8/01/2023

The PRIMA Bionic Vision System in Patients With Geographic Atrophy
The PRIMA Bionic Vision System in Patients with Geographic Atrophy

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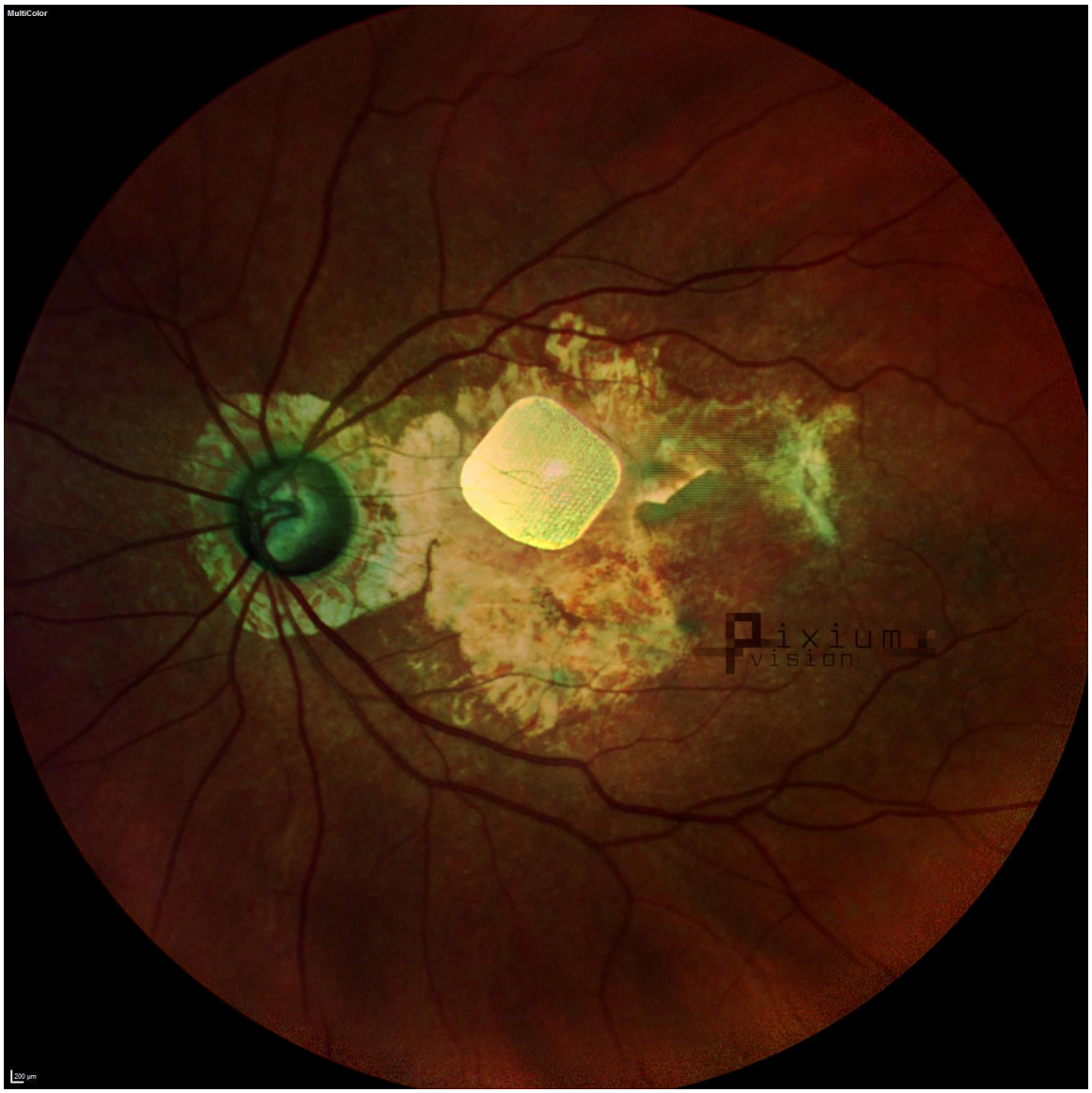
Objective: To report the visual acuity results up to 48 months after subretinal implantation of the PRIMA bionic vision system, designed to partially restore vision in patients suffering from geographic atrophy due to age-related macular degeneration (AMD).

Purpose: The PRIMA bionic vision system is designed to partially restore vision in patients suffering from geographic atrophy due to age-related macular degeneration (AMD). A camera mounted on a pair of glasses captures images from the environment. After processing, this information is sent by an infrared projector onto a subretinal photovoltaic implant. The 378 pixels of the implant convert the infrared light into electrical pulses which stimulate the remaining inner retinal neurons. PRIMA was implanted in 5 subjects with atrophic AMD in a feasibility trial in France. After mechanical, optical and electronic adjustment of the external components, the subjects were trained to use the device. Subjects underwent visual testing, including Octopus visual field, as well as visual acuity tests with Landolt rings and ETDRS charts. Subjects were able to benefit from image processing, including zoom. Here, we report visual acuity results up to 48 months after implantation.

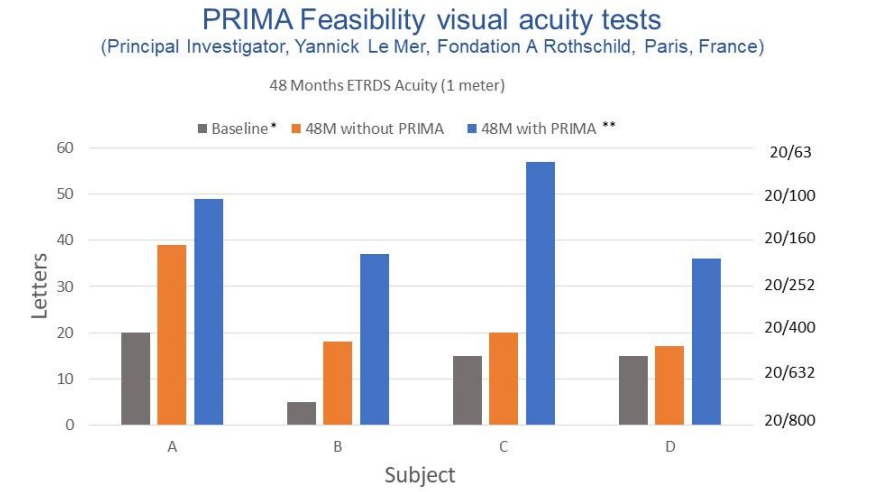
Methods: This was a prospective, non-randomized, non-masked feasibility study. Five subjects with atrophic AMD were implanted with the PRIMA device in one eye. All eyes implanted had geographic atrophy involving the foveal center and no central visual perception. Visual acuity was measured with Landolt rings and ETDRS letters both with and without the system.
Results: In all 5 patients, the implant was successfully placed under the central retina. The visual field test demonstrated that all subjects had perception elicited by the implant in the scotoma area. Visual acuity measurement with Landolt rings demonstrated an improvement of up to logMAR 0.87 (with versus without the system). ETDRS measurement demonstrated that subjects are able to recognize letters and sequences of letters with a visual acuity improvement of up to 37 letters (logMAR 0.74). The peripheral visual acuity did not decline after the surgery over a review period of up to 48 months following surgery.

Conclusion: The subretinal implantation of PRIMA in subjects with geographic atrophy due to AMD is feasible and safe, with no reduction of natural peripheral visual acuity. Visual acuity measurements showed that patients are able to reliably recognize letters and sequences of letters with visual acuity improvement that is clinically meaningful.

IRB APPROVAL Yes



Color fundus photo of the PRIMA subretinal prosthesis



* Test at Baseline is done with different ETDRS protocol and recalculated from logMAR to numbers of letters ** Image processing includes magnification

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PRIMA feasibility study visual acuity results at 48 months

8/01/2023

Efficacy and Safety of Anti-High Temperature Requirement A1 (aHtrA1) Fab in Geographic Atrophy (GA) Secondary to AMD: GAllego Phase 2 Randomized Trial

Efficacy and Safety of anti-High Temperature Requirement A1 (aHtrA1) Fab in Geographic Atrophy (GA) Secondary to AMD: GAllego Phase 2 Randomized Trial

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Objective: To investigate the safety, tolerability and efficacy of intravitreal injection (ITV) of aHtrA1 (FHTR2163 or galegenimab) in patients with GA secondary to age-related macular degeneration (AMD).

Purpose: *ARMS2/HTRA1* is a top locus identified in genome-wide association studies imparting increased risk of AMD. The serine protease HtrA1 is expressed in the retina. Inhibiting HtrA1 is hypothesized to slow progression of GA. GAllego is a Phase 2 randomized trial investigating the safety, tolerability, and efficacy of galegenimab, an anti-HtrA1 antigen-binding fragment (Fab), in patients with GA.

Methods: Eligible patients with BCVA letter score of ≥ 24 letters, prebaseline total GA lesion size 2.54~17.78 mm^2, and baseline GA lesion size 2.54~25.4 mm^2 in the study eye, were randomized 2:1:2 to receive 20 mg galegenimab every 4 weeks (Q4W) or every 8 weeks (Q8W), or sham Q4/8W. The primary endpoint was mean change in GA area from baseline to Week 72 as measured by fundus autofluorescence (FAF). A monitoring committee conducted periodic unmasked review of cumulative safety/limited efficacy data of the ongoing study. The committee recommended discontinuing the study early based on benefit/risk analysis. Efficacy data were assessed for patients with at least one post-baseline FAF measurement.

Results: A total of 373 patients were randomized, with 150 in the galegenimab Q4W arm, 75 in the galegenimab Q8W arm, and 148 in pooled sham arms. Baseline demographic and ocular characteristics among the three arms were reasonably balanced. The rate of intraocular inflammation (IOI) was 16/224 (7.1%), all among treated patients. Most cases of IOI were mild or moderate in severity and most resolved after treatment with topical steroids by the end of the study. There were no cases of occlusive retinal vasculitis (see Table 1). Among the 337 patients with at least one post-baseline GA area measurement, the least squares mean change in GA area from baseline to W72 was 2.67, 2.50, and 2.38 mm^2, respectively, for the Q4W galegenimab, Q8W galegenimab, and pooled sham arms. Differences between the treated and sham groups were not statistically significant. Additional subgroup analysis on efficacy, safety, and HtrA1 risk allele status are expected to be available at the time of presentation.

Conclusion: The GAllego phase 2 randomized trial of ITV aHtrA1 Fab, galegenimab, demonstrated that 20 mg of study drug administered every 4 week (Q4W) or every 8 week (Q8W) did not show a statistically significant difference in mean change in GA area from baseline to Week 72 compared with pooled sham arms and led to a high rate of IOI in patients with GA secondary to AMD.

IRB APPROVAL Yes

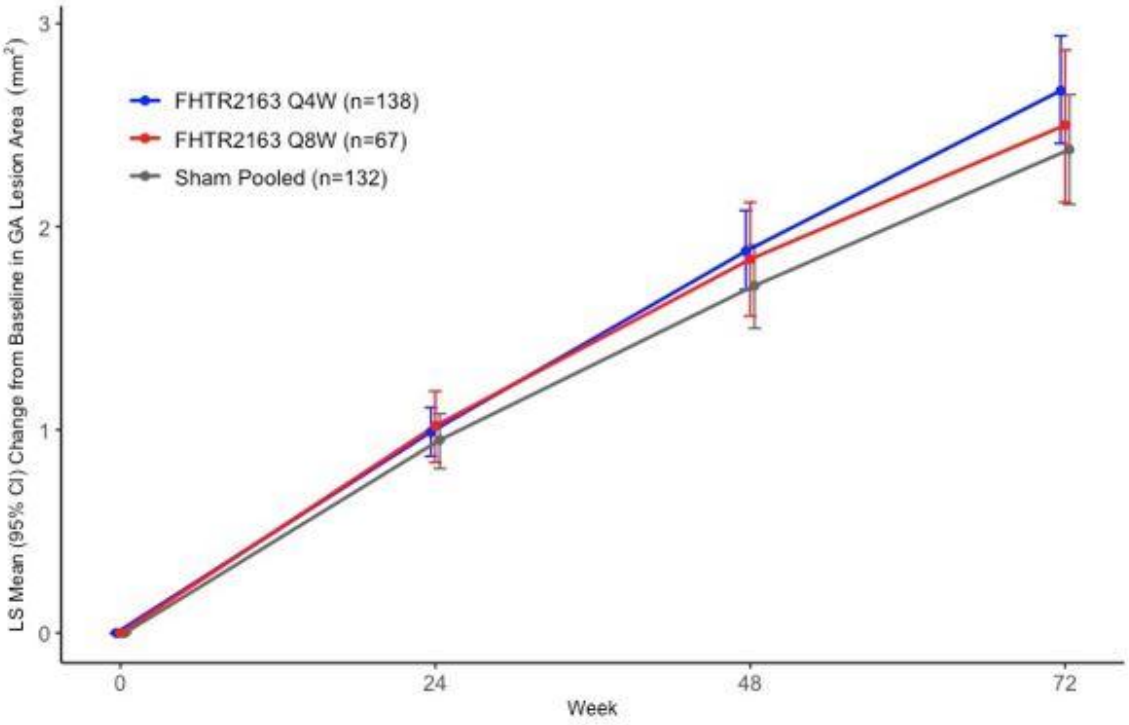

Figure 1. Least squares (LS) mean changes in GA area from baseline.

No. patients with IOI	16 (10 Q4W, 6 Q8W)[a]
Overall IOI rate	7.1% (16/224) total 6.7% (10/149) Q4W 8.0% (6/75) Q8W
Anterior segment only	3
Posterior segment only	7
Anterior and posterior segment	9
BCVA decrease (≥ 15 letters at time of diagnosis)	2
Vasculitis (non-occlusive)[b]	3
Treated with topical steroids only	10
Required oral or intravitreal steroids	5
IOI on galegenimab rechallenge (yes/no)[a]	3/1
Median number of injections to first IOI event (min-max)	3 [1-11]

[a] 3 of 4 patients rechallenged with study drug when this was allowed per protocol, manifested recurrent IOI, for a total of 19 events.
[b] Includes one possible Behcet's uveitis, HLA B51+. No cases of retinal artery or vein occlusion were reported.

Table 1. Intraocular inflammation overview.

8/01/2023

OTX-TKI for the Treatment of Neovascular Age-related Macular Degeneration: 12-Month Results From a U.S. Clinical Trial
OTX-TKI for the Treatment of Neovascular Age-related Macular Degeneration: 12-month Results from a U.S. Clinical Trial

- Robert Avery, MD

Objective: How long does the biological activity of OTX-TKI, a sustained release tyrosine kinase inhibitor implant, lasts in previously treated, controlled wet AMD patients, compared to aflibercept Q8W?
Purpose: To evaluate the safety, tolerability and biological activity of intravitreal axitinib implant (OTX-TKI) for the treatment of nAMD compared to aflibercept.
Methods: Prospective, randomized, double-masked U.S.-based clinical trial. Previously treated nAMD subjects with controlled retinal fluid were randomized (3:1) to OTX-TKI group or aflibercept group. OTX-TKI group received OTX-TKI 600 µg single implant at baseline and aflibercept at week 4. Aflibercept group received aflibercept Q8W starting at week 4. Adverse events (AEs), changes in visual acuity (BCVA using ETDRS letters), central subfield thickness (CSFT), and number of supplemental anti-VEGF injections were assessed through at least 12-months.
Results: The study enrolled 16 subjects in the OTX-TKI group and 5 subjects in the aflibercept group. No drug-related ocular or systemic serious AEs were reported in OTX-TKI subjects. Mean change in visual acuity and CSFT with OTX-TKI was comparable to aflibercept at all timepoints through month 12. 73% of OTX-TKI subjects did not receive supplemental injections up to 10 months and 60% did not receive supplemental injections up to 12 months. At month 12, four additional subjects received supplemental injections representing an 89% reduction in treatment burden over a 12-month period.
Conclusion: OTX-TKI maintained vision and CSFT comparably to aflibercept Q8W with 89% reduction in treatment burden over a 12-month period. Safety data showed OTX-TKI was generally well-tolerated. Pharmacodynamic effects observed in this trial support the characteristics of a potential treatment for nAMD with durability between 9-12 months following a single injection. Additional post-hoc analyses demonstrating therapeutic maintenance over 12 months, with supplemental treatment as needed, will be presented for the first time at ASRS 2023.

IRB APPROVAL Yes

8/01/2023

Port Delivery System with Ranibizumab (PDS) for Continuous Treatment in DME and DR: Additional Results from the Phase 3 Pagoda and Pavilion Trials

Port Delivery System with Ranibizumab (PDS) for Continuous Treatment in DME and DR: Additional Results from the Phase 3 Pagoda and Pavilion Trials

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Objective: To report new data for the PDS in diabetic macular edema (DME) and diabetic retinopathy (DR)
Purpose: The PDS is an innovative drug delivery system that includes a refillable ocular implant for continuous delivery of a customized formulation of ranibizumab (RBZ) into the vitreous. In the Pagoda trial for DME and the Pavilion trial for nonproliferative DR without center-involved DME (CI-DME), the PDS with RBZ 100 mg/mL was investigated with fixed refill-exchanges every 24 weeks (PDS Q24W) or 36 weeks (PDS Q36W), respectively. New results from the primary analyses are presented.
Methods: Pagoda (NCT04108156) and Pavilion (NCT04503551) are phase 3, ongoing, randomized, visual assessor–masked trials. Pagoda study arms: PDS Q24W vs intravitreal (IVT) RBZ 0.5 mg every 4 weeks (RBZ Q4W). Pavilion study arms: PDS Q36W vs control (observation plus supplemental IVT RBZ as required). Pagoda primary endpoint (PE): noninferiority (NI) of PDS Q24W based on BCVA change from baseline (BL) averaged over weeks (W) 60/64 (NI margin –4.5 ETDRS letters). Pavilion PE: superiority of PDS Q36W based on ≥2-step ETDRS-DRSS improvement from BL at W52. Additional endpoints including maintenance of driving vision (BCVA Snellen ≥20/40), stable vision (avoiding ≥3-line BCVA loss), and absence of protocol-defined DME will be presented for the first time.
Results: In Pagoda (PDS Q24W, n=381; RBZ Q4W, n=253), PDS Q24W was noninferior to RBZ Q4W in BCVA change from BL averaged over W60/64 (+9.4 vs +9.6 letters, respectively; difference [95% CI] 0.2 [–1.2 to 1.6]). At W64, 77.5% of PDS Q24W pts (vs 71.1% RBZ Q4W) had BCVA ≥20/40, 98.9% (vs 97.5% RBZ Q4W) avoided ≥3-line BCVA loss, and 82.6% (vs 78.3% RBZ Q4W) had DME absence.
In Pavilion (PDS Q36W, n=106; control, n=68), PDS Q36W was superior to control with 80.1% vs 9.0% of pts achieving ≥2-step ETDRS-DRSS improvement from BL at W52 (difference [95% CI], 71.1% [61.0–81.2]; *P*=<0.0001). At W52, 93.7% of PDS Q36W pts (vs 89.3% control) maintained BCVA ≥20/40 and 98.9% (vs 92.9% control) avoided ≥3-line BCVA loss. The rate of pts who did not develop CI-DME at W52 was significantly greater with PDS Q36W (92.9%) vs control (71.0%) (HR [95% CI], 0.2 [<0.1–0.5]; *P*=0.0001). The PDS was generally well tolerated in both trials with no new safety signals observed.
Conclusion: Pagoda and Pavilion both met their primary endpoints. The PDS, the first continuous delivery treatment platform for DME and DR, has the potential to provide functional and anatomical benefits, and prevent disease progression, without the need for frequent IVT injections.

IRB APPROVAL Yes