

**Table 14.2-2.1: Summary of Corneal Fluorescein Staining by NEI Scale (Full Analysis Set)**

Visit		Pro-ocular 0.5% (N=29) n (%)	Pro-ocular 1% (N=30) n (%)	Placebo (N=30) n (%)	Overall (N=89) n (%)
Baseline	n (missing)	29 (0)	30 (0)	30 (0)	89 (0)
	Mean (SD)	7.4 (3.00)	7.7 (2.88)	8.2 (3.47)	7.8 (3.11)
	Median	7.0	7.0	8.0	7.0
	Q1, Q3	5.0, 9.0	5.0, 10.0	5.0, 11.0	5.0, 10.0
	Min, Max	4, 15	4, 13	4, 15	4, 15
Week 2	n (missing)	28 (1)	28 (2)	30 (0)	86 (3)
	Mean (SD)	4.8 (3.51)	5.5 (3.88)	5.8 (2.98)	5.4 (3.45)
	Median	4.0	5.0	5.0	5.0
	Q1, Q3	2.0, 7.0	2.0, 8.5	4.0, 8.0	3.0, 7.0
	Min, Max	0, 15	0, 14	1, 12	0, 15
Week 2 change from Baseline	n (missing)	28 (1)	28 (2)	30 (0)	86 (3)
	Mean (SD)	-2.5 (3.91)	-2.1 (2.20)	-2.4 (3.54)	-2.3 (3.27)
	Median	-2.0	-2.0	-2.0	-2.0
	Q1, Q3	-4.0, 0.0	-3.0, 0.0	-5.0, 0.0	-4.0, 0.0
	Min, Max	-12, 8	-7, 2	-10, 3	-12, 8

**Table 14.2-2.1: Summary of Corneal Fluorescein Staining by NEI Scale (Full Analysis Set)**

Visit		Pro-ocular 0.5% (N=29) n (%)	Pro-ocular 1% (N=30) n (%)	Placebo (N=30) n (%)	Overall (N=89) n (%)
Week 4	n (missing)	28 (1)	29 (1)	30 (0)	87 (2)
	Mean (SD)	4.2 (2.02)	5.9 (3.19)	5.1 (3.10)	5.1 (2.88)
	Median	4.0	5.0	3.5	4.0
	Q1, Q3	2.5, 6.0	4.0, 9.0	3.0, 8.0	3.0, 7.0
	Min, Max	1, 8	1, 14	2, 12	1, 14
Week 4 change from Baseline	n (missing)	28 (1)	29 (1)	30 (0)	87 (2)
	Mean (SD)	-3.1 (3.52)	-1.9 (1.93)	-3.1 (3.38)	-2.7 (3.05)
	Median	-1.0	-2.0	-2.0	-2.0
	Q1, Q3	-6.0, -1.0	-3.0, 0.0	-5.0, -1.0	-4.0, -1.0
	Min, Max	-11, 0	-6, 2	-11, 1	-11, 2
Week 8	n (missing)	24 (5)	28 (2)	28 (2)	80 (9)
	Mean (SD)	4.0 (2.82)	4.8 (3.08)	4.9 (3.98)	4.6 (3.34)
	Median	4.5	4.0	4.0	4.0
	Q1, Q3	1.5, 6.0	3.0, 7.0	1.0, 6.5	2.0, 6.0
	Min, Max	0, 11	0, 11	0, 15	0, 15

**Table 14.2-2.1: Summary of Corneal Fluorescein Staining by NEI Scale (Full Analysis Set)**

Visit		Pro-ocular 0.5% (N=29) n (%)	Pro-ocular 1% (N=30) n (%)	Placebo (N=30) n (%)	Overall (N=89) n (%)
Week 8 change from Baseline	n (missing)	24 (5)	28 (2)	28 (2)	80 (9)
	Mean (SD)	-3.4 (3.94)	-3.1 (2.46)	-3.4 (4.51)	-3.3 (3.68)
	Median	-2.0	-3.0	-3.0	-3.0
	Q1, Q3	-5.0, 0.0	-4.0, -1.0	-6.5, -1.0	-5.5, -1.0
	Min, Max	-13, 1	-8, 0	-12, 9	-13, 9
Week 12	n (missing)	24 (5)	28 (2)	27 (3)	79 (10)
	Mean (SD)	4.2 (2.63)	5.9 (3.83)	4.4 (3.23)	4.9 (3.35)
	Median	4.0	4.5	4.0	4.0
	Q1, Q3	2.0, 6.0	3.0, 9.5	1.0, 7.0	2.0, 7.0
	Min, Max	0, 11	1, 13	0, 11	0, 13
Week 12 change from Baseline	n (missing)	24 (5)	28 (2)	27 (3)	79 (10)
	Mean (SD)	-2.9 (3.81)	-2.0 (2.36)	-4.0 (3.45)	-2.9 (3.30)
	Median	-1.0	-1.5	-3.0	-2.0
	Q1, Q3	-4.5, 0.0	-4.0, 0.0	-6.0, -1.0	-4.0, -1.0
	Min, Max	-12, 1	-7, 2	-12, 1	-12, 2

**Table 14.2-2.2: Analysis of Corneal Fluorescein Staining by NEI Scale (Full Analysis Set)**

Visit		Adjusted Mean		P-value
		n	LS Mean (95% CI)	
Week 2	1% Pro-ocular	28	-2.36 (-3.64, -1.08)	-
	0.5% Pro-ocular	28	-2.89 (-4.19, -1.58)	-
	Placebo	30	-2.38 (-3.69, -1.06)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		0.02 (-1.58, 1.61)	0.984
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		-0.51 (-2.10, 1.08)	0.524
Week 4	1% Pro-ocular	29	-1.93 (-2.98, -0.87)	-
	0.5% Pro-ocular	28	-3.37 (-4.44, -2.30)	-
	Placebo	30	-2.90 (-3.99, -1.81)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		0.97 (-0.33, 2.28)	0.142
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		-0.47 (-1.80, 0.86)	0.486
Week 8	1% Pro-ocular	28	-3.27 (-4.64, -1.90)	-
	0.5% Pro-ocular	24	-3.85 (-5.32, -2.39)	-
	Placebo	28	-3.44 (-4.90, -1.99)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		0.18 (-1.54, 1.89)	0.839
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		-0.41 (-2.21, 1.39)	0.652

N: total number of patients per group. n: number of non-missing observations. CI: Confidence Interval. The change from baseline is analysed by means of an ANCOVA model by Visit with treatment as fixed effect and baseline measure and stratification factor (male, female: menopausal, female: non-menopausal) as covariates.

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**Table 14.2-2.2: Analysis of Corneal Fluorescein Staining by NEI Scale (Full Analysis Set)**

Visit		Adjusted Mean		P-value
		n	LS Mean (95% CI)	
Week 12	1% Pro-ocular	28	-1.91 (-3.20, -0.61)	-
	0.5% Pro-ocular	24	-3.19 (-4.60, -1.77)	-
	Placebo	27	-3.64 (-5.02, -2.26)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		1.73 (0.14, 3.32)	0.034
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		0.45 (-1.23, 2.13)	0.597

N: total number of patients per group. n: number of non-missing observations. CI: Confidence Interval. The change from baseline is analysed by means of an ANCOVA model by Visit with treatment as fixed effect and baseline measure and stratification factor (male, female: menopausal, female: non-menopausal) as covariates.

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**Table 14.2-2.3: Summary of Corneal Fluorescein Staining by NEI Scale (Per-Protocol Set)**

Visit		Pro-ocular 0.5% (N=28) n (%)	Pro-ocular 1% (N=26) n (%)	Placebo (N=25) n (%)	Overall (N=79) n (%)
Baseline	n (missing)	28 (0)	26 (0)	25 (0)	79 (0)
	Mean (SD)	7.3 (3.02)	7.6 (2.79)	7.7 (3.13)	7.5 (2.95)
	Median	7.0	7.0	7.0	7.0
	Q1, Q3	5.0, 9.0	5.0, 9.0	5.0, 10.0	5.0, 9.0
	Min, Max	4, 15	4, 13	4, 15	4, 15
Week 2	n (missing)	27 (1)	26 (0)	25 (0)	78 (1)
	Mean (SD)	4.7 (3.52)	5.4 (3.64)	6.0 (2.86)	5.4 (3.36)
	Median	4.0	5.0	5.0	5.0
	Q1, Q3	2.0, 7.0	2.0, 8.0	4.0, 8.0	3.0, 7.0
	Min, Max	0, 15	0, 14	1, 12	0, 15
Week 2 change from Baseline	n (missing)	27 (1)	26 (0)	25 (0)	78 (1)
	Mean (SD)	-2.5 (3.98)	-2.2 (2.19)	-1.7 (3.14)	-2.2 (3.18)
	Median	-2.0	-2.0	-1.0	-2.0
	Q1, Q3	-4.0, 0.0	-3.0, 0.0	-4.0, 1.0	-4.0, 0.0
	Min, Max	-12, 8	-7, 2	-8, 3	-12, 8

**Table 14.2-2.3: Summary of Corneal Fluorescein Staining by NEI Scale (Per-Protocol Set)**

Visit		Pro-ocular 0.5% (N=28) n (%)	Pro-ocular 1% (N=26) n (%)	Placebo (N=25) n (%)	Overall (N=79) n (%)
Week 4	n (missing)	27 (1)	26 (0)	25 (0)	78 (1)
	Mean (SD)	4.1 (2.03)	6.0 (3.20)	5.2 (3.11)	5.1 (2.89)
	Median	4.0	5.0	3.0	4.0
	Q1, Q3	2.0, 6.0	4.0, 9.0	3.0, 8.0	3.0, 7.0
	Min, Max	1, 8	1, 14	2, 12	1, 14
Week 4 change from Baseline	n (missing)	27 (1)	26 (0)	25 (0)	78 (1)
	Mean (SD)	-3.0 (3.58)	-1.6 (1.79)	-2.5 (3.02)	-2.4 (2.92)
	Median	-1.0	-2.0	-1.0	-1.0
	Q1, Q3	-7.0, -1.0	-3.0, 0.0	-4.0, -1.0	-3.0, 0.0
	Min, Max	-11, 0	-5, 2	-11, 1	-11, 2
Week 8	n (missing)	24 (4)	25 (1)	23 (2)	72 (7)
	Mean (SD)	4.0 (2.82)	5.0 (3.08)	5.5 (4.07)	4.8 (3.36)
	Median	4.5	4.0	5.0	4.0
	Q1, Q3	1.5, 6.0	3.0, 7.0	2.0, 8.0	2.5, 6.5
	Min, Max	0, 11	0, 11	1, 15	0, 15

**Table 14.2-2.3: Summary of Corneal Fluorescein Staining by NEI Scale (Per-Protocol Set)**

Visit		Pro-ocular 0.5% (N=28) n (%)	Pro-ocular 1% (N=26) n (%)	Placebo (N=25) n (%)	Overall (N=79) n (%)
Week 8 change from Baseline	n (missing)	24 (4)	25 (1)	23 (2)	72 (7)
	Mean (SD)	-3.4 (3.94)	-2.8 (2.38)	-2.2 (3.94)	-2.8 (3.47)
	Median	-2.0	-2.0	-3.0	-2.0
	Q1, Q3	-5.0, 0.0	-4.0, -1.0	-4.0, 0.0	-4.0, -0.5
	Min, Max	-13, 1	-8, 0	-11, 9	-13, 9
Week 12	n (missing)	23 (5)	26 (0)	22 (3)	71 (8)
	Mean (SD)	3.9 (2.24)	5.7 (3.71)	4.5 (3.04)	4.7 (3.14)
	Median	4.0	4.0	4.5	4.0
	Q1, Q3	2.0, 6.0	3.0, 9.0	2.0, 7.0	2.0, 7.0
	Min, Max	0, 8	1, 13	0, 11	0, 13
Week 12 change from Baseline	n (missing)	23 (5)	26 (0)	22 (3)	71 (8)
	Mean (SD)	-3.0 (3.81)	-2.0 (2.09)	-3.4 (3.20)	-2.8 (3.10)
	Median	-1.0	-1.5	-3.0	-2.0
	Q1, Q3	-5.0, 0.0	-4.0, 0.0	-5.0, -1.0	-4.0, -1.0
	Min, Max	-12, 1	-6, 1	-12, 1	-12, 1



**Table 14.2-2.4: Analysis of Corneal Fluorescein Staining by NEI Scale (Per-Protocol Set)**

Visit		Adjusted Mean		P-value
		n	LS Mean (95% CI)	
Week 2	1% Pro-ocular	26	-2.36 (-3.67, -1.05)	-
	0.5% Pro-ocular	27	-2.87 (-4.17, -1.57)	-
	Placebo	25	-1.80 (-3.19, -0.42)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		-0.56 (-2.20, 1.09)	0.504
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		-1.06 (-2.70, 0.57)	0.199
Week 4	1% Pro-ocular	26	-1.65 (-2.75, -0.54)	-
	0.5% Pro-ocular	27	-3.30 (-4.37, -2.23)	-
	Placebo	25	-2.49 (-3.65, -1.33)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		0.84 (-0.55, 2.23)	0.232
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		-0.81 (-2.20, 0.58)	0.248
Week 8	1% Pro-ocular	25	-2.93 (-4.35, -1.51)	-
	0.5% Pro-ocular	24	-3.70 (-5.15, -2.26)	-
	Placebo	23	-2.41 (-3.96, -0.85)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		-0.52 (-2.34, 1.30)	0.570
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		-1.30 (-3.16, 0.57)	0.169

N: total number of patients per group. n: number of non-missing observations. CI: Confidence Interval. The change from baseline is analysed by means of an ANCOVA model by Visit with treatment as fixed effect and baseline measure and stratification factor (male, female: menopausal, female: non-menopausal) as covariates.

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**Table 14.2-2.4: Analysis of Corneal Fluorescein Staining by NEI Scale (Per-Protocol Set)**

Visit		Adjusted Mean		P-value
		n	LS Mean (95% CI)	
Week 12	1% Pro-ocular	26	-1.95 (-3.21, -0.69)	-
	0.5% Pro-ocular	23	-3.39 (-4.75, -2.02)	-
	Placebo	22	-3.26 (-4.69, -1.83)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		1.31 (-0.32, 2.94)	0.113
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		-0.12 (-1.81, 1.56)	0.883

N: total number of patients per group. n: number of non-missing observations. CI: Confidence Interval. The change from baseline is analysed by means of an ANCOVA model by Visit with treatment as fixed effect and baseline measure and stratification factor (male, female: menopausal, female: non-menopausal) as covariates.

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