Ladder Trial of the Port Delivery System With Ranibizumab: Initial Study Results

The Port Delivery System With Ranibizumab (PDS)

- Enables continuous delivery of ranibizumab into the vitreous

- Innovative drug delivery system
  - Permanent, refillable intraocular implant
  - Customized formulation of ranibizumab
  - Implant surgically placed at the pars plana
  - Refills performed in office

Ladder: A Phase 2 Randomized Active-Treatment-Controlled Clinical Trial of PDS for nAMD

Real-world Visual Acuity Outcomes Fall Short of Clinical Trial Results

- Frequent monitoring and injections impose a significant burden on patients, caregivers, and physicians
- Need a solution to reduce treatment burden and improve real-world patient outcomes

Ladder Eligibility: Patients With nAMD Responsive to Prior Anti-VEGF Treatment

- Disease
  - nAMD diagnosed within 9 months of screening
  - BCVA 20/20–20/200 Snellen equivalent (using ETDRS charts)

- Prior treatment with anti-VEGF injections
  - ≥ 2 anti-VEGF injections before screening
  - Ranibizumab must be most recent anti-VEGF treatment (≤ 7 days before screening)

- Demonstrated response to any anti-VEGF
  - Stable/improved BCVA or decreased CFT after initiation of anti-VEGF treatment
Study Design: PRN Refill of PDS vs Monthly Injections

Primary endpoint: Time to first required PDS refill

PDS refill performed if any of the following criteria were met due to nAMD disease activity:

- Increase in CFT
  - > 7.5 µm compared with average of last 2 visits

- Decrease in BCVA
  - > 5 ETDRS letters compared with average of last 2 visits

- Hemorrhage
  - New macular hemorrhage

Baseline Demographics and Ocular Characteristics: Generally Well Balanced Across Treatment Arms

Mean (SD) for age, years, no. of prior anti-VEGF injections, and time since nAMD diagnosis, months:

- Age, years:
  - Mean: 78.3 (11.9)
  - Range: 52 to 101

- No. of prior anti-VEGF injections:
  - Mean: 3.4 (1.5)
  - Range: 2 to 7

- Time since nAMD diagnosis, months:
  - Mean: 185.0 (61.6)
  - Range: 61 to 528

Vision Outcomes at 9 Months: PDS 100 mg/mL Comparable to Monthly Intravitreal Ranibizumab Injections

Mean BCVA change from baseline, patients previously treated with any anti-VEGF:

- Mean BCVA change:
  - PDS 100 mg/mL: 2.8 (1.6)
  - Monthly injections: 3.2 (1.8)

- 5 ETDRS letters compared with average of last 2 visits

1/28/2019
PDS ranibizumab 40 mg/mL
PDS ranibizumab 10 mg/mL
Intravitreal ranibizumab
PDS ranibizumab 100 mg/mL
PDS ranibizumab 0.5 mg monthly
Intravitreal ranibizumab

Injury, poisoning, and procedural complications
Infections and infestations
Nervous system disorders
Gastrointestinal disorders

Incidence > 1, n (%)
System Organ Class Preferred Term

Eye disorders
Events in PDS Arms Were Nonserious
Systemic Safety: Majority of GI, Injuries, and CNS Events in PDS Arms Were Nonserios

Mean CFT Change From Baseline ILM-Bruch's, Including PED Height
Mean CFT Change From Baseline ILM-RPE, Excluding PED Height

CFT Outcomes at 9 Months:
PDS Comparable to Monthly Intravitreal Injections

Drug Release Performance Verified in Explanted Implants

PDS-Associated Events: PDS Implantation Surgery and Refill Procedure Well Tolerated by Patients

Systemic Safety: PDS Comparable to Monthly Ranibizumab Injections

Oral Antithrombotic Substudy Results

No vitreous hemorrhages observed in patients on oral antithrombotic therapy that underwent PDS Implant insertion surgery using optimized surgical procedure
Conclusion

PDS Has the Potential to Reduce Intravitreal Injection Treatment Burden and Improve Real-world Clinical Outcomes

- In the PDS with ranibizumab 100 mg/mL treatment arm
  - Median time to first required refill was 15.0 months
  - 80% of patients went ≥ 6 months until the first refill
  - BCVA and anatomic outcomes comparable to those of monthly intravitreal ranibizumab

- PDS Implant insertion surgery and refill procedure were well tolerated
  - Systemic safety comparable to monthly intravitreal injections
  - Patients on oral antithrombotics able to interrupt treatment did not demonstrate an increased risk of vitreous hemorrhage

- Phase 3 program, Archway, using fixed 24-week interval dosing is underway

Video: PDS Optimized Implantation Surgical Procedure