

# Effect of intravitreal axitinib hydrogel injection (OTX-TKI) on ellipsoid zone integrity in non-proliferative diabetic retinopathy

Paulo H. Simoes da Silva<sup>1</sup>; Reem Amine<sup>1</sup>; Amy Tang<sup>1</sup>; Lyndsey Della Vecchia<sup>1</sup>; Neal Shah<sup>1</sup>; John Mamone<sup>1</sup>; Erin Flannigan<sup>1</sup>; Penina B. Schlesinger<sup>1</sup>; Jasmine Scafuro<sup>1</sup>; Julia L. Beilis<sup>1</sup>; Michelle Bonnay<sup>1</sup>; Karissa Zarbock<sup>1</sup>; Barret Schmidt<sup>1</sup>; Jamie Reese<sup>1</sup>; Sunil K. Srivastava<sup>1</sup>; Justis P. Ehlers<sup>1</sup>  
<sup>1</sup>Cleveland Clinic, Cleveland, OH, United States.

Poster #6346- A0140

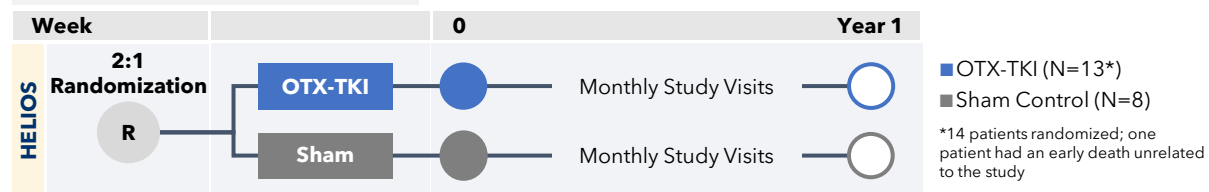
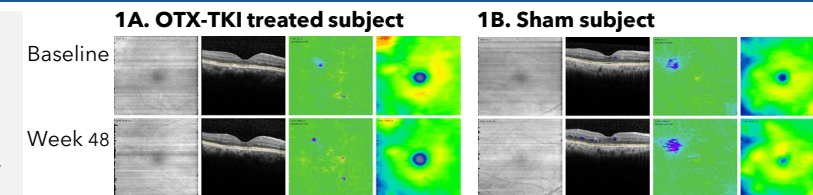
## PURPOSE

- The ellipsoid zone (EZ) may serve as a potential biomarker for therapy monitoring and visual acuity outcome prediction.<sup>1</sup>
- Diabetic retinopathy is the leading cause of blindness in working age adults, with a significant treatment gap—less than 1% of patients with non-proliferative diabetic retinopathy (NPDR) receive treatment.<sup>2-4</sup>
- This study aims to explore the effect of a single intravitreal injection of axitinib hydrogel (OTX-TKI) on the integrity of the ellipsoid zone in eyes with NPDR, with the goal of providing insight into potential therapeutic approaches for preserving retinal function and vision loss in this patient population.

## METHODS

- OTX-TKI is an investigational, sustained release hydrogel designed to deliver axitinib, a small molecule, multitarget tyrosine kinase inhibitor directly in the eye with intravitreal injection.
- Post-hoc analysis of the Phase 1 HELIOS trial, a randomized, controlled study comparing OTX-TKI to sham injection in NPDR patients (DRSS Level 43 or 57) without center-involved diabetic macular edema (CI-DME).
- Spectral-domain OCT scans were read in a masked fashion using an automated, higher-order, machine-learning platform with certified-reader validation and correction, as needed, to extract retinal layer features, including EZ-RPE thickness and volume measures.

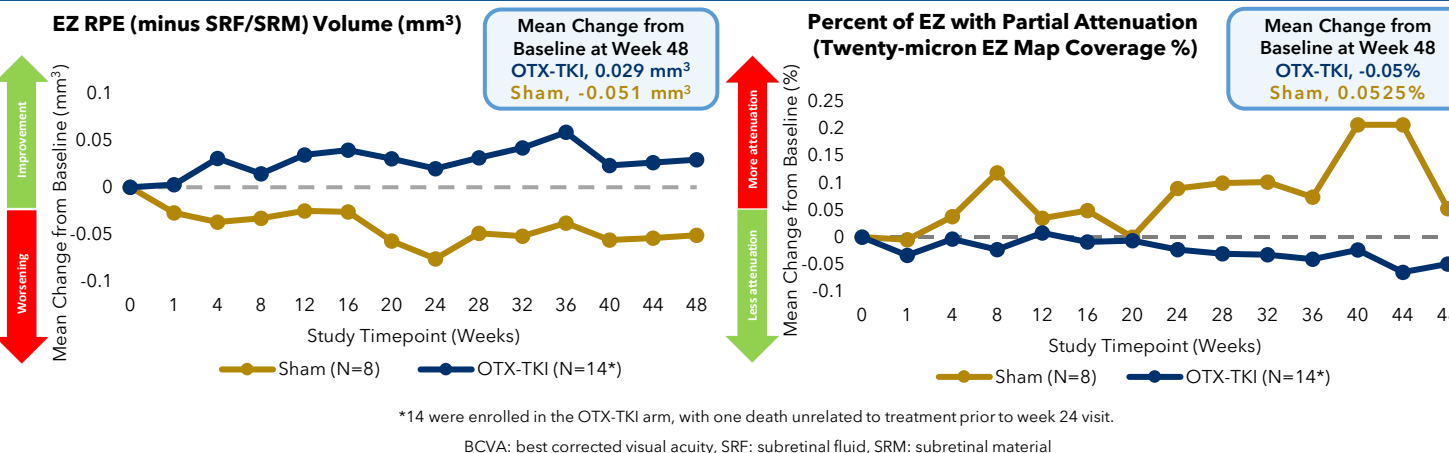
**Figure 1:** Two representative cases demonstrate longitudinal changes in *en face* retinal thickness and ellipsoid zone (EZ) mapping. EZ integrity was stabilized in the subject treated with intravitreal axitinib hydrogel injection, compared to the sham group.



**Figure 2:** Patients were randomized (2:1), dosed once with OTX-TKI or sham injections and were monitored for 52 weeks

## RESULTS

- No patients in the study received rescue anti-VEGF injections.
- Baseline EZ-RPE volume for both groups was 1.381 mm<sup>3</sup>. OTX-TKI eyes showed consistent increases in EZ-RPE volume from baseline at all visits from day 7 through week 48, with a mean increase of 0.020 mm<sup>3</sup> and 0.029 mm<sup>3</sup> at weeks 24 and 48, respectively, compared to a reduction of 0.076 mm<sup>3</sup> and 0.051 mm<sup>3</sup> in sham eyes, respectively.
- Baseline Twenty-micron EZ Map Coverage analyzed longitudinally was similar at baseline with relatively minimal EZ degradation in both arms (0.10% for the sham and 0.09% for the OTX-TKI arm). Across 48 weeks, the OTX-TKI arm remained relatively stable showing consistent and sustained drug effect over time, compared to the sham arm which exhibited greater fluctuation.



**Figure 3:** EZ RPE (minus SRF/SRM) Volume (mm<sup>3</sup>) (3A) and  $\leq 20 \mu\text{m}$  EZ Map Coverage (%) (3B) for randomized patients measured every 4 weeks

## CONCLUSIONS

- OTX-TKI may lead to stabilization or improvement of EZ integrity, as suggested by the observed EZ-RPE volume increase over 48 weeks in OTX-TKI-treated NPDR patients and the relatively stable partial EZ loss.
- These findings suggest a potential protective effect of OTX-TKI on photoreceptor structure, supporting its potential utility in early diabetic retinal disease management.