**7/17/2024**

**Wet AMD Symposium 1**

**Ixoberogene Soroparvovec (Ixo-vec) IVT Gene Therapy for Neovascular AMD: First-Time 26-Week Interim Analysis Results From the Phase 2 LUNA Study**


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- Sean Adrean, MD, FAAO, FASRS
- Mark Barakat, MD
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- Dante Pieramici, MD
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**Objective:** Assess the safety, tolerability, and efficacy of a single intravitreal (IVT) injection of ixoberogene soroparvovec (previously known as ADVM-022) in anti-VEGF treatment-experienced patients with neovascular age-related macular degeneration (nAMD).

**Purpose:** The burden of frequent anti-VEGF injections and real-world vision decline underscore persistent unmet needs for nAMD patients. Ixo-vec (AAV2.7m8-aflibercept) is an investigational gene therapy designed to provide continuous and consistent expression of aflibercept and has demonstrated vision preservation and sustained reduction in macular fluid through three years following a single IVT injection in the first-in-human OPTIC trial (NCT03748784). The ongoing Phase 2 LUNA study (NCT05536973) was designed to determine the optimal dose of Ixo-vec combined with enhanced corticosteroid prophylactic regimens for the treatment of nAMD.
**Study Design:** LUNA is a multicenter, randomized, double-masked, 60-month study in treatment-experienced nAMD patients with a demonstrated response to anti-VEGF therapy. Eligible participants were randomly allocated between two Ixo-vec doses, $6x10^{10}$ and $2x10^{11}$ vg/eye, and across multiple prophylactic regimens including local corticosteroids (topical difluprednate, IVT dexamethasone) with and without oral prednisone. The primary endpoints are incidence and severity of adverse events and mean change in BCVA from baseline to Week 52. Key secondary endpoints include change in CST, number of supplemental aflibercept injections, and the effectiveness of the prophylactic corticosteroid regimens in minimizing inflammation. A pre-specified interim analysis will be performed once all participants complete their Week 26 visit.


**Full abstract to be released at the conclusion of the presentation.**

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**7/17/2024**

**Wet AMD Symposium 1**

**Phase 2 Population Extension Cohort in the PRISM Trial Evaluating 4D-150 in Adults With Neovascular Age-related Macular Degeneration**


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- Vrinda Hershberger, MD, PhD
- Fuad Makkouk6, MD
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- Carol Chung, PhD
- Robert Kim, MD
- David Kirn, MD
- David Kirn, MD



**Objective:** Evaluate the safety and clinical activity of 4D-150 in adults with neovascular (wet) age-related macular degeneration.
**Purpose:** 4D-150 is an investigational intravitreal (IVT) genetic medicine comprising a retinotropic AAV vector (R100) and a dual-transgene cassette containing a codon-optimized sequence encoding aflibercept (AFLB) and an miRNA sequence targeting VEGF-C. In a first-in-human dose exploration study in adults with neovascular (wet) age-related macular degeneration (wAMD) who required frequent anti-VEGF injections, 4D-150 was safe and generally well tolerated and demonstrated clinical activity at all tested doses. Here we report first-time results from a Phase 2 open-label study evaluating 4D-150 in a wAMD population with a less frequent need for anti-VEGF injections and a broader range of disease activity compared to the previous cohorts.

**Study Design:** PRISM is a prospective ongoing, multicenter Phase 1/2 clinical trial (NCT05197270). In the population extension stage, eligible participants were adults (age, ≥50 years) with wAMD with subretinal or intraretinal fluid on optical coherence tomography and best corrected visual acuity (BCVA) of 34–83 letters. Participants were masked, randomized, and received IVT AFLB 2 mg on Day -7 and Day 28 and a single IVT injection of 4D-150 $3\times10^{10}$ vg/eye or $1\times10^{10}$ vg/eye on Day 1 (Figure 1). Study outcomes include the incidence and severity of adverse events, the proportion of participants who remain supplemental anti-VEGF injection-free, and change from baseline in BCVA and central subfield thickness (CST).
**Results:** A total of 32 participants received a single IVT injection of 4D-150 at a dose of either $3x10^{10}$ vg/eye (n=17) or $1x10^{10}$ vg/eye (n=15). Baseline characteristics are summarized in Table 1. As of 17 January 2024, the duration of follow-up ranged from 8 to 16 weeks. Interim analysis of safety outcomes demonstrated that 4D-150 was generally well tolerated; there were no 4D-150–related serious adverse events and no clinically significant ocular adverse events, including intraocular inflammation, endophthalmitis, retinal vasculitis, retinal artery occlusion and hypotony.
**Conclusions:** Interim safety data from the population extension stage of the PRISM clinical trial demonstrate that 4D-150 was generally well tolerated during follow-up for 8–16 weeks. Additional methods and data for the population extension cohort will be presented.


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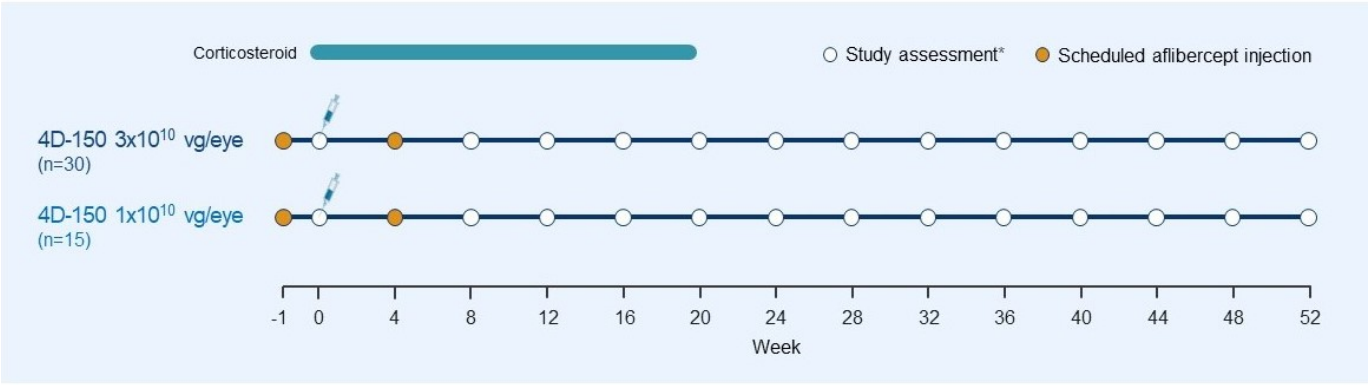
| | 4D-150 $3 \times 10^{10}$ vg/eye | 4D-150 $1 \times 10^{10}$ vg/eye | Total |
|---|---|---|---|
| N | 30 | 15 | 45 |
| Mean ±SD age, years | 77 ±7.7 | 78 ±8.6 | 77 ±7.9 |
| Female, n (%) | 20 (67) | 6 (40) | 26 (58) |
| Mean ±SD BCVA, ETDRS letters | 71 ±9.9 | 73 ±8.8 | 72 ±9.5 |
| Mean ±SD CST, µm | 336 ±135.0 | 314 ±70.8 | 329 ±117.1 |
| Mean annualized anti-VEGF injection rate | 8.3 | 10.7 | 9.0 |
| Mean ±SD anti-VEGF injections in prior 12 months, n | 4.4 ±2.0 | 4.3 ±2.1 | 4.4 ±2.0 |

BCVA, best corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

## Phase 2 Population Extension




*Visual acuity, optical coherence tomography, ophthalmic exam.

**7/17/2024**

**Wet AMD Symposium 1**

# Subretinal Delivery of Investigational ABBV-RGX-314 for Neovascular Age-Related Macular Degeneration: A Phase II Pharmacodynamic Study


- Edward Wood, MD, FASRS



**Objective:** To evaluate the pharmacodynamics of subretinally delivered investigational ABBV-RGX-314 produced by either a bioreactor or adherent cell culture manufacturing process in patients with neovascular age-related macular degeneration.
**Purpose:** ABBV-RGX-314 is an investigational single administration gene therapy designed to deliver a transgene for a soluble anti-VEGF Fab. This Phase II bridging study in patients with nAMD evaluates the clinical performance between subretinally delivered ABBV-RGX-314 produced with REGENXBIO's NAVXpress™ bioreactor platform process and the initial adherent cell culture process.
**Methods:** This study is a multi-center, open-label pharmacodynamic bridging study to evaluate subretinal delivery of ABBV-RGX-314 produced by either the NAVXpress platform process (Bioreactor, BRX) or the adherent cell culture manufacturing process (Hyperstack®, HS), which was used in the Phase I/IIa trial of ABBV-RGX-314 for the treatment of nAMD. Sixty patients are assigned to one of two dose levels ($6.4x10^{10}$ GC/eye or $1.3x10^{11}$ GC/eye) with half of the patients receiving BRX and half receiving HS at each dose level (n=15 for each of the four cohorts). ABBV-RGX-314 protein concentration in the eye at Month 6 is the primary endpoint; safety and tolerability, change from baseline in Best Corrected Visual Acuity (BCVA), change in central retinal thickness (CRT) and need for supplemental anti-VEGF injections are also being evaluated.
**Results:** All cohorts have fully enrolled. As of May 8, 2023, ABBV-RGX-314 was well tolerated in all cohorts. Five serious adverse events (AEs) were reported, none of which were considered related to ABBV-RGX-314. Through six months in the high dose (BRX and HS; n=30) and low dose (BRX; n=15) cohorts, ABBV-RGX-314 protein concentrations in the study eye were similar. These cohorts demonstrated stable-to-improved BCVA and CRT and meaningful reductions in anti-VEGF injection burden, with many injection-free patients. Common treatment emergent AEs through six months were mild-to-moderate and included post-operative conjunctival hemorrhage (38%), post-operative inflammation (31%), and retinal pigmentary changes (13%).
**Conclusion:** ABBV-RGX-314 produced by the NAVXpress platform process has been well-tolerated and demonstrated a similar clinical profile to the adherent cell culture process. Initial study results support the dose levels and cGMP commercial-ready material being evaluated in the ongoing ATMOSPHERE® and ASCENT™ pivotal trials.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**7/17/2024**

**Wet AMD Symposium 1**

# Assessing Supplemental Injection Use Across Groups in the Phase 2 DAVIO 2 Trial of EYP-1901 vs Aflibercept in Wet Age-Related Macular Degeneration


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- Stephanie Ruggiero, BS
- Monica Roy, OD, MPH
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**Objective:** Assess supplemental injection patterns in the DAVIO 2 trial of EYP-1901 vs standard of care (SoC) to determine therapeutic durability across patient types.
**Purpose:** A high treatment burden is associated with current biologics used to treat wet age-related macular degeneration (wAMD), resulting in a need for more durable therapies. EYP-1901 is a sustained-delivery therapy supplying the pan–vascular endothelial growth factor (VEGF) receptor inhibitor vorolanib in a bioerodible form of intravitreal (IVT) Durasert that consistently elutes drug for ~9 months in animal models, as was supported by the phase 1 DAVIO trial. DAVIO 2 is a phase 2, multicenter, prospective, randomized, double-masked, parallel study examining the efficacy of a single IVT injection of EYP-1901 vs aflibercept in eyes with wAMD. This analysis assessed the need for supplemental SoC injections in subgroups of eyes in DAVIO 2.
**Methods:** Previously treated eyes with wAMD were randomized on Day 1 to EYP-1901 2060 µg, EYP-1901 3090 µg, or SoC (aflibercept 2 mg q8W). All arms received aflibercept 2 mg on Day 1 and Weeks 4 and 8. EYP-1901 was administered as a single dose on Week 8. Eyes in all groups could receive supplemental SoC injections if they met specified best corrected visual acuity (BCVA) and/or anatomic criteria. The primary endpoint was the mean change in BCVA from Day 1 to Weeks 28 and 32 averaged. Secondary endpoints included reduction in treatment burden, mean change in central subfield thickness (CST), number of eyes free of anti-VEGF injections after induction, and number of aflibercept injections in each group after induction.
**Results:** One hundred fifty-six eyes received EYP-1901 2060 µg (n = 50), EYP-1901 3090 µg (n = 52), or SoC (n = 54). The mean difference in BCVA vs SoC at Weeks 28 and 32 averaged was -0.3 letters for EYP-1901 2060 µg and -0.4 letters for EYP-1901 3090 µg. The mean difference in CST from SoC was below 10 µm with both doses at Week 32. Treatment burden was reduced by 89% and 85% with EYP-1901 2060 µg and 3090 µg, and 65% and 64% of eyes were supplement-free up to 6 months. The number of eyes meeting criteria for supplemental injections in each treatment arm will be presented.
**Conclusion:** After 6 months of treatment, a single dose of EYP-1901 with protocol-specified SoC supplementation resulted in BCVA that was statistically non-inferior to SoC monotherapy for wAMD. Data showing the number of eyes in comparative subgroups meeting criteria for supplemental injections will be presented to demonstrate variances in wAMD control with SoC and the durable, sustained-delivery option EYP-1901.


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