Archway Phase 3 Trial of the Port Delivery System With Ranibizumab (PDS) for Neovascular Age-Related Macular Degeneration: Data Update and Key Surgical Pearls

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Purpose

To present results from the Archway September 2020 data cut and report key surgical pearls from the Port Delivery System with ranibizumab (PDS) implant insertion procedure

Introduction

- The PDS is an innovative drug delivery system for the continuous delivery of a customised formulation of ranibizumab into the vitreous through a refillable ocular implant[1,2]
- The PDS is US Food and Drug Administration approved for the treatment of neovascular age-related macular degeneration (nAMD) in adults who have responded to ≥ 2 anti–vascular endothelial growth factor (VEGF) injections[1]
- The phase 3 Archway trial (NCT03677934) evaluated safety and efficacy of the PDS for the treatment of nAMD[3]

Methods

- The phase 3 Archway trial evaluated non-inferiority and equivalence of the PDS with ranibizumab 100 mg/mL with fixed refill-exchanges every 24 weeks (PDS Q24W) versus intravitreal ranibizumab 0.5 mg injections every 4 weeks (monthly ranibizumab)[3]
- The primary endpoint was best-corrected visual acuity (BCVA) change from baseline averaged over weeks 36 and 40, with a non-inferiority margin of –4.5 letters and an equivalence margin of ± 4.5 letters[3]
- The September 2020 data cut extended Archway results to ≥ 48 weeks of follow-up, covering 2 complete refill-exchange intervals for patients treated with the PDS

Conclusions

- PDS Q24W maintained vision and anatomic outcomes comparable with monthly ranibizumab
  - Primary endpoint: PDS Q24W was non-inferior and equivalent for BCVA change at the average of weeks 36/40
  - BCVA change at the average of weeks 44/48 remained non-inferior through 2 refill-exchange intervals
  - Observed vision and anatomic results were comparable with monthly ranibizumab through week 48
  - Through 2 refill-exchange intervals, > 90% of PDS Q24W patients did not need supplemental ranibizumab treatment
  - Adverse events related to the PDS procedures are well understood, manageable and are continually being analysed to optimise patient outcomes
- Optimised surgical procedures support successful patient outcomes
  - Optimised implant insertion procedure mitigated post-operative vitreous haemorrhage
  - Adherence to specified methodology is key for maximising optimal outcomes with PDS procedures
  - Standardised surgical training and ongoing procedural evaluations are important for enhancing surgeon proficiency

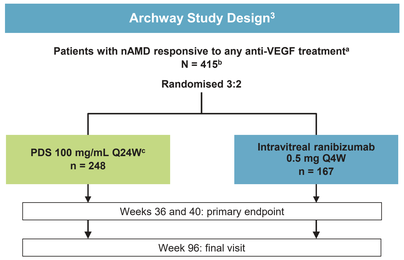
1. The Port Delivery System With Ranibizumab (PDS): Continuous Intravitreal Delivery of a Customised Formulation of Ranibizumab

- Permanent, refillable ocular implant
- Customised formulation of ranibizumab
- Implant surgically placed at the pars plana
- In-clinic refill-exchange procedures



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Archway Study Design[3]

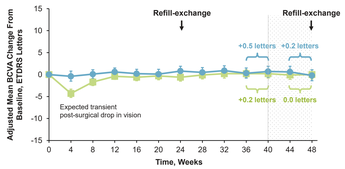


Archway, NCT03677934. [a] nAMD in study eye diagnosed within 9 months of screening; ≥ 3 intravitreal injections of any anti-VEGF agent within previous 6 months. [b] Efficacy- and safety-evaluable population. 418 total patients were enrolled, with 251 and 167 patients randomised to the PDS 100 mg/mL Q24W and intravitreal ranibizumab 0.5 mg Q4W arms, respectively; 3 patients in the PDS arm did not receive study treatment and were excluded from the efficacy- and safety-evaluable population. [c] Supplemental intravitreal ranibizumab 0.5 mg injections were available at the 2 visits preceding each refill-exchange procedure if protocol-specified disease activity criteria were met.
nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

2. Adjusted Mean BCVA and CPT Change From Baseline at Weeks 40 and 48 in Archway

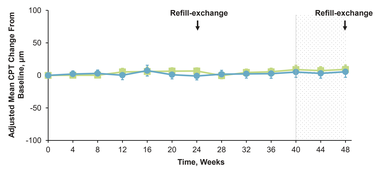
Adjusted Mean BCVA Change From Baseline[a]

Mean of 5.0 Previous Anti-VEGF Injections



Adjusted Mean CPT (ILM-RPE) Change From Baseline[b]

Mean of 5.0 Previous Anti-VEGF Injections

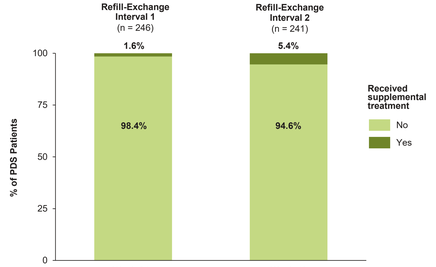


PDS 100 mg/mL Q24W (n = 248) — Intravitreal ranibizumab 0.5 mg Q4W (n = 167)

- PDS Q24W was non-inferior and equivalent to monthly ranibizumab at the average of weeks 36 and 40 (primary endpoint)[3] and non-inferior[c] at the average of weeks 44 and 48
- CPT outcomes were comparable across arms

Archway, NCT03677934. CPT defined as retinal thickness in the centre of the fovea measured between the ILM and the inner third of the RPE layer. [a] Adjusted means from an MMRM analysis through week 48. Adjusted means estimated using a MMRM with adjustment for change from baseline in BCVA as the response and included terms for treatment group, visit, treatment-by-visit interaction and baseline BCVA (< 74 vs ≥ 74 ETDRS letters). [b] Adjusted means from an MMRM analysis through week 40. MMRM adjustment for change from baseline in CPT score as the response and included terms for treatment group, visit, treatment-by-visit interaction and baseline BCVA (< 74 vs ≥ 74 ETDRS letters). Vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. [c] Equivalence not assessed per protocol. BCVA, best-corrected visual acuity; CPT, centre point thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ILM, internal limiting membrane; MMRM, mixed-effect model for repeated measures; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; RPE, retinal pigment epithelium; VEGF, vascular endothelial growth factor.

3. > 90% of Patients Did Not Receive Supplemental Treatment Before Each Refill-Exchange Procedure[a]



Supplemental intravitreal ranibizumab treatment criteria were based on BCVA and CST[b] changes due to nAMD disease activity

No patients who received supplemental treatment in interval 1 received supplemental treatment in interval 2

[a] For each interval, percentages of patients who did/did not receive supplemental treatment were calculated out of the number of patients who were on treatment and assessed for supplemental treatment for ≥ 1 visit (interval 1, week 16 or 20; interval 2, week 40 or 44). [b] CST was measured on SD-OCT from ILM-Bruch's and included PED height if present.
BCVA, best-corrected visual acuity; CST, central subfield thickness; ILM, internal limiting membrane; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; PED, pigment epithelial detachment; SD-OCT, spectral-domain optical coherence tomography.

4. OAESIs[a] Through an Average of 79 Weeks of Follow-up

Ocular adverse events in the PDS Q24W arm were manageable and well characterised in the clinical trial setting

	PDS 100 mg/mL Q24W (n = 248)		Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)	
MedDRA Preferred Term, n (%)[b]	Onset After Week 40	Overall[c]	Onset After Week 40	Overall[c]
Overall number of AESIs	**20**	**87**	**5**	**15**
Patients with ≥ 1 ocular AESI	**13 (5.2%)**	**55 (22.2%)**	**5 (3.0%)**	**15 (9.0%)**
Cataract[d]	11 (4.4%)	20 (8.1%)	2 (1.2%)	8 (4.8%)
Conjunctival bleb/conjunctival filtering bleb leak[e]	1 (0.4%)	17 (6.9%)	0	0
Conjunctival erosion	1 (0.4%)	6 (2.4%)	0	0
Conjunctival retraction	0	5 (2.0%)	0	0
Endophthalmitis	1 (0.4%)	4 (1.6%)	1 (0.6%)	1 (0.6%)
Hyphema	0	1 (0.4%)	0	0
Rhegmatogenous retinal detachment	0	2 (0.8%)	0	0
Tractional retinal detachment	0	0	0	0
Vitreous haemorrhage	2 (0.8%)	15 (6.0%)	2 (1.2%)	6 (3.6%)

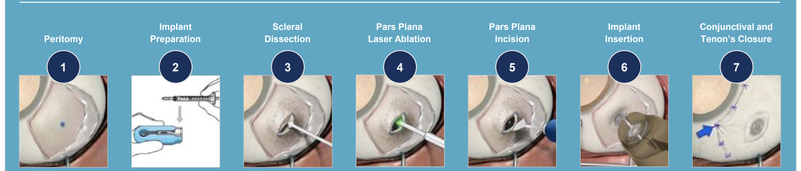
- 3 PDS patients experienced implant dislocation; 2 had onset after week 40
- 1 of 248 PDS-treated patients had irreversible vision loss due to an adverse event (*E. faecalis* endophthalmitis); no new events after week 40
- Systemic safety of PDS Q24W was generally comparable with monthly ranibizumab

[a] Protocol-defined OAESIs potentially related to the PDS implant or implant insertion procedure. [b] Frequency counts by MedDRA Preferred Term. Multiple occurrences of the same adverse event in an individual are counted only once for each column. [c] All data through the 11 September 2020 clinical cutoff date. [d] Includes terms: cataract, cataract nuclear, cataract cortical, cataract subcapsular. [e] In PDS trials, conjunctival bleb is an elevation of the conjunctiva above the implant flange; conjunctival filtering bleb leak is a post-surgical fluid accumulation under the conjunctiva. Observed data, all treated patients who received ≥ 1 dose of study drug according to the actual treatment. Month 1 visit includes data up to 37 days (monthly study visit + 7 days).
AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; OAESI, ocular adverse event of special interest; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

5. The PDS Surgical Procedures Have Evolved to Support Optimal Outcomes and Include 7 Critical Steps

Following all surgical steps as prescribed in the Instructions for Use is required to maximise optimal surgical outcomes

Critical Steps for Surgical Success

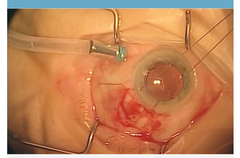


Control of haemostasis is critical at all steps to ensure optimal visualisation and minimise risk of post-operative vitreous haemorrhage

The content of this presentation does not constitute any form of training on the or any associated surgical procedures. In addition, the content of this presentation is not a substitute for training on PDS or any associated surgical procedures.
PDS, Port Delivery System with ranibizumab.

6. Precise Handling of the Conjunctiva and Tenon's Capsule and Anchorage of Both to the Limbus During Closure Are Crucial for Optimal Surgery Outcomes

Traction Suture



Traction Suture

- Placement of a traction suture before peritomy aids in visualisation of the superotemporal quadrant

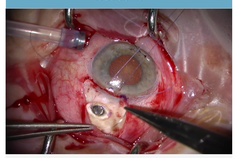
Peritomy



Crucial Steps in Peritomy

- Identify, preserve Tenon's capsule
- Use of non-toothed forceps
- Blunt dissection from limbus to fornix

Closure



Crucial Steps in Closure

- Both conjunctiva and Tenon's capsule should be sutured to anterior limbus with scleral bites
- Use of non-toothed forceps
- Multiple 3:1:1 sutures placed away from implant

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References

1. Susvimo [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2022.
2. Khanani AM et al. *Expert Opin Drug Deliv.* 2021;18(11):1571-1576.
3. Holekamp N et al. Archway Investigators. Ophthalmology. 2022;129(3):295-307.

Financial Disclosures

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- MM: Employee: F. Hoffmann-La Roche Ltd.

Study and Product Disclosures

- The Port Delivery System with ranibizumab (PDS) has been approved by the US Food and Drug Administration for the treatment of nAMD in adults who have previously responded to ≥ 2 anti-VEGF injections. Please note that the PDS has not been approved for use outside the United States
- The US Food and Drug Administration has issued a boxed warning for the PDS because it has been associated with a 3-fold higher rate of endophthalmitis compared with monthly intravitreal injections of ranibizumab[1]
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation

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