

Table 20 Summary of Intensity of Dryness / Irritation Patient Feeling assessed by SANDE (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 (%)
Frequency of Symptoms (mm)					
Baseline	n (missing)	29 (0)	30 (0)	30 (0)	89 (0)
	Mean (SD)	72.0 (26.58)	65.7 (28.12)	75.5 (23.69)	71.0 (26.21)
	Median	79.0	68.0	75.5	75.0
	Q1, Q3	54.0, 96.0	49.0, 88.0	62.0, 98.0	54.0, 96.0
	Min, Max	21, 100	0, 100	23, 100	0, 100
Week 12	n (missing)	25 (4)	28 (2)	27 (3)	80 (9)
	Mean (SD)	47.7 (28.56)	43.9 (30.52)	44.6 (26.51)	45.3 (28.29)
	Median	42.0	43.5	50.0	46.5
	Q1, Q3	30.0, 74.0	13.0, 68.5	26.0, 62.0	19.5, 69.0
	Min, Max	0, 100	2, 96	2, 100	0, 100
Week 12 change from Baseline	n (missing)	25 (4)	28 (2)	27 (3)	80 (9)
	Mean (SD)	-27.6 (27.43)	-22.3 (24.60)	-31.5 (27.50)	-27.0 (26.44)
	Median	-24.0	-18.5	-35.0	-23.5
	Q1, Q3	-45.0, -7.0	-40.0, -2.0	-49.0, -5.0	-46.0, -3.0
	Min, Max	-94, 28	-77, 21	-91, 3	-94, 28
Severity of Symptoms (mm)					
Baseline	n (missing)	29 (0)	30 (0)	30 (0)	89 (0)
	Mean (SD)	69.1 (26.54)	63.0 (31.31)	74.5 (23.11)	68.9 (27.30)
	Median	75.0	69.5	73.5	74.0
	Q1, Q3	48.0, 96.0	37.0, 90.0	53.0, 97.0	48.0, 96.0
	Min, Max	19, 100	1, 100	30, 100	1, 100
Week 12	n (missing)	25 (4)	28 (2)	27 (3)	80 (9)
	Mean (SD)	46.0 (28.71)	43.0 (33.54)	43.8 (26.17)	44.2 (29.36)
	Median	43.0	33.5	49.0	46.0
	Q1, Q3	30.0, 67.0	9.0, 76.5	16.0, 64.0	15.5, 66.5
	Min, Max	0, 100	3, 100	2, 100	0, 100

Visit		Pro-ocular 0.5% (N=29) n (%)	Pro-ocular 1% (N=30) n (%)	Placebo (N=30) n (%)	Overall (N=89) n (%)
Week 12 change from Baseline	n (missing)	25 (4)	28 (2)	27 (3)	80 (9)
	Mean (SD)	-25.7 (28.30)	-20.6 (22.31)	-32.3 (27.77)	-26.2 (26.29)
	Median	-19.0	-21.5	-35.0	-25.0
	Q1, Q3	-43.0, -9.0	-38.0, -2.0	-53.0, -4.0	-46.0, -4.5
	Min, Max	-73, 30	-68, 30	-90, 13	-90, 30
Global Score (mm)					
Baseline	n (missing)	29 (0)	30 (0)	30 (0)	89 (0)
	Mean (SD)	70.2 (26.01)	63.9 (29.25)	74.7 (22.97)	69.6 (26.29)
	Median	77.0	68.2	73.2	73.0
	Q1, Q3	54.4, 93.5	43.9, 87.5	58.7, 97.0	53.5, 94.0
	Min, Max	20, 100	0, 100	28, 100	0, 100
Week 12	n (missing)	25 (4)	28 (2)	27 (3)	80 (9)
	Mean (SD)	46.6 (28.22)	42.8 (31.54)	44.0 (26.14)	44.4 (28.45)
	Median	42.5	35.2	49.0	43.6
	Q1, Q3	30.0, 68.5	10.6, 72.4	18.3, 61.5	18.1, 66.8
	Min, Max	0, 100	2, 95	2, 100	0, 100
Week 12 change from Baseline	n (missing)	25 (4)	28 (2)	27 (3)	80 (9)
	Mean (SD)	-26.6 (27.60)	-21.6 (22.35)	-31.9 (27.20)	-26.7 (25.77)
	Median	-22.6	-22.1	-38.1	-23.3
	Q1, Q3	-44.6, -9.0	-37.6, -3.0	-50.5, -4.5	-46.4, -4.5
	Min, Max	-83, 30	-69, 21	-91, 5	-91, 30
Global Score LOCF (mm)					
Baseline	n (missing)	29 (0)	30 (0)	30 (0)	89 (0)
	Mean (SD)	70.2 (26.01)	63.9 (29.25)	74.7 (22.97)	69.6 (26.29)
	Median	77.0	68.2	73.2	73.0
	Q1, Q3	54.4, 93.5	43.9, 87.5	58.7, 97.0	53.5, 94.0
	Min, Max	20, 100	0, 100	28, 100	0, 100
Week 12	n (missing)	29 (0)	30 (0)	30 (0)	89 (0)
	Mean (SD)	48.4 (28.23)	44.1 (32.25)	45.1 (25.62)	45.8 (28.57)
	Median	43.1	35.2	49.3	47.4
	Q1, Q3	30.0, 70.4	11.2, 74.6	25.5, 61.5	20.8, 68.5
	Min, Max	0, 100	2, 98	2, 100	0, 100
Week 12 change from Baseline	n (missing)	29 (0)	30 (0)	30 (0)	89 (0)
	Mean (SD)	-21.8 (30.07)	-19.9 (22.66)	-29.7 (26.89)	-23.8 (26.71)
	Median	-17.5	-18.6	-24.8	-19.2
	Q1, Q3	-42.5, -5.0	-37.1, -1.5	-49.6, -4.5	-44.6, -4.3
	Min, Max	-83, 54	-69, 21	-91, 5	-91, 54

Source: Table 14.2.2.25, Statistical Output in Appendix 16.2.

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Table 21 Analysis of Intensity of Dryness / Irritation Patient Feeling assessed by SANDE (Full Analysis Set)

Visit: Week 12	Adjusted Mean		
	n	LS Mean (95% CI)	P-value
Frequency of Symptoms			
1% Pro-ocular	28	-23.17 (-34.24;-12.11)	-
0.5% Pro-ocular	25	-24.46 (-36.00;-12.93)	-
Placebo	27	-28.43 (-39.93;-16.92)	-
LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		5.25 (-8.35;18.85)	0.444
LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		3.96 (-9.89;17.81)	0.570
Severity of Symptoms			
1% Pro-ocular	28	-20.68 (-31.70;-9.66)	-
0.5% Pro-ocular	25	-22.49 (-33.95;-11.02)	-
Placebo	27	-28.09 (-39.56;-16.62)	-
LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		7.41 (-6.20;21.02)	0.282
LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		5.60 (-8.20;19.40)	0.421
Global Score			
1% Pro-ocular	28	-22.06 (-32.92;-11.21)	-
0.5% Pro-ocular	25	-23.49 (-34.78;-12.19)	-
Placebo	27	-28.23 (-39.51;-16.94)	-
LS Mean Difference, 1% Pro-ocular – Placebo (95% CI)		6.16 (-7.22;19.55)	0.362
LS Mean Difference, 0.5% Pro-ocular – Placebo (95% CI)		4.74 (-8.84;18.31)	0.489

Source: Table 14.2.2.26, Statistical Output in Appendix 16.2.

Global Score, Intensity of Dryness / Irritation Patient Feeling assessed by SANDE at Week 12 (with LOCF): Combined analyses of the Frequency and Severity scale.

Abbreviations: 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.