Pharmacokinetic (PK) Profile of the Port Delivery System With Ranibizumab (PDS) in the Phase 2 Ladder Trial

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Purpose:
The PDS is an investigational drug delivery system that includes a pars plana implant for continuous delivery of ranibizumab into the vitreous. Ranibizumab release from the implant follows first-order kinetics and is mediated by passive diffusion. In the phase 2 Ladder trial (NCT02510794) in patients with nAMD (N=220), serum samples were collected to characterize the PK of ranibizumab after the initial fill and subsequent refills of the PDS implant.

Methods:
In the PDS 10, 40, and 100 mg/mL arms, serum PK samples were collected at randomization; day (D) 1 ≥60 minutes following implant insertion; D1, 7, and 14 after implant insertion; at monthly study visits; and at D1 and 7 after each refill. In the monthly intravitreal ranibizumab 0.5 mg arm, serum samples were collected at randomization; months (M) 1, 3, 6, and 9; and the final study visit to assess Ctrough levels. Serum ranibizumab concentrations were measured using a validated enzyme-linked immunosorbent assay with a lower quantification limit of 15 pg/mL.

Results:
Independent of timing and number of refills, median serum ranibizumab concentrations at M9 were 27.9, 110, and 235 pg/mL in the PDS 10, 40, and 100 mg/mL arms, respectively, and 56.1 pg/mL in the monthly intravitreal ranibizumab arm. Individual serum concentrations over time generally support that PDS is continuously delivering ranibizumab for extended durations consistently across patients within each arm. Following implant insertion and before first refill, geometric mean (coefficient of variation) serum ranibizumab concentrations were 243 (146%), 160 (155%), 101 (137%), and 50.8 (108%) pg/mL at M6, 9, 12, and 16, respectively, in PDS 100 mg/mL patients who never received ranibizumab injections in the study eye or fellow eye after implant insertion or prior intravitreal bevacizumab treatment. For all PDS arms, serum concentration versus time profiles were consistent following implant insertion and across refills.

Conclusions:
The PDS implant continuously releases ranibizumab for extended durations, including through M16 in the PDS 100 mg/mL arm. These findings provide PK data to support median time to first refill of 15.8 months observed in PDS 100 mg/mL patients, which was associated with sustained visual gains comparable with monthly intravitreal ranibizumab.