Safety of Suprachoroidal Injection Procedure Utilizing a Microinjector Across Three Retinal Disorders

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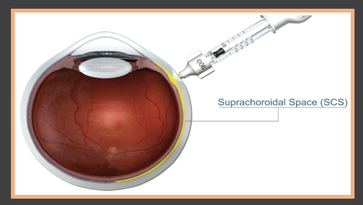


Purpose

- Suprachoroidal injection (SCI) via SCS Microinjector® is an investigational ocular injection developed to provide high, compartmentalized drug concentrations to chorioretinal layers via the suprachoroidal space (SCS).
- This post hoc study evaluated safety of SCIs across multiple clinical trials involving an investigational proprietary suspension of triamcinolone acetonide (CLS-TA), focusing on serious adverse events (SAEs) and events occurring on the day of the injection procedure.

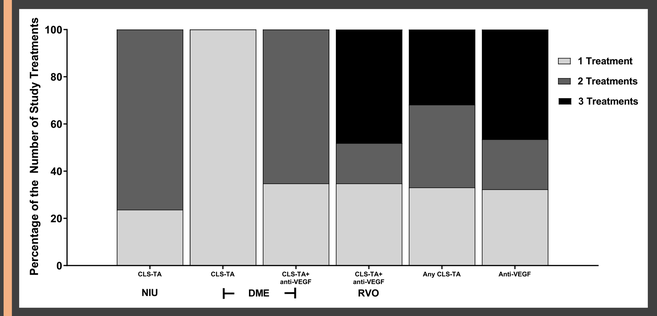
Methods

- Datasets were assessed from 8 clinical trials involving three separate disease states:
  - Noninfectious uveitis (NIU)
  - Diabetic macular edema (DME)
  - Retinal vein occlusion (RVO)
- Patients who received one or more SCI were included, either as monotherapy or in conjunction with an intravitreal (IVT) anti-VEGF.
- Disposition, exposure, demographics and baseline characteristics were summarized by disease state and study treatment.
- Rare but SAEs known to occur with intraocular injections, including lens injury, suprachoroidal hemorrhage, retinal tear, retinal detachment, endophthalmitis and reduced visual acuity were assessed.
- Treatment emergent adverse events (TEAEs) assessed included eye pain on the day of the procedure.
- Outcomes were compared to control eyes randomized to receive IVT anti-VEGF monotherapy in conjunction with a sham SCI.

Disposition

	NIU	DME			RVO	Across All Disease States	
Disposition and Exposure	CLS-TA	CLS-TA	CLS-TA + IVT Anti-VEGF	Any CLS-TA	CLS-TA + IVT Anti-VEGF	Any CLS-TA	IVT Anti-VEGF + SCI Sham
Patients, N	156	10	46	56	414	626	449
Completed, n (%)	151 (96.8)	9 (90.0)	40 (87.0)	49 (87.5)	153 (37.0)	353 (56.4)	189 (42.1)
Discontinued, n (%)	5 (3.2)	1 (10.0)	6 (13.0)	7 (12.5)	247 (62.1)	269 (43.0)	258 (57.5)
Adverse events	0 (0.0)	0 (0.0)	3 (6.5)	3 (5.4)	2 (0.5)	5 (0.8)	7 (1.6)
Non-compliance	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
Withdrawal of consent	3 (1.9)	1 (10.0)	3 (6.5)	4 (7.1)	9 (2.2)	16 (2.6)	4 (0.9)
Lost to follow-up	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.4)	7 (1.1)	16 (3.6)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	240 (58.0)	240 (38.3)	232 (51.7)
Mean Length of follow-up (range), days	154.4 (29-217)	176.8 (124-196)	171.7 (65-217)	172.6 (65-217)	198.0 (15-391)	184.8 (15-391)	196.5 (22-397)

Exposure to Study Treatments



Demographics and Baseline Characteristics

	NIU	DME			RVO	Across All Disease States	
Demographics and Baseline Characteristics	CLS-TA	CLS-TA	CLS-TA + IVT Anti-VEGF	Any CLS-TA	CLS-TA + IVT Anti-VEGF	Any CLS-TA	IVT Anti-VEGF + SCI Sham
Patients, N	156	10	46	56	414	626	449
Mean age (range), y	51.1 (18-92)	63.1 (46-73)	60.2 (28-82)	60.7 (28-82)	65.4 (31-93)	61.4 (18-93)	63.6 (19-97)
Females, n (%)	91 (58.3)	4 (40.0)	14 (30.4)	18 (32.1)	188 (45.4)	297 (47.4)	198 (44.1)
Whites, n (%)	89 (57.1)	6 (60.0)	37 (80.4)	43 (76.8)	278 (67.1)	410 (65.5)	311 (69.3)
Phakic, n (%)	79 (50.6)	4 (40.0)	39 (84.8)	43 (76.8)	335 (80.9)	457 (73.0)	364 (81.1)
Mean ETDRS BCVA (range), letters	58.9 (9-90)	67.2 (54-81)	59.3 (34-83)	60.7 (34-83)	50.7 (10-80)	53.7 (9-90)	51.9 (16-86)
Snellen equivalent (range)	20/80 (20/800-20/15)	20/50 (20/100-20/26)	20/80 (20/250-20/26)	20/64 (20/250-20/26)	20/100 (20/100-20/32)	20/100 (20/800-20/15)	20/100 (20/500-20/20)
Mean CST (range), µm	455.1 (176-857)	472.7 (328-691)	479.9 (301-954)	478.6 (301-954)	650.7 (255-1676)	586.5 (176-1676)	652.4 (220-1527)

Serious Adverse Events in the Study Eye

	NIU	DME			RVO	Across All Disease States	
Serious Adverse Events	Total CLS-TA	CLS-TA	CLS-TA + IVT Anti-VEGF	Total CLS-TA	CLS-TA + IVT Anti-VEGF	Total CLS-TA	Total IVT Anti-VEGF + SCI Sham
Patients at risk, N	156	10	46	56	414	626	449
Patients with ≥1 event	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)	6 (1.0)	4 (0.9)
Endophthalmitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Intraocular pressure increased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	3 (0.5)	0 (0.0)
Retinal detachment	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
Ulcerative keratitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Visual acuity reduced	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	2 (0.3)	0 (0.0)
Vitreous haemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

Eye Pain Related Treatment-Emergent Adverse Events Temporally Related to the Treatment Procedure

	NIU	DME			RVO	Across All Disease States	
Treatment-Emergent Adverse Events	Total CLS-TA	CLS-TA	CLS-TA + IVT Anti-VEGF	Total CLS-TA	CLS-TA + IVT Anti-VEGF	Total CLS-TA	Total IVT Anti-VEGF + SCI Sham
Patients at risk, N	156	10	46	56	414	626	449
Patients with ≥1 event	18 (11.5)	0 (0.0)	0 (0.0)	0 (0.0)	25 (6.0)	43 (6.9)	7 (1.6)
Eye pain	12 (7.7)	0 (0.0)	0 (0.0)	0 (0.0)	19 (4.6)	31 (5.0)	4 (0.9)
Ocular discomfort	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	2 (0.3)	2 (0.4)
Injection site discomfort	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
Injection site pain	8 (5.1)	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.4)	14 (2.2)	1 (0.2)

Results

- 626 patients received one or more SCI, either as monotherapy (N=166) or in conjunction with IVT anti-VEGF (N=460) with the majority (>66%) receiving 2 or more study treatments.
- Three of 626 patients experienced 3 SAEs of interest, all occurring in patients receiving multiple SCI injections.
  - One NIU monotherapy patient experienced retinal detachment, and 2 RVO patients receiving combination therapy experienced reduced vision; each were deemed not related to treatment by a masked Investigator.
- There were no SAEs involving lens injury, suprachoroidal hemorrhage, endophthalmitis, or retinal tear in patients receiving SCIs, either alone or in conjunction with anti-VEGF.
- In the control, 449 patients received IVT anti-VEGF in conjunction with a sham SCI. Three RVO patients experienced 3 SAEs of interest, including retinal detachment, vitreous hemorrhage and endophthalmitis. Each was deemed not related to treatment by a masked Investigator.
- 18 of 156 (11.5%) NIU patients, 0 of 56 DME patients and 25 of 414 (6.0%) RVO patients experienced a TEAE related to eye pain on the day of the procedure.

Conclusions

- Overall, across 8 clinical trials involving NIU, DME and RVO, the safety profile of SCI, either as monotherapy or in conjunction with IVT anti-VEGF injections, is comparable to IVT anti-VEGF injections alone for events occurring during or after the procedures.
- Overall incidence of eye pain (6.9%) observed in SCIs with CLS-TA is comparable to labeled incidences with IVT aflibercept in wet AMD (9%), DME (9%), and RVO (10.4%)[1].

References

1. *Regeneron Pharmaceutical, Inc. EYLEA® [prescribing information]* Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; 2017