Southeast Retina Center

Safety and Tolerability Study of Suprachoroidal Injection of CLS-AX in Neovascular AMD Patients with Persistent Activity Following Anti-VEGF Therapy

(OASIS, NCT04626128; Extension Study NCT NCT05131646)

C0310

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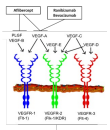
PURPOSE

Assess the safety and tolerability of a single dose of CLS-AX (axitinib injectable suspension), for suprachoroidal injection (SCS injection) in patients with active subfoveal CNV secondary to neovascular age-related macular degeneration (nAMD)

BACKGROUND

CLS-AX: axitinib injectable suspension for suprachoroidal use

- Highly potent
- Inhibits VEGFR-1, VEGFR-2, VEGFR-3 receptors
- Better ocular cell biocompatibility than other TKIs
- Preclinical models showed durability at effective concentrations to at least 6 months



SCS Injection with a microinjector:

- Targeted, compartmentalized, bioavailable to posterior ocular tissues
- Procedure & device validated with approved product for suprachoroidal use (XIPERE®, Bausch + Lomb)

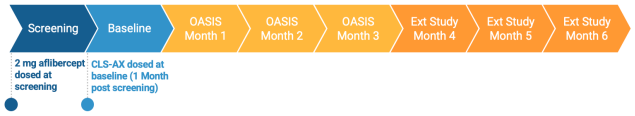
Scan to view SCS injection

SCS injection in OASIS patient

OASIS & EXTENSION

First In-human Study of axitinib in the SCS, a Phase 1/2a Clinical Trial

- **OASIS:** Phase 1/2a open-label, dose escalation study with 3 months follow-up
- **Extension:** optional non-interventional study of additional 3 months follow-up for patients in cohorts 2-4.
- **Eligibility:** nAMD patients with active CNV previously treated with anti-VEGF standard of care



- **Treatments:** Single dose of CLS-AX via SCS injection at doses of 0.03, 0.1, 0.5 and 1.0 mg one month after IVT aflibercept
- **Primary Endpoint:** Safety and tolerability over 3 to 6 months following CLS-AX administration

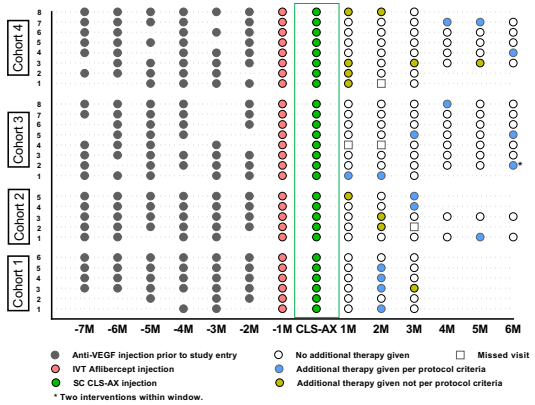
RESULTS

CLS-AX via SCS injection was safe and well-tolerated in all cohorts

- No serious adverse events (SAEs)
- No treatment emergent adverse events (TEAEs) related to study treatment
- No dose limiting toxicities
- No adverse events related to inflammation, vasculitis or vascular occlusion
- No vitreous "floaters" or dispersion of CLS-AX into the vitreous
- No retinal detachment
- No endophthalmitis
- No adverse events related to intraocular pressure

Treatments Pre & Post CLS-AX

77 – 85% Reduction in Treatment Burden in Cohorts 3 and 4



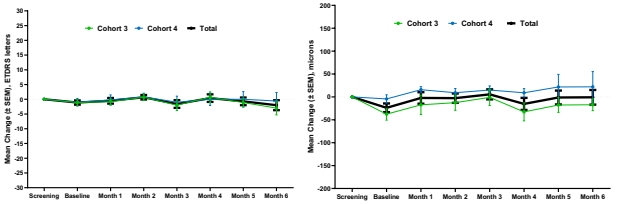
Demographics

Wet AMD Disease Characteristics	COHORT 1 0.03 mg	COHORT 2 0.1 mg		COHORT 3 0.5 mg		COHORT 4 1.0 mg		TOTAL	
	OASIS	OASIS	Extension	OASIS	Extension	OASIS	Extension	OASIS	Extension
No. of participants	6	5	2	8	7	8	5	27	14
Mean age (range), years	81.8 (66-93)	78.2 (65-90)	74.0 (70-78)	86.3 (75-97)	87.9 (81-97)	76.5 (66-83)	79.6 (74-83)	80.9 (65-97)	82.9 (70-97)
Mean baseline best corrected visual acuity (range), letters	59.0 (29-74)	65.6 (52-75)	60.0 (52-68)	58.5 (37-74)	59.0 (37-74)	65.8 (50-74)	71.2 (69-74)	62.1 (29-75)	63.5 (37-74)
Mean baseline central subfield retinal thickness (range), µm	231.2 (208-294)	209.4 (184-227)	213.5 (200-227)	202.0 (175-238)	201.9 (175-238)	218.8 (152-295)	214.8 (197-234)	214.8 (152-295)	208.1 (175-238)
Mean duration of nAMD diagnosis (range), months	50.13 (12.4-110.3)	49.78 (24.7-81.3)	44.30 (33.9-54.7)	66.64 (6.8-102.1)	67.29 (6.8-102.1)	48.21 (4.5-132.8)	36.42 (6.1-103.4)	54.39 (4.5-132.8)	52.98 (6.1-103.4)
Number of anti-VEGF injections reported prior to IVT aflibercept at Screening, mean (range)	26.8 (7-41)	24.2 (12-39)	23.0 (12-34)	37.0 (6-90)	38.9 (6-90)	28.8 (5-89)	33.2 (6-89)	29.9 (5-90)	34.6 (6-90)
Annualized number of anti-VEGF injections prior to IVT aflibercept at Screening, mean (range)	9.36 (6.3-12.7)	9.54 (5.4-12.2)	8.81 (5.4-12.2)	8.47 (4.9-11.8)	8.84 (4.9-11.9)	11.96 (8.9-13.6)	12.01 (10.5-13.1)	9.90 (4.9-13.6)	9.97 (4.9-13.1)

BIOLOGIC EFFECT in EXTENSION, *post hoc analysis*

Higher Dose Cohorts (3 & 4) showed Stable BCVA & CST

Mean Change in BCVA (left) and CST (right) from Screening to Month 6



Cohort 3: n=5; Cohort 4: n=7

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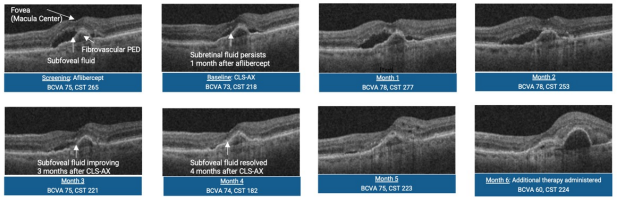
Case Study



Cohort 3, Subject 2: 89 prior anti-VEGF injections with persistent subfoveal fluid 1 month after aflibercept at screening. Subretinal fluid gradually resolves through 4 months after CLS-AX with stable BCVA and improved CST.

CONCLUSION

- CLS-AX administered via SCS Injection for nAMD was safe and well-tolerated and exhibited early signs of durability and reduction in treatment burden.
- CLS-AX will be evaluated in a Phase 2b Clinical Trial, ODYSSEY, for nAMD.

Source: Viral S. Kansara, Leroy W. Muya, Thomas A. Ciulla; Evaluation of Long-Lasting Potential of Suprachoroidal Axitinib Suspension Via Ocular and Systemic Disposition in Rabbits. *Trans. Vis. Sci. Tech.* 2021;10(7):19. Theile et al. Multikinase Inhibitors as a New Approach in Neovascular Age-Related Macular Degeneration (AMD) Treatment: In Vitro Safety Evaluations of Axitinib, Pazopanib and Sorafenib for Intraocular Use. Klin Monatsbl Augenheilkd 2013; 230: 247-254. | Image by Mikael Häggström, used with permission.