

## **Intravitreal Ziv-aflibercept in Patients with Diabetic Macular Edema Refractory to Intravitreal Bevacizumab.**

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**Purpose:** To evaluate the efficacy of intravitreal ziv-aflibercept (IVZ) in patients with diabetic macular edema resistant to intravitreal bevacizumab (IVB). **Method:** This prospective study was conducted between October 2017 and March 2018. Patients who had persistent macular edema, defined as <10% improvement in central macular thickness (CMT) on optical coherence tomography (OCT), after at least three IVB injections were eligible for this study. Patients were switched to IVZ and response to treatment after at least two injections was measured. Best corrected visual acuity (BCVA) as well as CMT and macular volume (MV) on OCT after receiving a series of IVB were compared to response after IVZ.

**Results:** A total of 55 eyes from 35 patients were included in this study. Mean age was 62 (49-75) year old. Twenty patients (57%) were male. Patients received an average of 8 (3-15) IVB injections before being switched to IVZ. All patients received at least two IVZ injections.

Mean BCVA improved from 0.85 logMAR at baseline (the time of medication switch) to 0.7 LogMAR (P=0.03) one month after receiving the second IVZ. Mean CMT and MV decreased from 493  $\mu\text{m}$  and 11  $\mu\text{m}^3$  to 348  $\mu\text{m}$  and 10  $\mu\text{m}^3$  (P<0.0001), respectively, after two IVZ injections. Patients experienced a significant improvement in CMT and MV after their first IVZ

injection ( $P < 0.0001$ ) while the change in BCVA reached statistical significance after the second IVZ injection ( $P: 0.016$ ). In 23 eyes which received three injections, BCVA improved from 0.85 at baseline to 0.5 LogMAR one month after third monthly IVZ injection ( $P < 0.002$ ) while CMT and MV decreased from 520  $\mu\text{m}$  and 11  $\mu\text{m}^3$  to 312  $\mu\text{m}$  and 9.7  $\mu\text{m}^3$ , respectively ( $P < 0.0001$ ). There were no adverse events for patients who received IVZ, including no cases of endophthalmitis.

Conclusion: IVZ was associated with improvements in vision and anatomic outcomes in patients with diabetic macular edema refractory to IVB. IVZ is a promising therapy which mitigates the costs associated with aflibercept while demonstrating good treatment response and a favorable safety profile. This option may be especially promising for low or middle income countries.