Macular Atrophy (MA) in the Phase 2 Ladder Trial

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Purpose:
To determine the rate of MA prevalence and incidence in Ladder trial participants.

Methods:
Ladder (NCT02510794; N=220) compared the Port Delivery System with ranibizumab (PDS) filled with 3 customized formulations of ranibizumab vs monthly intravitreal ranibizumab 0.5 mg in eyes with nAMD that were responsive to ≥ 2 injections of any standard-of-care anti-VEGF agent. The Duke Reading Center assessed MA at screening, months 4 and 9, and the final visit. Patients with subfoveal MA at screening were excluded from trial enrollment. MA presence was assessed using SD-OCT according to the Classification of Atrophy Meetings guidelines. MA area was determined by FAF. SD-OCT and near infrared scanning laser ophthalmoscopic images were used to help define the MA margins when necessary. Two Readers assessed MA area. If values reported differed by >10%, they were arbitrated by a third Reader; areas differing by <10% were averaged. The worst-observation-carried-forward approach was used to impute missing data.

Results:
At baseline, after initial intravitreal anti-VEGF treatment, MA not involving the fovea was observed in 14.5%, 11.5%, and 13.6% of eyes in the PDS 10 mg/mL, 40 mg/mL, and 100 mg/mL arms, respectively, and in 7.3% of eyes in the monthly ranibizumab arm. Mean MA area (mm²) at baseline was 0.8, 1.4, and 0.9 in the PDS arms, respectively, and 1.8 in the monthly ranibizumab arm. At the last assessment, which varied across patients due to variable time on study (mean, 22.1 months; range, 10.8–37.6 months), MA was observed in 38.6%, 40.0%, 40.4%, and 45.7% of eyes in the PDS 10 mg/mL, 40 mg/mL, 100 mg/mL, and monthly ranibizumab arms, respectively. Mean change in MA area (mm²) at last assessment was +2.5, +1.6, +1.1 and +1.2, respectively. The percentages of patients without MA at baseline who developed MA at last assessment were 29%, 32%, 31%, and 41%, respectively.

Conclusions:
Rates of MA in Ladder were comparable across treatment arms. Continuous delivery of ranibizumab through the PDS was not associated with an increased incidence or enlargement of MA compared with monthly ranibizumab injections. Future analyses of larger PDS datasets will be used to validate these observations.