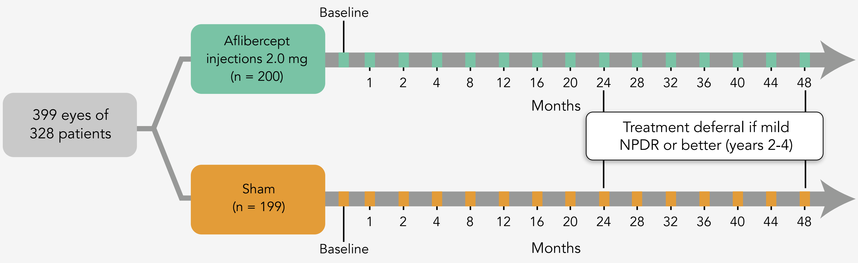
Effect of Intravitreous Anti-Vascular Endothelial Growth Factor (VEGF) vs Sham Treatment for Prevention of Vision-Threatening Complications of Diabetic Retinopathy (DR): The Protocol W Randomized Clinical Trial

Maturi RK, Glassman AR, Josic K, et al. *JAMA Ophthalmol*. 2021 Jul 1;139(7):701-712. doi:10.1001/jamaophthalmol.2021.0606
Maturi R, Ashraf M. Protocol W: A Summary of 2-Year Results. *Retina Today*. September 2021.

Protocol W is a Phase 3, prospective, multicenter study by the DRCR Retina Network that included eyes with moderate-to-severe non-proliferative diabetic retinopathy (NPDR) without baseline center-involved diabetic macular edema (CI-DME). This study was designed as a long-term evaluation of the efficacy of intravitreous aflibercept injections compared with sham treatment in preventing potentially vision-threatening complications in eyes with moderate to severe NPDR.

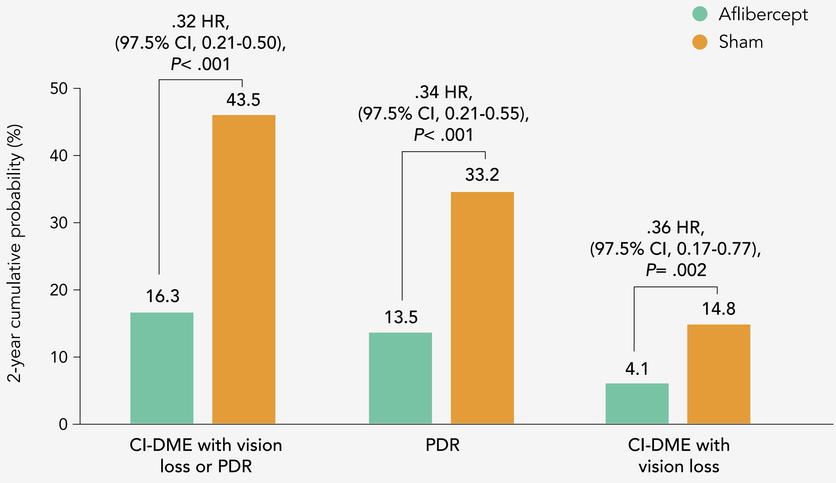
Eyes were randomized to treatment groups of aflibercept 2.0 mg or sham injections at baseline through 2 years, with treatment deferral between 2 and 4 years if the eye had mild NPDR or better.



Aflibercept was administered in both groups if CI-DME with vision loss* or high-risk PDR developed. The primary outcome of the study was either the development of CI-DME (>10% increase in CST from baseline) with vision loss* or the development of PDR at the completion of the last 2-year visit.

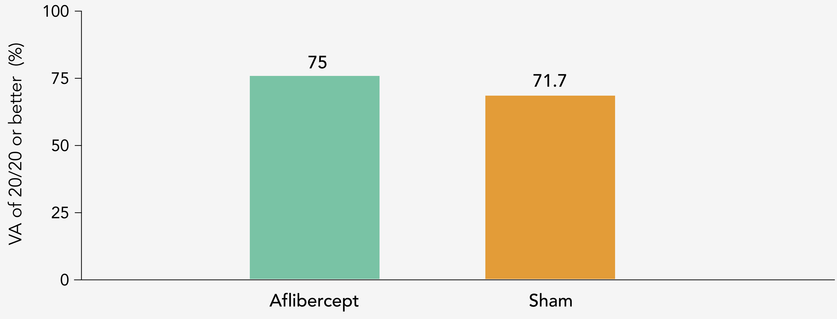
*≥10 letters at 1 visit or 5-9 letters at 2 consecutive visits.
PDR = proliferative diabetic retinopathy; CST = central subfoveal thickness; VA = visual acuity.

Preventive treatment with aflibercept resulted in a *threefold reduction* in the development of CI-DME with vision loss and nearly *twofold reduction* in the development of new-onset PDR.



HR = hazard ratio.

At 2 years, there was no significant difference in the mean change in visual acuity between the aflibercept group and the sham group.



The vast majority of eyes in both groups had a VA of 20/20 or better, with few eyes losing 10 or more letters at 2 years (6.9% vs 8.4%). This suggests that initiating treatment after the development of complications achieves similar visual outcomes at 2 years compared with preventive use of anti-VEGF injections.

Conclusions

The results of this study suggest that early aflibercept treatment in eyes with NPDR results in a reduction in the development of both PDR and CI-DME with decreased vision at 2 years. However, this preventive therapy did not translate to better visual acuity compared with sham injection. Long-term follow-up is necessary to determine whether visual outcomes will remain similar at 4 years or whether preventing PDR and CI-DME will result in better visual outcomes in eyes treated early with aflibercept.