End-of-Study Results for the Ladder Phase 2 Trial of the Port Delivery System with Ranibizumab for Neovascular Age-Related Macular Degeneration

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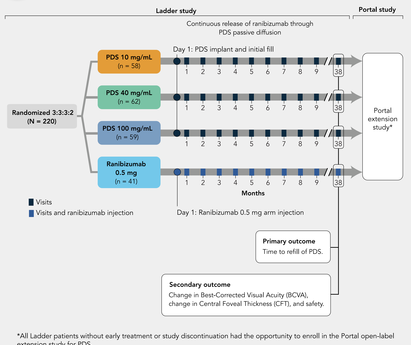
Vision gains in neovascular age-related macular degeneration (nAMD) patients receiving anti-VEGF treatment may decline over time. Consistent treatment is vital for maintaining vision, while interruptions may lead to loss of gains. This study presents end-of-study findings from the Ladder trial, assessing the Port Delivery System (PDS) with ranibizumab for nAMD treatment. PDS is an innovative drug delivery system designed to reduce treatment burden through the continuous intravitreal delivery of a specialized formulation of ranibizumab.

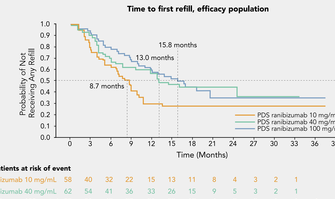
The Ladder trial was a phase 2, multicenter, randomized, active treatment-controlled, dose-ranging clinical trial of the PDS for nAMD conducted at 49 sites in the United States.



*All Ladder patients without early treatment or study discontinuation had the opportunity to enroll in the Portal open-label extension study for PDS.

The median time to first refill was 8.7 months, 13 months, and 15.8 months for PDS 10 mg/mL, 40 mg/mL, and 100 mg/mL respectively.

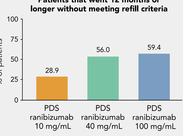
Time to first refill, efficacy population



No. of patients at risk of event

PDS ranibizumab 10 mg/mL	58	40	32	22	15	13	11	8	4	3	2	1
PDS ranibizumab 40 mg/mL	62	54	41	36	33	26	15	9	5	3	2	1
PDS ranibizumab 100 mg/mL	59	51	43	37	31	23	12	4	2	2	1	1

Patients that went 12 months or longer without meeting refill criteria

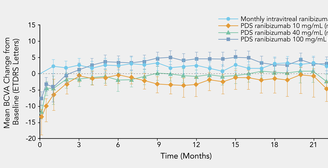


Refill criteria:
1. Increase in CFT ≥75 µm on OCT: avg. previous 2 CFT measurements
2. Increase in CFT ≥100 µm from lowest CFT in study
3. Decrease of ≥5 letters in BCVA compared to avg. previous 2 measurements
4. Decrease of ≥10 letters from best BCVA
5. Presence of new macular hemorrhage

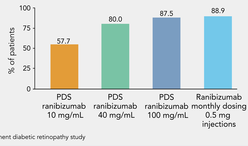
CFT = central foveal thickness, BCVA = best-corrected visual acuity

A dose response was observed across the PDS treatment arms, with the patients in the PDS 100 mg/mL arm experiencing improved BCVA gains from baseline over time.

BCVA change from baseline in the efficacy population



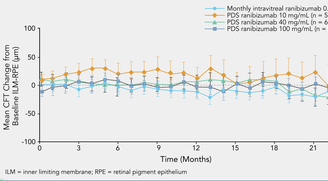
Patients maintaining baseline vision at month 22



ETDRS = early treatment diabetic retinopathy study

CFT change from baseline generally was stable over time and comparable in the PDS 100 mg/mL and monthly intravitreal ranibizumab 0.5 mg injection arms.

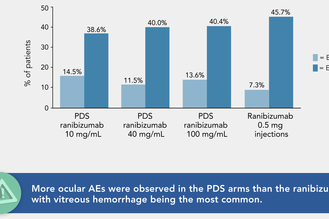
Mean CFT from the ILM to the RPE in the efficacy population



ILM = inner limiting membrane; RPE = retinal pigment epithelium

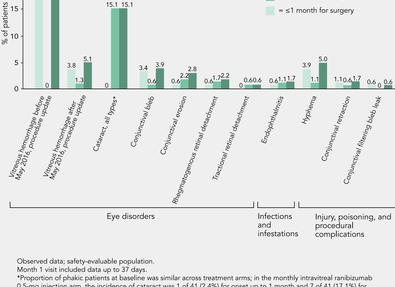
The percentage of patients with macular atrophy were similar across treatment arms and monthly intravitreal ranibizumab 0.5 mg injection arms at both baseline and end of study.

Patients with macular atrophy



More ocular AEs were observed in the PDS arms than the ranibizumab arm, with vitreous hemorrhage being the most common.

PDS with ranibizumab-associated adverse events



Observed data; safety-evaluable population.
Month 1 visit included data up to 37 days.
*Proportion of phakic patients at baseline was similar across treatment arms; in the monthly intravitreal ranibizumab 0.5-mg injection arm, the incidence of cataract was 1 of 41 (2.4%) for onset up to 1 month and 7 of 41 (17.1%) for onset more than 1 month.

Conclusions

Over a mean of 22 months on study, vision and anatomic outcomes were comparable between the PDS 100 mg/mL and monthly intravitreal ranibizumab 0.5 mg arms, with a lower total number of ranibizumab treatments with the PDS. The consistent outcomes observed with the PDS indicate that sustained intravitreal VEGF suppression through continuous drug delivery may be the key to reducing the anti-VEGF treatment burden without sacrificing long-term efficacy in patients with nAMD.