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Intravitreal Aflibercept Injection (IAI) for Moderately Severe to Severe Nonproliferative Diabetic Retinopathy (NPDR): The Phase 3 PANORAMA Study

David M. Brown, MD, on behalf of the PANORAMA study investigators

Retina Consultants of Houston, Houston, TX

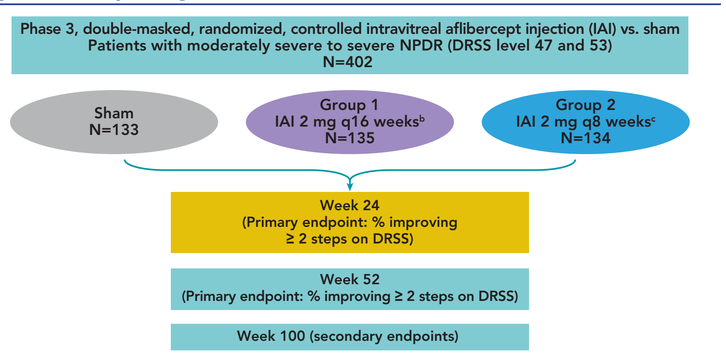
BACKGROUND

DIABETIC RETINOPATHY AND ITS TREATMENT OPTIONS

- Diabetic retinopathy (DR) is the leading cause of blindness in working-age adults in the United States.[1,2]
- An estimated 4 million U.S. adults 40 years and older have DR,[2] characterized by complex microvascular changes in the retina mediated by hyperglycemia and its myriad downstream effects.
- Several factors are associated with an increased risk of DR progression, primarily duration of disease, elevated hemoglobin A1c (HbA1c) levels, and systemic hypertension.[1]
- Panretinal photocoagulation (PRP) has long been a standard of care for proliferative diabetic retinopathy (PDR).[3] PRP, however, is inherently destructive to the retina and may cause peripheral vision loss and exacerbation of diabetic macular edema (DME). Despite timely intervention with PRP, some patients may still experience vision loss.[4]
- Corticosteroids may play a role in the treatment of PDR due to their anti-inflammatory and anti-angiogenic properties. When used, they are typically adjunctive therapy along with PRP.[5] Steroids are prone to adverse events such as cataract formation and increased intraocular pressure.
- In the VISTA and VIVID trials, significantly more eyes receiving intravitreal aflibercept injection (IAI) versus those in the laser control group had a ≥2-step improvement in the Diabetic Retinopathy Severity Scale (DRSS) score.[6,7] In an integrated safety analysis, the most frequent serious ocular adverse event through week 100 was cataract (2.4%, 1.0%, and 0.3% for 2q4, 2q8, and control).[7]
- The PANORAMA study was designed to evaluate IAI compared to sham in the treatment of moderately severe to severe non-proliferative diabetic retinopathy (NPDR) in patients without DME at baseline.

METHODS

Figure 1. Study Design[a]



[a]The PANORAMA study was funded by Regeneron Pharmaceuticals, Inc, Tarrytown, New York, and Bayer HealthCare, Berlin, Germany.
[b]After 3 initial monthly doses and 1 q8 interval
[c]After 5 initial monthly doses
Patients will be stratified by baseline DRSS level
DRSS = Diabetic Retinopathy Severity Scale; NPDR = non-proliferative diabetic retinopathy

RESULTS

Table 1. Disposition and Baseline Demographics

	Sham	Group 1	Group 2	All IAI	Total
Patients who completed week 24, n (%)	119 (89.5%)	129 (95.6%)	132 (98.5%)	261 (97.0%)	380 (94.5%)
N (FAS/SAF)	133	135	134	269	402
Age, years (SD)	55.8 (10.31)	55.4 (11.13)	55.8 (10.19)	55.6 (10.66)	55.7 (10.53)
Women, n (%)	64 (48.1%)	60 (44.4%)	53 (39.6%)	113 (42.0%)	177 (44.0%)
Race, n (%)					
White	107 (80.5%)	99 (73.3%)	104 (77.6%)	203 (75.5%)	310 (77.1%)
Black or African American	13 (9.8%)	16 (11.9%)	12 (9.0%)	28 (10.4%)	41 (10.2%)
Asian	4 (3.0%)	12 (8.9%)	7 (5.2%)	19 (7.1%)	23 (5.7%)
Other	9 (6.8%)	8 (5.9%)	11 (8.2%)	19 (7.1%)	28 (7.0%)
Hb A1c (%)	8.5 (1.54)	8.6 (1.69)	8.4 (1.64)	8.5 (1.66)	8.5 (1.62)
Duration of Diabetes, years (SD)	15.5 (9.34)	13.7 (8.61)	14.0 (9.69)	13.8 (9.15)	14.4 (9.24)
Diabetes type 2	123 (92.5%)	121 (89.6%)	124 (92.5%)	245 (91.1%)	368 (91.5%)

Group 1: 3 monthly doses followed by 1 q8 interval, Group 2: 5 monthly doses
FAS = full analysis set; SAF = safety analysis set

Table 2. Baseline Disease Characteristics

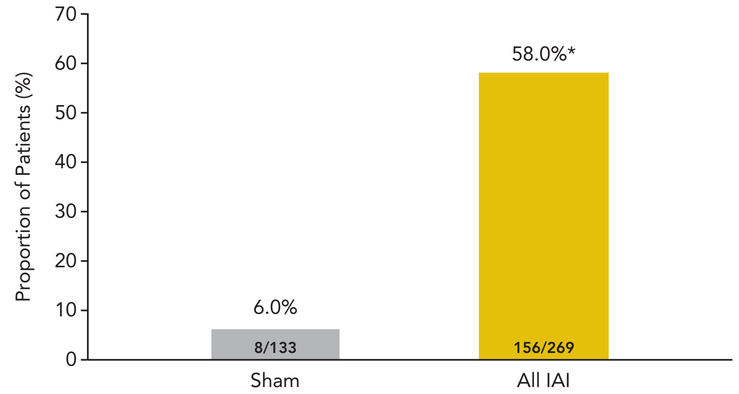
	Sham	Group 1	Group 2	All IAI	Total
N (FAS/SAF)	133	135	134	269	402
ETDRS BCVA (letters), mean (SD) Snellen Equivalent	82.7 (6.03) 20/25	82.2 (6.63) 20/25	82.3 (5.15) 20/25	82.3 (5.93) 20/25	82.4 (5.96) 20/25
Central retinal thickness, µm (SD)	249.4 (38.41)	246.0 (34.34)	246.8 (31.59)	246.4 (32.94)	247.4 (34.82)
DRSS					
Level 47	99 (74.4%)	102 (75.6%)	101 (75.4%)	203 (75.5%)	302 (75.1%)
Level 53	34 (25.6%)	33 (24.4%)	33 (24.6%)	66 (24.5%)	100 (24.9%)

Group 1: 3 monthly doses followed by 1 q8 interval, Group 2: 5 monthly doses
BCVA = best-corrected visual acuity; FAS = full analysis set; SAF = safety analysis set

TREATMENT EXPERIENCE

- IAI patients received, on average, 4.4 injections through week 24.

Figure 2. Proportion of Patients with ≥2-Step Improvement from Baseline in DRSS Score



*p < 0.0001 vs. sham
LOCF; Sham n=133, All IAI n=269

SAFETY

- There were no new safety signals in the trial.
- There was one case of mild intraocular inflammation (IOI) in a patient treated with IAI (0.085 percent rate per injection), which is consistent with the rate of IOI seen in previous clinical trials.

CONCLUSIONS

- The proportion of patients with ≥2-step improvement in the DRSS score was significantly greater in the IAI group vs sham at week 24
- No new safety signals were identified

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