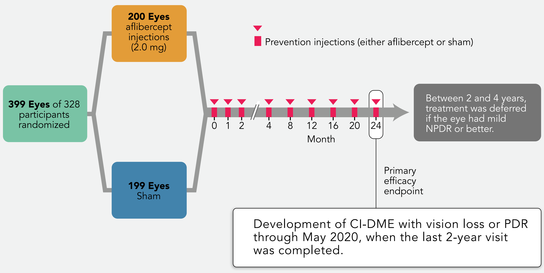
Effect of Intravitreous Anti–Vascular Endothelial Growth Factor vs Sham Treatment for Prevention of Vision-Threatening Complications of Diabetic Retinopathy: The Protocol W Randomized Clinical Trial

Maturi RK, Glassman AR, Josic K, et al. *JAMA Ophthalmol*. 2021;139(7):701-712.
doi:10.1001/jamaophthalmol.2021.0606

The role of anti–vascular endothelial growth factor injections for the management of nonproliferative diabetic retinopathy (NPDR) without center-involved diabetic macular edema (CI-DME) has not been clearly established. This study was designed to determine the efficacy of intravitreous aflibercept injections compared with sham treatment in preventing potentially vision-threatening complications in eyes with moderate to severe NPDR.

Data was collected from 328 adults (399 eyes) with moderate to severe NPDR (Early Treatment Diabetic Retinopathy Study severity level, 43-53), without CI-DME. Analyses followed the intent-to-treat principle.

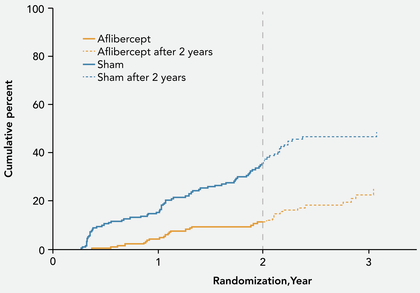


Aflibercept was administered in both groups if CI-DME with vision loss (≥10 letters at 1 visit or 5-9 letters at 2 consecutive visits) or high-risk proliferative diabetic retinopathy (PDR) developed.

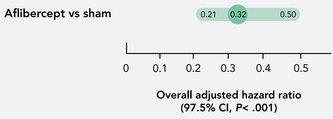
Among the 328 participants, 57.6% were men (230 of 399 eyes) with a mean age of 56 [SD: 11] years.

Aflibercept injections reduced the development of vision-threating complications compared with sham treatment.

Time from randomization to development of PDR or CI-DME with vision loss



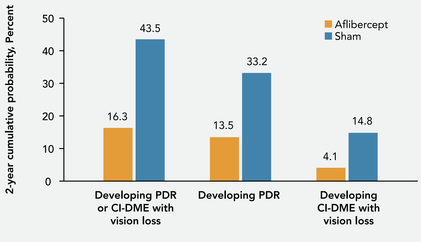
No. at risk				
Aflibercept	200	173	133	35
Sham	199	153	101	22



The overall adjusted hazard ratio for aflibercept vs sham favored aflibercept.

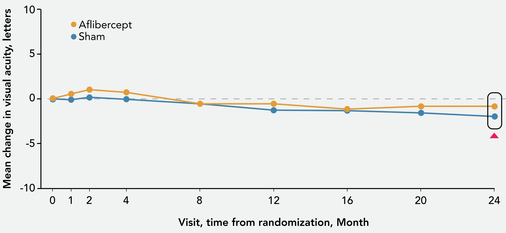
Aflibercept treatment reduced the probability of developing PDR or CI-DME with vision loss.

2-year cumulative probability of developing PDR or CI-DME with vision loss



Through 2 years, preventive treatment did not confer visual acuity benefit compared with observation plus aflibercept if complications developed.

Mean change in visual acuity through 2 years



No. of eyes								
Aflibercept	200	194	163	189	174	180	161	144	160
Sham	199	188	153	189	174	181	166	151	166

▲ The mean (SD) change in visual acuity from baseline to 2 years was -0.9 (5.8) letters with aflibercept and -2.0 (6.1) letters with sham (adjusted mean difference, 0.5 letters [97.5% CI, -1.0 to 1.9 letters]; *P*= .47).

Conclusions

In this randomized clinical trial, among eyes with moderate to severe NPDR, the proportion of eyes that developed PDR or vision-reducing CI-DME was lower with periodic aflibercept compared with sham treatment. However, through 2 years, preventive treatment did not confer visual acuity benefit compared with observation plus treatment with aflibercept only after development of PDR or vision-reducing CI-DME. The 4-year results will be important to assess longer-term visual acuity outcomes.