Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

Definition of study eye

For enrolled subjects, both eyes were evaluated, and the eye with the smaller MRD-1 was defined as the study eye. If MRD-1 was the same in both eyes, the eye with the greater visual field deficit was defined as the study eye. If ptosis was present in both eyes and MRD-1 was ≤0 in one eye, then the eye with measurable MRD-1 (≥0.5 mm) was defined as the study eye.

Randomization

Randomization schemes were created by an independent biostatistician using a block design. Study sites accessed the Interactive Web Response System to randomize subjects to study treatment and to assign the study medication kit to be dispensed. Drug kit and randomization numbers were recorded in each subject's electronic case report form.

eTable 1. Subject disposition and demographics, individual studies included in pooled analysis.

	Study RVL-1201-201 (N=140)		Study RVL-1201-202 (N=164)	
	Oxymetazoline 0.1% (n=94)	**Vehicle (n=46)**	**Oxymetazoline 0.1% (n=109)**	**Vehicle (n=55)**
Subjects enrolled	94	46	109	55
Subjects completing all visits, n (%)	90 (95.7%)	45 (97.8%)	108 (99.1%)	53 (96.4%)
Compliance with treatment, mean % (SD)[a]	97.4 (11.9)	95.7 (15.0)	98.7 (4.5)	98.5 (4.4)
Treatment exposure, mean days (SD)	41.6 (6.4)	42.7 (1.6)	42.4 (2.9)	41.6 (7.0)
Age, years				
Mean (SD)	64.7 (12.2)	65.5 (12.5)	63.6 (14.3)	63.3 (16.5)
Min, max	22, 83	26, 85	20, 92	14, 85
Sex, n (%)				
Female	74 (78.7%)	32 (69.6%)	77 (70.6%)	39 (70.9%)
Male	20 (21.3%)	14 (30.4%)	32 (29.4%)	16 (29.1%)
Race, n (%)				
White	78 (83.0%)	42 (91.3%)	99 (90.8%)	50 (90.9%)
Black	12 (12.8%)	3 (6.5%)	6 (5.5%)	3 (5.5%)
Asian	2 (2.1%)	1 (2.2%)	4 (3.7%)	2 (3.6%)
American Indian	2 (2.1%)	0	0	0
Ethnicity, n (%)				

Not Hispanic/Latino	74 (78.7%)	35 (76.1%)	96 (88.1%)	49 (89.1%)
Hispanic/Latino	20 (21.3%)	11 (23.9%)	13 (11.9%)	6 (10.9%)
Baseline points seen, top 4 rows, LPFT				
Mean (SD)	17.0 (4.4)	16.9 (5.2)	17.6 (4.9)	17.6 (5.5)
Median	17.0	17.0	18.0	18.0
Minimum, maximum	8, 27	2, 25	8, 27	10, 26
Baseline MRD-1, mm				
Mean (SD)	1.16 (0.66)	1.03 (0.68)	1.04 (0.74)	1.07 (0.70)
Median	1.00	1.00	1.00	1.00
Minimum, maximum	0.0, 3.0	0.0, 2.0	0.0, 2.0	0.0, 2.0

LPFT, Leicester Peripheral Field Test; MRD-1, Marginal Reflex Distance; SD, standard deviation

[a] Percentage of opened vials returned relative to the number of vials that should have been used during the treatment period

eTable 2. Primary (mean change from baseline in the number of points seen in the top 4 rows on the Leicester Peripheral Field Test (LPFT)) and secondary (mean change from baseline in Marginal Reflex Distance 1 (MRD-1)) efficacy outcomes, individual studies included in pooled analysis.

	Study RVL-1201-201 (N=140)		**Study RVL-1201-202 (N=164)**	
	Oxymetazoline 0.1% (n=94)	**Vehicle (n=46)**	**Oxymetazoline 0.1% (n=109)**	**Vehicle (n=55)**
LPFT				
Points at baseline, mean (SD)	17.0 (4.4)	16.9 (5.2)	17.6 (4.9)	17.6 (5.5)
Day 1, hour 6				
Change from baseline, mean (SD)	5.2 (6.0)	1.5 (3.9)	6.3 (6.7)	2.1 (4.3)
Mean difference (95% CI), p value [a]	3.67 (2.00, 5.34), p < 0.0001		4.23 (2.36, 6.09), p < 0.0001	
Day 14, hour 2				
Change from baseline, mean (SD)	6.4 (5.0)	2.2 (5.8)	7.7 (6.4)	2.4 (5.3)
Mean difference (95% CI), p value [a]	4.20 (2.30, 6.10), p < 0.0001		5.30 (3.45, 7.14), p < 0.0001	
MRD-1				
Baseline MRD-1, mean mm (SD)	1.16 (0.66)	1.03 (0.58)	1.04 (0.74)	1.07 (0.70)
Day 1, hour 6				
Change from baseline, mean (SD)	0.94 (0.92)	0.67 (1.00)	0.98 (0.87)	0.35 (0.57)
Mean difference (95% CI), p value [a]	0.27 (-0.07, 0.61), p = 0.028		0.61 (0.37, 0.86), p < 0.0001	

Day 14, hour 2				
Change from baseline, mean (SD)	1.09 (0.80)	0.58 (0.88)	1.22 (0.93)	0.43 (0.73)
Mean difference (95% CI), p value [a]	0.52 (0.22, 0.81), p = 0.0004		0.78 (0.50, 1.06), p < 0.0001	

CI, confidence interval; SD, standard deviation

[a] p versus vehicle, from ANCOVA model with treatment as a fixed factor and baseline score as a covariate

eTable 3. Summary of treatment-emergent adverse events (TEAEs), individual studies included in pooled analysis.

	Study RVL-1201-201 (N=140)		Study RVL-1201-202 (N=164)	
	Oxymetazoline 0.1% (n=94)	**Vehicle (n=46)**	**Oxymetazoline 0.1% (n=109)**	**Vehicle (n=55)**
Subjects reporting any TEAE, n (%)	29 (30.9%)	15 (32.6%)	35 (32.1%)	21 (38.2%)
Total TEAEs reported	65	27	65	46
Subjects reporting TEAE by number of TEAEs, n (%)				
0 TEAEs	65 (69.1%)	31 (67.4%)	74 (67.9%)	34 (61.8%)
1 TEAE	9 (9.6%)	9 (19.6%)	15 (13.8%)	9 (16.4%)
>1 TEAE	20 (21.3%)	6 (13.0%)	20 (18.3%)	12 (21.8%)
Subjects reporting TEAE by maximum intensity, n (%)[a]				
Mild	23 (24.5%)	9 (19.6%)	29 (26.6%)	16 (29.1%)
Moderate	4 (4.3%)	6 (13.0%)	6 (5.5%)	5 (9.1%)
Severe	2 (2.1%)	0	0	0
Subjects reporting TEAE by relationship to study drug, n (%)[b]				
Not suspected	18 (19.1%)	11 (23.9%)	22 (20.2%)	16 (29.1%)
Suspected	11 (11.7%)	4 (8.7%)	13 (11.9%)	5 (9.1%)
Subjects reporting any serious TEAE, n (%)	1 (1.1%)	0	1 (0.9%)	1 (1.8%)
Subjects reporting any TEAE leading to discontinuation, n (%)	3 (3.2%)	1 (2.2%)	1 (0.9%)	1 (1.8%)

TEAEs reported for ≥2% of subjects, by MedDRA Preferred Term, events:n (%)				
Punctate keratitis	11:7 (7.4%)	2:2 (4.3%)	8:4 (3.7%)	1:1 (1.8%)
Vision blurred	10:5 (5.3%)	0:0	2:2 (1.8%)	0:0
Ocular hyperemia	5:3 (3.2%)	0:0	0:0	0:0
Conjunctival hyperemia	0:0	0:0	10:6 (5.5%)	2:1 (1.8%)
Eye pain	0:0	0:0	4:3 (2.8%)	0:0
Eye pruritus	0:0	2:1 (2.2%)	0:0	4:2 (3.6%)
Vitreous detachment	0:0	2:2 (4.3%)	0:0	0:0
Instillation site pain	8:4 (4.3%)	0:0	3:2 (1.8%)	0:0
Instillation site complication	2:1 (1.1%)	0:0	0:0	4:2 (3.6%)
Upper respiratory tract infection	2:2 (2.1%)	1:1 (2.2%)	0:0	1:1 (1.8%)
Vital dye staining on cornea	4:2 (2.1%)	0:0	2:1 (0.9%)	4:3 (5.5%)
Headache	2:2 (2.1%)	0:0	0:0	1:1 (1.8%)

MedDRA, Medial Dictionary for Regulatory Activities

[a] Subjects reporting ≥1 TEAE counted once at the maximum intensity of all reported TEAEs

[b] Subjects reporting the same TEAE at more than one relationship counted at the greatest relationship