

Table 14.2-2.32: Summary of Non-Invasive Keratograph Tear Film Break Up Time (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)	28 (1)	27 (3)	30 (0)	85 (4)
	Mean (SD)	4.2 (1.96)	5.1 (3.26)	5.8 (4.76)	5.0 (3.58)
	Median	4.0	3.7	3.7	3.7
	Q1, Q3	3.0, 4.3	3.0, 6.7	2.3, 7.3	3.0, 6.0
	Min, Max	2, 11	2, 15	2, 23	2, 23
Week 2	n (missing)	25 (4)	27 (3)	30 (0)	82 (7)
	Mean (SD)	6.7 (3.76)	6.5 (4.07)	5.8 (3.14)	6.3 (3.63)
	Median	6.0	4.7	4.8	5.0
	Q1, Q3	4.0, 9.3	3.7, 8.0	3.3, 7.7	3.7, 9.0
	Min, Max	0, 14	2, 16	2, 14	0, 16
Week 2 change from Baseline	n (missing)	25 (4)	26 (4)	30 (0)	81 (8)
	Mean (SD)	2.6 (3.86)	1.5 (4.84)	0.0 (4.43)	1.3 (4.48)
	Median	1.7	0.5	0.3	0.7
	Q1, Q3	0.0, 5.3	-1.0, 3.0	-1.3, 2.7	-0.7, 3.0
	Min, Max	-3, 12	-8, 13	-14, 8	-14, 13

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Week 4	n (missing)	25 (4)	25 (5)	29 (1)	79 (10)
	Mean (SD)	7.8 (4.73)	6.2 (4.70)	5.7 (3.35)	6.6 (4.30)
	Median	6.7	4.3	4.0	4.3
	Q1, Q3	4.3, 11.3	4.0, 6.0	3.0, 7.7	3.7, 8.7
	Min, Max	3, 21	3, 22	2, 16	2, 22
Week 4 change from Baseline	n (missing)	25 (4)	25 (5)	29 (1)	79 (10)
	Mean (SD)	3.5 (5.14)	1.0 (4.81)	-0.1 (6.09)	1.4 (5.56)
	Median	2.0	0.3	0.0	0.7
	Q1, Q3	0.0, 7.7	-1.3, 2.0	-2.0, 2.0	-1.0, 3.3
	Min, Max	-5, 16	-9, 12	-20, 13	-20, 16
Week 8	n (missing)	21 (8)	24 (6)	28 (2)	73 (16)
	Mean (SD)	7.2 (3.95)	5.8 (3.56)	6.8 (4.41)	6.5 (4.00)
	Median	6.0	4.8	5.2	5.3
	Q1, Q3	4.3, 8.3	3.5, 7.2	3.3, 9.0	3.7, 8.3
	Min, Max	3, 17	2, 17	2, 21	2, 21

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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)	21 (8)	24 (6)	28 (2)	73 (16)
	Mean (SD)	3.0 (4.20)	1.0 (4.70)	1.8 (4.56)	1.8 (4.51)
	Median	2.0	1.0	1.0	1.0
	Q1, Q3	0.0, 4.3	-1.2, 3.0	-0.2, 3.8	-0.3, 3.7
	Min, Max	-2, 13	-10, 14	-7, 19	-10, 19
Week 12	n (missing)	23 (6)	26 (4)	27 (3)	76 (13)
	Mean (SD)	6.6 (3.53)	6.6 (4.70)	6.1 (3.81)	6.4 (4.01)
	Median	4.7	5.5	5.3	5.2
	Q1, Q3	4.0, 10.7	3.3, 8.3	3.0, 9.0	3.3, 9.2
	Min, Max	2, 14	2, 19	2, 17	2, 19
Week 12 change from Baseline	n (missing)	23 (6)	26 (4)	27 (3)	76 (13)
	Mean (SD)	2.3 (3.78)	1.4 (5.43)	1.1 (4.57)	1.6 (4.64)
	Median	1.0	0.0	0.3	0.3
	Q1, Q3	-0.7, 6.3	-1.0, 2.7	-1.0, 4.0	-1.0, 3.5
	Min, Max	-2, 10	-9, 16	-10, 11	-10, 16

Table 14.2-2.33: Analysis of Non-Invasive Keratograph Tear Film Break Up Time (Full Analysis Set)

Visit		Adjusted Mean		P-value
		n	LS Mean (95% CI)	
Week 2	1% Pro-ocular	26	1.56 (-0.01, 3.14)	-
	0.5% Pro-ocular	25	1.94 (0.35, 3.54)	-
	Placebo	30	0.48 (-1.09, 2.05)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		1.09 (-0.82, 2.99)	0.260
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		1.47 (-0.50, 3.43)	0.141
Week 4	1% Pro-ocular	25	1.71 (-0.27, 3.68)	-
	0.5% Pro-ocular	25	3.25 (1.35, 5.15)	-
	Placebo	29	1.26 (-0.65, 3.17)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		0.45 (-1.89, 2.78)	0.704
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		1.99 (-0.39, 4.37)	0.101
Week 8	1% Pro-ocular	24	1.19 (-0.60, 2.98)	-
	0.5% Pro-ocular	21	2.58 (0.70, 4.46)	-
	Placebo	28	2.30 (0.50, 4.11)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		-1.11 (-3.30, 1.08)	0.315
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		0.27 (-2.03, 2.58)	0.813

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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Page 1 of 2

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Visit		Adjusted Mean		P-value
		n	LS Mean (95% CI)	
Week 12	1% Pro-ocular	26	1.53 (-0.35, 3.41)	-
	0.5% Pro-ocular	23	1.70 (-0.24, 3.64)	-
	Placebo	27	1.10 (-0.80, 3.01)	-
	LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		0.43 (-1.81, 2.67)	0.705
	LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		0.59 (-1.74, 2.93)	0.613

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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Page 2 of 2