Intravitreal Afiblercept Injection for Nonproliferative Diabetic Retinopathy: Results from the PANORAMA Study

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Purpose:
To investigate efficacy and safety of intravitreal aflibercept injection (IAI) versus sham in moderately severe-to-severe nonproliferative diabetic retinopathy (NPDR) without diabetic macular edema (DME).

Methods:
Adult patients with DRSS 47 or 53, absence of CI-DME, and baseline BCVA ≥69 letters (approximately ≥20/40) received either IAI 2 mg q16 weeks after 3 monthly doses and one q8 interval (2q16, n=135), IAI 2 mg q8 weeks after 5 monthly doses (2q8, n=134), or sham (n=133). After week 52, the 2q8 group switched to PRN dosing (IAI was administered at each visit unless DRSS score was ≤35); the 2q16 and sham groups remained on fixed dosing. Primary endpoint was the proportion of eyes with a ≥2-step DRSS improvement at week 52. Additional endpoints included vision-threatening complications (VTC; proliferative diabetic retinopathy and/or anterior segment neovascularization) or CI-DME event rates through weeks 52 and 100. Event rates were based on the Kaplan–Meier method; risk reduction was based on calculated hazard ratios.

Results:
Through week 52, 65.2% (2q16) and 79.9% (2q8) versus 15.0% (sham) had a ≥2-step DRSS improvement (P<0.0001 for both comparisons). Corresponding proportions at week 100, were 62.2% (2q16), 50.0% (2q8) and 12.8% (sham) (nominal P<0.0001 for both). Through week 52, VTC event rate was 4% (2q16) and 2.4% (2q8) versus 20.1% (sham) (P<0.0001 for both). IAI significantly reduced VTC risk by 85% (2q16) and 88% (2q8) versus sham. Through week 100, VTC rates were lower with IAI (2q16 and 2q8) versus sham (9.1% 6.9% and 30.6%, respectively; nominal P<0.0001) with a corresponding risk reduction of 77% (2q16) and 83% (2q8) versus sham. The CI-DME event rate was lower with 2q16 and 2q8 versus sham through week 52 (7.0%, 8.5% and 27.6%; P<0.0001 for both) and week 100 (11.3%, 14.4% and 38.4%; nominal P<0.0001); IAI reduced CI-DME risk by 79% and 73% (2q16 and 2q8) at week 52 and 76% and 68% (2q16 and 2q8) at week 100. No new safety signals were identified.

Conclusions:
IAI improved diabetic retinopathy and prevented disease progression in moderately severe-to-severe NPDR without DME.