Anhang 4-G

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Garadacimab (Andembry®)

CSL Behring GmbH

Modul 4 A- Anhang 4-G

Routinemäßige Prävention von wiederkehrenden Attacken des hereditären Angioödems bei Patienten ab einem Alter von 12 Jahren

Vollständige Darstellung der Subgruppenanalysen

Stand: 01.03.2025

Darstellung des Aufbaus der Subgruppenanalyse

Die Subgruppenanalysen werden zunächst nach den verschiedenen Endpunkten dargestellt. Anschließend wird die Subgruppe „Alter“ als separate Kategorie aufgeführt, wobei für jeden Endpunkt eine entsprechende Analyse durchgeführt wird.

Inhaltsverzeichnis

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4.1 Anzahl von HAE-Attacken während der Behandlungsphase

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.008
time-normalized baseline attack rate during Run-in Period		0.644
Subgroup		0.096
Interaction Treatment*Subgroup		
Gender = Male		130
Total Number of HAE Attacks during Treatment Period	8	11 (44.00)
Number of Subjects observed during Treatment Period, n (%) [2]	15 (38.46)	
Time-normalized Number of HAE Attacks Per Month		11
Number Observed	15	2.15 (1.473)
Mean (SD)	0.09 (0.122)	0.44
Standard Error	0.03	2.10
Median	0.00	1.00, 3.47
1st Quartile, 3rd Quartile	0.00, 0.17	0.2, 4.4
Minimum, Maximum	0.0, 0.3	2.22 (0.210)
LS Means (Standard Error)[1]	0.08 (0.853)	0.03 (0.01, 0.19)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-96.619 (-99.395, -81.103)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Male		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	15	11
Mean (SD)	1.05 (1.460)	25.75 (17.679)
Standard Error	0.38	5.33
Median	0.00	25.19
1st Quartile, 3rd Quartile	0.00, 2.01	11.98, 41.69
Minimum, Maximum	0.0, 4.0	2.2, 53.1
LS Means (Standard Error)[1]	0.90 (0.853)	26.65 (0.210)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.03 (0.01, 0.19)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-96.619 (-99.395, -81.103)
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Female		136
Total Number of HAE Attacks during Treatment Period	55	
Number of Subjects observed during Treatment Period, n (%) [2]	24 (61.54)	14 (56.00)
Time-normalized Number of HAE Attacks Per Month		
Number Observed	24	14
Mean (SD)	0.38 (0.853)	1.90 (1.218)
Standard Error	0.17	0.33
Median	0.00	1.35
1st Quartile, 3rd Quartile	0.00, 0.33	1.00, 3.03
Minimum, Maximum	0.0, 3.8	0.2, 4.2
LS Means (Standard Error)[1]	0.32 (0.350)	1.94 (0.206)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.16 (0.07, 0.37)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-83.535 (-92.672, -63.005)
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Female		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	24	14
Mean (SD)	4.62 (10.231)	22.84 (14.617)
Standard Error	2.09	3.91
Median	0.00	16.24
1st Quartile, 3rd Quartile	0.00, 3.98	11.98, 36.32
Minimum, Maximum	0.0, 45.9	2.0, 50.7
LS Means (Standard Error)[1]	3.83 (0.350)	23.26 (0.206)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.16 (0.07, 0.37)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-83.535 (-92.672, -63.005)
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.016
time-normalized baseline attack rate during Run-in Period		0.754
Subgroup		0.227
Interaction Treatment*Subgroup		
Region = EU (Germany, Hungary, Netherlands)		118
Total Number of HAE Attacks during Treatment Period	12	9 (36.00)
Number of Subjects observed during Treatment Period, n (%) [2]	11 (28.21)	
Time-normalized Number of HAE Attacks Per Month		9
Number Observed	11	2.20 (1.496)
Mean (SD)	0.19 (0.366)	0.50
Standard Error	0.11	1.19
Median	0.00	1.00, 3.47
1st Quartile, 3rd Quartile	0.00, 0.17	0.7, 4.2
Minimum, Maximum	0.0, 1.2	2.21 (0.254)
LS Means (Standard Error)[1]	0.09 (0.936)	0.04 (0.01, 0.27)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-95.881 (-99.372, -72.986)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = EU (Germany, Hungary, Netherlands)		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	11	9
Mean (SD)	2.26 (4.390)	26.37 (17.950)
Standard Error	1.32	5.98
Median	0.00	14.28
1st Quartile, 3rd Quartile	0.00, 2.02	11.98, 41.69
Minimum, Maximum	0.0, 14.9	8.5, 50.7
LS Means (Standard Error)[1]	1.09 (0.936)	26.53 (0.254)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.04 (0.01, 0.27)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-95.881 (-99.372, -72.986)
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)		148
Total Number of HAE Attacks during Treatment Period	51	
Number of Subjects observed during Treatment Period, n (%) [2]	28 (71.79)	16 (64.00)
Time-normalized Number of HAE Attacks Per Month		
Number Observed	28	16
Mean (SD)	0.30 (0.777)	1.90 (1.237)
Standard Error	0.15	0.31
Median	0.00	1.73
1st Quartile, 3rd Quartile	0.00, 0.32	1.08, 2.84
Minimum, Maximum	0.0, 3.8	0.2, 4.4
LS Means (Standard Error)[1]	0.28 (0.394)	1.99 (0.228)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.14 (0.06, 0.35)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-85.957 (-94.297, -65.422)
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	28	16
Mean (SD)	3.64 (9.323)	22.86 (14.847)
Standard Error	1.76	3.71
Median	0.00	20.80
1st Quartile, 3rd Quartile	0.00, 3.84	12.94, 34.07
Minimum, Maximum	0.0, 45.9	2.0, 53.1
LS Means (Standard Error)[1]	3.35 (0.394)	23.82 (0.228)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.14 (0.06, 0.35)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-85.957 (-94.297, -65.422)
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.017
time-normalized baseline attack rate during Run-in Period		0.366
Subgroup		0.267
Interaction Treatment*Subgroup		
Age at First Diagnosis = <=17 years		138
Total Number of HAE Attacks during Treatment Period	25	12 (48.00)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.15)	
Time-normalized Number of HAE Attacks Per Month		12
Number Observed	18	2.39 (1.344)
Mean (SD)	0.24 (0.435)	0.39
Standard Error	0.10	2.32
Median	0.00	1.16, 3.38
1st Quartile, 3rd Quartile	0.00, 0.33	0.2, 4.4
Minimum, Maximum	0.0, 1.5	2.42 (0.227)
LS Means (Standard Error)[1]	0.16 (0.606)	0.07 (0.02, 0.23)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-93.437 (-98.156, -76.645)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = <=17 years		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	18	12
Mean (SD)	2.83 (5.219)	28.66 (16.129)
Standard Error	1.23	4.66
Median	0.00	27.87
1st Quartile, 3rd Quartile	0.00, 3.91	13.93, 40.51
Minimum, Maximum	0.0, 18.1	2.0, 53.1
LS Means (Standard Error)[1]	1.90 (0.606)	29.00 (0.227)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.07 (0.02, 0.23)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-93.437 (-98.156, -76.645)
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = >17 years		128
Total Number of HAE Attacks during Treatment Period	38	
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.85)	13 (52.00)
Time-normalized Number of HAE Attacks Per Month		
Number Observed	21	13
Mean (SD)	0.30 (0.851)	1.66 (1.231)
Standard Error	0.19	0.34
Median	0.00	1.27
1st Quartile, 3rd Quartile	0.00, 0.17	0.83, 2.56
Minimum, Maximum	0.0, 3.8	0.2, 4.2
LS Means (Standard Error)[1]	0.28 (0.438)	1.80 (0.236)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.16 (0.06, 0.42)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-84.285 (-94.100, -58.143)
Two-sided Wilcoxon Test, p-value		<0.001

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	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = >17 years		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	21	13
Mean (SD)	3.61 (10.212)	19.93 (14.772)
Standard Error	2.23	4.10
Median	0.00	15.30
1st Quartile, 3rd Quartile	0.00, 2.05	9.93, 30.78
Minimum, Maximum	0.0, 45.9	2.2, 49.9
LS Means (Standard Error)[1]	3.39 (0.438)	21.57 (0.236)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.16 (0.06, 0.42)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-84.285 (-94.100, -58.143)
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.792
time-normalized baseline attack rate during Run-in Period		0.125
Subgroup		0.434
Interaction Treatment*Subgroup		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month Total		129
Number of HAE Attacks during Treatment Period	19	17 (68.00)
Number of Subjects observed during Treatment Period, n (%) [2]	24 (61.54)	
Time-normalized Number of HAE Attacks Per Month		17
Number Observed	24	1.60 (1.023)
Mean (SD)	0.13 (0.272)	0.25
Standard Error	0.06	1.27
Median	0.00	0.83, 2.34
1st Quartile, 3rd Quartile	0.00, 0.24	0.2, 3.3
Minimum, Maximum	0.0, 1.2	1.53 (0.254)
LS Means (Standard Error)[1]	0.14 (0.575)	0.09 (0.03, 0.29)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-91.025 (-97.214, -71.086)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	24	17
Mean (SD)	1.61 (3.262)	19.25 (12.273)
Standard Error	0.67	2.98
Median	0.00	15.30
1st Quartile, 3rd Quartile	0.00, 2.91	9.93, 28.10
Minimum, Maximum	0.0, 14.9	2.0, 39.3
LS Means (Standard Error)[1]	1.64 (0.575)	18.32 (0.254)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.09 (0.03, 0.29)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.025 (-97.214, -71.086)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >=3 attacks/month Total		137
Number of HAE Attacks during Treatment Period	44	
Number of Subjects observed during Treatment Period, n (%) [2]	15 (38.46)	8 (32.00)
Time-normalized Number of HAE Attacks Per Month		
Number Observed	15	8
Mean (SD)	0.49 (1.031)	2.87 (1.506)
Standard Error	0.27	0.53
Median	0.00	3.42
1st Quartile, 3rd Quartile	0.00, 0.34	1.17, 4.19
Minimum, Maximum	0.0, 3.8	1.0, 4.4
LS Means (Standard Error)[1]	0.45 (0.497)	2.78 (0.238)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.16 (0.06, 0.41)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-83.697 (-93.568, -58.674)
Two-sided Wilcoxon Test, p-value		0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >=3 attacks/month		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	15	8
Mean (SD)	5.87 (12.370)	34.47 (18.070)
Standard Error	3.19	6.39
Median	0.00	41.02
1st Quartile, 3rd Quartile	0.00, 4.04	14.02, 50.31
Minimum, Maximum	0.0, 45.9	12.0, 53.1
LS Means (Standard Error)[1]	5.44 (0.497)	33.36 (0.238)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.16 (0.06, 0.41)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-83.697 (-93.568, -58.674)
Two-sided Wilcoxon Test, p-value		0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.038
time-normalized baseline attack rate during Run-in Period		0.914
Subgroup		0.662
Interaction Treatment*Subgroup		
History of Laryngeal Attack = No		101
Total Number of HAE Attacks during Treatment Period	17	8 (32.00)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.15)	
Time-normalized Number of HAE Attacks Per Month		8
Number Observed	18	2.13 (1.298)
Mean (SD)	0.16 (0.297)	0.46
Standard Error	0.07	1.84
Median	0.00	1.00, 3.24
1st Quartile, 3rd Quartile	0.00, 0.17	0.7, 4.2
Minimum, Maximum	0.0, 1.2	2.02 (0.267)
LS Means (Standard Error)[1]	0.17 (0.646)	0.08 (0.02, 0.33)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-91.538 (-97.851, -66.683)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = No		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	18	8
Mean (SD)	1.93 (3.570)	25.51 (15.578)
Standard Error	0.84	5.51
Median	0.00	22.03
1st Quartile, 3rd Quartile	0.00, 2.05	11.98, 38.86
Minimum, Maximum	0.0, 14.9	8.5, 49.9
LS Means (Standard Error)[1]	2.05 (0.646)	24.21 (0.267)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.08 (0.02, 0.33)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.538 (-97.851, -66.683)
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = Yes		165
Total Number of HAE Attacks during Treatment Period	46	
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.85)	17 (68.00)
Time-normalized Number of HAE Attacks Per Month		
Number Observed	21	17
Mean (SD)	0.36 (0.890)	1.96 (1.356)
Standard Error	0.19	0.33
Median	0.00	1.34
1st Quartile, 3rd Quartile	0.00, 0.33	1.16, 3.03
Minimum, Maximum	0.0, 3.8	0.2, 4.4
LS Means (Standard Error)[1]	0.26 (0.463)	2.09 (0.212)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.12 (0.04, 0.35)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-87.501 (-95.578, -64.668)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.1.aS: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = Yes		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	21	17
Mean (SD)	4.38 (10.677)	23.46 (16.266)
Standard Error	2.33	3.95
Median	0.00	16.05
1st Quartile, 3rd Quartile	0.00, 3.91	13.90, 36.32
Minimum, Maximum	0.0, 45.9	2.0, 53.1
LS Means (Standard Error)[1]	3.14 (0.463)	25.13 (0.212)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.12 (0.04, 0.35)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-87.501 (-95.578, -64.668)
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

4.2 Anzahl von HAE-Attacken während der Behandlungsphase, die während der Behandlungsphase ein On-Demand-Medikament erfordern

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Generalized Linear Model [1], p-value		<0.001
Treatment		<0.001
time-normalized baseline attack rate during Run-in Period		0.663
Subgroup		0.132
Interaction Treatment*Subgroup		
Gender = Male		116
Total Number of HAE Attacks during Treatment Period	6	11 (44.00)
Number of Subjects observed during Treatment Period, n (%) [2]	15 (38.46)	
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	15	11
Mean (SD)	0.07 (0.120)	1.85 (1.647)
Standard Error	0.03	0.50
Median	0.00	1.05
1st Quartile, 3rd Quartile	0.00, 0.17	0.50, 3.47
Minimum, Maximum	0.0, 0.3	0.0, 4.4
LS Means (Standard Error)[1]	0.05 (1.029)	2.01 (0.231)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.02 (0.00, 0.20)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-97.503 (-99.683, -80.326)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.

[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Male		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	15	11
Mean (SD)	0.79 (1.445)	22.24 (19.761)
Standard Error	0.37	5.96
Median	0.00	12.59
1st Quartile, 3rd Quartile	0.00, 2.01	5.96, 41.69
Minimum, Maximum	0.0, 4.0	0.0, 53.1
LS Means (Standard Error)[1]	0.60 (1.029)	24.17 (0.231)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.02 (0.00, 0.20)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-97.503 (-99.683, -80.326)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Female		130
Total Number of HAE Attacks during Treatment Period	48	
Number of Subjects observed during Treatment Period, n (%) [2]	24 (61.54)	14 (56.00)
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	24	14
Mean (SD)	0.34 (0.829)	1.81 (1.221)
Standard Error	0.17	0.33
Median	0.00	1.35
1st Quartile, 3rd Quartile	0.00, 0.25	0.96, 2.81
Minimum, Maximum	0.0, 3.8	0.2, 4.2
LS Means (Standard Error)[1]	0.24 (0.414)	1.75 (0.218)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.14 (0.05, 0.34)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-86.489 (-94.573, -66.366)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Female		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	24	14
Mean (SD)	4.03 (9.947)	21.71 (14.650)
Standard Error	2.03	3.92
Median	0.00	16.24
1st Quartile, 3rd Quartile	0.00, 3.01	11.47, 33.72
Minimum, Maximum	0.0, 45.9	2.0, 50.7
LS Means (Standard Error)[1]	2.84 (0.414)	21.05 (0.218)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.14 (0.05, 0.34)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-86.489 (-94.573, -66.366)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Generalized Linear Model [1], p-value		0.002
Treatment		0.006
time-normalized baseline attack rate during Run-in Period		0.987
Subgroup		0.233
Interaction Treatment*Subgroup		
Region = EU (Germany, Hungary, Netherlands)		113
Total Number of HAE Attacks during Treatment Period	11	9 (36.00)
Number of Subjects observed during Treatment Period, n (%) [2]	11 (28.21)	
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	11	9
Mean (SD)	0.17 (0.370)	2.10 (1.548)
Standard Error	0.11	0.52
Median	0.00	1.16
1st Quartile, 3rd Quartile	0.00, 0.17	0.85, 3.47
Minimum, Maximum	0.0, 1.2	0.4, 4.2
LS Means (Standard Error)[1]	0.05 (1.161)	1.86 (0.298)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.03 (0.00, 0.27)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-97.185 (-99.705, -73.094)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = EU (Germany, Hungary, Netherlands)		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	11	9
Mean (SD)	2.08 (4.443)	25.22 (18.577)
Standard Error	1.34	6.19
Median	0.00	13.97
1st Quartile, 3rd Quartile	0.00, 2.02	10.20, 41.69
Minimum, Maximum	0.0, 14.9	4.2, 50.7
LS Means (Standard Error)[1]	0.63 (1.161)	22.26 (0.298)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.03 (0.00, 0.27)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-97.185 (-99.705, -73.094)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)		133
Total Number of HAE Attacks during Treatment Period	43	
Number of Subjects observed during Treatment Period, n (%) [2]	28 (71.79)	16 (64.00)
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	28	16
Mean (SD)	0.26 (0.752)	1.68 (1.324)
Standard Error	0.14	0.33
Median	0.00	1.35
1st Quartile, 3rd Quartile	0.00, 0.17	0.50, 2.60
Minimum, Maximum	0.0, 3.8	0.0, 4.4
LS Means (Standard Error)[1]	0.22 (0.490)	1.84 (0.266)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.12 (0.04, 0.35)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-88.307 (-96.132, -64.656)
Two-sided Wilcoxon Test, p-value		<0.001

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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	28	16
Mean (SD)	3.06 (9.020)	20.11 (15.886)
Standard Error	1.70	3.97
Median	0.00	16.24
1st Quartile, 3rd Quartile	0.00, 2.00	6.00, 31.22
Minimum, Maximum	0.0, 45.9	0.0, 53.1
LS Means (Standard Error)[1]	2.59 (0.490)	22.11 (0.266)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.12 (0.04, 0.35)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-88.307 (-96.132, -64.656)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.002
time-normalized baseline attack rate during Run-in Period		0.222
Subgroup		0.094
Interaction Treatment*Subgroup		
Age at First Diagnosis = <=17 years		126
Total Number of HAE Attacks during Treatment Period	17	12 (48.00)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.15)	
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		12
Number Observed	18	2.12 (1.536)
Mean (SD)	0.16 (0.339)	0.44
Standard Error	0.08	2.32
Median	0.00	0.77, 3.25
1st Quartile, 3rd Quartile	0.00, 0.17	0.0, 4.4
Minimum, Maximum	0.0, 1.2	2.37 (0.258)
LS Means (Standard Error)[1]	0.07 (0.862)	0.03 (0.01, 0.17)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-97.027 (-99.492, -82.590)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = <=17 years		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	18	12
Mean (SD)	1.94 (4.073)	25.48 (18.435)
Standard Error	0.96	5.32
Median	0.00	27.87
1st Quartile, 3rd Quartile	0.00, 2.01	9.27, 39.00
Minimum, Maximum	0.0, 14.9	0.0, 53.1
LS Means (Standard Error)[1]	0.85 (0.862)	28.43 (0.258)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.03 (0.01, 0.17)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-97.027 (-99.492, -82.590)
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = >17 years		120
Total Number of HAE Attacks during Treatment Period	37	
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.85)	13 (52.00)
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	21	13
Mean (SD)	0.29 (0.853)	1.56 (1.243)
Standard Error	0.19	0.34
Median	0.00	1.00
1st Quartile, 3rd Quartile	0.00, 0.17	0.83, 2.39
Minimum, Maximum	0.0, 3.8	0.2, 4.0
LS Means (Standard Error)[1]	0.24 (0.497)	1.51 (0.266)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.16 (0.05, 0.47)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-84.002 (-94.611, -52.507)
Two-sided Wilcoxon Test, p-value		<0.001

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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = >17 years		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	21	13
Mean (SD)	3.51 (10.237)	18.68 (14.917)
Standard Error	2.23	4.14
Median	0.00	11.98
1st Quartile, 3rd Quartile	0.00, 2.05	9.93, 28.73
Minimum, Maximum	0.0, 45.9	2.2, 47.9
LS Means (Standard Error)[1]	2.89 (0.497)	18.08 (0.266)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.16 (0.05, 0.47)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-84.002 (-94.611, -52.507)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.129
time-normalized baseline attack rate during Run-in Period		0.265
Subgroup		0.785
Interaction Treatment*Subgroup		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month Total Number of HAE Attacks during Treatment Period		116
	15	17 (68.00)
Number of Subjects observed during Treatment Period, n (%) [2]	24 (61.54)	
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	24	17
Mean (SD)	0.11 (0.267)	1.41 (1.030)
Standard Error	0.05	0.25
Median	0.00	1.05
1st Quartile, 3rd Quartile	0.00, 0.08	0.50, 2.34
Minimum, Maximum	0.0, 1.2	0.2, 3.1
LS Means (Standard Error)[1]	0.13 (0.695)	1.52 (0.261)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.08 (0.02, 0.35)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.640 (-97.992, -65.197)
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	24	17
Mean (SD)	1.27 (3.202)	16.88 (12.363)
Standard Error	0.65	3.00
Median	0.00	12.59
1st Quartile, 3rd Quartile	0.00, 0.98	6.05, 28.10
Minimum, Maximum	0.0, 14.9	2.0, 37.4
LS Means (Standard Error)[1]	1.53 (0.695)	18.26 (0.261)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.08 (0.02, 0.35)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.640 (-97.992, -65.197)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >=3 attacks/month		130
Total Number of HAE Attacks during Treatment Period	39	
Number of Subjects observed during Treatment Period, n (%) [2]	15 (38.46)	8 (32.00)
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	15	8
Mean (SD)	0.43 (1.002)	2.73 (1.692)
Standard Error	0.26	0.60
Median	0.00	3.42
1st Quartile, 3rd Quartile	0.00, 0.34	1.17, 4.11
Minimum, Maximum	0.0, 3.8	0.0, 4.4
LS Means (Standard Error)[1]	0.26 (0.605)	2.35 (0.257)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.03, 0.34)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-89.182 (-96.534, -66.231)
Two-sided Wilcoxon Test, p-value		0.003

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Source: 16.2.5.4; UNBLINDED

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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >=3 attacks/month		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	15	8
Mean (SD)	5.20 (12.023)	32.72 (20.304)
Standard Error	3.10	7.18
Median	0.00	41.02
1st Quartile, 3rd Quartile	0.00, 4.04	14.02, 49.32
Minimum, Maximum	0.0, 45.9	0.0, 53.1
LS Means (Standard Error)[1]	3.06 (0.605)	28.24 (0.257)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.03, 0.34)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-89.182 (-96.534, -66.231)
Two-sided Wilcoxon Test, p-value		0.003

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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
Generalized Linear Model [1], p-value		0.001
Treatment		0.006
time-normalized baseline attack rate during Run-in Period		0.833
Subgroup		0.919
Interaction Treatment*Subgroup		
History of Laryngeal Attack = No		92
Total Number of HAE Attacks during Treatment Period	15	8 (32.00)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.15)	
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	18	8
Mean (SD)	0.14 (0.302)	1.94 (1.475)
Standard Error	0.07	0.52
Median	0.00	1.84
1st Quartile, 3rd Quartile	0.00, 0.17	0.68, 3.24
Minimum, Maximum	0.0, 1.2	0.0, 4.0
LS Means (Standard Error)[1]	0.15 (0.726)	1.78 (0.298)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.08 (0.02, 0.38)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.770 (-98.225, -61.846)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = No		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	18	8
Mean (SD)	1.71 (3.623)	23.24 (17.705)
Standard Error	0.85	6.26
Median	0.00	22.03
1st Quartile, 3rd Quartile	0.00, 2.05	8.11, 38.86
Minimum, Maximum	0.0, 14.9	0.0, 47.9
LS Means (Standard Error)[1]	1.76 (0.726)	21.33 (0.298)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.08 (0.02, 0.38)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.770 (-98.225, -61.846)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = Yes		154
Total Number of HAE Attacks during Treatment Period	39	
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.85)	17 (68.00)
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	21	17
Mean (SD)	0.31 (0.862)	1.78 (1.395)
Standard Error	0.19	0.34
Median	0.00	1.16
1st Quartile, 3rd Quartile	0.00, 0.16	0.83, 2.81
Minimum, Maximum	0.0, 3.8	0.2, 4.4
LS Means (Standard Error)[1]	0.18 (0.569)	1.93 (0.227)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.09 (0.03, 0.31)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-90.879 (-97.319, -68.965)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.bS: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = Yes		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	21	17
Mean (SD)	3.71 (10.344)	21.34 (16.739)
Standard Error	2.26	4.06
Median	0.00	13.97
1st Quartile, 3rd Quartile	0.00, 1.95	9.93, 33.72
Minimum, Maximum	0.0, 45.9	2.0, 53.1
LS Means (Standard Error)[1]	2.11 (0.569)	23.10 (0.227)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.09 (0.03, 0.31)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-90.879 (-97.319, -68.965)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

4.3 Zeit bis zur ersten HAE-Attacke nach Tag 1

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Gender		
Cox-proportional hazards model results [5]		
p-value		
Treatment (CSL312 vs. Placebo)		
Subgroup		<0.001
Interaction Treatment*Subgroup		0.081
		0.318

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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Source: 16.2.5.6; UNBLINDED

[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Gender Gender = Male	15 (38.5)	11 (44.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	6 (40.0)	11 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1]	9 (60.0)	0
Attack-free or one HAE Attack after Study Day 1[1]	13 (86.7)	1 (9.1)
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	15.00
1st, 3rd Quartile[3]	93.00, -	8.00, 23.00
Minimum, Maximum[4]	10.0, 145.0	1.0, 123.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		
Hazard Ratio and 95% Confidence Interval p-value		
Treatment (CSL312 vs. Placebo)		-2.11 (0.566)
		0.12 (0.040, 0.369)
		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Gender Gender = Female	24 (61.5)	14 (56.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	9 (37.5)	14 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1]	15 (62.5)	0
Attack-free or one HAE Attack after Study Day 1[1]	16 (66.7)	1 (7.1)
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	6.00
1st, 3rd Quartile[3]	47.00, -	4.00, 13.00
Minimum, Maximum[4]	4.0, 98.0	1.0, 61.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		
Hazard Ratio and 95% Confidence Interval p-value		
Treatment (CSL312 vs. Placebo)		-2.34 (0.501)
		0.10 (0.036, 0.258)
		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Region		
Cox-proportional hazards model results [5]		
p-value		
Treatment (CSL312 vs. Placebo)		
Subgroup		<0.001
Interaction Treatment*Subgroup		0.344
		0.671

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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Region		
Region = EU (Germany, Hungary, Netherlands)	11 (28.2)	9 (36.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	5 (45.5)	9 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1] Attack-free or one HAE Attack after Study Day 1[1]	6 (54.5) 9 (81.8)	0 0
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	8.00
1st, 3rd Quartile[3]	98.00, -	5.00, 16.00
Minimum, Maximum[4]	21.0, 145.0	2.0, 23.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		
Hazard Ratio and 95% Confidence Interval p-value		
Treatment (CSL312 vs. Placebo)		
		-3.24 (1.069)
		0.04 (0.005, 0.317)
		0.002

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)	28 (71.8)	16 (64.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	10 (35.7)	16 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1] Attack-free or one HAE Attack after Study Day 1[1]	18 (64.3) 20 (71.4)	0 2 (12.5)
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	12.50
1st, 3rd Quartile[3]	63.00, -	4.00, 18.00
Minimum, Maximum[4]	4.0, 87.0	1.0, 123.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		
Hazard Ratio and 95% Confidence Interval p-value		
Treatment (CSL312 vs. Placebo)		
		-1.93 (0.424)
		0.15 (0.063, 0.334)
		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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Source: 16.2.5.6; UNBLINDED

[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age at First Diagnosis		
Cox-proportional hazards model results [5]		
p-value		
Treatment (CSL312 vs. Placebo)		
Subgroup		<0.001
Interaction Treatment*Subgroup		0.097
		0.661

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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Source: 16.2.5.6; UNBLINDED

[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age at First Diagnosis Age at First Diagnosis = <=17	18 (46.2)	12 (48.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	8 (44.4)	12 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1]	10 (55.6)	0
Attack-free or one HAE Attack after Study Day 1[1]	13 (72.2)	1 (8.3)
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	8.00
1st, 3rd Quartile[3]	28.00, -	2.50, 14.50
Minimum, Maximum[4]	4.0, 145.0	1.0, 61.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		
Hazard Ratio and 95% Confidence Interval p-value		
Treatment (CSL312 vs. Placebo)		
		-2.22 (0.569)
		0.11 (0.035, 0.330)
		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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Source: 16.2.5.6; UNBLINDED

[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age at First Diagnosis Age at First Diagnosis = >17	21 (53.8)	13 (52.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	7 (33.3)	13 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1] Attack-free or one HAE Attack after Study Day 1[1]	14 (66.7) 16 (76.2)	0 1 (7.7)
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	13.00
1st, 3rd Quartile[3]	87.00, -	6.00, 23.00
Minimum, Maximum[4]	8.0, 114.0	4.0, 123.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		
Hazard Ratio and 95% Confidence Interval p-value		
Treatment (CSL312 vs. Placebo)		
		-2.19 (0.496)
		0.11 (0.042, 0.295)
		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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Source: 16.2.5.6; UNBLINDED

[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Baseline Attack rate observed during Run-in Period		
Cox-proportional hazards model results [5]		
p-value		
Treatment (CSL312 vs. Placebo)		
Subgroup		<0.001
Interaction Treatment*Subgroup		0.060
		0.459

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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Baseline Attack rate observed during Run-in Period Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month	24 (61.5)	17 (68.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	8 (33.3)	17 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1] Attack-free or one HAE Attack after Study Day 1[1]	16 (66.7)	0
	18 (75.0)	2 (11.8)
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	14.00
1st, 3rd Quartile[3]	71.50, -	5.00, 23.00
Minimum, Maximum[4]	9.0, 98.0	1.0, 123.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		-2.11 (0.451)
Hazard Ratio and 95% Confidence Interval		0.12 (0.050, 0.293)
p-value		<0.001
Treatment (CSL312 vs. Placebo)		

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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month	15 (38.5)	8 (32.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	7 (46.7)	8 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1]	8 (53.3)	0
Attack-free or one HAE Attack after Study Day 1[1]	11 (73.3)	0
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	8.00
1st, 3rd Quartile[3]	87.00, -	3.00, 12.00
Minimum, Maximum[4]	4.0, 145.0	1.0, 16.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		
Hazard Ratio and 95% Confidence Interval p-value		
Treatment (CSL312 vs. Placebo)		
		-2.70 (0.819)
		0.07 (0.014, 0.335)
		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: History of Laryngeal Attack		
Cox-proportional hazards model results [5]		
p-value		
Treatment (CSL312 vs. Placebo)		
Subgroup		<0.001
Interaction Treatment*Subgroup		0.593
		0.960

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s.sas
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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: History of Laryngeal Attack History of Laryngeal Attack = No	18 (46.2)	8 (32.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	8 (44.4)	8 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1] Attack-free or one HAE Attack after Study Day 1[1]	10 (55.6) 14 (77.8)	0 0
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	12.00
1st, 3rd Quartile[3]	87.00, -	8.00, 15.50
Minimum, Maximum[4]	10.0, 114.0	6.0, 19.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		-3.72 (1.090)
Hazard Ratio and 95% Confidence Interval p-value		0.02 (0.003, 0.205)
Treatment (CSL312 vs. Placebo)		<0.001

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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

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GAP Table 14.2.4.5.1aS: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: History of Laryngeal Attack History of Laryngeal Attack = Yes	21 (53.8)	17 (68.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	7 (33.3)	17 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1] Attack-free or one HAE Attack after Study Day 1[1]	14 (66.7) 15 (71.4)	0 2 (11.8)
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	6.00
1st, 3rd Quartile[3]	71.00, -	4.00, 23.00
Minimum, Maximum[4]	4.0, 145.0	1.0, 123.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results [5]		
Parameter Estimate and Standard Error		
Hazard Ratio and 95% Confidence Interval p-value		
Treatment (CSL312 vs. Placebo)		
		-2.17 (0.498)
		0.11 (0.043, 0.303)
		<0.001

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[1] Percentages are based on the Intention-to-Treat Analysis Set.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1
[5] Cox-proportional hazards (regression) model with treatment group and adjusted for stratification variables as used for randomization or with treatment group only for subgroup category.

4.4 Anzahl von moderaten und schweren HAE-Attacken

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.006
time-normalized baseline attack rate during Run-in Period		0.486
Subgroup		0.351
Interaction Treatment*Subgroup		
Gender = Male		89
Total Number of HAE Attacks during Treatment Period	4	11 (44.00)
Number of Subjects observed during Treatment Period, n (%) [2]	15 (38.46)	
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	15	11
Mean (SD)	0.04 (0.099)	1.44 (1.363)
Standard Error	0.03	0.41
Median	0.00	0.83
1st Quartile, 3rd Quartile	0.00, 0.00	0.50, 2.48
Minimum, Maximum	0.0, 0.3	0.2, 4.4
LS Means (Standard Error)[1]	0.05 (1.006)	1.55 (0.214)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.03 (0.00, 0.23)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-96.934 (-99.592, -76.981)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson

chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.

[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Male		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	15	11
Mean (SD)	0.53 (1.185)	17.34 (16.359)
Standard Error	0.31	4.93
Median	0.00	9.98
1st Quartile, 3rd Quartile	0.00, 0.00	5.99, 29.78
Minimum, Maximum	0.0, 4.0	2.2, 53.1
LS Means (Standard Error)[1]	0.57 (1.006)	18.62 (0.214)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.03 (0.00, 0.23)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-96.934 (-99.592, -76.981)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Female		
Total Number of HAE Attacks during Treatment Period	25	84
Number of Subjects observed during Treatment Period, n (%) [2]	24 (61.54)	14 (56.00)
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	24	14
Mean (SD)	0.18 (0.363)	1.26 (0.983)
Standard Error	0.07	0.26
Median	0.00	0.89
1st Quartile, 3rd Quartile	0.00, 0.17	0.67, 2.34
Minimum, Maximum	0.0, 1.2	0.0, 2.8
LS Means (Standard Error)[1]	0.12 (0.494)	1.25 (0.222)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.09 (0.03, 0.27)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-90.862 (-96.944, -72.682)
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Female		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	24	14
Mean (SD)	2.12 (4.358)	15.07 (11.801)
Standard Error	0.89	3.15
Median	0.00	10.73
1st Quartile, 3rd Quartile	0.00, 2.02	7.98, 28.10
Minimum, Maximum	0.0, 14.0	0.0, 33.7
LS Means (Standard Error)[1]	1.37 (0.494)	15.04 (0.222)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.09 (0.03, 0.27)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-90.862 (-96.944, -72.682)
Two-sided Wilcoxon Test, p-value		<0.001

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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Generalized Linear Model [1], p-value		0.003
Treatment		0.009
time-normalized baseline attack rate during Run-in Period		0.789
Subgroup		0.592
Interaction Treatment*Subgroup		
Region = EU (Germany, Hungary, Netherlands)		69
Total Number of HAE Attacks during Treatment Period	9	9 (36.00)
Number of Subjects observed during Treatment Period, n (%) [2]	11 (28.21)	
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	11	9
Mean (SD)	0.14 (0.323)	1.29 (1.019)
Standard Error	0.10	0.34
Median	0.00	0.83
1st Quartile, 3rd Quartile	0.00, 0.17	0.53, 2.48
Minimum, Maximum	0.0, 1.1	0.3, 2.7
LS Means (Standard Error)[1]	0.06 (1.017)	1.50 (0.283)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.04 (0.00, 0.33)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-96.039 (-99.528, -66.754)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = EU (Germany, Hungary, Netherlands)		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	11	9
Mean (SD)	1.70 (3.878)	15.43 (12.226)
Standard Error	1.17	4.08
Median	0.00	9.93
1st Quartile, 3rd Quartile	0.00, 2.01	6.37, 29.78
Minimum, Maximum	0.0, 12.7	4.1, 32.5
LS Means (Standard Error)[1]	0.71 (1.017)	17.96 (0.283)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.04 (0.00, 0.33)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-96.039 (-99.528, -66.754)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)		104
Total Number of HAE Attacks during Treatment Period	20	
Number of Subjects observed during Treatment Period, n (%) [2]	28 (71.79)	16 (64.00)
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	28	16
Mean (SD)	0.12 (0.291)	1.37 (1.239)
Standard Error	0.05	0.31
Median	0.00	1.00
1st Quartile, 3rd Quartile	0.00, 0.08	0.58, 2.08
Minimum, Maximum	0.0, 1.2	0.0, 4.4
LS Means (Standard Error)[1]	0.10 (0.537)	1.36 (0.227)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.07 (0.02, 0.23)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-92.704 (-97.688, -76.975)
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	28	16
Mean (SD)	1.43 (3.490)	16.43 (14.870)
Standard Error	0.66	3.72
Median	0.00	12.03
1st Quartile, 3rd Quartile	0.00, 0.94	7.00, 24.91
Minimum, Maximum	0.0, 14.0	0.0, 53.1
LS Means (Standard Error)[1]	1.19 (0.537)	16.31 (0.227)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.07 (0.02, 0.23)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-92.704 (-97.688, -76.975)
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.003
time-normalized baseline attack rate during Run-in Period		0.015
Subgroup		0.308
Interaction Treatment*Subgroup		
Age at First Diagnosis = <=17 years		108
Total Number of HAE Attacks during Treatment Period	15	12 (48.00)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.15)	
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	18	12
Mean (SD)	0.14 (0.335)	1.87 (1.262)
Standard Error	0.08	0.36
Median	0.00	2.08
1st Quartile, 3rd Quartile	0.00, 0.00	0.75, 2.70
Minimum, Maximum	0.0, 1.1	0.0, 4.4
LS Means (Standard Error)[1]	0.08 (0.665)	2.04 (0.202)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.04 (0.01, 0.16)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-95.956 (-98.993, -83.755)
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = <=17 years		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	18	12
Mean (SD)	1.71 (4.019)	22.47 (15.145)
Standard Error	0.95	4.37
Median	0.00	24.91
1st Quartile, 3rd Quartile	0.00, 0.00	8.98, 32.38
Minimum, Maximum	0.0, 12.7	0.0, 53.1
LS Means (Standard Error)[1]	0.99 (0.665)	24.53 (0.202)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.04 (0.01, 0.16)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-95.956 (-98.993, -83.755)
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = >17 years		
Total Number of HAE Attacks during Treatment Period	14	65
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.85)	13 (52.00)
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	21	13
Mean (SD)	0.11 (0.266)	0.85 (0.779)
Standard Error	0.06	0.22
Median	0.00	0.68
1st Quartile, 3rd Quartile	0.00, 0.16	0.50, 0.96
Minimum, Maximum	0.0, 1.2	0.0, 3.1
LS Means (Standard Error)[1]	0.09 (0.568)	0.92 (0.259)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.10 (0.03, 0.34)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-90.013 (-97.079, -65.856)
Two-sided Wilcoxon Test, p-value		<0.001

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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = >17 years		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	21	13
Mean (SD)	1.33 (3.193)	10.16 (9.353)
Standard Error	0.70	2.59
Median	0.00	8.21
1st Quartile, 3rd Quartile	0.00, 1.88	5.99, 11.47
Minimum, Maximum	0.0, 14.0	0.0, 37.4
LS Means (Standard Error)[1]	1.11 (0.568)	11.09 (0.259)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.10 (0.03, 0.34)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-90.013 (-97.079, -65.856)
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.013
time-normalized baseline attack rate during Run-in Period		0.288
Subgroup		0.665
Interaction Treatment*Subgroup		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month Total Number of HAE Attacks during Treatment Period		95
	12	17 (68.00)
Number of Subjects observed during Treatment Period, n (%) [2]	24 (61.54)	
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		17
Number Observed	24	1.20 (0.980)
Mean (SD)	0.09 (0.231)	0.24
Standard Error	0.05	0.83
Median	0.00	0.53, 1.81
1st Quartile, 3rd Quartile	0.00, 0.00	0.0, 3.1
Minimum, Maximum	0.0, 1.1	1.22 (0.220)
LS Means (Standard Error)[1]	0.10 (0.612)	0.08 (0.02, 0.28)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-92.226 (-97.818, -72.303)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	24	17
Mean (SD)	1.03 (2.770)	14.37 (11.755)
Standard Error	0.57	2.85
Median	0.00	9.93
1st Quartile, 3rd Quartile	0.00, 0.00	6.37, 21.72
Minimum, Maximum	0.0, 12.7	0.0, 37.4
LS Means (Standard Error)[1]	1.14 (0.612)	14.60 (0.220)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.08 (0.02, 0.28)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-92.226 (-97.818, -72.303)
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >=3 attacks/month		
Total Number of HAE Attacks during Treatment Period	17	78
Number of Subjects observed during Treatment Period, n (%) [2]	15 (38.46)	8 (32.00)
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	15	8
Mean (SD)	0.19 (0.379)	1.64 (1.462)
Standard Error	0.10	0.52
Median	0.00	1.08
1st Quartile, 3rd Quartile	0.00, 0.17	0.67, 2.59
Minimum, Maximum	0.0, 1.2	0.0, 4.4
LS Means (Standard Error)[1]	0.09 (0.723)	1.72 (0.240)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.05 (0.01, 0.23)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-94.970 (-98.879, -77.432)
Two-sided Wilcoxon Test, p-value		0.003

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >=3 attacks/month		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	15	8
Mean (SD)	2.28 (4.543)	19.66 (17.547)
Standard Error	1.17	6.20
Median	0.00	13.02
1st Quartile, 3rd Quartile	0.00, 2.01	7.98, 31.12
Minimum, Maximum	0.0, 14.0	0.0, 53.1
LS Means (Standard Error)[1]	1.04 (0.723)	20.61 (0.240)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.05 (0.01, 0.23)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-94.970 (-98.879, -77.432)
Two-sided Wilcoxon Test, p-value		0.003

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.004
time-normalized baseline attack rate during Run-in Period		0.637
Subgroup		0.437
Interaction Treatment*Subgroup		
History of Laryngeal Attack = No		52
Total Number of HAE Attacks during Treatment Period	12	8 (32.00)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.15)	
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	18	8
Mean (SD)	0.11 (0.262)	1.10 (0.971)
Standard Error	0.06	0.34
Median	0.00	0.83
1st Quartile, 3rd Quartile	0.00, 0.16	0.51, 1.50
Minimum, Maximum	0.0, 1.1	0.0, 3.1
LS Means (Standard Error)[1]	0.12 (0.620)	1.26 (0.300)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.10 (0.03, 0.37)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-90.289 (-97.478, -62.611)
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = No		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	18	8
Mean (SD)	1.37 (3.147)	13.22 (11.656)
Standard Error	0.74	4.12
Median	0.00	9.98
1st Quartile, 3rd Quartile	0.00, 1.88	6.18, 18.04
Minimum, Maximum	0.0, 12.7	0.0, 37.4
LS Means (Standard Error)[1]	1.47 (0.620)	15.10 (0.300)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.10 (0.03, 0.37)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-90.289 (-97.478, -62.611)
Two-sided Wilcoxon Test, p-value		<0.001

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = Yes		121
Total Number of HAE Attacks during Treatment Period	17	
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.85)	17 (68.00)
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	21	17
Mean (SD)	0.14 (0.329)	1.45 (1.228)
Standard Error	0.07	0.30
Median	0.00	0.96
1st Quartile, 3rd Quartile	0.00, 0.00	0.66, 2.48
Minimum, Maximum	0.0, 1.2	0.0, 4.4
LS Means (Standard Error)[1]	0.07 (0.701)	1.49 (0.196)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.04 (0.01, 0.19)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-95.532 (-98.949, -81.006)
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.dS: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach –Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = Yes		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	21	17
Mean (SD)	1.62 (3.942)	17.41 (14.731)
Standard Error	0.86	3.57
Median	0.00	11.47
1st Quartile, 3rd Quartile	0.00, 0.00	7.94, 29.78
Minimum, Maximum	0.0, 14.0	0.0, 53.1
LS Means (Standard Error)[1]	0.80 (0.701)	17.86 (0.196)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.04 (0.01, 0.19)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-95.532 (-98.949, -81.006)
Two-sided Wilcoxon Test, p-value		<0.001

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

4.5 Anzahl von schweren HAE-Attacken

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Generalized Linear Model [1], p-value		
Treatment		0.048
time-normalized baseline attack rate during Run-in Period		0.158
Subgroup		0.717
Interaction Treatment*Subgroup		0.578
Gender = Male		
Total Number of HAE Attacks during Treatment Period	1	8
Number of Subjects observed during Treatment Period, n (%) [2]	15 (38.46)	11 (44.00)
Time-normalized Number of Severe HAE Attacks Treatment Per Month		
Number Observed	15	11
Mean (SD)	0.01 (0.041)	0.12 (0.238)
Standard Error	0.01	0.07
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 0.18
Minimum, Maximum	0.0, 0.2	0.0, 0.7
LS Means (Standard Error)[1]	0.01 (1.165)	0.14 (0.412)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.09 (0.01, 0.98)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.327 (-99.229, -2.399)
Two-sided Wilcoxon Test, p-value		0.137

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The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical)

and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.

[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Male		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	15	11
Mean (SD)	0.13 (0.486)	1.48 (2.852)
Standard Error	0.13	0.86
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 2.20
Minimum, Maximum	0.0, 1.9	0.0, 7.9
LS Means (Standard Error)[1]	0.14 (1.165)	1.63 (0.412)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.09 (0.01, 0.98)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.327 (-99.229, -2.399)
Two-sided Wilcoxon Test, p-value		0.137

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Female		
Total Number of HAE Attacks during Treatment Period	5	13
Number of Subjects observed during Treatment Period, n (%) [2]	24 (61.54)	14 (56.00)
Time-normalized Number of Severe HAE Attacks Treatment Per Month		
Number Observed	24	14
Mean (SD)	0.04 (0.086)	0.18 (0.198)
Standard Error	0.02	0.05
Median	0.00	0.08
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 0.33
Minimum, Maximum	0.0, 0.3	0.0, 0.5
LS Means (Standard Error)[1]	0.03 (0.543)	0.17 (0.329)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.19 (0.06, 0.63)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-81.257 (-94.432, -36.907)
Two-sided Wilcoxon Test, p-value		0.017

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Gender		
Gender = Female		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	24	14
Mean (SD)	0.42 (1.029)	2.12 (2.381)
Standard Error	0.21	0.64
Median	0.00	0.99
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 4.01
Minimum, Maximum	0.0, 4.0	0.0, 6.1
LS Means (Standard Error)[1]	0.37 (0.543)	1.98 (0.329)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.19 (0.06, 0.63)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-81.257 (-94.432, -36.907)
Two-sided Wilcoxon Test, p-value		0.017

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Generalized Linear Model [1], p-value		0.010
Treatment		0.052
time-normalized baseline attack rate during Run-in Period		0.022
Subgroup		0.252
Interaction Treatment*Subgroup		
Region = EU (Germany, Hungary, Netherlands)		14
Total Number of HAE Attacks during Treatment Period	2	9 (36.00)
Number of Subjects observed during Treatment Period, n (%) [2]	11 (28.21)	
Time-normalized Number of Severe HAE Attacks Treatment Per Month		9
Number Observed	11	0.26 (0.237)
Mean (SD)	0.03 (0.069)	0.08
Standard Error	0.02	0.33
Median	0.00	0.00, 0.34
1st Quartile, 3rd Quartile	0.00, 0.00	0.0, 0.7
Minimum, Maximum	0.0, 0.2	0.28 (0.314)
LS Means (Standard Error)[1]	0.02 (0.979)	0.07 (0.01, 0.53)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-93.133 (-99.103, -47.419)
Two-sided Wilcoxon Test, p-value		0.018

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.

[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = EU (Germany, Hungary, Netherlands)		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	11	9
Mean (SD)	0.37 (0.834)	3.11 (2.848)
Standard Error	0.25	0.95
Median	0.00	3.99
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 4.04
Minimum, Maximum	0.0, 2.1	0.0, 7.9
LS Means (Standard Error)[1]	0.23 (0.979)	3.31 (0.314)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.07 (0.01, 0.53)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-93.133 (-99.103, -47.419)
Two-sided Wilcoxon Test, p-value		0.018

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)		
Total Number of HAE Attacks during Treatment Period	4	7
Number of Subjects observed during Treatment Period, n (%) [2]	28 (71.79)	16 (64.00)
Time-normalized Number of Severe HAE Attacks Treatment Per Month		
Number Observed	28	16
Mean (SD)	0.02 (0.074)	0.09 (0.180)
Standard Error	0.01	0.04
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 0.09
Minimum, Maximum	0.0, 0.3	0.0, 0.5
LS Means (Standard Error)[1]	0.02 (0.587)	0.08 (0.460)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.31 (0.07, 1.34)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-68.697 (-92.714, 34.495)
Two-sided Wilcoxon Test, p-value		0.168

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The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Region		
Region = RoW (Canada, Israel, Japan, United States)		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	28	16
Mean (SD)	0.28 (0.891)	1.12 (2.158)
Standard Error	0.17	0.54
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 1.10
Minimum, Maximum	0.0, 4.0	0.0, 6.1
LS Means (Standard Error)[1]	0.29 (0.587)	0.92 (0.460)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.31 (0.07, 1.34)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-68.697 (-92.714, 34.495)
Two-sided Wilcoxon Test, p-value		0.168

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Generalized Linear Model [1], p-value		0.001
Treatment		0.057
time-normalized baseline attack rate during Run-in Period		0.017
Subgroup		0.503
Interaction Treatment*Subgroup		
Age at First Diagnosis = <=17 years		15
Total Number of HAE Attacks during Treatment Period	4	12 (48.00)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.15)	
Time-normalized Number of Severe HAE Attacks Treatment Per Month		12
Number Observed	18	0.23 (0.259)
Mean (SD)	0.04 (0.092)	0.07
Standard Error	0.02	0.17
Median	0.00	0.00, 0.49
1st Quartile, 3rd Quartile	0.00, 0.00	0.0, 0.7
Minimum, Maximum	0.0, 0.3	0.26 (0.285)
LS Means (Standard Error)[1]	0.03 (0.617)	0.11 (0.03, 0.41)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-89.278 (-97.196, -58.995)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		0.023

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Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.

[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = <=17 years		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	18	12
Mean (SD)	0.45 (1.110)	2.82 (3.107)
Standard Error	0.26	0.90
Median	0.00	2.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 5.85
Minimum, Maximum	0.0, 4.0	0.0, 7.9
LS Means (Standard Error)[1]	0.34 (0.617)	3.15 (0.285)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.03, 0.41)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-89.278 (-97.196, -58.995)
Two-sided Wilcoxon Test, p-value		0.023

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = >17 years		
Total Number of HAE Attacks during Treatment Period	2	6
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.85)	13 (52.00)
Time-normalized Number of Severe HAE Attacks Treatment Per Month		
Number Observed	21	13
Mean (SD)	0.02 (0.049)	0.08 (0.130)
Standard Error	0.01	0.04
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 0.17
Minimum, Maximum	0.0, 0.2	0.0, 0.3
LS Means (Standard Error)[1]	0.02 (0.780)	0.07 (0.459)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.23 (0.04, 1.39)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-76.590 (-96.044, 38.535)
Two-sided Wilcoxon Test, p-value		0.093

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Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age at First Diagnosis		
Age at First Diagnosis = >17 years		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	21	13
Mean (SD)	0.19 (0.585)	0.94 (1.565)
Standard Error	0.13	0.43
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 1.99
Minimum, Maximum	0.0, 2.0	0.0, 4.0
LS Means (Standard Error)[1]	0.20 (0.780)	0.87 (0.459)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.23 (0.04, 1.39)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-76.590 (-96.044, 38.535)
Two-sided Wilcoxon Test, p-value		0.093

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Generalized Linear Model [1], p-value		0.076
Treatment		0.385
time-normalized baseline attack rate during Run-in Period		0.023
Subgroup		0.439
Interaction Treatment*Subgroup		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month Total		7
Number of HAE Attacks during Treatment Period	3	17 (68.00)
Number of Subjects observed during Treatment Period, n (%) [2]	24 (61.54)	
Time-normalized Number of Severe HAE Attacks Treatment Per Month		17
Number Observed	24	0.09 (0.153)
Mean (SD)	0.02 (0.056)	0.04
Standard Error	0.01	0.00
Median	0.00	0.00, 0.17
1st Quartile, 3rd Quartile	0.00, 0.00	0.0, 0.5
Minimum, Maximum	0.0, 0.2	0.08 (0.421)
LS Means (Standard Error)[1]	0.02 (0.642)	0.26 (0.06, 1.15)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-74.407 (-94.310, 15.117)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		0.131

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.

[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	24	17
Mean (SD)	0.25 (0.677)	1.05 (1.835)
Standard Error	0.14	0.45
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 1.99
Minimum, Maximum	0.0, 2.1	0.0, 5.6
LS Means (Standard Error)[1]	0.25 (0.642)	0.99 (0.421)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.26 (0.06, 1.15)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-74.407 (-94.310, 15.117)
Two-sided Wilcoxon Test, p-value		0.131

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
Produced: 21MAR2024 07:28
Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >=3 attacks/month Total		
Number of HAE Attacks during Treatment Period	3	14
Number of Subjects observed during Treatment Period, n (%) [2]	15 (38.46)	8 (32.00)
Time-normalized Number of Severe HAE Attacks Treatment Per Month		
Number Observed	15	8
Mean (SD)	0.03 (0.094)	0.29 (0.265)
Standard Error	0.02	0.09
Median	0.00	0.33
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 0.51
Minimum, Maximum	0.0, 0.3	0.0, 0.7
LS Means (Standard Error)[1]	0.03 (0.654)	0.28 (0.312)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.03, 0.46)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-88.590 (-97.150, -54.328)
Two-sided Wilcoxon Test, p-value		0.010

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = >=3 attacks/month		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	15	8
Mean (SD)	0.40 (1.125)	3.52 (3.174)
Standard Error	0.29	1.12
Median	0.00	4.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 6.10
Minimum, Maximum	0.0, 4.0	0.0, 7.9
LS Means (Standard Error)[1]	0.38 (0.654)	3.30 (0.312)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.03, 0.46)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-88.590 (-97.150, -54.328)
Two-sided Wilcoxon Test, p-value		0.010

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
Generalized Linear Model [1], p-value		0.685
Treatment		0.223
time-normalized baseline attack rate during Run-in Period		0.082
Subgroup		0.156
Interaction Treatment*Subgroup		
History of Laryngeal Attack = No		2
Total Number of HAE Attacks during Treatment Period	3	8 (32.00)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.15)	
Time-normalized Number of Severe HAE Attacks Treatment Per Month		8
Number Observed	18	0.04 (0.118)
Mean (SD)	0.03 (0.064)	0.04
Standard Error	0.02	0.00
Median	0.00	0.00, 0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.0, 0.3
Minimum, Maximum	0.0, 0.2	0.05 (0.828)
LS Means (Standard Error)[1]	0.03 (0.675)	0.65 (0.08, 5.26)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-35.112 (-91.989, 425.569)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		
Two-sided Wilcoxon Test, p-value		0.930

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Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.

[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = No		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	18	8
Mean (SD)	0.33 (0.768)	0.50 (1.411)
Standard Error	0.18	0.50
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 0.00
Minimum, Maximum	0.0, 2.1	0.0, 4.0
LS Means (Standard Error)[1]	0.35 (0.675)	0.54 (0.828)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.65 (0.08, 5.26)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-35.112 (-91.989, 425.569)
Two-sided Wilcoxon Test, p-value		0.930

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
Produced: 21MAR2024 07:28
Source: 16.2.5.4; UNBLINDED

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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = Yes		
Total Number of HAE Attacks during Treatment Period	3	19
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.85)	17 (68.00)
Time-normalized Number of Severe HAE Attacks Treatment Per Month		
Number Observed	21	17
Mean (SD)	0.02 (0.080)	0.21 (0.231)
Standard Error	0.02	0.06
Median	0.00	0.17
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 0.34
Minimum, Maximum	0.0, 0.3	0.0, 0.7
LS Means (Standard Error)[1]	0.02 (0.693)	0.21 (0.276)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.10 (0.02, 0.44)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-89.634 (-97.532, -56.453)
Two-sided Wilcoxon Test, p-value		0.003

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
Produced: 21MAR2024 07:28 Page 19 of 60
Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

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GAP Table 14.2.1.2.1.gS: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = Yes		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	21	17
Mean (SD)	0.29 (0.959)	2.47 (2.767)
Standard Error	0.21	0.67
Median	0.00	1.99
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 4.04
Minimum, Maximum	0.0, 4.0	0.0, 7.9
LS Means (Standard Error)[1]	0.26 (0.693)	2.47 (0.276)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.10 (0.02, 0.44)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-89.634 (-97.532, -56.453)
Two-sided Wilcoxon Test, p-value		0.003

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
Produced: 21MAR2024 07:28
Source: 16.2.5.4; UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and Subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and Subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

4.6 Reduktion der Anzahl der HAE-Attacken um 50 %, 70 % und 90 %

CSL312_3001

GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 50% [2][3] Non-responders with Reduction of < 50% [2][3]	37 (94.9) 2 (5.1)	8 (32.0) 17 (68.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(83.11, 98.58)	(17.21, 51.59)
Logistic Regression , p-value		
Treatment <		0.008
Subgroup		0.693
Interaction Treatment*Subgroup		0.393

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
Produced: 21MAR2024 07:30 Page 1 of 90
Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup:			
Gender			
Gender = Male			
Subjects Included in the Analysis, n	15	11	
Responders with Reduction of >= 50% [2][3]	15 (100.0)	3 (27.3)	
Odds Ratio and 95% Confidence Interval and p-value		75.29 (3.464, 1636.462)	<0.001
Relative Risk and 95% Confidence Interval and p-value		3.67 (1.397, 9.624)	0.008
Risk Difference and 95% Confidence Interval and p-value		0.73 (0.464, 0.990)	<0.001
Gender = Female			
Subjects Included in the Analysis, n	24	14	
Responders with Reduction of >= 50% [2][3]	22 (91.7)	5 (35.7)	
Odds Ratio and 95% Confidence Interval and p-value		19.80 (3.228, 121.467)	<0.001
Relative Risk and 95% Confidence Interval and p-value		2.57 (1.258, 5.237)	0.010
Risk Difference and 95% Confidence Interval and p-value		0.56 (0.285, 0.834)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
Produced: 21MAR2024 07:30 Page 2 of 90
Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [1]	39 (100.0) 0	25 (100.0) 0
Responders with Reduction of >= 70% [2][3] Non-responders with Reduction of < 70% [2][3]	36 (92.3) 3 (7.7)	4 (16.0) 21 (84.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 70% [4]	(79.68, 97.35)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		0.004
Subgroup		0.790
Interaction Treatment*Subgroup		0.480

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
Produced: 21MAR2024 07:30 Page 3 of 90
Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup:			
Gender			
Gender = Male			
Subjects Included in the Analysis, n	15	11	
Responders with Reduction of >= 70% [2][3]	15 (100.0)	2 (18.2)	
Odds Ratio and 95% Confidence Interval and p-value		117.80 (5.089, 2726.883)	<0.001
Relative Risk and 95% Confidence Interval and p-value		5.50 (1.570, 19.266)	0.008
Risk Difference and 95% Confidence Interval and p-value		0.82 (0.590, 1.000)	<0.001
Gender = Female			
Subjects Included in the Analysis, n	24	14	
Responders with Reduction of >= 70% [2][3]	21 (87.5)	2 (14.3)	
Odds Ratio and 95% Confidence Interval and p-value		42.00 (6.129, 287.814)	<0.001
Relative Risk and 95% Confidence Interval and p-value		6.13 (1.683, 22.295)	0.006
Risk Difference and 95% Confidence Interval and p-value		0.73 (0.506, 0.958)	<0.001

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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [1]	39 (100.0) 0	25 (100.0) 0
Responders with Reduction of >= 90% [2][3] Non-responders with Reduction of < 90% [2][3]	29 (74.4) 10 (25.6)	2 (8.0) 23 (92.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 90% [4]	(58.92, 85.43)	(2.22, 24.97)
Logistic Regression , p-value		
Treatment		0.001
Subgroup		0.859
Interaction Treatment*Subgroup		0.593

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup:			
Gender			
Gender = Male			
Subjects Included in the Analysis, n	15	11	
Responders with Reduction of >= 90% [2][3]	13 (86.7)	1 (9.1)	
Odds Ratio and 95% Confidence Interval and p-value		65.00 (5.136, 822.595)	<0.001
Relative Risk and 95% Confidence Interval and p-value		9.53 (1.456, 62.431)	0.019
Risk Difference and 95% Confidence Interval and p-value		0.78 (0.534, 1.000)	<0.001
Gender = Female			
Subjects Included in the Analysis, n	24	14	
Responders with Reduction of >= 90% [2][3]	16 (66.7)	1 (7.1)	
Odds Ratio and 95% Confidence Interval and p-value		26.00 (2.870, 235.570)	<0.001
Relative Risk and 95% Confidence Interval and p-value		9.33 (1.382, 63.012)	0.022
Risk Difference and 95% Confidence Interval and p-value		0.60 (0.363, 0.827)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 50% [2][3]	37 (94.9)	8 (32.0)
Non-responders with Reduction of < 50% [2][3]	2 (5.1)	17 (68.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(83.11, 98.58)	(17.21, 51.59)
Logistic Regression , p-value		
Treatment		0.018
Subgroup		0.915
Interaction Treatment*Subgroup		0.525

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	11	9	
Responders with Reduction of >= 50% [2][3]	10 (90.9)	3 (33.3)	
Odds Ratio and 95% Confidence Interval and p-value		20.00 (1.676, 238.630)	0.009
Relative Risk and 95% Confidence Interval and p-value		2.73 (1.063, 7.000)	0.037
Risk Difference and 95% Confidence Interval and p-value		0.58 (0.224, 0.927)	0.001
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	28	16	
Responders with Reduction of >= 50% [2][3]	27 (96.4)	5 (31.3)	
Odds Ratio and 95% Confidence Interval and p-value		59.40 (6.207, 568.436)	<0.001
Relative Risk and 95% Confidence Interval and p-value		3.09 (1.487, 6.405)	0.002
Risk Difference and 95% Confidence Interval and p-value		0.65 (0.414, 0.889)	<0.001

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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Region		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [1]	39 (100.0) 0	25 (100.0) 0
Responders with Reduction of >= 70% [2][3] Non-responders with Reduction of < 70% [2][3]	36 (92.3) 3 (7.7)	4 (16.0) 21 (84.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 70% [4]	(79.68, 97.35)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		0.003
Subgroup		0.621
Interaction Treatment*Subgroup		0.844

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	11	9	
Responders with Reduction of >= 70% [2][3]	10 (90.9)	1 (11.1)	
Odds Ratio and 95% Confidence Interval and p-value		80.00 (4.299, 1488.604)	<0.001
Relative Risk and 95% Confidence Interval and p-value		8.18 (1.277, 52.416)	0.027
Risk Difference and 95% Confidence Interval and p-value		0.80 (0.531, 1.000)	<0.001
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	28	16	
Responders with Reduction of >= 70% [2][3]	26 (92.9)	3 (18.8)	
Odds Ratio and 95% Confidence Interval and p-value		56.33 (8.350, 380.062)	<0.001
Relative Risk and 95% Confidence Interval and p-value		4.95 (1.777, 13.805)	0.002
Risk Difference and 95% Confidence Interval and p-value		0.74 (0.527, 0.955)	<0.001

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[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Region		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [1]	39 (100.0) 0	25 (100.0) 0
Responders with Reduction of >= 90% [2][3] Non-responders with Reduction of < 90% [2][3]	29 (74.4) 10 (25.6)	2 (8.0) 23 (92.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 90% [4]	(58.92, 85.43)	(2.22, 24.97)
Logistic Regression , p-value		
Treatment		0.012
Subgroup		0.481
Interaction Treatment*Subgroup		0.384

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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	11	9	
Responders with Reduction of >= 90% [2][3]	9 (81.8)	0	
Odds Ratio and 95% Confidence Interval and p-value		72.20 (3.043, 1713.302)	<0.001
Relative Risk and 95% Confidence Interval and p-value		15.83 (1.046, 239.676)	NE
Risk Difference and 95% Confidence Interval and p-value		0.82 (0.590, 1.000)	<0.001
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	28	16	
Responders with Reduction of >= 90% [2][3]	20 (71.4)	2 (12.5)	
Odds Ratio and 95% Confidence Interval and p-value		17.50 (3.218, 95.157)	<0.001
Relative Risk and 95% Confidence Interval and p-value		5.71 (1.530, 21.335)	0.010
Risk Difference and 95% Confidence Interval and p-value		0.59 (0.356, 0.822)	<0.001

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[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 50% [2][3]	37 (94.9)	8 (32.0)
Non-responders with Reduction of < 50% [2][3]	2 (5.1)	17 (68.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(83.11, 98.58)	(17.21, 51.59)
Logistic Regression , p-value		
Treatment		<0.001
Subgroup		0.127
Interaction Treatment*Subgroup		0.457

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	18	12	
Responders with Reduction of >= 50% [2][3]	17 (94.4)	2 (16.7)	
Odds Ratio and 95% Confidence Interval and p-value		85.00 (6.809, 1061.028)	<0.001
Relative Risk and 95% Confidence Interval and p-value		5.67 (1.591, 20.180)	0.007
Risk Difference and 95% Confidence Interval and p-value		0.78 (0.542, 1.000)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Reduction of >= 50% [2][3]	20 (95.2)	6 (46.2)	
Odds Ratio and 95% Confidence Interval and p-value		23.33 (2.374, 229.333)	0.001
Relative Risk and 95% Confidence Interval and p-value		2.06 (1.138, 3.741)	0.017
Risk Difference and 95% Confidence Interval and p-value		0.49 (0.205, 0.777)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 70% [2][3]	36 (92.3)	4 (16.0)
Non-responders with Reduction of < 70% [2][3]	3 (7.7)	21 (84.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 70% [4]	(79.68, 97.35)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		<0.001
Subgroup		0.930
Interaction Treatment*Subgroup		0.546

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	18	12	
Responders with Reduction of >= 70% [2][3]	16 (88.9)	2 (16.7)	
Odds Ratio and 95% Confidence Interval and p-value		40.00 (4.834, 330.994)	<0.001
Relative Risk and 95% Confidence Interval and p-value		5.33 (1.489, 19.099)	0.010
Risk Difference and 95% Confidence Interval and p-value		0.72 (0.466, 0.978)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Reduction of >= 70% [2][3]	20 (95.2)	2 (15.4)	
Odds Ratio and 95% Confidence Interval and p-value		110.00 (8.933, 1354.455)	<0.001
Relative Risk and 95% Confidence Interval and p-value		6.19 (1.724, 22.230)	0.005
Risk Difference and 95% Confidence Interval and p-value		0.80 (0.582, 1.000)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [1]	39 (100.0) 0	25 (100.0) 0
Responders with Reduction of >= 90% [2][3] Non-responders with Reduction of < 90% [2][3]	29 (74.4) 10 (25.6)	2 (8.0) 23 (92.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 90% [4]	(58.92, 85.43)	(2.22, 24.97)
Logistic Regression , p-value		
Treatment		0.004
Subgroup		0.953
Interaction Treatment*Subgroup		0.858

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	18	12	
Responders with Reduction of >= 90% [2][3]	13 (72.2)	1 (8.3)	
Odds Ratio and 95% Confidence Interval and p-value		28.60 (2.890, 283.063)	<0.001
Relative Risk and 95% Confidence Interval and p-value		8.67 (1.299, 57.844)	0.026
Risk Difference and 95% Confidence Interval and p-value		0.64 (0.380, 0.898)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Reduction of >= 90% [2][3]	16 (76.2)	1 (7.7)	
Odds Ratio and 95% Confidence Interval and p-value		38.40 (3.952, 373.087)	<0.001
Relative Risk and 95% Confidence Interval and p-value		9.90 (1.484, 66.102)	0.018
Risk Difference and 95% Confidence Interval and p-value		0.68 (0.452, 0.918)	<0.001

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 50% [2][3]	37 (94.9)	8 (32.0)
Non-responders with Reduction of < 50% [2][3]	2 (5.1)	17 (68.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(83.11, 98.58)	(17.21, 51.59)
Logistic Regression , p-value		
Treatment		<0.001
Subgroup		0.687
Interaction Treatment*Subgroup		0.615

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	24	17	
Responders with Reduction of >= 50% [2][3]	23 (95.8)	5 (29.4)	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	55.20 (5.774, 527.734)	<0.001
and 95% Confidence Interval and p-value	Risk Difference and 95%	3.26 (1.553, 6.837)	0.002
Confidence Interval and p-value		0.66 (0.433, 0.895)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders with Reduction of >= 50% [2][3]	14 (93.3)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	23.33 (1.948, 279.429)	0.005
and 95% Confidence Interval and p-value	Risk Difference and 95%	2.49 (1.007, 6.151)	0.048
Confidence Interval and p-value		0.56 (0.200, 0.917)	0.002

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 70% [2][3]	36 (92.3)	4 (16.0)
Non-responders with Reduction of < 70% [2][3]	3 (7.7)	21 (84.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 70% [4]	(79.68, 97.35)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		<0.001
Subgroup		0.409
Interaction Treatment*Subgroup		0.197

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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	24	17	
Responders with Reduction of >= 70% [2][3]	23 (95.8)	2 (11.8)	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	172.50 (14.345, 2074.395)	<0.001
and 95% Confidence Interval and p-value	Risk Difference and 95%	8.15 (2.210, 30.024)	0.002
Confidence Interval and p-value		0.84 (0.668, 1.000)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders with Reduction of >= 70% [2][3]	13 (86.7)	2 (25.0)	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	19.50 (2.192, 173.486)	0.004
and 95% Confidence Interval and p-value	Risk Difference and 95%	3.47 (1.027, 11.702)	0.045
Confidence Interval and p-value		0.62 (0.271, 0.963)	<0.001

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 90% [2][3]	29 (74.4)	2 (8.0)
Non-responders with Reduction of < 90% [2][3]	10 (25.6)	23 (92.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 90% [4]	(58.92, 85.43)	(2.22, 24.97)
Logistic Regression , p-value		
Treatment		<0.001
Subgroup		0.552
Interaction Treatment*Subgroup		0.626

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	24	17	
Responders with Reduction of >= 90% [2][3]	18 (75.0)	2 (11.8)	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	22.50 (3.946, 128.296)	<0.001
and 95% Confidence Interval and p-value	Risk Difference and 95%	6.38 (1.699, 23.916)	0.006
Confidence Interval and p-value		0.63 (0.401, 0.864)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders with Reduction of >= 90% [2][3]	11 (73.3)	0	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	43.44 (2.051, 920.363)	0.001
and 95% Confidence Interval and p-value	Risk Difference and 95%	12.94 (0.860, 194.654)	NE
Confidence Interval and p-value		0.73 (0.510, 0.957)	<0.001

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 50% [2][3]	37 (94.9)	8 (32.0)
Non-responders with Reduction of < 50% [2][3]	2 (5.1)	17 (68.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(83.11, 98.58)	(17.21, 51.59)
Logistic Regression , p-value		
Treatment		0.008
Subgroup		0.687
Interaction Treatment*Subgroup		0.758

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	18	8	
Responders with Reduction of >= 50% [2][3]	17 (94.4)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value		28.33 (2.389, 336.008)	0.002
Relative Risk and 95% Confidence Interval and p-value		2.52 (1.022, 6.204)	0.045
Risk Difference and 95% Confidence Interval and p-value		0.57 (0.218, 0.921)	0.002
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	21	17	
Responders with Reduction of >= 50% [2][3]	20 (95.2)	5 (29.4)	
Odds Ratio and 95% Confidence Interval and p-value		48.00 (4.993, 461.449)	<0.001
Relative Risk and 95% Confidence Interval and p-value		3.24 (1.541, 6.805)	0.002
Risk Difference and 95% Confidence Interval and p-value		0.66 (0.423, 0.893)	<0.001

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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 70% [2][3]	36 (92.3)	4 (16.0)
Non-responders with Reduction of < 70% [2][3]	3 (7.7)	21 (84.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 70% [4]	(79.68, 97.35)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		0.003
Subgroup		0.409
Interaction Treatment*Subgroup		0.843

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	18	8	
Responders with Reduction of >= 70% [2][3]	17 (94.4)	2 (25.0)	
Odds Ratio and 95% Confidence Interval and p-value		51.00 (3.886, 669.408)	<0.001
Relative Risk and 95% Confidence Interval and p-value		3.78 (1.132, 12.611)	0.031
Risk Difference and 95% Confidence Interval and p-value		0.69 (0.376, 1.000)	<0.001
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	21	17	
Responders with Reduction of >= 70% [2][3]	19 (90.5)	2 (11.8)	
Odds Ratio and 95% Confidence Interval and p-value		71.25 (8.959, 566.669)	<0.001
Relative Risk and 95% Confidence Interval and p-value		7.69 (2.077, 28.480)	0.002
Risk Difference and 95% Confidence Interval and p-value		0.79 (0.589, 0.985)	<0.001

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [1]	39 (100.0) 0	25 (100.0) 0
Responders with Reduction of >= 90% [2][3] Non-responders with Reduction of < 90% [2][3]	29 (74.4) 10 (25.6)	2 (8.0) 23 (92.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 90% [4]	(58.92, 85.43)	(2.22, 24.97)
Logistic Regression , p-value		
Treatment		0.015
Subgroup		0.552
Interaction Treatment*Subgroup		0.478

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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GAP Table 14.2.2.1.2.aS: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	18	8	
Responders with Reduction of >= 90% [2][3]	14 (77.8)	0	
Odds Ratio and 95% Confidence Interval and p-value		54.78 (2.615, 1147.374)	<0.001
Relative Risk and 95% Confidence Interval and p-value		13.74 (0.918, 205.494)	NE
Risk Difference and 95% Confidence Interval and p-value		0.78 (0.586, 0.970)	<0.001
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	21	17	
Responders with Reduction of >= 90% [2][3]	15 (71.4)	2 (11.8)	
Odds Ratio and 95% Confidence Interval and p-value		18.75 (3.248, 108.228)	<0.001
Relative Risk and 95% Confidence Interval and p-value		6.07 (1.606, 22.948)	0.008
Risk Difference and 95% Confidence Interval and p-value		0.60 (0.350, 0.843)	<0.001

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

4.7 Reduktion der Anzahl der HAE-Attacken um 100 %

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of 100% (attack-free) [2][3] Non-responders with Reduction of < 100% [2][3]	24 (61.5) 15 (38.5)	0 25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(45.90, 75.11)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.028
Subgroup		0.913
Interaction Treatment*Subgroup		0.878

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup:			
Gender			
Gender = Male			
Subjects Included in the Analysis, n	15	11	
Responders with Reduction of 100% (attack-free) [2][3]	9 (60.0)	0	
Odds Ratio and 95% Confidence Interval and p-value		33.62 (1.670, 676.570)	0.002
Relative Risk and 95% Confidence Interval and p-value		14.25 (0.917, 221.474)	NE
Risk Difference and 95% Confidence Interval and p-value		0.60 (0.352, 0.848)	<0.001
Gender = Female			
Subjects Included in the Analysis, n	24	14	
Responders with Reduction of 100% (attack-free) [2][3]	15 (62.5)	0	
Odds Ratio and 95% Confidence Interval and p-value		47.32 (2.520, 888.405)	<0.001
Relative Risk and 95% Confidence Interval and p-value		18.60 (1.198, 288.763)	NE
Risk Difference and 95% Confidence Interval and p-value		0.63 (0.431, 0.819)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of 100% (attack-free) [2][3] Non-responders with Reduction of < 100% [2][3]	24 (61.5) 15 (38.5)	0 25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(45.90, 75.11)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.059
Subgroup		0.795
Interaction Treatment*Subgroup		0.672

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	11	9	
Responders with Reduction of 100% (attack-free) [2][3]	6 (54.5)	0	
Odds Ratio and 95% Confidence Interval and p-value		22.45 (1.051, 479.928)	0.010
Relative Risk and 95% Confidence Interval and p-value		10.83 (0.692, 169.682)	NE
Risk Difference and 95% Confidence Interval and p-value		0.55 (0.251, 0.840)	<0.001
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	28	16	
Responders with Reduction of 100% (attack-free) [2][3]	18 (64.3)	0	
Odds Ratio and 95% Confidence Interval and p-value		58.14 (3.156, 1071.197)	<0.001
Relative Risk and 95% Confidence Interval and p-value		21.69 (1.394, 337.413)	NE
Risk Difference and 95% Confidence Interval and p-value		0.64 (0.465, 0.820)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of 100% (attack-free) [2][3] Non-responders with Reduction of < 100% [2][3]	24 (61.5) 15 (38.5)	0 25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(45.90, 75.11)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.029
Subgroup		0.971
Interaction Treatment*Subgroup		0.813

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup:			
Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	18	12	
Responders with Reduction of 100% (attack-free) [2][3]	10 (55.6)	0	
Odds Ratio and 95% Confidence Interval and p-value		30.88 (1.588, 600.652)	0.002
Relative Risk and 95% Confidence Interval and p-value		14.37 (0.920, 224.294)	NE
Risk Difference and 95% Confidence Interval and p-value		0.56 (0.326, 0.785)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Reduction of 100% (attack-free) [2][3]	14 (66.7)	0	
Odds Ratio and 95% Confidence Interval and p-value		52.20 (2.713, 1004.463)	<0.001
Relative Risk and 95% Confidence Interval and p-value		18.45 (1.194, 285.349)	NE
Risk Difference and 95% Confidence Interval and p-value		0.67 (0.465, 0.868)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of 100% (attack-free) [2][3] Non-responders with Reduction of < 100% [2][3]	24 (61.5) 15 (38.5)	0 25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(45.90, 75.11)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.006
Subgroup		0.735
Interaction Treatment*Subgroup		0.574

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	24	17	
Responders with Reduction of 100% (attack-free) [2][3]	16 (66.7)	0	
Odds Ratio and 95% Confidence Interval and p-value Relative Risk		67.94 (3.626, 1272.873)	<0.001
and 95% Confidence Interval and p-value Risk Difference and 95%		23.76 (1.523, 370.734)	NE
Confidence Interval and p-value		0.67 (0.478, 0.855)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders with Reduction of 100% (attack-free) [2][3]	8 (53.3)	0	
Odds Ratio and 95% Confidence Interval and p-value Relative Risk		19.27 (0.944, 393.401)	0.012
and 95% Confidence Interval and p-value Risk Difference and 95%		9.56 (0.622, 147.025)	NE
Confidence Interval and p-value		0.53 (0.281, 0.786)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of 100% (attack-free) [2][3] Non-responders with Reduction of < 100% [2][3]	24 (61.5) 15 (38.5)	0 25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(45.90, 75.11)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.059
Subgroup		0.735
Interaction Treatment*Subgroup		0.601

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

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Gap Analysis (Database lock: 24Jun2022)

GAP Table 14.2.2.1.2.bS: Number and proportion of HAE attack-free patient - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	18	8	
Responders with Reduction of 100% (attack-free) [2][3]	10 (55.6)	0	
Odds Ratio and 95% Confidence Interval and p-value		21.00 (1.054, 418.476)	0.008
Relative Risk and 95% Confidence Interval and p-value		9.95 (0.653, 151.598)	NE
Risk Difference and 95% Confidence Interval and p-value		0.56 (0.326, 0.785)	<0.001
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	21	17	
Responders with Reduction of 100% (attack-free) [2][3]	14 (66.7)	0	
Odds Ratio and 95% Confidence Interval and p-value		67.67 (3.555, 1287.814)	<0.001
Relative Risk and 95% Confidence Interval and p-value		23.73 (1.518, 370.976)	NE
Risk Difference and 95% Confidence Interval and p-value		0.67 (0.465, 0.868)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps.sas
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Source: 16.2.5.5; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

4.8 Gesundheitszustand (EQ-5D-5L VAS)

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 15 [2][5]	8 (20.5)	0
Non-responders with Change from Baseline of < 15 [2][5]	31 (79.5)	25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(10.78, 35.53)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.620
Subgroup		0.913
Interaction Treatment*Subgroup		0.480

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap07si.sas
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Source: 16.2.5.8; UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	15	11	
Responders with Change from Baseline of >= 15 [2][5]	1 (6.7)	0	
Odds Ratio and 95% Confidence Interval and p-value		2.38 (0.088, 64.050)	0.392
Relative Risk and 95% Confidence Interval and p-value		2.25 (0.100, 50.541)	NE
Risk Difference and 95% Confidence Interval and p-value		0.07 (-0.060, 0.193)	0.301
Gender = Female			
Subjects Included in the Analysis, n	24	14	
Responders with Change from Baseline of >= 15 [2][5]	7 (29.2)	0	
Odds Ratio and 95% Confidence Interval and p-value		12.43 (0.653, 236.537)	0.027
Relative Risk and 95% Confidence Interval and p-value		9.00 (0.553, 146.562)	NE
Risk Difference and 95% Confidence Interval and p-value		0.29 (0.110, 0.474)	0.002

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 7 [2][5]	13 (33.3)	4 (16.0)
Non-responders with Change from Baseline of < 7 [2][5]	26 (66.7)	21 (84.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(20.63, 49.02)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		0.174
Subgroup		0.157
Interaction Treatment*Subgroup		0.298

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	15	11	
Responders with Change from Baseline of >= 7 [2][5]	4 (26.7)	0	
Odds Ratio and 95% Confidence Interval and p-value		9.00 (0.433, 187.006)	0.068
Relative Risk and 95% Confidence Interval and p-value		6.75 (0.401, 113.726)	NE
Risk Difference and 95% Confidence Interval and p-value		0.27 (0.043, 0.490)	0.020
Gender = Female			
Subjects Included in the Analysis, n	24	14	
Responders with Change from Baseline of >= 7 [2][5]	9 (37.5)	4 (28.6)	
Odds Ratio and 95% Confidence Interval and p-value		1.50 (0.361, 6.230)	0.581
Relative Risk and 95% Confidence Interval and p-value		1.31 (0.495, 3.483)	0.585
Risk Difference and 95% Confidence Interval and p-value		0.09 (-0.217, 0.395)	0.567

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 15 [2][5]	8 (20.5)	0
Non-responders with Change from Baseline of < 15 [2][5]	31 (79.5)	25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(10.78, 35.53)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.344
Subgroup		0.795
Interaction Treatment*Subgroup		0.779

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	11	9	
Responders with Change from Baseline of >= 15 [2][5]	2 (18.2)	0	
Odds Ratio and 95% Confidence Interval and p-value		5.00 (0.211, 118.650)	0.189
Relative Risk and 95% Confidence Interval and p-value		4.17 (0.225, 77.108)	NE
Risk Difference and 95% Confidence Interval and p-value		0.18 (-0.046, 0.410)	0.118
Region = RoW (Canada, Israel, Japan, United States)			
Subjects Included in the Analysis, n	28	16	
Responders with Change from Baseline of >= 15 [2][5]	6 (21.4)	0	
Odds Ratio and 95% Confidence Interval and p-value		9.53 (0.501, 181.371)	0.049
Relative Risk and 95% Confidence Interval and p-value		7.62 (0.457, 127.016)	NE
Risk Difference and 95% Confidence Interval and p-value		0.21 (0.062, 0.366)	0.006

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 7 [2][5]	13 (33.3)	4 (16.0)
Non-responders with Change from Baseline of < 7 [2][5]	26 (66.7)	21 (84.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(20.63, 49.02)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		0.662
Subgroup		0.621
Interaction Treatment*Subgroup		0.764

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	11	9	
Responders with Change from Baseline of >= 7 [2][5]	2 (18.2)	1 (11.1)	
Odds Ratio and 95% Confidence Interval and p-value		1.78 (0.134, 23.520)	0.668
Relative Risk and 95% Confidence Interval and p-value		1.64 (0.175, 15.263)	0.666
Risk Difference and 95% Confidence Interval and p-value		0.07 (-0.236, 0.377)	0.651
Region = RoW (Canada, Israel, Japan, United States)			
Subjects Included in the Analysis, n	28	16	
Responders with Change from Baseline of >= 7 [2][5]	11 (39.3)	3 (18.8)	
Odds Ratio and 95% Confidence Interval and p-value		2.80 (0.647, 12.155)	0.164
Relative Risk and 95% Confidence Interval and p-value		2.10 (0.684, 6.416)	0.195
Risk Difference and 95% Confidence Interval and p-value		0.21 (-0.058, 0.469)	0.126

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 15 [2][5]	8 (20.5)	0
Non-responders with Change from Baseline of < 15 [2][5]	31 (79.5)	25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(10.78, 35.53)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.200
Subgroup		0.971
Interaction Treatment*Subgroup		0.961

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	18	12	
Responders with Change from Baseline of >= 15 [2][5]	4 (22.2)	0	
Odds Ratio and 95% Confidence Interval and p-value		7.76 (0.379, 158.680)	0.085
Relative Risk and 95% Confidence Interval and p-value		6.16 (0.361, 104.902)	NE
Risk Difference and 95% Confidence Interval and p-value		0.22 (0.030, 0.414)	0.023
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Change from Baseline of >= 15 [2][5]	4 (19.0)	0	
Odds Ratio and 95% Confidence Interval and p-value		6.94 (0.343, 140.398)	0.099
Relative Risk and 95% Confidence Interval and p-value		5.73 (0.333, 98.406)	NE
Risk Difference and 95% Confidence Interval and p-value		0.19 (0.023, 0.358)	0.026

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 7 [2][5]	13 (33.3)	4 (16.0)
Non-responders with Change from Baseline of < 7 [2][5]	26 (66.7)	21 (84.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(20.63, 49.02)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		0.205
Subgroup		0.930
Interaction Treatment*Subgroup		0.774

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	18	12	
Responders with Change from Baseline of >= 7 [2][5]	7 (38.9)	2 (16.7)	
Odds Ratio and 95% Confidence Interval and p-value		3.18 (0.531, 19.051)	0.201
Relative Risk and 95% Confidence Interval and p-value		2.33 (0.580, 9.381)	0.233
Risk Difference and 95% Confidence Interval and p-value		0.22 (-0.086, 0.531)	0.158
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Change from Baseline of >= 7 [2][5]	6 (28.6)	2 (15.4)	
Odds Ratio and 95% Confidence Interval and p-value		2.20 (0.371, 13.038)	0.385
Relative Risk and 95% Confidence Interval and p-value		1.86 (0.439, 7.863)	0.400
Risk Difference and 95% Confidence Interval and p-value		0.13 (-0.143, 0.407)	0.348

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 15 [2][5]	8 (20.5)	0
Non-responders with Change from Baseline of < 15 [2][5]	31 (79.5)	25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(10.78, 35.53)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.194
Subgroup		0.735
Interaction Treatment*Subgroup		0.949

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	24	17	
Responders with Change from Baseline of >= 15 [2][5]	4 (16.7)	0	
Odds Ratio and 95% Confidence Interval and p-value		7.68 (0.386, 152.866)	0.080
Relative Risk and 95% Confidence Interval and p-value		6.48 (0.372, 112.951)	NE
Risk Difference and 95% Confidence Interval and p-value		0.17 (0.018, 0.316)	0.028
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of >= 15 [2][5]	4 (26.7)	0	
Odds Ratio and 95% Confidence Interval and p-value		6.65 (0.314, 140.925)	0.116
Relative Risk and 95% Confidence Interval and p-value		5.06 (0.306, 83.693)	NE
Risk Difference and 95% Confidence Interval and p-value		0.27 (0.043, 0.490)	0.020

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 7 [2][5]	13 (33.3)	4 (16.0)
Non-responders with Change from Baseline of < 7 [2][5]	26 (66.7)	21 (84.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(20.63, 49.02)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		0.302
Subgroup		0.409
Interaction Treatment*Subgroup		0.970

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NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	24	17	
Responders with Change from Baseline of >= 7 [2][5]	6 (25.0)	2 (11.8)	
Odds Ratio and 95% Confidence Interval and p-value		2.50 (0.438, 14.255)	0.298
Relative Risk and 95% Confidence Interval and p-value		2.13 (0.486, 9.286)	0.316
Risk Difference and 95% Confidence Interval and p-value		0.13 (-0.099, 0.364)	0.262
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of >= 7 [2][5]	7 (46.7)	2 (25.0)	
Odds Ratio and 95% Confidence Interval and p-value		2.62 (0.395, 17.458)	0.321
Relative Risk and 95% Confidence Interval and p-value		1.87 (0.500, 6.963)	0.353
Risk Difference and 95% Confidence Interval and p-value		0.22 (-0.175, 0.609)	0.279

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 15 [2][5]	8 (20.5)	0
Non-responders with Change from Baseline of < 15 [2][5]	31 (79.5)	25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(10.78, 35.53)	(0.00, 13.32)
Logistic Regression , p-value		
Treatment		0.576
Subgroup		0.735
Interaction Treatment*Subgroup		0.449

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	18	8	
Responders with Change from Baseline of >= 15 [2][5]	2 (11.1)	0	
Odds Ratio and 95% Confidence Interval and p-value		2.58 (0.111, 59.934)	0.336
Relative Risk and 95% Confidence Interval and p-value		2.37 (0.126, 44.397)	NE
Risk Difference and 95% Confidence Interval and p-value		0.11 (-0.034, 0.256)	0.134
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	21	17	
Responders with Change from Baseline of >= 15 [2][5]	6 (28.6)	0	
Odds Ratio and 95% Confidence Interval and p-value		14.68 (0.763, 282.272)	0.018
Relative Risk and 95% Confidence Interval and p-value		10.64 (0.642, 176.348)	NE
Risk Difference and 95% Confidence Interval and p-value		0.29 (0.092, 0.479)	0.004

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 7 [2][5]	13 (33.3)	4 (16.0)
Non-responders with Change from Baseline of < 7 [2][5]	26 (66.7)	21 (84.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(20.63, 49.02)	(6.40, 34.65)
Logistic Regression , p-value		
Treatment		0.567
Subgroup		0.745
Interaction Treatment*Subgroup		0.697

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i: Analysis of Responders for Change from Baseline for EQ-5d-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	18	8	
Responders with Change from Baseline of >= 7 [2][5]	4 (22.2)	1 (12.5)	
Odds Ratio and 95% Confidence Interval and p-value		2.00 (0.187, 21.431)	0.569
Relative Risk and 95% Confidence Interval and p-value		1.78 (0.234, 13.494)	0.578
Risk Difference and 95% Confidence Interval and p-value		0.10 (-0.202, 0.396)	0.524
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	21	17	
Responders with Change from Baseline of >= 7 [2][5]	9 (42.9)	3 (17.6)	
Odds Ratio and 95% Confidence Interval and p-value		3.50 (0.768, 15.958)	0.101
Relative Risk and 95% Confidence Interval and p-value		2.43 (0.777, 7.590)	0.127
Risk Difference and 95% Confidence Interval and p-value		0.25 (-0.027, 0.531)	0.076

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

4.9 WPAI:GH Frage 6

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [6]	37 (100.0) 3 (8.1)	23 (100.0) 3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with Change from Baseline of > -15 [2][5]	0 37 (100.0)	0 23 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(0.00, 9.41)	(0.00, 14.31)
Logistic Regression , p-value		
Treatment		NE
Subgroup		NE
Interaction Treatment*Subgroup		NE

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap11si.sas
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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: Gender		
Gender = Male		
Subjects Included in the Analysis, n	14	10
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE
Gender = Female		
Subjects Included in the Analysis, n	23	13
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap11si.sas
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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	37 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	3 (8.1)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	0	0
Non-responders with Change from Baseline of > -15 [2][5]	37 (100.0)	23 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(0.00, 9.41)	(0.00, 14.31)
Logistic Regression , p-value		
Treatment		NE
Subgroup		NE
Interaction Treatment*Subgroup		NE

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap11si.sas
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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: Region		
Region = EU (Germany, Hungary, Netherlands)		
Subjects Included in the Analysis, n	10	9
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	27	14
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [6]	37 (100.0) 3 (8.1)	23 (100.0) 3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with Change from Baseline of > -15 [2][5]	0 37 (100.0)	0 23 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(0.00, 9.41)	(0.00, 14.31)
Logistic Regression , p-value		
Treatment		NE
Subgroup		NE
Interaction Treatment*Subgroup		NE

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap11si.sas
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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: Age at First Diagnosis		
Age at First Diagnosis = <=17 years		
Subjects Included in the Analysis, n	16	10
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE
Age at First Diagnosis = >17 years		
Subjects Included in the Analysis, n	21	13
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE

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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [6]	37 (100.0) 3 (8.1)	23 (100.0) 3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with Change from Baseline of > -15 [2][5]	0 37 (100.0)	0 23 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(0.00, 9.41)	(0.00, 14.31)
Logistic Regression , p-value		
Treatment		NE
Subgroup		NE
Interaction Treatment*Subgroup		NE

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap11si.sas
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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: Baseline Attack rate observed during Run-in Period		
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month		
Subjects Included in the Analysis, n	22	15
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value Relative Risk		NE
and 95% Confidence Interval and p-value Risk Difference and 95%		NE
Confidence Interval and p-value		NE
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month		
Subjects Included in the Analysis, n	15	8
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value Relative Risk		NE
and 95% Confidence Interval and p-value Risk Difference and 95%		NE
Confidence Interval and p-value		NE

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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	37 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	3 (8.1)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	0	0
Non-responders with Change from Baseline of > -15 [2][5]	37 (100.0)	23 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(0.00, 9.41)	(0.00, 14.31)
Logistic Regression , p-value		
Treatment		NE
Subgroup		NE
Interaction Treatment*Subgroup		NE

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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i: Analysis of Responders for Change from Baseline for WPAI:GH Q6 at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3] Subgroup: History of Laryngeal Attack		
History of Laryngeal Attack = No		
Subjects Included in the Analysis, n	17	8
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE
History of Laryngeal Attack = Yes		
Subjects Included in the Analysis, n	20	15
Responders with Change from Baseline of <= -15 [2][5]	0	0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap11si.sas
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Source: 16.2.5.9; UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] WPAI:GH is only answered from patients of age >= 16 years. Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes). Question 6 "During the past seven days, how much did your health problems affect your ability to perform your normal daily activities, excluding your job?" can be answered on a scale from 0 = Health problems had no effect on my daily activities to 10 = Health problems completely prevented me from performing my daily activities.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

4.10 AE-QoL

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Functioning [3] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	26 (74.3)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	9 (25.7)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(57.93, 85.84)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.027
Subgroup		0.562
Interaction Treatment*Subgroup		0.898

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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Functioning [3] Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	13	10	
Responders with Change from Baseline of <= -15 [2][5]	9 (69.2)	2 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		9.00 (1.285, 63.025)	0.022
Relative Risk and 95% Confidence Interval and p-value		3.46 (0.951, 12.594)	0.060
Risk Difference and 95% Confidence Interval and p-value		0.49 (0.140, 0.845)	0.006
Gender = Female			
Subjects Included in the Analysis, n	22	13	
Responders with Change from Baseline of <= -15 [2][5]	17 (77.3)	4 (30.8)	
Odds Ratio and 95% Confidence Interval and p-value		7.65 (1.635, 35.798)	0.007
Relative Risk and 95% Confidence Interval and p-value		2.51 (1.077, 5.854)	0.033
Risk Difference and 95% Confidence Interval and p-value		0.47 (0.159, 0.771)	0.003

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
Produced: 25APR2024 10:56
Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Functioning [3] Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	26 (74.3)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	9 (25.7)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(57.93, 85.84)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.009
Subgroup		0.736
Interaction Treatment*Subgroup		0.239

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
Produced: 25APR2024 10:56
Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Functioning [3] Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	10	9	
Responders with Change from Baseline of <= -15 [2][5]	9 (90.0)	2 (22.2)	
Odds Ratio and 95% Confidence Interval and p-value		31.50 (2.350, 422.299)	0.004
Relative Risk and 95% Confidence Interval and p-value		4.05 (1.172, 13.989)	0.027
Risk Difference and 95% Confidence Interval and p-value		0.68 (0.349, 1.000)	<0.001
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	25	14	
Responders with Change from Baseline of <= -15 [2][5]	17 (68.0)	4 (28.6)	
Odds Ratio and 95% Confidence Interval and p-value		5.31 (1.269, 22.244)	0.019
Relative Risk and 95% Confidence Interval and p-value		2.38 (0.996, 5.685)	0.051
Risk Difference and 95% Confidence Interval and p-value		0.39 (0.095, 0.693)	0.010

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Functioning [3]		
Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [6]	35 (100.0) 2 (5.7)	23 (100.0) 3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with Change from Baseline of > -15 [2][5]	26 (74.3) 9 (25.7)	6 (26.1) 17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(57.93, 85.84)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.006
Subgroup		0.073
Interaction Treatment*Subgroup		0.035

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Functioning [3]			
Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	14	10	
Responders with Change from Baseline of <= -15 [2][5]	12 (85.7)	0	
Odds Ratio and 95% Confidence Interval and p-value		105.00 (4.521, 2438.704)	<0.001
Relative Risk and 95% Confidence Interval and p-value		18.33 (1.211, 277.616)	NE
Risk Difference and 95% Confidence Interval and p-value		0.86 (0.674, 1.000)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Change from Baseline of <= -15 [2][5]	14 (66.7)	6 (46.2)	
Odds Ratio and 95% Confidence Interval and p-value		2.33 (0.565, 9.639)	0.245
Relative Risk and 95% Confidence Interval and p-value		1.44 (0.746, 2.796)	0.275
Risk Difference and 95% Confidence Interval and p-value		0.21 (-0.133, 0.543)	0.234

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Functioning [3]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1] Subjects	35 (100.0)	23 (100.0)
with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with	26 (74.3)	6 (26.1)
Change from Baseline of > -15 [2][5]	9 (25.7)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(57.93, 85.84)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.006
Subgroup		0.369
Interaction Treatment*Subgroup		0.791

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Functioning [3]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	14 (70.0)	3 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value Relative Risk and		9.33 (1.911, 45.583)	0.004
95% Confidence Interval and p-value Risk Difference and 95%		3.50 (1.222, 10.022)	0.020
Confidence Interval and p-value		0.50 (0.215, 0.785)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month Subjects			
Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	12 (80.0)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value		6.67 (0.987, 45.036)	0.046
Relative Risk and 95% Confidence Interval and p-value		2.13 (0.842, 5.405)	0.110
Risk Difference and 95% Confidence Interval and p-value		0.43 (0.033, 0.817)	0.034

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
Produced: 25APR2024 10:56
Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Functioning [3]		
Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1] Subjects	35 (100.0)	23 (100.0)
with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with	26 (74.3)	6 (26.1)
Change from Baseline of > -15 [2][5]	9 (25.7)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(57.93, 85.84)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.187
Subgroup		0.369
Interaction Treatment*Subgroup		0.210

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Functioning [3]			
Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	10 (66.7)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value		3.33 (0.557, 19.949)	0.189
Relative Risk and 95% Confidence Interval and p-value		1.78 (0.678, 4.659)	0.242
Risk Difference and 95% Confidence Interval and p-value		0.29 (-0.120, 0.703)	0.165
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	16 (80.0)	3 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		16.00 (3.001, 85.304)	<0.001
Relative Risk and 95% Confidence Interval and p-value		4.00 (1.420, 11.267)	0.009
Risk Difference and 95% Confidence Interval and p-value		0.60 (0.332, 0.868)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fatigue and Mood [3] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	22 (62.9)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	13 (37.1)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(46.34, 76.83)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.347
Subgroup		0.562
Interaction Treatment*Subgroup		0.372

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fatigue and Mood [3] Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	13	10	
Responders with Change from Baseline of <= -15 [2][5]	5 (38.5)	2 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		2.50 (0.370, 16.888)	0.351
Relative Risk and 95% Confidence Interval and p-value		1.92 (0.466, 7.936)	0.366
Risk Difference and 95% Confidence Interval and p-value		0.18 (-0.178, 0.547)	0.318
Gender = Female			
Subjects Included in the Analysis, n	22	13	
Responders with Change from Baseline of <= -15 [2][5]	17 (77.3)	4 (30.8)	
Odds Ratio and 95% Confidence Interval and p-value		7.65 (1.635, 35.798)	0.007
Relative Risk and 95% Confidence Interval and p-value		2.51 (1.077, 5.854)	0.033
Risk Difference and 95% Confidence Interval and p-value		0.47 (0.159, 0.771)	0.003

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fatigue and Mood [3] Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	22 (62.9)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	13 (37.1)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(46.34, 76.83)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.046
Subgroup		0.099
Interaction Treatment*Subgroup		0.165

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
Produced: 25APR2024 10:56
Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fatigue and Mood [3] Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	10	9	
Responders with Change from Baseline of <= -15 [2][5]	6 (60.0)	0	
Odds Ratio and 95% Confidence Interval and p-value		27.44 (1.252, 601.572)	0.006
Relative Risk and 95% Confidence Interval and p-value		11.82 (0.759, 184.130)	NE
Risk Difference and 95% Confidence Interval and p-value		0.60 (0.296, 0.904)	<0.001
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	25	14	
Responders with Change from Baseline of <= -15 [2][5]	16 (64.0)	6 (42.9)	
Odds Ratio and 95% Confidence Interval and p-value		2.37 (0.623, 9.025)	0.207
Relative Risk and 95% Confidence Interval and p-value		1.49 (0.762, 2.926)	0.243
Risk Difference and 95% Confidence Interval and p-value		0.21 (-0.109, 0.532)	0.196

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
Produced: 25APR2024 10:56
Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fatigue and Mood [3] Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	22 (62.9)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	13 (37.1)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(46.34, 76.83)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.041
Subgroup		0.562
Interaction Treatment*Subgroup		0.580

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
Produced: 25APR2024 10:56
Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fatigue and Mood [3] Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	14	10	
Responders with Change from Baseline of <= -15 [2][5]	9 (64.3)	2 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		7.20 (1.081, 47.962)	0.036
Relative Risk and 95% Confidence Interval and p-value		3.21 (0.876, 11.790)	0.078
Risk Difference and 95% Confidence Interval and p-value		0.44 (0.090, 0.796)	0.014
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Change from Baseline of <= -15 [2][5]	13 (61.9)	4 (30.8)	
Odds Ratio and 95% Confidence Interval and p-value		3.66 (0.840, 15.913)	0.082
Relative Risk and 95% Confidence Interval and p-value		2.01 (0.833, 4.859)	0.120
Risk Difference and 95% Confidence Interval and p-value		0.31 (-0.014, 0.637)	0.061

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fatigue and Mood [3]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1] Subjects	35 (100.0)	23 (100.0)
with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with	22 (62.9)	6 (26.1)
Change from Baseline of > -15 [2][5]	13 (37.1)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(46.34, 76.83)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.015
Subgroup		0.931
Interaction Treatment*Subgroup		0.610

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fatigue and Mood [3]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	14 (70.0)	4 (26.7)	
Odds Ratio and 95% Confidence Interval and p-value Relative Risk and		6.42 (1.444, 28.511)	0.012
95% Confidence Interval and p-value Risk Difference and 95%		2.62 (1.081, 6.372)	0.033
Confidence Interval and p-value		0.43 (0.133, 0.734)	0.005
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month Subjects			
Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	8 (53.3)	2 (25.0)	
Odds Ratio and 95% Confidence Interval and p-value		3.43 (0.516, 22.802)	0.202
Relative Risk and 95% Confidence Interval and p-value		2.13 (0.587, 7.752)	0.250
Risk Difference and 95% Confidence Interval and p-value		0.28 (-0.109, 0.675)	0.157

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fatigue and Mood [3]		
Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	22 (62.9)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	13 (37.1)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(46.34, 76.83)	(12.55, 46.47)
Logistic Regression , p-value		
Treatment		0.187
Subgroup		0.369
Interaction Treatment*Subgroup		0.626

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fatigue and Mood [3]			
Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	10 (66.7)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value		3.33 (0.557, 19.949)	0.189
Relative Risk and 95% Confidence Interval and p-value		1.78 (0.678, 4.659)	0.242
Risk Difference and 95% Confidence Interval and p-value		0.29 (-0.120, 0.703)	0.165
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	12 (60.0)	3 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		6.00 (1.274, 28.254)	0.020
Relative Risk and 95% Confidence Interval and p-value		3.00 (1.025, 8.777)	0.045
Risk Difference and 95% Confidence Interval and p-value		0.40 (0.105, 0.695)	0.008

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fears and Shame [3] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.027
Subgroup		0.859
Interaction Treatment*Subgroup		0.733

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fears and Shame [3] Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	13	10	
Responders with Change from Baseline of <= -15 [2][5]	9 (69.2)	2 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		9.00 (1.285, 63.025)	0.022
Relative Risk and 95% Confidence Interval and p-value		3.46 (0.951, 12.594)	0.060
Risk Difference and 95% Confidence Interval and p-value		0.49 (0.140, 0.845)	0.006
Gender = Female			
Subjects Included in the Analysis, n	22	13	
Responders with Change from Baseline of <= -15 [2][5]	14 (63.6)	3 (23.1)	
Odds Ratio and 95% Confidence Interval and p-value		5.83 (1.231, 27.632)	0.022
Relative Risk and 95% Confidence Interval and p-value		2.76 (0.973, 7.814)	0.056
Risk Difference and 95% Confidence Interval and p-value		0.41 (0.101, 0.710)	0.009

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fears and Shame [3] Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.107
Subgroup		0.964
Interaction Treatment*Subgroup		0.760

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fears and Shame [3] Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	10	9	
Responders with Change from Baseline of <= -15 [2][5]	6 (60.0)	2 (22.2)	
Odds Ratio and 95% Confidence Interval and p-value		5.25 (0.698, 39.476)	0.105
Relative Risk and 95% Confidence Interval and p-value		2.70 (0.719, 10.136)	0.141
Risk Difference and 95% Confidence Interval and p-value		0.38 (-0.030, 0.785)	0.069
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	25	14	
Responders with Change from Baseline of <= -15 [2][5]	17 (68.0)	3 (21.4)	
Odds Ratio and 95% Confidence Interval and p-value		7.79 (1.690, 35.924)	0.006
Relative Risk and 95% Confidence Interval and p-value		3.17 (1.123, 8.964)	0.029
Risk Difference and 95% Confidence Interval and p-value		0.47 (0.184, 0.748)	0.001

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fears and Shame [3] Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.040
Subgroup		0.107
Interaction Treatment*Subgroup		0.258

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fears and Shame [3] Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	14	10	
Responders with Change from Baseline of <= -15 [2][5]	8 (57.1)	0	
Odds Ratio and 95% Confidence Interval and p-value		27.46 (1.347, 560.053)	0.004
Relative Risk and 95% Confidence Interval and p-value		12.47 (0.802, 193.845)	NE
Risk Difference and 95% Confidence Interval and p-value		0.57 (0.312, 0.831)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Change from Baseline of <= -15 [2][5]	15 (71.4)	5 (38.5)	
Odds Ratio and 95% Confidence Interval and p-value		4.00 (0.925, 17.302)	0.061
Relative Risk and 95% Confidence Interval and p-value		1.86 (0.887, 3.888)	0.101
Risk Difference and 95% Confidence Interval and p-value		0.33 (0.002, 0.657)	0.049

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fears and Shame [3]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1] Subjects	35 (100.0)	23 (100.0)
with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with	23 (65.7)	5 (21.7)
Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.003
Subgroup		0.196
Interaction Treatment*Subgroup		0.157

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fears and Shame [3]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	14 (70.0)	2 (13.3)	
Odds Ratio and 95% Confidence Interval and p-value Relative Risk and		15.17 (2.585, 88.990)	0.001
95% Confidence Interval and p-value Risk Difference and 95%		5.25 (1.400, 19.687)	0.014
Confidence Interval and p-value		0.57 (0.302, 0.831)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month Subjects			
Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	9 (60.0)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value		2.50 (0.428, 14.607)	0.314
Relative Risk and 95% Confidence Interval and p-value		1.60 (0.597, 4.286)	0.350
Risk Difference and 95% Confidence Interval and p-value		0.23 (-0.192, 0.642)	0.290

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fears and Shame [3]		
Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.309
Subgroup		0.196
Interaction Treatment*Subgroup		0.157

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fears and Shame [3]			
Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	9 (60.0)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value		2.50 (0.428, 14.607)	0.314
Relative Risk and 95% Confidence Interval and p-value		1.60 (0.597, 4.286)	0.350
Risk Difference and 95% Confidence Interval and p-value		0.23 (-0.192, 0.642)	0.290
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	14 (70.0)	2 (13.3)	
Odds Ratio and 95% Confidence Interval and p-value		15.17 (2.585, 88.990)	0.001
Relative Risk and 95% Confidence Interval and p-value		5.25 (1.400, 19.687)	0.014
Risk Difference and 95% Confidence Interval and p-value		0.57 (0.302, 0.831)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Nutrition [3] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	14 (40.0)	2 (8.7)
Non-responders with Change from Baseline of > -15 [2][5]	21 (60.0)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(25.55, 56.43)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.049
Subgroup		0.846
Interaction Treatment*Subgroup		0.703

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Nutrition [3] Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	13	10	
Responders with Change from Baseline of <= -15 [2][5]	7 (53.8)	1 (10.0)	
Odds Ratio and 95% Confidence Interval and p-value		10.50 (1.015, 108.577)	0.032
Relative Risk and 95% Confidence Interval and p-value		5.38 (0.784, 36.960)	0.087
Risk Difference and 95% Confidence Interval and p-value		0.44 (0.110, 0.767)	0.009
Gender = Female			
Subjects Included in the Analysis, n	22	13	
Responders with Change from Baseline of <= -15 [2][5]	7 (31.8)	1 (7.7)	
Odds Ratio and 95% Confidence Interval and p-value		5.60 (0.603, 52.004)	0.106
Relative Risk and 95% Confidence Interval and p-value		4.14 (0.571, 29.957)	0.160
Risk Difference and 95% Confidence Interval and p-value		0.24 (-0.001, 0.484)	0.051

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Nutrition [3] Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	14 (40.0)	2 (8.7)
Non-responders with Change from Baseline of > -15 [2][5]	21 (60.0)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(25.55, 56.43)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.120
Subgroup		0.429
Interaction Treatment*Subgroup		0.464

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Nutrition [3] Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	10	9	
Responders with Change from Baseline of <= -15 [2][5]	4 (40.0)	0	
Odds Ratio and 95% Confidence Interval and p-value		13.15 (0.600, 288.328)	0.038
Relative Risk and 95% Confidence Interval and p-value		8.18 (0.501, 133.665)	NE
Risk Difference and 95% Confidence Interval and p-value		0.40 (0.096, 0.704)	0.010
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	25	14	
Responders with Change from Baseline of <= -15 [2][5]	10 (40.0)	2 (14.3)	
Odds Ratio and 95% Confidence Interval and p-value		4.00 (0.733, 21.838)	0.099
Relative Risk and 95% Confidence Interval and p-value		2.80 (0.712, 11.019)	0.141
Risk Difference and 95% Confidence Interval and p-value		0.26 (-0.008, 0.523)	0.058

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Nutrition [3]		
Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	14 (40.0)	2 (8.7)
Non-responders with Change from Baseline of > -15 [2][5]	21 (60.0)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(25.55, 56.43)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.059
Subgroup		0.367
Interaction Treatment*Subgroup		0.233

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Nutrition [3]			
Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	14	10	
Responders with Change from Baseline of <= -15 [2][5]	7 (50.0)	0	
Odds Ratio and 95% Confidence Interval and p-value		21.00 (1.033, 426.960)	0.009
Relative Risk and 95% Confidence Interval and p-value		11.00 (0.700, 172.924)	NE
Risk Difference and 95% Confidence Interval and p-value		0.50 (0.238, 0.762)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Change from Baseline of <= -15 [2][5]	7 (33.3)	2 (15.4)	
Odds Ratio and 95% Confidence Interval and p-value		2.75 (0.474, 15.964)	0.256
Relative Risk and 95% Confidence Interval and p-value		2.17 (0.528, 8.884)	0.283
Risk Difference and 95% Confidence Interval and p-value		0.18 (-0.102, 0.461)	0.211

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Nutrition [3]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1] Subjects	35 (100.0)	23 (100.0)
with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with	14 (40.0)	2 (8.7)
Change from Baseline of > -15 [2][5]	21 (60.0)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(25.55, 56.43)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.019
Subgroup		0.641
Interaction Treatment*Subgroup		0.304

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Nutrition [3]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	10 (50.0)	1 (6.7)	
Odds Ratio and 95% Confidence Interval and p-value		14.00 (1.536, 127.621)	0.007
Relative Risk and 95% Confidence Interval and p-value		7.50 (1.074, 52.377)	0.042
Risk Difference and 95% Confidence Interval and p-value		0.43 (0.180, 0.686)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	4 (26.7)	1 (12.5)	
Odds Ratio and 95% Confidence Interval and p-value		2.55 (0.234, 27.709)	0.443
Relative Risk and 95% Confidence Interval and p-value		2.13 (0.284, 16.023)	0.461
Risk Difference and 95% Confidence Interval and p-value		0.14 (-0.179, 0.462)	0.386

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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Nutrition [3]		
Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1] Subjects	35 (100.0)	23 (100.0)
with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with	14 (40.0)	2 (8.7)
Change from Baseline of > -15 [2][5]	21 (60.0)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(25.55, 56.43)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.127
Subgroup		0.641
Interaction Treatment*Subgroup		0.899

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Nutrition [3]			
Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	7 (46.7)	1 (12.5)	
Odds Ratio and 95% Confidence Interval and p-value		6.13 (0.597, 62.821)	0.109
Relative Risk and 95% Confidence Interval and p-value		3.73 (0.552, 25.250)	0.177
Risk Difference and 95% Confidence Interval and p-value		0.34 (0.001, 0.683)	0.050
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	7 (35.0)	1 (6.7)	
Odds Ratio and 95% Confidence Interval and p-value		7.54 (0.813, 69.906)	0.052
Relative Risk and 95% Confidence Interval and p-value		5.25 (0.721, 38.233)	0.102
Risk Difference and 95% Confidence Interval and p-value		0.28 (0.039, 0.528)	0.023

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.057
Subgroup		0.859
Interaction Treatment*Subgroup		0.931

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	13	10	
Responders with Change from Baseline of <= -15 [2][5]	8 (61.5)	2 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		6.40 (0.947, 43.234)	0.051
Relative Risk and 95% Confidence Interval and p-value		3.08 (0.829, 11.426)	0.093
Risk Difference and 95% Confidence Interval and p-value		0.42 (0.053, 0.778)	0.025
Gender = Female			
Subjects Included in the Analysis, n	22	13	
Responders with Change from Baseline of <= -15 [2][5]	15 (68.2)	3 (23.1)	
Odds Ratio and 95% Confidence Interval and p-value		7.14 (1.484, 34.384)	0.011
Relative Risk and 95% Confidence Interval and p-value		2.95 (1.052, 8.298)	0.040
Risk Difference and 95% Confidence Interval and p-value		0.45 (0.150, 0.752)	0.003

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -6 [2][5]	29 (82.9)	11 (47.8)
Non-responders with Change from Baseline of > -6 [2][5]	6 (17.1)	12 (52.2)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(67.32, 91.90)	(29.24, 67.04)
Logistic Regression , p-value		
Treatment		0.187
Subgroup		0.855
Interaction Treatment*Subgroup		0.520

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	13	10	
Responders with Change from Baseline of <= -6 [2][5]	10 (76.9)	5 (50.0)	
Odds Ratio and 95% Confidence Interval and p-value		3.33 (0.557, 19.949)	0.189
Relative Risk and 95% Confidence Interval and p-value		1.54 (0.774, 3.060)	0.219
Risk Difference and 95% Confidence Interval and p-value		0.27 (-0.116, 0.655)	0.171
Gender = Female			
Subjects Included in the Analysis, n	22	13	
Responders with Change from Baseline of <= -6 [2][5]	19 (86.4)	6 (46.2)	
Odds Ratio and 95% Confidence Interval and p-value		7.39 (1.441, 37.883)	0.012
Relative Risk and 95% Confidence Interval and p-value		1.87 (1.017, 3.444)	0.044
Risk Difference and 95% Confidence Interval and p-value		0.40 (0.096, 0.709)	0.010

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.045
Subgroup		0.338
Interaction Treatment*Subgroup		0.572

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	10	9	
Responders with Change from Baseline of <= -15 [2][5]	6 (60.0)	1 (11.1)	
Odds Ratio and 95% Confidence Interval and p-value		12.00 (1.053, 136.794)	0.032
Relative Risk and 95% Confidence Interval and p-value		5.40 (0.795, 36.683)	0.084
Risk Difference and 95% Confidence Interval and p-value		0.49 (0.122, 0.855)	0.009
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	25	14	
Responders with Change from Baseline of <= -15 [2][5]	17 (68.0)	4 (28.6)	
Odds Ratio and 95% Confidence Interval and p-value		5.31 (1.269, 22.244)	0.019
Relative Risk and 95% Confidence Interval and p-value		2.38 (0.996, 5.685)	0.051
Risk Difference and 95% Confidence Interval and p-value		0.39 (0.095, 0.693)	0.010

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: Region		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -6 [2][5]	29 (82.9)	11 (47.8)
Non-responders with Change from Baseline of > -6 [2][5]	6 (17.1)	12 (52.2)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(67.32, 91.90)	(29.24, 67.04)
Logistic Regression , p-value		
Treatment		0.023
Subgroup		0.270
Interaction Treatment*Subgroup		0.222

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	10	9	
Responders with Change from Baseline of <= -6 [2][5]	9 (90.0)	3 (33.3)	
Odds Ratio and 95% Confidence Interval and p-value		18.00 (1.496, 216.620)	0.013
Relative Risk and 95% Confidence Interval and p-value		2.70 (1.048, 6.959)	0.040
Risk Difference and 95% Confidence Interval and p-value		0.57 (0.207, 0.926)	0.002
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	25	14	
Responders with Change from Baseline of <= -6 [2][5]	20 (80.0)	8 (57.1)	
Odds Ratio and 95% Confidence Interval and p-value		3.00 (0.709, 12.694)	0.133
Relative Risk and 95% Confidence Interval and p-value		1.40 (0.854, 2.295)	0.182
Risk Difference and 95% Confidence Interval and p-value		0.23 (-0.074, 0.532)	0.139

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.020
Subgroup		0.253
Interaction Treatment*Subgroup		0.365

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	14	10	
Responders with Change from Baseline of <= -15 [2][5]	9 (64.3)	1 (10.0)	
Odds Ratio and 95% Confidence Interval and p-value		16.20 (1.565, 167.738)	0.009
Relative Risk and 95% Confidence Interval and p-value		6.43 (0.962, 42.978)	0.055
Risk Difference and 95% Confidence Interval and p-value		0.54 (0.230, 0.855)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Change from Baseline of <= -15 [2][5]	14 (66.7)	4 (30.8)	
Odds Ratio and 95% Confidence Interval and p-value		4.50 (1.017, 19.902)	0.045
Relative Risk and 95% Confidence Interval and p-value		2.17 (0.908, 5.170)	0.081
Risk Difference and 95% Confidence Interval and p-value		0.36 (0.037, 0.681)	0.029

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -6 [2][5]	29 (82.9)	11 (47.8)
Non-responders with Change from Baseline of > -6 [2][5]	6 (17.1)	12 (52.2)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(67.32, 91.90)	(29.24, 67.04)
Logistic Regression , p-value		
Treatment		0.002
Subgroup		0.027
Interaction Treatment*Subgroup		0.018

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	14	10	
Responders with Change from Baseline of <= -6 [2][5]	13 (92.9)	2 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		52.00 (4.032, 670.597)	<0.001
Relative Risk and 95% Confidence Interval and p-value		4.64 (1.333, 16.174)	0.016
Risk Difference and 95% Confidence Interval and p-value		0.73 (0.446, 1.000)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders with Change from Baseline of <= -6 [2][5]	16 (76.2)	9 (69.2)	
Odds Ratio and 95% Confidence Interval and p-value		1.42 (0.303, 6.686)	0.660
Relative Risk and 95% Confidence Interval and p-value		1.10 (0.713, 1.699)	0.665
Risk Difference and 95% Confidence Interval and p-value		0.07 (-0.240, 0.380)	0.660

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [6]	35 (100.0) 2 (5.7)	23 (100.0) 3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with Change from Baseline of > -15 [2][5]	23 (65.7) 12 (34.3)	5 (21.7) 18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.003
Subgroup		0.196
Interaction Treatment*Subgroup		0.157

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	14 (70.0)	2 (13.3)	
Odds Ratio and 95% Confidence Interval and p-value Relative Risk and		15.17 (2.585, 88.990)	0.001
95% Confidence Interval and p-value Risk Difference and 95%		5.25 (1.400, 19.687)	0.014
Confidence Interval and p-value		0.57 (0.302, 0.831)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month Subjects			
Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	9 (60.0)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value		2.50 (0.428, 14.607)	0.314
Relative Risk and 95% Confidence Interval and p-value		1.60 (0.597, 4.286)	0.350
Risk Difference and 95% Confidence Interval and p-value		0.23 (-0.192, 0.642)	0.290

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [1] Subjects	35 (100.0)	23 (100.0)
with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -6 [2][5] Non-responders with	29 (82.9)	11 (47.8)
Change from Baseline of > -6 [2][5]	6 (17.1)	12 (52.2)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(67.32, 91.90)	(29.24, 67.04)
Logistic Regression , p-value		
Treatment		0.009
Subgroup		0.309
Interaction Treatment*Subgroup		0.320

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -6 [2][5]	17 (85.0)	6 (40.0)	
Odds Ratio and 95% Confidence Interval and p-value Relative Risk and		8.50 (1.709, 42.279)	0.006
95% Confidence Interval and p-value Risk Difference and 95%		2.13 (1.113, 4.057)	0.022
Confidence Interval and p-value		0.45 (0.157, 0.743)	0.003
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month Subjects			
Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -6 [2][5]	12 (80.0)	5 (62.5)	
Odds Ratio and 95% Confidence Interval and p-value		2.40 (0.355, 16.213)	0.373
Relative Risk and 95% Confidence Interval and p-value		1.28 (0.707, 2.317)	0.415
Risk Difference and 95% Confidence Interval and p-value		0.18 (-0.217, 0.567)	0.381

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression , p-value		
Treatment		0.309
Subgroup		0.196
Interaction Treatment*Subgroup		0.157

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -15 [2][5]	9 (60.0)	3 (37.5)	
Odds Ratio and 95% Confidence Interval and p-value		2.50 (0.428, 14.607)	0.314
Relative Risk and 95% Confidence Interval and p-value		1.60 (0.597, 4.286)	0.350
Risk Difference and 95% Confidence Interval and p-value		0.23 (-0.192, 0.642)	0.290
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -15 [2][5]	14 (70.0)	2 (13.3)	
Odds Ratio and 95% Confidence Interval and p-value		15.17 (2.585, 88.990)	0.001
Relative Risk and 95% Confidence Interval and p-value		5.25 (1.400, 19.687)	0.014
Risk Difference and 95% Confidence Interval and p-value		0.57 (0.302, 0.831)	<0.001

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -6 [2][5]	29 (82.9)	11 (47.8)
Non-responders with Change from Baseline of > -6 [2][5]	6 (17.1)	12 (52.2)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(67.32, 91.90)	(29.24, 67.04)
Logistic Regression , p-value		
Treatment		0.654
Subgroup		0.015
Interaction Treatment*Subgroup		0.029

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	15	8	
Responders with Change from Baseline of <= -6 [2][5]	12 (80.0)	7 (87.5)	
Odds Ratio and 95% Confidence Interval and p-value		0.57 (0.049, 6.606)	0.658
Relative Risk and 95% Confidence Interval and p-value		0.91 (0.635, 1.316)	0.630
Risk Difference and 95% Confidence Interval and p-value		-0.07 (-0.381, 0.231)	0.631
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	20	15	
Responders with Change from Baseline of <= -6 [2][5]	17 (85.0)	4 (26.7)	
Odds Ratio and 95% Confidence Interval and p-value		15.58 (2.910, 83.455)	<0.001
Relative Risk and 95% Confidence Interval and p-value		3.19 (1.350, 7.526)	0.008
Risk Difference and 95% Confidence Interval and p-value		0.58 (0.310, 0.856)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si.sas
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Source: 16.2.5.7; UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] AE-QoL is only answered from patients of age >= 18 years. The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [2]	39 (100.0)	23 (92.0)
Subjects with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	31 (79.5)	2 (8.7)
Non-Responders (None/Poor/Fair/Good) [3]	8 (20.5)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(64.47, 89.22)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.004
Subgroup		0.846
Interaction Treatment*Subgroup		0.889

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1] Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	15	10	
Responders (Excellent) [3]	12 (80.0)	1 (10.0)	
Odds Ratio and 95% Confidence Interval and p-value		36.00 (3.193, 405.897)	<0.001
Relative Risk and 95% Confidence Interval and p-value		8.00 (1.225, 52.246)	0.030
Risk Difference and 95% Confidence Interval and p-value		0.70 (0.425, 0.975)	<0.001
Gender = Female			
Subjects Included in the Analysis, n	24	13	
Responders (Excellent) [3]	19 (79.2)	1 (7.7)	
Odds Ratio and 95% Confidence Interval and p-value		45.60 (4.733, 439.357)	<0.001
Relative Risk and 95% Confidence Interval and p-value		10.29 (1.548, 68.413)	0.016
Risk Difference and 95% Confidence Interval and p-value		0.71 (0.497, 0.932)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1] Subgroup: Region		
Subjects Included in the Analysis, n (%) [2] Subjects	39 (100.0)	23 (92.0)
with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	31 (79.5)	2 (8.7)
Non-Responders (None/Poor/Fair/Good) [3]	8 (20.5)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(64.47, 89.22)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.036
Subgroup		0.429
Interaction Treatment*Subgroup		0.936

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1] Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	11	9	
Responders (Excellent) [3]	7 (63.6)	0	
Odds Ratio and 95% Confidence Interval and p-value		31.67 (1.463, 685.302)	0.004
Relative Risk and 95% Confidence Interval and p-value		12.50 (0.810, 192.996)	NE
Risk Difference and 95% Confidence Interval and p-value		0.64 (0.352, 0.921)	<0.001
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	28	14	
Responders (Excellent) [3]	24 (85.7)	2 (14.3)	
Odds Ratio and 95% Confidence Interval and p-value		36.00 (5.755, 225.179)	<0.001
Relative Risk and 95% Confidence Interval and p-value		6.00 (1.648, 21.840)	0.007
Risk Difference and 95% Confidence Interval and p-value		0.71 (0.490, 0.939)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1]		
Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [2] Subjects	39 (100.0)	23 (92.0)
with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	31 (79.5)	2 (8.7)
Non-Responders (None/Poor/Fair/Good) [3]	8 (20.5)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(64.47, 89.22)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.004
Subgroup		0.846
Interaction Treatment*Subgroup		0.774

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1]			
Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	18	10	
Responders (Excellent) [3]	14 (77.8)	1 (10.0)	
Odds Ratio and 95% Confidence Interval and p-value		31.50 (3.017, 328.930)	<0.001
Relative Risk and 95% Confidence Interval and p-value		7.78 (1.192, 50.754)	0.032
Risk Difference and 95% Confidence Interval and p-value		0.68 (0.410, 0.945)	<0.001
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	21	13	
Responders (Excellent) [3]	17 (81.0)	1 (7.7)	
Odds Ratio and 95% Confidence Interval and p-value		51.00 (5.049, 515.110)	<0.001
Relative Risk and 95% Confidence Interval and p-value		10.52 (1.583, 69.973)	0.015
Risk Difference and 95% Confidence Interval and p-value		0.73 (0.511, 0.954)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [2] Subjects	39 (100.0)	23 (92.0)
with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	31 (79.5)	2 (8.7)
Non-Responders (None/Poor/Fair/Good) [3]	8 (20.5)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(64.47, 89.22)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		<0.001
Subgroup		0.500
Interaction Treatment*Subgroup		0.991

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	24	15	
Responders (Excellent) [3]	21 (87.5)	2 (13.3)	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	45.50 (6.682, 309.807)	<0.001
and 95% Confidence Interval and p-value	Risk Difference and 95%	6.56 (1.790, 24.057)	0.005
Confidence Interval and p-value		0.74 (0.525, 0.959)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders (Excellent) [3]	10 (66.7)	0	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	32.45 (1.563, 673.745)	0.003
and 95% Confidence Interval and p-value	Risk Difference and 95%	11.81 (0.781, 178.773)	NE
Confidence Interval and p-value		0.67 (0.428, 0.905)	<0.001

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1]		
Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [2] Subjects	39 (100.0)	23 (92.0)
with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	31 (79.5)	2 (8.7)
Non-Responders (None/Poor/Fair/Good) [3]	8 (20.5)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(64.47, 89.22)	(2.42, 26.80)
Logistic Regression , p-value		
Treatment		0.022
Subgroup		0.500
Interaction Treatment*Subgroup		0.839

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.4.hS: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1]			
Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	18	8	
Responders (Excellent) [3]	13 (72.2)	0	
Odds Ratio and 95% Confidence Interval and p-value		41.73 (2.037, 854.685)	<0.001
Relative Risk and 95% Confidence Interval and p-value		12.79 (0.852, 192.017)	NE
Risk Difference and 95% Confidence Interval and p-value		0.72 (0.515, 0.929)	<0.001
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	21	15	
Responders (Excellent) [3]	18 (85.7)	2 (13.3)	
Odds Ratio and 95% Confidence Interval and p-value		39.00 (5.683, 267.664)	<0.001
Relative Risk and 95% Confidence Interval and p-value		6.43 (1.749, 23.635)	0.005
Risk Difference and 95% Confidence Interval and p-value		0.72 (0.496, 0.952)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1] Subgroup: Gender		
Subjects Included in the Analysis, n (%) [2]	38 (97.4)	24 (96.0)
Subjects with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	25 (65.8)	3 (12.5)
Non-Responders (None/Poor/Fair/Good) [3]	13 (34.2)	21 (87.5)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.89, 78.79)	(4.34, 31.00)
Logistic Regression , p-value		
Treatment		0.020
Subgroup		0.755
Interaction Treatment*Subgroup		0.839

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1] Subgroup: Gender			
Gender = Male			
Subjects Included in the Analysis, n	14	10	
Responders (Excellent) [3]	9 (64.3)	1 (10.0)	
Odds Ratio and 95% Confidence Interval and p-value		16.20 (1.565, 167.738)	0.009
Relative Risk and 95% Confidence Interval and p-value		6.43 (0.962, 42.978)	0.055
Risk Difference and 95% Confidence Interval and p-value		0.54 (0.230, 0.855)	<0.001
Gender = Female			
Subjects Included in the Analysis, n	24	14	
Responders (Excellent) [3]	16 (66.7)	2 (14.3)	
Odds Ratio and 95% Confidence Interval and p-value		12.00 (2.147, 67.067)	0.002
Relative Risk and 95% Confidence Interval and p-value		4.67 (1.254, 17.363)	0.022
Risk Difference and 95% Confidence Interval and p-value		0.52 (0.261, 0.787)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1] Subgroup: Region		
Subjects Included in the Analysis, n (%) [2] Subjects	38 (97.4)	24 (96.0)
with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	25 (65.8)	3 (12.5)
Non-Responders (None/Poor/Fair/Good) [3]	13 (34.2)	21 (87.5)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.89, 78.79)	(4.34, 31.00)
Logistic Regression , p-value		
Treatment		0.064
Subgroup		0.874
Interaction Treatment*Subgroup		0.751

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1] Subgroup: Region			
Region = EU (Germany, Hungary, Netherlands)			
Subjects Included in the Analysis, n	11	9	
Responders (Excellent) [3]	6 (54.5)	1 (11.1)	
Odds Ratio and 95% Confidence Interval and p-value		9.60 (0.876, 105.166)	0.048
Relative Risk and 95% Confidence Interval and p-value		4.91 (0.716, 33.653)	0.105
Risk Difference and 95% Confidence Interval and p-value		0.43 (0.076, 0.793)	0.018
Region = RoW (Canada, Israel, Japan, United States) Subjects Included in the Analysis, n	27	15	
Responders (Excellent) [3]	19 (70.4)	2 (13.3)	
Odds Ratio and 95% Confidence Interval and p-value		15.44 (2.813, 84.718)	<0.001
Relative Risk and 95% Confidence Interval and p-value		5.28 (1.419, 19.623)	0.013
Risk Difference and 95% Confidence Interval and p-value		0.57 (0.327, 0.814)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1]		
Subgroup: Age at First Diagnosis		
Subjects Included in the Analysis, n (%) [2] Subjects with imputed values, n (%) [2]	38 (97.4) 0	24 (96.0) 0
Responders (Excellent) [3]	25 (65.8)	3 (12.5)
Non-Responders (None/Poor/Fair/Good) [3]	13 (34.2)	21 (87.5)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.89, 78.79)	(4.34, 31.00)
Logistic Regression , p-value		
Treatment		0.044
Subgroup		0.544
Interaction Treatment*Subgroup		0.260

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1]			
Subgroup: Age at First Diagnosis			
Age at First Diagnosis = <=17 years			
Subjects Included in the Analysis, n	18	12	
Responders (Excellent) [3]	10 (55.6)	2 (16.7)	
Odds Ratio and 95% Confidence Interval and p-value		6.25 (1.054, 37.070)	0.036
Relative Risk and 95% Confidence Interval and p-value		3.33 (0.881, 12.615)	0.076
Risk Difference and 95% Confidence Interval and p-value		0.39 (0.077, 0.701)	0.014
Age at First Diagnosis = >17 years			
Subjects Included in the Analysis, n	20	12	
Responders (Excellent) [3]	15 (75.0)	1 (8.3)	
Odds Ratio and 95% Confidence Interval and p-value		33.00 (3.363, 323.811)	<0.001
Relative Risk and 95% Confidence Interval and p-value		9.00 (1.355, 59.783)	0.023
Risk Difference and 95% Confidence Interval and p-value		0.67 (0.421, 0.913)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1]		
Subgroup: Baseline Attack rate observed during Run-in Period		
Subjects Included in the Analysis, n (%) [2] Subjects with imputed values, n (%) [2]	38 (97.4) 0	24 (96.0) 0
Responders (Excellent) [3]	25 (65.8)	3 (12.5)
Non-Responders (None/Poor/Fair/Good) [3]	13 (34.2)	21 (87.5)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.89, 78.79)	(4.34, 31.00)
Logistic Regression , p-value		
Treatment		0.003
Subgroup		0.372
Interaction Treatment*Subgroup		0.732

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1]			
Subgroup: Baseline Attack rate observed during Run-in Period			
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month			
Subjects Included in the Analysis, n	23	16	
Responders (Excellent) [3]	17 (73.9)	3 (18.8)	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	12.28 (2.573, 58.589)	<0.001
and 95% Confidence Interval and p-value	Risk Difference and 95%	3.94 (1.382, 11.248)	0.010
Confidence Interval and p-value		0.55 (0.289, 0.814)	<0.001
Baseline Attack rate observed during Run-in Period = >= 3 attacks/month			
Subjects Included in the Analysis, n	15	8	
Responders (Excellent) [3]	8 (53.3)	0	
Odds Ratio and 95% Confidence Interval and p-value	Relative Risk	19.27 (0.944, 393.401)	0.012
and 95% Confidence Interval and p-value	Risk Difference and 95%	9.56 (0.622, 147.025)	NE
Confidence Interval and p-value		0.53 (0.281, 0.786)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1]		
Subgroup: History of Laryngeal Attack		
Subjects Included in the Analysis, n (%) [2]	38 (97.4)	24 (96.0)
Subjects with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	25 (65.8)	3 (12.5)
Non-Responders (None/Poor/Fair/Good) [3]	13 (34.2)	21 (87.5)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.89, 78.79)	(4.34, 31.00)
Logistic Regression , p-value		
Treatment		0.069
Subgroup		0.372
Interaction Treatment*Subgroup		0.783

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
Produced: 21MAR2024 07:32
Source: 16.2.5.10; UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.5.hS: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1]			
Subgroup: History of Laryngeal Attack			
History of Laryngeal Attack = No			
Subjects Included in the Analysis, n	17	8	
Responders (Excellent) [3]	9 (52.9)	0	
Odds Ratio and 95% Confidence Interval and p-value		19.00 (0.947, 381.063)	0.012
Relative Risk and 95% Confidence Interval and p-value		9.50 (0.620, 145.506)	NE
Risk Difference and 95% Confidence Interval and p-value		0.53 (0.292, 0.767)	<0.001
History of Laryngeal Attack = Yes			
Subjects Included in the Analysis, n	21	16	
Responders (Excellent) [3]	16 (76.2)	3 (18.8)	
Odds Ratio and 95% Confidence Interval and p-value		13.87 (2.778, 69.206)	<0.001
Relative Risk and 95% Confidence Interval and p-value		4.06 (1.425, 11.585)	0.009
Risk Difference and 95% Confidence Interval and p-value		0.57 (0.310, 0.839)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05bs.sas
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Source: 16.2.5.10; UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period."
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

4.12 Verträglichkeit

GAP Table 14.3.1.1.5S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) - Subgroup Analysis (Safety Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Gender		
Number (%) of Subjects with at least 1 TEAE	25 (64.1)	15 (60.0)
Logistic Regression, p-value		
Treatment		0.239
Subgroup		0.040
Interaction Treatment*Subgroup		0.165
Gender = Male, n (%) [1]		4 (16.0)
Odds Ratio and 95% Confidence Interval	9 (23.1)	0.389 (0.082, 1.840)
p-value		0.237
Relative Risk and 95% Confidence Interval		0.656 (0.331, 1.301)
p-value		0.228
Risk Difference and 95% Confidence Interval		-0.229 (-0.590, 0.132)
p-value		0.213
Gender = Female, n (%) [1]		11 (44.0)
Odds Ratio and 95% Confidence Interval		1.513 (0.410, 5.586)
p-value	16 (41.0)	0.539
Relative Risk and 95% Confidence Interval		1.304 (0.553, 3.073)
p-value		0.544
Risk Difference and 95% Confidence Interval		0.095 (-0.198, 0.388)
p-value		0.526

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap13_2.sas
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Source: 16.2.7.2, UNBLINDED

n = number of subjects with at least 1 event.
[1] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).

GAP Table 14.3.1.1.5S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) – Subgroup Analysis (Safety Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Region		
Number (%) of Subjects with at least 1 TEAE	25 (64.1)	15 (60.0)
Logistic Regression, p-value		
Treatment		0.442
Subgroup		0.611
Interaction Treatment*Subgroup		0.529
Region = EU (Germany, Hungary, Netherlands), n (%) [1]		6 (24.0)
Odds Ratio and 95% Confidence Interval	9 (23.1)	0.533 (0.100, 2.839)
p-value		0.469
Relative Risk and 95% Confidence Interval		0.677 (0.239, 1.917)
p-value		0.463
Risk Difference and 95% Confidence Interval		-0.147 (-0.534, 0.240)
p-value		0.457
Region = RoW (Canada, Israel, Japan, United States), n (%) [1]		9 (36.0)
Odds Ratio and 95% Confidence Interval		0.984 (0.299, 3.243)
p-value	16 (41.0)	0.980
Relative Risk and 95% Confidence Interval		0.992 (0.527, 1.867)
p-value		0.979
Risk Difference and 95% Confidence Interval		-0.004 (-0.301, 0.293)
p-value		0.979

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap13_2.sas
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Source: 16.2.7.2, UNBLINDED

n = number of subjects with at least 1 event.
[1] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).

GAP Table 14.3.1.1.5S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) – Subgroup Analysis (Safety Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age at First Diagnosis		
Number (%) of Subjects with at least 1 TEAE	25 (64.1)	15 (60.0)
Logistic Regression, p-value		
Treatment		0.364
Subgroup		0.331
Interaction Treatment*Subgroup		0.341
Age at First Diagnosis = <=17 years, n (%) [1]		6 (24.0)
Odds Ratio and 95% Confidence Interval	12 (30.8)	0.643 (0.160, 2.585)
p-value		0.539
Relative Risk and 95% Confidence Interval		0.796 (0.393, 1.611)
p-value		0.526
Risk Difference and 95% Confidence Interval		-0.110 (-0.454, 0.234)
p-value		0.531
Age at First Diagnosis = >17 years, n (%) [1]		9 (36.0)
Odds Ratio and 95% Confidence Interval		1.038 (0.273, 3.957)
p-value	13 (33.3)	0.957
Relative Risk and 95% Confidence Interval		1.023 (0.461, 2.271)
p-value		0.956
Risk Difference and 95% Confidence Interval		0.009 (-0.313, 0.331)
p-value		0.956

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap13_2.sas
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n = number of subjects with at least 1 event.
[1] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).

GAP Table 14.3.1.1.5S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) - Subgroup Analysis (Safety Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Baseline Attack rate observed during Run-in Period		
Number (%) of Subjects with at least 1 TEAE	25 (64.1)	15 (60.0)
Logistic Regression, p-value		
Treatment		0.812
Subgroup		0.861
Interaction Treatment*Subgroup		0.980
Baseline Attack rate observed during Run-in Period = 1 to <3 attacks/month, n (%) [1]	15 (38.5)	10 (40.0)
Odds Ratio and 95% Confidence Interval		0.917 (0.273, 3.081)
p-value		0.889
Relative Risk and 95% Confidence Interval		0.952 (0.480, 1.887)
p-value		0.888
Risk Difference and 95% Confidence Interval		-0.021 (-0.319, 0.277)
p-value		0.888
Baseline Attack rate observed during Run-in Period = >=3 attacks/month, n (%) [1]	10 (25.6)	5 (20.0)
Odds Ratio and 95% Confidence Interval		0.700 (0.145, 3.370)
p-value		0.662
Relative Risk and 95% Confidence Interval		0.824 (0.355, 1.909)
p-value		0.651
Risk Difference and 95% Confidence Interval		-0.088 (-0.477, 0.300)
p-value		0.656

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap13_2.sas
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Source: 16.2.7.2, UNBLINDED

n = number of subjects with at least 1 event.
[1] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).

GAP Table 14.3.1.1.5S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) – Subgroup Analysis (Safety Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: History of Laryngeal Attack		
Number (%) of Subjects with at least 1 TEAE	25 (64.1)	15 (60.0)
Logistic Regression, p-value		
Treatment		0.598
Subgroup		0.486
Interaction Treatment*Subgroup		0.740
History of Laryngeal Attack = No, n (%) [1]		4 (16.0)
Odds Ratio and 95% Confidence Interval	11 (28.2)	0.655 (0.134, 3.186)
p-value		0.605
Relative Risk and 95% Confidence Interval		0.810 (0.379, 1.730)
p-value		0.586
Risk Difference and 95% Confidence Interval		-0.106 (-0.497, 0.286)
p-value		0.597
History of Laryngeal Attack = Yes, n (%) [1]		11 (44.0)
Odds Ratio and 95% Confidence Interval		0.884 (0.257, 3.046)
p-value	14 (35.9)	0.847
Relative Risk and 95% Confidence Interval		0.929 (0.446, 1.935)
p-value		0.845
Risk Difference and 95% Confidence Interval		-0.030 (-0.328, 0.269)
p-value		0.845

n = number of subjects with at least 1 event.
[1] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).

GAP Table 14.3.1.1.4S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) and at least 10% of Patients in Any Arm at System Organ Class or Preferred Term Level – Subgroup Analysis (Safety Analysis Set)

MedDRA System Organ Class MedDRA Preferred Term [1]	CSL312 200mg (N=39)	Placebo (N=25)
General disorders and administration site conditions, n (%) [2][3]	4 (10.3)	9 (36.0)
Logistic Regression, p-value		
Treatment		0.739
Subgroup		0.028
Interaction Treatment*Subgroup		0.049

n = number of subjects with at least 1 event. NE = Not Estimable.
[1] Adverse events are coded using MedDRA version 25.0.
[2] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).
[3] Only System Organ Classes and preferred Terms are shown with at least 10% of all patients in at least one treatment arm.

GAP Table 14.3.1.1.4S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) and at least 10% of Patients in Any Arm at System Organ Class or Preferred Term Level – Subgroup Analysis (Safety Analysis Set)

MedDRA System Organ Class MedDRA Preferred Term [1]	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Region		
General disorders and administration site conditions, n (%) [2][3]	4 (10.3)	9 (36.0)
Logistic Regression, p-value		
Treatment		0.214
Subgroup		0.511
Interaction Treatment*Subgroup		0.719

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n = number of subjects with at least 1 event. NE = Not Estimable.
[1] Adverse events are coded using MedDRA version 25.0.
[2] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).
[3] Only System Organ Classes and preferred Terms are shown with at least 10% of all patients in at least one treatment arm.

GAP Table 14.3.1.1.4S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) and at least 10% of Patients in Any Arm at System Organ Class or Preferred Term Level – Subgroup Analysis (Safety Analysis Set)

MedDRA System Organ Class MedDRA Preferred Term [1]	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age at First Diagnosis		
General disorders and administration site conditions, n (%) [2][3] Logistic Regression, p-value	4 (10.3)	9 (36.0)
Treatment		0.342
Subgroup		0.064
Interaction Treatment*Subgroup		0.638

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap08s.sas
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n = number of subjects with at least 1 event. NE = Not Estimable.
[1] Adverse events are coded using MedDRA version 25.0.
[2] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).
[3] Only System Organ Classes and preferred Terms are shown with at least 10% of all patients in at least one treatment arm.

GAP Table 14.3.1.1.4S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) and at least 10% of Patients in Any Arm at System Organ Class or Preferred Term Level – Subgroup Analysis (Safety Analysis Set)

MedDRA System Organ Class MedDRA Preferred Term [1]	CSL312 200mg (N=39)	Placebo (N=25)
General disorders and administration site conditions, n (%) [2][3]	4 (10.3)	9 (36.0)
Logistic Regression, p-value		
Treatment		0.050
Subgroup		0.323
Interaction Treatment*Subgroup		0.560

n = number of subjects with at least 1 event. NE = Not Estimable.
[1] Adverse events are coded using MedDRA version 25.0.
[2] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).
[3] Only System Organ Classes and preferred Terms are shown with at least 10% of all patients in at least one treatment arm.

GAP Table 14.3.1.1.4S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) and at least 10% of Patients in Any Arm at System Organ Class or Preferred Term Level – Subgroup Analysis (Safety Analysis Set)

MedDRA System Organ Class MedDRA Preferred Term [1]	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: History of Laryngeal Attack		
General disorders and administration site conditions, n (%) [2][3]	4 (10.3)	9 (36.0)
Logistic Regression, p-value		
Treatment		0.134
Subgroup		0.915
Interaction Treatment*Subgroup		0.956

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap08s.sas
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n = number of subjects with at least 1 event. NE = Not Estimable.
[1] Adverse events are coded using MedDRA version 25.0.
[2] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).
[3] Only System Organ Classes and preferred Terms are shown with at least 10% of all patients in at least one treatment arm.

4.13 Anzahl von HAE-Attacken während der Behandlungsphase, Subgruppe Alter

GAP Table 14.2.1.1.aS2: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.034
time-normalized baseline attack rate during Run-in Period		0.530
Subgroup		0.940
Interaction Treatment*Subgroup		
Age <=41years		135
Total Number of HAE Attacks during Treatment Period	27	16 (64.0)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.2)	
Time-normalized Number of HAE Attacks Per Month		16
Number Observed	18	1.76 (1.245)
Mean (SD)	0.25 (0.431)	0.31
Standard Error	0.10	1.23
Median	0.08	0.85, 2.68
1st Quartile, 3rd Quartile	0.00, 0.33	0.2, 4.2
Minimum, Maximum	0.0, 1.5	1.87 (0.237)
LS Means (Standard Error)[1]	0.20 (0.568)	0.10 (0.03, 0.36)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-89.571 (-96.997, -63.777)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		<0.001
Two-sided Wilcoxon Test, p-value		

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and subgroup variable are

excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.1.aS2: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age <=41years		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	18	16
Mean (SD)	3.05 (5.176)	21.07 (14.941)
Standard Error	1.22	3.74
Median	1.00	14.79
1st Quartile, 3rd Quartile	0.00, 3.99	10.23, 32.21
Minimum, Maximum	0.0, 18.1	2.0, 50.7
LS Means (Standard Error)[1]	2.34 (0.568)	22.45 (0.237)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.10 (0.03, 0.36)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-89.571 (-96.997, -63.777)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.1.aS2: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age >41years		
Total Number of HAE Attacks during Treatment Period	36	131
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.8)	9 (36.0)
Time-normalized Number of HAE Attacks Per Month		
Number Observed	21	9
Mean (SD)	0.28 (0.853)	2.46 (1.380)
Standard Error	0.19	0.46
Median	0.00	2.56
1st Quartile, 3rd Quartile	0.00, 0.17	1.34, 3.36
Minimum, Maximum	0.0, 3.8	0.8, 4.4
LS Means (Standard Error)[1]	0.26 (0.456)	2.32 (0.237)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.04, 0.30)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-88.933 (-95.910, -70.059)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.1.aS2: Primary Efficacy Analysis: Time-normalized Number of HAE Attacks Per Month/Year Using Wilcoxon and Poisson Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age >41years		
Time-normalized Number of HAE Attacks Per Year		
Number Observed	21	9
Mean (SD)	3.41 (10.242)	29.54 (16.562)
Standard Error	2.23	5.52
Median	0.00	30.78
1st Quartile, 3rd Quartile	0.00, 2.00	16.05, 40.36
Minimum, Maximum	0.0, 45.9	9.9, 53.1
LS Means (Standard Error)[1]	3.08 (0.456)	27.80 (0.237)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.04, 0.30)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-88.933 (-95.910, -70.059)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model. Interaction of treatment and subgroup variable are excluded from the model for the subgroup analysis.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

4.14 Anzahl von HAE-Attacken, die während der Behandlungsphase ein On-Demand-Medikament erfordern, Subgruppe Alter

GAP Table 14.2.1.2.1.bS2: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.007
time-normalized baseline attack rate during Run-in Period		0.621
Subgroup		0.570
Interaction Treatment*Subgroup		
Age <=41years		117
Total Number of HAE Attacks during Treatment Period	19	16 (64.0)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.2)	
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		16
Number Observed	18	1.49 (1.338)
Mean (SD)	0.18 (0.339)	0.33
Standard Error	0.08	1.00
Median	0.00	0.43, 2.58
1st Quartile, 3rd Quartile	0.00, 0.17	0.0, 4.2
Minimum, Maximum	0.0, 1.2	1.70 (0.260)
LS Means (Standard Error)[1]	0.11 (0.745)	0.06 (0.01, 0.31)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-93.656 (-98.711, -68.785)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		<0.001
Two-sided Wilcoxon Test, p-value		

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.bS2: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age <=41years		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	18	16
Mean (SD)	2.16 (4.071)	17.93 (16.053)
Standard Error	0.96	4.01
Median	0.00	12.03
1st Quartile, 3rd Quartile	0.00, 2.05	5.10, 30.91
Minimum, Maximum	0.0, 14.9	0.0, 50.7
LS Means (Standard Error)[1]	1.30 (0.745)	20.41 (0.260)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.06 (0.01, 0.31)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-93.656 (-98.711, -68.785)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.bS2: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age >41years		129
Total Number of HAE Attacks during Treatment Period	35	
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.8)	9 (36.0)
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Month		
Number Observed	21	9
Mean (SD)	0.28 (0.855)	2.42 (1.355)
Standard Error	0.19	0.45
Median	0.00	2.39
1st Quartile, 3rd Quartile	0.00, 0.00	1.34, 3.36
Minimum, Maximum	0.0, 3.8	0.8, 4.4
LS Means (Standard Error)[1]	0.22 (0.490)	2.05 (0.254)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.04, 0.31)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-89.212 (-96.195, -69.415)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.bS2: Time-normalized Number of HAE Attacks Per Month Requiring On-demand Treatment Using Wilcoxon and Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age >41years		
Time-normalized Number of HAE Attacks requiring on-demand treatment Per Year		
Number Observed	21	9
Mean (SD)	3.32 (10.265)	29.09 (16.257)
Standard Error	2.24	5.42
Median	0.00	28.73
1st Quartile, 3rd Quartile	0.00, 0.00	16.05, 40.36
Minimum, Maximum	0.0, 45.9	9.9, 53.1
LS Means (Standard Error)[1]	2.65 (0.490)	24.54 (0.254)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.11 (0.04, 0.31)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-89.212 (-96.195, -69.415)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

4.15 Zeit bis zur ersten HAE-Attacke nach Tag 1, Subgruppe Alter

GAP Table 14.2.4.5.1.aS2: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age	
Cox-proportional hazards model results [5]	
p-value	
Treatment (CSL312 vs. Placebo)	
Subgroup	<0.001
Interaction Treatment*Subgroup	0.386
	0.100

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s_2.sas
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[1] Percentages are based on the Intention-to-Treat Analysis Set in respective subgroup.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1.
[5] Cox-proportional hazards (regression) model with treatment group, subgroup and interaction term or with treatment group only for subgroup category.

GAP Table 14.2.4.5.1.aS2: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age Age		
<=41years	18 (46.2)	16 (64.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	9 (50.0)	16 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1]	9 (50.0)	0
Attack-free or one HAE Attack after Study Day 1[1]	12 (66.7)	2 (12.5)
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	11.50
1st, 3rd Quartile[3]	28.00, -	4.50, 19.50
Minimum, Maximum[4]	4.0, 145.0	1.0, 123.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results, Treatment (CSL312 vs. Placebo) [5]		
Parameter Estimate and Standard Error		-1.66 (0.451)
Hazard Ratio and 95% Confidence Interval		0.19 (0.078, 0.459)
p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s_2.sas
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Source: 16.2.5.6, UNBLINDED

[1] Percentages are based on the Intention-to-Treat Analysis Set in respective subgroup.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1.
[5] Cox-proportional hazards (regression) model with treatment group, subgroup and interaction term or with treatment group only for subgroup category.

GAP Table 14.2.4.5.1.aS2: Summary and Cox-proportional Hazards Model Time-to-First HAE Attack after Study Day 1 – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age		
Age >41years	21 (53.8)	9 (36.0)
Subjects with ...		
at Least one HAE Attack after Study Day 1[1]	6 (28.6)	9 (100.0)
no HAE Attacks after Study Day 1 (attack-free)[1]	15 (71.4)	0
Attack-free or one HAE Attack after Study Day 1[1]	17 (81.0)	0
Time-to-First HAE Attack after Study Day 1[2]		
Median[3]	-	8.00
1st, 3rd Quartile[3]	114.00, -	6.00, 17.00
Minimum, Maximum[4]	8.0, 114.0	1.0, 23.0
Median Time Ratio (CSL312 against Placebo)		-
Cox-proportional hazards model results, Treatment (CSL312 vs. Placebo) [5]		
Parameter Estimate and Standard Error		-3.92 (1.084)
Hazard Ratio and 95% Confidence Interval		0.02 (0.002, 0.166)
p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap10s_2.sas
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Source: 16.2.5.6, UNBLINDED

[1] Percentages are based on the Intention-to-Treat Analysis Set in respective subgroup.
[2] Subjects who do not experience a HAE attack are censored at the end of the Treatment Period (Visit Day 182) or at the study completion date.
[3] The median, 1st, and 3rd quartile times are defined as the times for which the Kaplan-Meier estimates for the time to event functions are equal to 0.5, 0.25, and 0.75, respectively. If the time-to-event function is horizontal at 0.5, 0.25, and 0.75, the median or percentiles are calculated as the average of the 2 values between which the time to event function is horizontal.
[4] Minimum and maximum are based on observed time to First HAE attack after Study Day 1.
[5] Cox-proportional hazards (regression) model with treatment group, subgroup and interaction term or with treatment group only for subgroup category.

4.16 Anzahl von moderaten bis schweren HAE-Attacken, Subgruppe Alter

GAP Table 14.2.1.2.1.dS2: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Generalized Linear Model [1], p-value		<0.001
Treatment		0.003
time-normalized baseline attack rate during Run-in Period		0.665
Subgroup		0.509
Interaction Treatment*Subgroup		
Age <=41years		97
Total Number of HAE Attacks during Treatment Period	18	16 (64.0)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.2)	
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		16
Number Observed	18	1.29 (1.007)
Mean (SD)	0.17 (0.334)	0.25
Standard Error	0.08	0.89
Median	0.00	0.52, 2.41
1st Quartile, 3rd Quartile	0.00, 0.17	0.0, 2.8
Minimum, Maximum	0.0, 1.1	1.32 (0.210)
LS Means (Standard Error)[1]	0.11 (0.575)	0.09 (0.02, 0.29)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-91.476 (-97.507, -70.858)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		<0.001
Two-sided Wilcoxon Test, p-value		

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.

[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.dS2: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age <=41years		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	18	16
Mean (SD)	2.05 (4.002)	15.42 (12.087)
Standard Error	0.94	3.02
Median	0.00	10.73
1st Quartile, 3rd Quartile	0.00, 2.05	6.21, 28.94
Minimum, Maximum	0.0, 12.7	0.0, 33.7
LS Means (Standard Error)[1]	1.35 (0.575)	15.82 (0.210)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.09 (0.02, 0.29)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-91.476 (-97.507, -70.858)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.dS2: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age >41years		
Total Number of HAE Attacks during Treatment Period	11	76
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.8)	9 (36.0)
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Month		
Number Observed	21	9
Mean (SD)	0.09 (0.262)	1.43 (1.416)
Standard Error	0.06	0.47
Median	0.00	0.83
1st Quartile, 3rd Quartile	0.00, 0.00	0.68, 1.34
Minimum, Maximum	0.0, 1.2	0.0, 4.4
LS Means (Standard Error)[1]	0.07 (0.627)	1.51 (0.235)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.05 (0.01, 0.18)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-95.210 (-98.716, -82.139)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.dS2: Time-normalized Number of Moderate or Severe HAE Attacks Per Month Using Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age >41years		
Time-normalized Number of Moderate or Severe HAE Attacks Treatment Per Year		
Number Observed	21	9
Mean (SD)	1.04 (3.145)	17.21 (16.987)
Standard Error	0.69	5.66
Median	0.00	9.98
1st Quartile, 3rd Quartile	0.00, 0.00	8.21, 16.05
Minimum, Maximum	0.0, 14.0	0.0, 53.1
LS Means (Standard Error)[1]	0.87 (0.627)	18.12 (0.235)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.05 (0.01, 0.18)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-95.210 (-98.716, -82.139)
Two-sided Wilcoxon Test, p-value		<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

4.17 Anzahl von schweren HAE-Attacken, Subgruppe Alter

GAP Table 14.2.1.2.1.gS2: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Generalized Linear Model [1], p-value		0.017
Treatment		0.133
time-normalized baseline attack rate during Run-in Period		0.701
Subgroup		0.754
Interaction Treatment*Subgroup		
Age <=41years		13
Total Number of HAE Attacks during Treatment Period	4	16 (64.0)
Number of Subjects observed during Treatment Period, n (%) [2]	18 (46.2)	
Time-normalized Number of Severe HAE Attacks Treatment Per Month		16
Number Observed	18	0.16 (0.229)
Mean (SD)	0.04 (0.092)	0.06
Standard Error	0.02	0.00
Median	0.00	0.00, 0.33
1st Quartile, 3rd Quartile	0.00, 0.00	0.0, 0.7
Minimum, Maximum	0.0, 0.3	0.17 (0.322)
LS Means (Standard Error)[1]	0.03 (0.626)	0.18 (0.05, 0.74)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		-81.629 (-95.452, -25.790)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		0.105
Two-sided Wilcoxon Test, p-value		

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length

of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.gS2: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age <=41years		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	18	16
Mean (SD)	0.45 (1.110)	1.87 (2.744)
Standard Error	0.26	0.69
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 4.01
Minimum, Maximum	0.0, 4.0	0.0, 7.9
LS Means (Standard Error)[1]	0.36 (0.626)	1.98 (0.322)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.18 (0.05, 0.74)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-81.629 (-95.452, -25.790)
Two-sided Wilcoxon Test, p-value		0.105

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.gS2: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age >41years		
Total Number of HAE Attacks during Treatment Period	2	8
Number of Subjects observed during Treatment Period, n (%) [2]	21 (53.8)	9 (36.0)
Time-normalized Number of Severe HAE Attacks Treatment Per Month		
Number Observed	21	9
Mean (SD)	0.02 (0.049)	0.15 (0.197)
Standard Error	0.01	0.07
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 0.33
Minimum, Maximum	0.0, 0.2	0.0, 0.5
LS Means (Standard Error)[1]	0.02 (0.821)	0.13 (0.427)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.13 (0.02, 0.78)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-87.402 (-97.965, -22.016)
Two-sided Wilcoxon Test, p-value		0.022

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

GAP Table 14.2.1.2.1.gS2: Time-normalized Number of Severe HAE Attacks Per Month Using Wilcoxon and Poisson Model Approach – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Age >41years		
Time-normalized Number of Severe HAE Attacks Treatment Per Year		
Number Observed	21	9
Mean (SD)	0.19 (0.585)	1.79 (2.361)
Standard Error	0.13	0.79
Median	0.00	0.00
1st Quartile, 3rd Quartile	0.00, 0.00	0.00, 3.99
Minimum, Maximum	0.0, 2.0	0.0, 6.1
LS Means (Standard Error)[1]	0.20 (0.821)	1.61 (0.427)
mean time-normalized number of HAE attacks ratio for CSL312 relative to placebo, 95% Confidence Interval [1]		0.13 (0.02, 0.78)
percentage difference in the mean time-normalized number of HAE attacks for CSL312 to placebo, 95% Confidence Interval		-87.402 (-97.965, -22.016)
Two-sided Wilcoxon Test, p-value		0.022

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn01gaps.sas
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Source: 16.2.5.4, UNBLINDED

The specified model did not converge.
[1] Using a generalized linear model for count data assuming a Poisson distribution with the logarithm as link function and Pearson chi-square scaling of standard errors to account for potential over dispersion. The model includes treatment (categorical) and the time-normalized baseline attack rate during Run-in Period (continuous) as covariate, the subgroup variable (categorical) and interaction of treatment and subgroup variable. To account for the length of subject treatment, the logarithm of the length of subject treatment (days) is used as an offset variable in the model.
[2] Percentages are based on the Intention-to-Treat Analysis Set.

4.18 Reduktion der Anzahl der HAE-Attacken um 50 %, 70 % und 90 %, Subgruppe Alter

GAP Table 14.2.2.1.2.aS2: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 50% [2][3]	37 (94.9)	8 (32.0)
Non-responders with Reduction of < 50% [2][3]	2 (5.1)	17 (68.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(83.11, 98.58)	(17.21, 51.59)
Logistic Regression, p-value		
Treatment		0.002
Subgroup		0.915
Interaction Treatment*Subgroup		0.969

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps_2.sas
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Source: 16.2.5.5, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)].
Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.1.2.aS2: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	18	16	
Responders with Reduction of >= 50% [2][3]	17 (94.4)	5 (31.3)	
Odds Ratio and 95% Confidence Interval and p-value		37.40 (3.837, 364.570)	<0.001
Relative Risk and 95% Confidence Interval and p-value		3.02 (1.449, 6.305)	0.003
Risk Difference and 95% Confidence Interval and p-value		0.63 (0.381, 0.883)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Reduction of >= 50% [2][3]	20 (95.2)	3 (33.3)	
Odds Ratio and 95% Confidence Interval and p-value		40.00 (3.486, 458.984)	<0.001
Relative Risk and 95% Confidence Interval and p-value		2.86 (1.129, 7.233)	0.027
Risk Difference and 95% Confidence Interval and p-value		0.62 (0.298, 0.940)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps_2.sas
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Source: 16.2.5.5, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)].
Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.1.2.aS2: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 70% [2][3]	36 (92.3)	4 (16.0)
Non-responders with Reduction of < 70% [2][3]	3 (7.7)	21 (84.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 70% [4]	(79.68, 97.35)	(6.40, 34.65)
Logistic Regression, p-value		
Treatment		<0.001
Subgroup		0.621
Interaction Treatment*Subgroup		0.389

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)].
Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.1.2.aS2: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	18	16	
Responders with Reduction of >= 70% [2][3]	16 (88.9)	3 (18.8)	
Odds Ratio and 95% Confidence Interval and p-value		34.67 (5.016, 239.573)	<0.001
Relative Risk and 95% Confidence Interval and p-value		4.74 (1.687, 13.319)	0.003
Risk Difference and 95% Confidence Interval and p-value		0.70 (0.461, 0.942)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Reduction of >= 70% [2][3]	20 (95.2)	1 (11.1)	
Odds Ratio and 95% Confidence Interval and p-value		160.00 (8.887, 2880.460)	<0.001
Relative Risk and 95% Confidence Interval and p-value		8.57 (1.347, 54.532)	0.023
Risk Difference and 95% Confidence Interval and p-value		0.84 (0.617, 1.000)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps_2.sas
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Source: 16.2.5.5, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)].
Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.1.2.aS2: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of >= 90% [2][3]	29 (74.4)	2 (8.0)
Non-responders with Reduction of < 90% [2][3]	10 (25.6)	23 (92.0)
95% Wilson Confidence Interval for Subjects with a Reduction of >= 90% [4]	(58.92, 85.43)	(2.22, 24.97)
Logistic Regression, p-value		
Treatment		0.005
Subgroup		0.481
Interaction Treatment*Subgroup		0.304

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)].
Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.1.2.aS2: Analysis of Responders With Reduction in the Attack Rate during the Treatment Period compared to the Run-in Period – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	18	16	
Responders with Reduction of >= 90% [2][3]	12 (66.7)	2 (12.5)	
Odds Ratio and 95% Confidence Interval and p-value		14.00 (2.370, 82.717)	0.002
Relative Risk and 95% Confidence Interval and p-value		5.33 (1.401, 20.306)	0.014
Risk Difference and 95% Confidence Interval and p-value		0.54 (0.270, 0.813)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Reduction of >= 90% [2][3]	17 (81.0)	0	
Odds Ratio and 95% Confidence Interval and p-value		73.89 (3.582, 1524.141)	<0.001
Relative Risk and 95% Confidence Interval and p-value		15.91 (1.059, 239.083)	NE
Risk Difference and 95% Confidence Interval and p-value		0.81 (0.642, 0.977)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps_2.sas
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Source: 16.2.5.5, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)].
Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

4.19 Reduktion der Anzahl der HAE-Attacken um 100 %, Subgruppe Alter

GAP Table 14.2.2.1.2.bS2: Number and proportion of HAE attack-free patient - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Study Period: 6-Month Treatment		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [1]	0	0
Responders with Reduction of 100% (attack-free) [2][3]	24 (61.5)	0
Non-responders with Reduction of < 100% [2][3]	15 (38.5)	25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(45.90, 75.11)	(0.00, 13.32)
Logistic Regression, p-value		
Treatment		0.024
Subgroup		0.795
Interaction Treatment*Subgroup		0.887

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps_2.sas
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Source: 16.2.5.5, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)].
Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.1.2.bS2: Number and proportion of HAE attack-free patient - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Study Period: 6-Month Treatment			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	18	16	
Responders with Reduction of 100% (attack-free) [2][3]	9 (50.0)	0	
Odds Ratio and 95% Confidence Interval and p-value		33.00 (1.721, 632.846)	0.001
Relative Risk and 95% Confidence Interval and p-value		17.00 (1.068, 270.623)	NE
Risk Difference and 95% Confidence Interval and p-value		0.50 (0.269, 0.731)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Reduction of 100% (attack-free) [2][3]	15 (71.4)	0	
Odds Ratio and 95% Confidence Interval and p-value		45.31 (2.284, 898.868)	<0.001
Relative Risk and 95% Confidence Interval and p-value		14.09 (0.933, 212.868)	NE
Risk Difference and 95% Confidence Interval and p-value		0.71 (0.521, 0.908)	<0.001

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_tn06gaps_2.sas
Produced: 22NOV2024 03:34 Page 2 of 6
Source: 16.2.5.5, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The percentage reduction in the time-normalized number of HAE attacks per month is calculated as 100*(1 – (time-normalized number of HAE attacks per month under CSL312 treatment or Placebo / time-normalized number of HAE attacks per month during Run-in)]. Subjects whose time-normalized number of HAE attacks per month cannot be calculated in any of the periods are excluded from the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

4.20 Gesundheitszustand (EQ-5D-5L VAS), Subgruppe Alter

GAP Table 14.2.2.1.2.fS.i2: Analysis of Responders for Change from Baseline for EQ-5D-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	39 (100.0) 3	25 (100.0)
Subjects with imputed values, n (%) [6]	(7.7)	3 (12.0)
Responders with Change from Baseline of >= 15 [2][5]	8 (20.5)	0
Non-responders with Change from Baseline of < 15 [2][5]	31 (79.5)	25 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(10.78, 35.53)	(0.00, 13.32)
Logistic Regression, p-value		
Treatment		0.209
Subgroup		0.795
Interaction Treatment*Subgroup		0.943

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap07si_2.sas
Produced: 22NOV2024 03:32 Page 1 of 4
Source: 16.2.5.8, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i2: Analysis of Responders for Change from Baseline for EQ-5D-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	18	16	
Responders with Change from Baseline of >= 15 [2][5]	3 (16.7)	0	
Odds Ratio and 95% Confidence Interval and p-value		7.45 (0.355, 156.279)	0.092
Relative Risk and 95% Confidence Interval and p-value		6.26 (0.348, 112.699)	NE
Risk Difference and 95% Confidence Interval and p-value		0.17 (-0.005, 0.339)	0.058
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of >= 15 [2][5]	5 (23.8)	0	
Odds Ratio and 95% Confidence Interval and p-value		6.33 (0.314, 127.602)	0.115
Relative Risk and 95% Confidence Interval and p-value		5.00 (0.305, 81.968)	NE
Risk Difference and 95% Confidence Interval and p-value		0.24 (0.056, 0.420)	0.010

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap07si_2.sas
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Source: 16.2.5.8, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i2: Analysis of Responders for Change from Baseline for EQ-5D-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Domain: VAS [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	39 (100.0)	25 (100.0)
Subjects with imputed values, n (%) [6]	3 (7.7)	3 (12.0)
Responders with Change from Baseline of >= 7 [2][5]	13 (33.3)	4 (16.0)
Non-responders with Change from Baseline of < 7 [2][5]	26 (66.7)	21 (84.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(20.63, 49.02)	(6.40, 34.65)
Logistic Regression, p-value		
Treatment		0.167
Subgroup		0.529
Interaction Treatment*Subgroup		0.593

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.fS.i2: Analysis of Responders for Change from Baseline for EQ-5D-5L VAS at Day 182 – Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Domain: VAS [3]			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	18	16	
Responders with Change from Baseline of >= 7 [2][5]	6 (33.3)	2 (12.5)	
Odds Ratio and 95% Confidence Interval and p-value		3.50 (0.592, 20.679)	0.159
Relative Risk and 95% Confidence Interval and p-value		2.67 (0.624, 11.388)	0.185
Risk Difference and 95% Confidence Interval and p-value		0.21 (-0.063, 0.480)	0.133
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of >= 7 [2][5]	7 (33.3)	2 (22.2)	
Odds Ratio and 95% Confidence Interval and p-value		1.75 (0.285, 10.742)	0.550
Relative Risk and 95% Confidence Interval and p-value		1.50 (0.384, 5.866)	0.560
Risk Difference and 95% Confidence Interval and p-value		0.11 (-0.227, 0.449)	0.520

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap07si_2.sas
Produced: 22NOV2024 03:32
Source: 16.2.5.8, UNBLINDED

NE = Not Estimable.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] VAS = visual analogue scale, which measures overall health status on a vertical visual analogue scale ranging from 0 (worst imaginable health status) to 100 (best imaginable health state).
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subject with missing VAS at Day 182 are imputed as Non-responders.

4.21 WPAI:GH Frage 6, Subgruppe Alter

GAP Table 14.2.2.1.6.gS.i2: Analysis of Responders for Change from Baseline for WPAI:GH Q6: Problem Affect Regular Daily Activity at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	37 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	3 (8.1)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	0	0
Non-responders with Change from Baseline of > -15 [2][5]	37 (100.0)	23 (100.0)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(0.00, 9.41)	(0.00, 14.31)
Logistic Regression, p-value		
Treatment		NE
Subgroup		NE
Interaction Treatment*Subgroup		NE

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap11si_2.sas
Produced: 22NOV2024 03:33
Source: 16.2.5.9, UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes).
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.6.gS.i2: Analysis of Responders for Change from Baseline for WPAI:GH Q6: Problem Affect Regular Daily Activity at Day 182 Analysis – Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=16 Years))

	CSL312 200mg (N=37)	Placebo (N=23)
Domain: Q6: Problem affect regular Daily activity [3]		
Subgroup: Age		
Age <=41years		
Subjects Included in the Analysis, n	16 0	14
Responders with Change from Baseline of <= -15 [2][5]		0
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		NE
Age >41years	21 0	9
Subjects Included in the Analysis, n		0
Responders with Change from Baseline of <= -15 [2][5]		NE
Odds Ratio and 95% Confidence Interval and p-value		NE
Relative Risk and 95% Confidence Interval and p-value		NE
Risk Difference and 95% Confidence Interval and p-value		

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap11si_2.sas
Produced: 22NOV2024 03:33 Page 2 of 2
Source: 16.2.5.9, UNBLINDED

NE = Not Estimable.
WPAI:GH is only answered from patients of age >= 16 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] Scores are expressed as impairment percentages, with higher scores indicating greater impairment and less productivity (i.e., worse outcomes).
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=16 years with missing WPAI:GH Q6 at Day 182 are imputed as Non-responders.

4.22 AE-QoL, Subgruppe Alter

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Functioning [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	26 (74.3)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	9 (25.7)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(57.93, 85.84)	(12.55, 46.47)
Logistic Regression, p-value		
Treatment		0.004
Subgroup		0.024
Interaction Treatment*Subgroup		0.082

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Functioning [3]			
Subgroup: Age			
Age <=41years		14	
Subjects Included in the Analysis, n	14	1 (7.1)	
Responders with Change from Baseline of <= -15 [2][5]	10 (71.4)	32.50 (3.127, 337.813)	
Odds Ratio and 95% Confidence Interval and p-value		10.00 (1.470, 68.040)	<0.001
Relative Risk and 95% Confidence Interval and p-value		0.64 (0.370, 0.915)	0.019
Risk Difference and 95% Confidence Interval and p-value			<0.001
Age >41years		9	
Subjects Included in the Analysis, n	21	5 (55.6)	
Responders with Change from Baseline of <= -15 [2][5]	16 (76.2)	2.56 (0.489, 13.389)	
Odds Ratio and 95% Confidence Interval and p-value		1.37 (0.729, 2.579)	0.266
Relative Risk and 95% Confidence Interval and p-value		0.21 (-0.166, 0.579)	0.327
Risk Difference and 95% Confidence Interval and p-value			0.277

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fatigue and Mood [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	22 (62.9)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	13 (37.1)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(46.34, 76.83)	(12.55, 46.47)
Logistic Regression, p-value		
Treatment		0.012
Subgroup		0.528
Interaction Treatment*Subgroup		0.308

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fatigue and Mood [3]			
Subgroup: Age			
Age <=41years		14	
Subjects Included in the Analysis, n	14		
Responders with Change from Baseline of <= -15 [2][5]	10 (71.4)	3 (21.4)	
Odds Ratio and 95% Confidence Interval and p-value		9.17 (1.634, 51.427)	0.009
Relative Risk and 95% Confidence Interval and p-value		3.33 (1.159, 9.586)	0.025
Risk Difference and 95% Confidence Interval and p-value		0.50 (0.180, 0.820)	0.002
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -15 [2][5]	12 (57.1)	3 (33.3)	
Odds Ratio and 95% Confidence Interval and p-value		2.67 (0.521, 13.655)	0.240
Relative Risk and 95% Confidence Interval and p-value		1.71 (0.634, 4.639)	0.289
Risk Difference and 95% Confidence Interval and p-value		0.24 (-0.136, 0.612)	0.212

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fears and Shame [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression, p-value		0.005
Treatment		0.029
Subgroup		0.013
Interaction Treatment*Subgroup		

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fears and Shame [3]			
Subgroup: Age			
Age <=41years		14	
Subjects Included in the Analysis, n	14	0	
Responders with Change from Baseline of <= -15 [2][5]	11 (78.6)		
Odds Ratio and 95% Confidence Interval and p-value		95.29 (4.456, 2037.478)	<0.001
Relative Risk and 95% Confidence Interval and p-value		23.00 (1.486, 356.016)	NE
Risk Difference and 95% Confidence Interval and p-value		0.79 (0.571, 1.000)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -15 [2][5]	12 (57.1)	5 (55.6)	
Odds Ratio and 95% Confidence Interval and p-value		1.07 (0.221, 5.145)	0.937
Relative Risk and 95% Confidence Interval and p-value		1.03 (0.515, 2.054)	0.936
Risk Difference and 95% Confidence Interval and p-value		0.02 (-0.372, 0.403)	0.936

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Nutrition [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	14 (40.0)	2 (8.7)
Non-responders with Change from Baseline of > -15 [2][5]	21 (60.0)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(25.55, 56.43)	(2.42, 26.80)
Logistic Regression, p-value		
Treatment		0.093
Subgroup		0.744
Interaction Treatment*Subgroup		0.910

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Nutrition [3]			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	14	14	
Responders with Change from Baseline of <= -15 [2][5]	5 (35.7)	1 (7.1)	
Odds Ratio and 95% Confidence Interval and p-value		7.22 (0.718, 72.696)	
Relative Risk and 95% Confidence Interval and p-value		5.00 (0.666, 37.511)	0.070
Risk Difference and 95% Confidence Interval and p-value		0.29 (0.001, 0.571)	0.118
			0.049
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -15 [2][5]	9 (42.9)	1 (11.1)	
Odds Ratio and 95% Confidence Interval and p-value		6.00 (0.632, 57.004)	
Relative Risk and 95% Confidence Interval and p-value		3.86 (0.570, 26.119)	0.097
Risk Difference and 95% Confidence Interval and p-value		0.32 (0.023, 0.612)	0.167
			0.035

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression, p-value		0.004
Treatment		0.058
Subgroup		0.054
Interaction Treatment*Subgroup		

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3]			
Subgroup: Age			
Age <=41years		14	
Subjects Included in the Analysis, n	14	1 (7.1)	
Responders with Change from Baseline of <= -15 [2][5]	10 (71.4)	32.50 (3.127, 337.813)	
Odds Ratio and 95% Confidence Interval and p-value		10.00 (1.470, 68.040)	<0.001
Relative Risk and 95% Confidence Interval and p-value		0.64 (0.370, 0.915)	0.019
Risk Difference and 95% Confidence Interval and p-value			<0.001
Age >41years		9	
Subjects Included in the Analysis, n	21	4 (44.4)	
Responders with Change from Baseline of <= -15 [2][5]	13 (61.9)	2.03 (0.417, 9.886)	
Odds Ratio and 95% Confidence Interval and p-value		1.39 (0.623, 3.112)	0.385
Relative Risk and 95% Confidence Interval and p-value		0.17 (-0.211, 0.560)	0.419
Risk Difference and 95% Confidence Interval and p-value			0.375

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -6 [2][5]	29 (82.9)	11 (47.8)
Non-responders with Change from Baseline of > -6 [2][5]	6 (17.1)	12 (52.2)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(67.32, 91.90)	(29.24, 67.04)
Logistic Regression, p-value		0.005
Treatment		0.009
Subgroup		0.005
Interaction Treatment*Subgroup		

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3]			
Subgroup: Age			
Age <=41years		14	
Subjects Included in the Analysis, n	14		
Responders with Change from Baseline of <= -6 [2][5]	14 (100.0)	3 (21.4)	
Odds Ratio and 95% Confidence Interval and p-value		95.29 (4.456, 2037.478)	<0.001
Relative Risk and 95% Confidence Interval and p-value		4.67 (1.712, 12.724)	0.003
Risk Difference and 95% Confidence Interval and p-value		0.79 (0.571, 1.000)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -6 [2][5]	15 (71.4)	8 (88.9)	
Odds Ratio and 95% Confidence Interval and p-value		0.31 (0.032, 3.068)	0.308
Relative Risk and 95% Confidence Interval and p-value		0.80 (0.563, 1.147)	0.228
Risk Difference and 95% Confidence Interval and p-value		-0.17 (-0.457, 0.107)	0.225

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NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Functioning [3] Subgroup: Age		
Subjects Included in the Analysis, n (%) [1] Subjects with imputed values, n (%) [6]	35 (100.0) 2 (5.7)	23 (100.0) 3 (13.0)
Responders with Change from Baseline of <= -15 [2][5] Non-responders with Change from Baseline of > -15 [2][5] 95% Wilson Confidence Interval for the Percentage of Responders [4]	26 (74.3) 9 (25.7) (57.93, 85.84)	6 (26.1) 17 (73.9) (12.55, 46.47)
Logistic Regression, p-value		
Treatment		0.004
Subgroup		0.024
Interaction Treatment*Subgroup		0.082

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si_2.sas
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NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Functioning [3] Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	14	14	
Responders with Change from Baseline of <= -15 [2][5]	10 (71.4)	1 (7.1)	
Odds Ratio and 95% Confidence Interval and p-value		32.50 (3.127, 337.813)	<0.001
Relative Risk and 95% Confidence Interval and p-value		10.00 (1.470, 68.040)	0.019
Risk Difference and 95% Confidence Interval and p-value		0.64 (0.370, 0.915)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -15 [2][5]	16 (76.2)	5 (55.6)	
Odds Ratio and 95% Confidence Interval and p-value		2.56 (0.489, 13.389)	0.266
Relative Risk and 95% Confidence Interval and p-value		1.37 (0.729, 2.579)	0.327
Risk Difference and 95% Confidence Interval and p-value		0.21 (-0.166, 0.579)	0.277

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NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fatigue and Mood [3] Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	22 (62.9)	6 (26.1)
Non-responders with Change from Baseline of > -15 [2][5]	13 (37.1)	17 (73.9)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(46.34, 76.83)	(12.55, 46.47)
Logistic Regression, p-value		
Treatment		0.012
Subgroup		0.528
Interaction Treatment*Subgroup		0.308

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si_2.sas
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Source: 16.2.5.7, UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fatigue and Mood [3] Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	14	14	
Responders with Change from Baseline of <= -15 [2][5]	10 (71.4)	3 (21.4)	
Odds Ratio and 95% Confidence Interval and p-value		9.17 (1.634, 51.427)	0.009
Relative Risk and 95% Confidence Interval and p-value		3.33 (1.159, 9.586)	0.025
Risk Difference and 95% Confidence Interval and p-value		0.50 (0.180, 0.820)	0.002
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -15 [2][5]	12 (57.1)	3 (33.3)	
Odds Ratio and 95% Confidence Interval and p-value		2.67 (0.521, 13.655)	0.240
Relative Risk and 95% Confidence Interval and p-value		1.71 (0.634, 4.639)	0.289
Risk Difference and 95% Confidence Interval and p-value		0.24 (-0.136, 0.612)	0.212

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si_2.sas
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NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Fears and Shame [3] Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression, p-value		
Treatment		0.005
Subgroup		0.029
Interaction Treatment*Subgroup		0.013

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Fears and Shame [3] Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	14	14	
Responders with Change from Baseline of <= -15 [2][5]	11 (78.6)	0	
Odds Ratio and 95% Confidence Interval and p-value		95.29 (4.456, 2037.478)	<0.001
Relative Risk and 95% Confidence Interval and p-value		23.00 (1.486, 356.016)	NE
Risk Difference and 95% Confidence Interval and p-value		0.79 (0.571, 1.000)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -15 [2][5]	12 (57.1)	5 (55.6)	
Odds Ratio and 95% Confidence Interval and p-value		1.07 (0.221, 5.145)	0.937
Relative Risk and 95% Confidence Interval and p-value		1.03 (0.515, 2.054)	0.936
Risk Difference and 95% Confidence Interval and p-value		0.02 (-0.372, 0.403)	0.936

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Source: 16.2.5.7, UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Nutrition [3] Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	14 (40.0)	2 (8.7)
Non-responders with Change from Baseline of > -15 [2][5]	21 (60.0)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(25.55, 56.43)	(2.42, 26.80)
Logistic Regression, p-value		
Treatment		0.093
Subgroup		0.744
Interaction Treatment*Subgroup		0.910

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si_2.sas
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Source: 16.2.5.7, UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Nutrition [3] Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	14	14	
Responders with Change from Baseline of <= -15 [2][5]	5 (35.7)	1 (7.1)	
Odds Ratio and 95% Confidence Interval and p-value		7.22 (0.718, 72.696)	0.070
Relative Risk and 95% Confidence Interval and p-value		5.00 (0.666, 37.511)	0.118
Risk Difference and 95% Confidence Interval and p-value		0.29 (0.001, 0.571)	0.049
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -15 [2][5]	9 (42.9)	1 (11.1)	
Odds Ratio and 95% Confidence Interval and p-value		6.00 (0.632, 57.004)	0.097
Relative Risk and 95% Confidence Interval and p-value		3.86 (0.570, 26.119)	0.167
Risk Difference and 95% Confidence Interval and p-value		0.32 (0.023, 0.612)	0.035

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value - baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -15 [2][5]	23 (65.7)	5 (21.7)
Non-responders with Change from Baseline of > -15 [2][5]	12 (34.3)	18 (78.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.15, 79.17)	(9.66, 41.90)
Logistic Regression, p-value		
Treatment		0.004
Subgroup		0.058
Interaction Treatment*Subgroup		0.054

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si_2.sas
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NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	14	14	
Responders with Change from Baseline of <= -15 [2][5]	10 (71.4)	1 (7.1)	
Odds Ratio and 95% Confidence Interval and p-value		32.50 (3.127, 337.813)	<0.001
Relative Risk and 95% Confidence Interval and p-value		10.00 (1.470, 68.040)	0.019
Risk Difference and 95% Confidence Interval and p-value		0.64 (0.370, 0.915)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -15 [2][5]	13 (61.9)	4 (44.4)	
Odds Ratio and 95% Confidence Interval and p-value		2.03 (0.417, 9.886)	0.385
Relative Risk and 95% Confidence Interval and p-value		1.39 (0.623, 3.112)	0.419
Risk Difference and 95% Confidence Interval and p-value		0.17 (-0.211, 0.560)	0.375

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si_2.sas Produced: 22NOV2024 03:35

Source: 16.2.5.7, UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)
Domain: Total AE QoL Score [3] Subgroup: Age		
Subjects Included in the Analysis, n (%) [1]	35 (100.0)	23 (100.0)
Subjects with imputed values, n (%) [6]	2 (5.7)	3 (13.0)
Responders with Change from Baseline of <= -6 [2][5]	29 (82.9)	11 (47.8)
Non-responders with Change from Baseline of > -6 [2][5]	6 (17.1)	12 (52.2)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(67.32, 91.90)	(29.24, 67.04)
Logistic Regression, p-value		
Treatment		0.005
Subgroup		0.009
Interaction Treatment*Subgroup		0.005

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

GAP Table 14.2.2.1.2.eS.i2: Analysis of Responders for Change from Baseline in AE-QoL Domains and Total Score at Day 182 - Non-Responder Imputation - Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set Including Only Adult Population (age >=18 Years))

	CSL312 200mg (N=35)	Placebo (N=23)	
Domain: Total AE QoL Score [3] Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	14	14	
Responders with Change from Baseline of <= -6 [2][5]	14 (100.0)	3 (21.4)	
Odds Ratio and 95% Confidence Interval and p-value		95.29 (4.456, 2037.478)	<0.001
Relative Risk and 95% Confidence Interval and p-value		4.67 (1.712, 12.724)	0.003
Risk Difference and 95% Confidence Interval and p-value		0.79 (0.571, 1.000)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders with Change from Baseline of <= -6 [2][5]	15 (71.4)	8 (88.9)	
Odds Ratio and 95% Confidence Interval and p-value		0.31 (0.032, 3.068)	0.308
Relative Risk and 95% Confidence Interval and p-value		0.80 (0.563, 1.147)	0.228
Risk Difference and 95% Confidence Interval and p-value		-0.17 (-0.457, 0.107)	0.225

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap05si_2.sas
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Source: 16.2.5.7, UNBLINDED

NE = Not Estimable.
AE-QoL is only answered from patients of age >= 18 years.
[1] Percentages are based on the number of subjects in the analysis set (N).
[2] Percentages are based on the number of subjects included in the analysis.
[3] The scores are expressed in percentage impairment (0-100%). Higher scores indicate more impairment.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.
[5] Change from Baseline derived as: visit value – baseline value.
[6] Percentages are based on the number of subjects in the analysis (N). Subjects >=18 years with missing AE-QoL at Day 182 are imputed as Non-responders.

4.23 SGART und IGART, Subgruppe Alter

GAP Table 14.2.2.4.hS2: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [2]	39 (100.0)	23 (92.0)
Subjects with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	31 (79.5)	2 (8.7)
Non-Responders (None/Poor/Fair/Good) [3]	8 (20.5)	21 (91.3)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(64.47, 89.22)	(2.42, 26.80)
Logistic Regression, p-value		
Treatment		<0.001
Subgroup		0.429
Interaction Treatment*Subgroup		0.612

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period.".
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

GAP Table 14.2.2.4.hS2: Analysis of Responder of IGART Responses by Study Visit – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1]			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	18	14	
Responders (Excellent) [3]	15 (83.3)	2 (14.3)	
Odds Ratio and 95% Confidence Interval and p-value		30.00 (4.296, 209.508)	<0.001
Relative Risk and 95% Confidence Interval and p-value		5.83 (1.590, 21.396)	0.008
Risk Difference and 95% Confidence Interval and p-value		0.69 (0.439, 0.942)	<0.001
Age >41years			
Subjects Included in the Analysis, n	21	9	
Responders (Excellent) [3]	16 (76.2)	0	
Odds Ratio and 95% Confidence Interval and p-value		57.00 (2.829, 1148.418)	<0.001
Relative Risk and 95% Confidence Interval and p-value		15.00 (0.996, 225.975)	NE
Risk Difference and 95% Confidence Interval and p-value		0.76 (0.580, 0.944)	<0.001

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Source: 16.2.5.10, UNBLINDED

NE = Not Estimable.
[1] Investigators have to respond to the following question: "Considering all of the ways HAE affects your patient, please rate your patient's response to the study medication provided to prevent HAE attacks during this Treatment Period.".
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.5.hS2: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Visit: Visit Day 182 [1]		
Subgroup: Age		
Subjects Included in the Analysis, n (%) [2]	38 (97.4)	24 (96.0)
Subjects with imputed values, n (%) [2]	0	0
Responders (Excellent) [3]	25 (65.8)	3 (12.5)
Non-Responders (None/Poor/Fair/Good) [3]	13 (34.2)	21 (87.5)
95% Wilson Confidence Interval for the Percentage of Responders [4]	(49.89, 78.79)	(4.34, 31.00)
Logistic Regression, p-value		
Treatment		0.031
Subgroup		0.312
Interaction Treatment*Subgroup		0.252

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period.".
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson’s asymptotic confidence limits.

GAP Table 14.2.2.5.hS2: Analysis of Responder of SGART Responses by Study Visit – Subgroup Analysis by Median Age (Intention-to-Treat Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)	
Visit: Visit Day 182 [1]			
Subgroup: Age			
Age <=41years			
Subjects Included in the Analysis, n	18	15	
Responders (Excellent) [3]	11 (61.1)	3 (20.0)	
Odds Ratio and 95% Confidence Interval and p-value		6.29 (1.294, 30.538)	0.019
Relative Risk and 95% Confidence Interval and p-value		3.06 (1.041, 8.972)	0.042
Risk Difference and 95% Confidence Interval and p-value		0.41 (0.108, 0.714)	0.008
Age >41years			
Subjects Included in the Analysis, n	20	9	
Responders (Excellent) [3]	14 (70.0)	0	
Odds Ratio and 95% Confidence Interval and p-value		42.38 (2.130, 843.285)	<0.001
Relative Risk and 95% Confidence Interval and p-value		13.81 (0.913, 208.954)	NE
Risk Difference and 95% Confidence Interval and p-value		0.70 (0.499, 0.901)	<0.001

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Source: 16.2.5.10, UNBLINDED

[1] Subjects have to respond to the following question: "Considering all of the ways HAE affects you, please rate your response to the study medication you were given to prevent HAE attacks during this Treatment Period.".
[2] Percentages are based on the number of subjects in the analysis (N).
[3] Percentages are based on the number of subjects included in the analysis.
[4] The 95% confidence interval is based on Wilson's asymptotic confidence limits.

4.24 Verträglichkeit, Subgruppe Alter

GAP Table 14.3.1.1.5S: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) – Subgroup Analysis (Safety Analysis Set)

	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age		
Number (%) of Subjects with at least 1 TEAE	25 (64.1)	15 (60.0)
Logistic Regression, p-value		
Treatment		0.534
Subgroup		0.611
Interaction Treatment*Subgroup		0.554
Age <=41years, n (%) [1]		9 (36.0)
Odds Ratio and 95% Confidence Interval	12 (30.8)	0.750 (0.203, 2.770)
p-value		0.670
Relative Risk and 95% Confidence Interval		0.850 (0.407, 1.775)
p-value		0.665
Risk Difference and 95% Confidence Interval		-0.071 (-0.391, 0.249)
p-value		0.665
Age >41years, n (%) [1]		6 (24.0)
Odds Ratio and 95% Confidence Interval		0.923 (0.218, 3.916)
p-value	13 (33.3)	0.915
Relative Risk and 95% Confidence Interval		0.957 (0.431, 2.124)
p-value		0.913
Risk Difference and 95% Confidence Interval		-0.020 (-0.377, 0.337)
p-value		0.914

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap13_2.sas
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Source: 16.2.7.2, UNBLINDED

n = number of subjects with at least 1 event.
[1] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).
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GAP Table 14.3.1.1.4S2: Number of Patients with at least 1 Treatment-Emergent Adverse Events (TEAE) and at least 10% of Patients in Any Arm at System Organ Class or Preferred Term Level – Subgroup Analysis by Median Age (Safety Analysis Set)

MedDRA System Organ Class MedDRA Preferred Term [1]	CSL312 200mg (N=39)	Placebo (N=25)
Subgroup: Age		
General disorders and administration site conditions, n (%) [2][3]	4 (10.3)	9 (36.0)
Logistic Regression, p-value		
Treatment		0.067
Subgroup		0.531
Interaction Treatment*Subgroup		0.337

0

CSL Behring / CSL312_3001: /projects/csbeh253590/stats/gap/prog/tables/t_gap08s_2.sas
Produced: 22NOV2024 03:33
Source: 16.2.7.2, UNBLINDED

n = number of subjects with at least 1 event.
[1] Adverse events are coded using MedDRA version 25.0.
[2] Percentages are calculated with the number of subjects in the Safety Analysis Set as the denominator (N).
[3] Only System Organ Classes and preferred Terms are shown with at least 10% of all patients in at least one treatment arm.

4.25 Subgruppenergebnisse aus dem indirekten Vergleich

Endpunkt	Effektschätzer	unteres 95% KI	oberes 95% KI	p-Wert	Effektschätzer	Gruppe	Subgruppe	Interaktionswert
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	2,340	0,608	9,006	0,2164	RR	Region	Europe	0,4203
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	1,272	0,685	2,360	0,4462	RR	Region	RoW	0,4203
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	13,997	0,699	280,117	0,0843	OR	Region	Europe	0,4203
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	2,204	0,340	14,302	0,4074	OR	Region	RoW	0,4203
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	0,508	-0,035	1,051	0,0667	RD	Region	Europe	0,4203
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	0,164	-0,231	0,559	0,4162	RD	Region	RoW	0,4203
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	2,926	1,259	6,801	0,0126	RR	Gender	Female	0,0353
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	0,746	0,288	1,936	0,5475	RR	Gender	Male	0,0353
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	18,997	2,533	142,481	0,0042	OR	Gender	Female	0,0353
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	0,185	0,010	3,537	0,2624	OR	Gender	Male	0,0353
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	0,631	0,217	1,045	0,0028	RD	Gender	Female	0,0353
Angioedema Quality of Life Questionnaire (AE-QoL), Gesamtscore, MID = 6	-0,213	-0,716	0,290	0,4065	RD	Gender	Male	0,0353
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	0,84494	0,161315	4,425632	0,8419	RR	Region	Europe	0,539169
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	1,545	0,577426	4,13391	0,3863	RR	Region	RoW	0,539169
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	3,428767	0,153706	76,48639	0,4367	OR	Region	Europe	0,539169
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	17,19247	1,377202	214,6244	0,0272	OR	Region	RoW	0,539169
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	0,208	-0,28348	0,699481	0,4068	RD	Region	Europe	0,539169
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	0,946	0,598985	1,293015	0	RD	Region	RoW	0,539169
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	1,399	0,523	3,744	0,5038	RR	Gender	Female	0,7003
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	0,960	0,185	4,985	0,9610	RR	Gender	Male	0,7003
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	6,769	0,781	58,673	0,0826	OR	Gender	Female	0,7003
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	9,583	0,272	337,424	0,2136	OR	Gender	Male	0,7003
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	0,302	-0,083	0,687	0,1239	RD	Gender	Female	0,7003
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 50 %	0,296	-0,107	0,699	0,1501	RD	Gender	Male	0,7003
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	2,216	0,140	35,131	0,5726	RR	Region	Europe	0,8184
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	1,547	0,408	5,861	0,5210	RR	Region	RoW	0,8184
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	16,363	0,382	701,586	0,1449	OR	Region	Europe	0,8184

Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	8,802	0,905	85,645	0,0610	OR	Region	RoW	0,8184
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	0,576	0,176	0,976	0,0047	RD	Region	Europe	0,8184
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	0,333	0,014	0,652	0,0407	RD	Region	RoW	0,8184
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	3,254	0,696	15,215	0,1338	RR	Gender	Female	0,1901
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	0,337	0,016	6,916	0,4803	RR	Gender	Male	0,1901
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	16,381	1,692	158,632	0,0158	OR	Gender	Female	0,1901
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	3,116	0,041	235,836	0,6066	OR	Gender	Male	0,1901
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	0,526	0,182	0,870	0,0027	RD	Gender	Female	0,1901
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 70 %	0,272	-0,066	0,610	0,1146	RD	Gender	Male	0,1901
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	3,409	0,062	186,976	0,5483	RR	Region	Europe	0,8825
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	2,447	0,400	14,977	0,3328	RR	Region	RoW	0,8825
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	13,284	0,154	1148,956	0,2557	OR	Region	Europe	0,8825
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	6,250	0,661	59,133	0,1100	OR	Region	RoW	0,8825
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	0,680	0,358	1,002	0,0000	RD	Region	Europe	0,8825
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	0,442	0,133	0,751	0,0051	RD	Region	RoW	0,8825
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	6,191	0,584	65,642	0,1302	RR	Gender	Female	0,4149
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	1,114	0,038	32,727	0,9502	RR	Gender	Male	0,4149
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	16,109	1,048	247,613	0,0462	OR	Gender	Female	0,4149
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	5,471	0,108	277,520	0,3962	OR	Gender	Male	0,4149
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	0,541	0,236	0,846	0,0005	RD	Gender	Female	0,4149
Anteil der Ansprecher (Patienten mit einer relativen Reduktion von adjustierten bestätigten HAE-Attacken um mindestens 90 %	0,510	0,170	0,850	0,0032	RD	Gender	Male	0,4149
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	3,887	0,060	251,739	0,5234	RR	Region	Europe	0,5534
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	21,690	0,455	1033,097	0,1185	RR	Region	RoW	0,5534
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	7,483	0,083	672,888	0,3806	OR	Region	Europe	0,5534

Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	58,140	1,003	3370,774	0,0498	OR	Region	RoW	0,5534
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	0,481	0,129	0,833	0,0074	RD	Region	Europe	0,5534
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	0,640	0,436	0,844	0,0000	RD	Region	RoW	0,5534
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	49,600	0,759	3240,320	0,0671	RR	Gender	Female	0,3792
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	3,664	0,065	206,440	0,5278	RR	Gender	Male	0,3792
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	130,718	1,580	10817,132	0,0305	OR	Gender	Female	0,3792
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	7,720	0,102	587,120	0,3551	OR	Gender	Male	0,3792
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	0,665	0,445	0,885	0,0000	RD	Gender	Female	0,3792
Anzahl und Anteil der Patienten ohne bestätigte HAE-Attacke während der Behandlungsphase	0,497	0,186	0,808	0,0017	RD	Gender	Male	0,3792
Anzahl von HAE-Attacken während der Behandlungsphase	0,069	0,012	0,392	0,0026	RR	Region	Europe	0,1915
Anzahl von HAE-Attacken während der Behandlungsphase	0,259	0,099	0,679	0,0060	RR	Region	RoW	0,1915
Anzahl von HAE-Attacken während der Behandlungsphase	0,225	0,090	0,565	0,0015	RR	Gender	Female	0,2694
Anzahl von HAE-Attacken während der Behandlungsphase	0,081	0,017	0,387	0,0016	RR	Gender	Male	0,2694
Rate der bestätigten HAE-Attacken, welche eine akute Behandlung erfordern	0,048	0,005	0,436	0,0070	RR	Region	Europe	0,1737
Rate der bestätigten HAE-Attacken, welche eine akute Behandlung erfordern	0,273	0,083	0,899	0,0328	RR	Region	RoW	0,1737
Rate der bestätigten HAE-Attacken, welche eine akute Behandlung erfordern	0,222	0,076	0,652	0,0062	RR	Gender	Female	0,2439
Rate der bestätigten HAE-Attacken, welche eine akute Behandlung erfordern	0,056	0,007	0,439	0,0062	RR	Gender	Male	0,2439
Rate von moderaten oder schweren bestätigten HAEAttacken	0,105	0,031	0,350	0,0002	RR	Gender	Female	0,9300
Rate von moderaten oder schweren bestätigten HAEAttacken	0,094	0,011	0,794	0,0299	RR	Gender	Male	0,9300
Rate von moderaten oder schweren bestätigten HAE-Attacken	0,053	0,005	0,532	0,0126	RR	Region	Europe	0,4899
Rate von moderaten oder schweren bestätigten HAE-Attacken	0,135	0,036	0,506	0,0030	RR	Region	RoW	0,4899
Zeit bis zur ersten bestätigten HAE-Attacke	0,048	0,005	0,444	0,0075	HR	Region	Europe	0,2234
Zeit bis zur ersten bestätigten HAE-Attacke	0,218	0,080	0,596	0,0030	HR	Region	RoW	0,2234
Zeit bis zur ersten bestätigten HAE-Attacke	0,088	0,028	0,274	0,0000	HR	Gender	Female	0,1116
Zeit bis zur ersten bestätigten HAE-Attacke	0,372	0,095	1,457	0,1556	HR	Gender	Male	0,1116
Anzahl der Patienten mit ≥ 1 UE	0,480	0,040	5,754	0,5623	OR	Region	Europe	0,5684
Anzahl der Patienten mit ≥ 1 UE	0,870	0,133	5,704	0,8846	OR	Region	RoW	0,5684
Anzahl der Patienten mit ≥ 1 UE	0,660	0,213	2,045	0,4713	RR	Region	Europe	0,5684
Anzahl der Patienten mit ≥ 1 UE	0,970	0,489	1,925	0,9299	RR	Region	RoW	0,5684
Anzahl der Patienten mit ≥ 1 UE	-0,128	-0,640	0,384	0,6243	RD	Region	Europe	0,5684
Anzahl der Patienten mit ≥ 1 UE	0,014	-0,354	0,382	0,9405	RD	Region	RoW	0,5684
Anzahl der Patienten mit ≥ 1 UE	1,755	0,324	9,503	0,5139	OR	Gender	Female	0,1229
Anzahl der Patienten mit ≥ 1 UE	0,117	0,010	1,347	0,0852	OR	Gender	Male	0,1229
Anzahl der Patienten mit ≥ 1 UE	1,398	0,519	3,765	0,5078	RR	Gender	Female	0,1229
Anzahl der Patienten mit ≥ 1 UE	0,515	0,233	1,138	0,1007	RR	Gender	Male	0,1229

Anzahl der Patienten mit ≥ 1 UE	-0,838	-1,403	-0,273	0,0036	RD	Gender	Female	0,1229
Anzahl der Patienten mit ≥ 1 UE	-0,039	-0,505	0,427	0,8696	RD	Gender	Male	0,1229

HAE: hereditäres Angioödem (hereditary angioedema); HR: Hazard Ratio; MID: Bedeutsamkeitsschwelle klinischer Relevanz (minimal important difference); OR: odds ratio; RD: risk difference; RR: rate ratio; RoW: Rest of World; UE: unerwünschtes Ereignis