Analysis of Retinal Fluid and Vision Outcomes in the Archway Phase 3 Trial of the Port Delivery System With Ranibizumab (PDS) in Patients With nAMD

Arshad M. Khanani, MD, MA, FASRS[1]; Steven Blotner, MS[2]; Shamika Gune, MD[2]; and Merce Morral, MD[3]

[1] Sierra Eye Institute, Reno, NV, USA; [2] Genentech, Inc., South San Francisco, CA, USA; [3] F. Hoffmann-La Roche Ltd., Basel, Switzerland

Key Clinical Question

What is the relationship between retinal fluid and vision outcomes in patients with neovascular age-related macular degeneration (nAMD) treated in the phase 3 Archway trial of the Port Delivery System with ranibizumab (PDS)?

Introduction

- The PDS is an innovative drug delivery system for the continuous delivery of a customised formulation of ranibizumab into the vitreous and is approved by the US Food and Drug Administration for the treatment of nAMD in adults who have previously responded to ≥ 2 anti–vascular endothelial growth factor (VEGF) injections[1]
- The phase 3 Archway trial (NCT03677934) demonstrated that[2,3]:
  - The PDS with ranibizumab 100 mg/mL with fixed refill-exchanges every 24 weeks (PDS Q24W) was non-inferior and equivalent to intravitreal ranibizumab 0.5 mg injections every 4 weeks (monthly ranibizumab) for best-corrected visual acuity (BCVA) change at the average of weeks 36/40 (primary endpoint)
  - PDS Q24W maintained vision and anatomic outcomes comparable with monthly ranibizumab through 2 years (96 weeks)
  - Through each of the 4 PDS treatment intervals, ~95% of PDS Q24W patients assessed did not receive supplemental ranibizumab treatment[a]
  - 93.2% of PDS Q24W patients preferred PDS treatment over intravitreal injections at week 40
  - Adverse events related to the PDS procedures were generally manageable, with learnings continually implemented to optimise patient outcomes[b]

[a] Supplemental intravitreal ranibizumab 0.5 mg injections were available at the 2 visits preceding each refill-exchange procedure if the following protocol-specified disease activity criteria were met: decrease of ≥ 15 letters from the best-recorded BCVA in the study OR increase of ≥ 100 µm in CST on SD-OCT from the lowest CST measurement in the study OR increase of ≥ 100 µm in CST on SD-OCT from the lowest CST measurement in the study associated with a decrease of ≥ 10 letters from the best-recorded BCVA during the study. [b] 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.

Methods

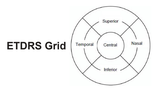
- In the phase 3 Archway trial, patients with nAMD were randomised to PDS Q24W or monthly ranibizumab[2]
- Spectral-domain optical coherence tomography (SD-OCT) images at each monthly visit were graded for subretinal fluid (SRF) or intraretinal fluid (IRF) up to week 40
- Analysis outcomes included:
  - Proportion of patients with either SRF or IRF (and SRF and/or IRF in the centre 1 mm) over 40 weeks
  - Change in BCVA from baseline in study eyes in the presence or absence of SRF/IRF up to week 40

Conclusions

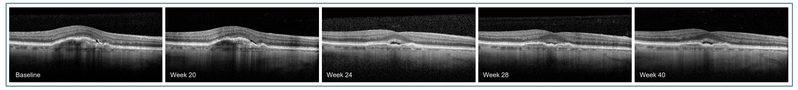
- In Archway, incidence of retinal fluid (SRF and/or IRF) was generally similar in the PDS Q24W and monthly ranibizumab treatment arms and remained consistent over time
- Vision outcomes on study were comparable, regardless of the overall presence or absence of SRF and/or IRF in either treatment arm
- The presence of IRF in the centre 1 mm was associated with worse vision outcomes, consistent with other trials
- Continuous delivery of ranibizumab with PDS Q24W maintained vision outcomes, regardless of the overall presence or absence of retinal fluid

1. SD-OCT Images From Archway Were Graded for SRF/IRF

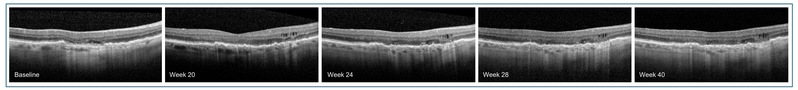
- SD-OCT images from the Archway trial were subject to dual-read grading, with the entire macula reviewed for SRF and IRF, graded YES/NO
- If graded YES for SRF/IRF, images were further reviewed for SRF/IRF at the centre 1 mm



Patient With SRF Present

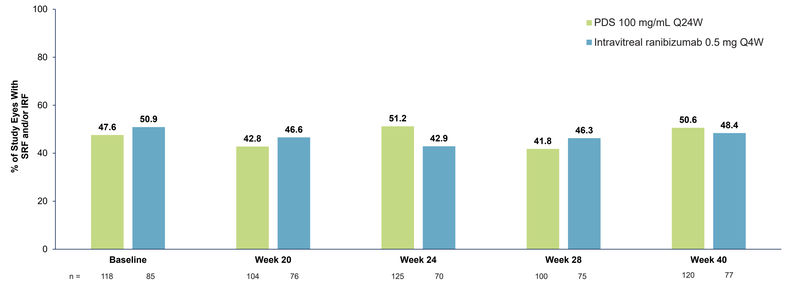


Patient With IRF Present



Archway, NCT03677934.
ETDRS, Early Treatment Diabetic Retinopathy Study; IRF, intraretinal fluid; SD-OCT, spectral-domain optical coherence tomography; SRF, subretinal fluid.

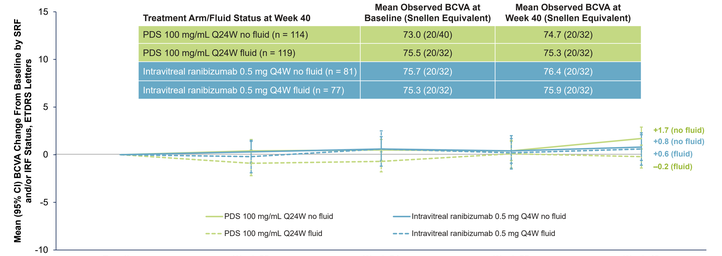
2. Percentage of Study Eyes With SRF and/or IRF Was Similar Between Treatment Arms and Over Time



Archway, NCT03677934.
IRF, intraretinal fluid; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; SRF, subretinal fluid.

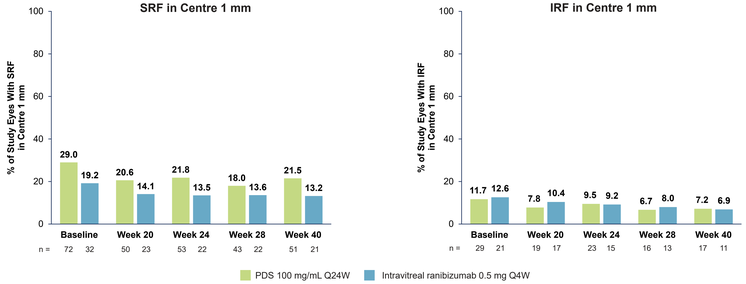
3. Vision Outcomes Were Similar Between Treatment Arms Both With and Without SRF and/or IRF

Treatment Arm/Fluid Status at Week 40	Mean Observed BCVA at Baseline (Snellen Equivalent)	Mean Observed BCVA at Week 40 (Snellen Equivalent)
PDS 100 mg/mL Q24W no fluid (n = 114)	73.0 (20/40)	74.7 (20/32)
PDS 100 mg/mL Q24W fluid (n = 119)	75.5 (20/32)	75.3 (20/32)
Intravitreal ranibizumab 0.5 mg Q4W no fluid (n = 81)	75.7 (20/32)	76.4 (20/32)
Intravitreal ranibizumab 0.5 mg Q4W fluid (n = 77)	75.3 (20/32)	75.9 (20/32)



Archway, NCT03677934.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; IRF, intraretinal fluid; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; SRF, subretinal fluid.

4. Fluid Dynamics in the Centre 1 mm Were Similar Between Treatment Arms; Relatively Few Patients Had Fluid Presence in the Centre 1 mm

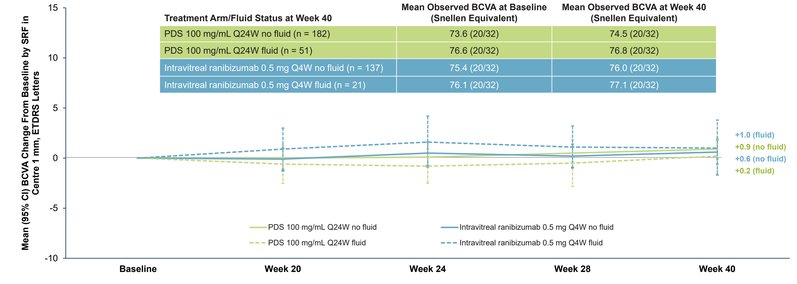




Archway, NCT03677934.
IRF, intraretinal fluid; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; SRF, subretinal fluid.

5. Vision Outcomes Were Similar Between Treatment Arms Both With and Without SRF in the Centre 1 mm

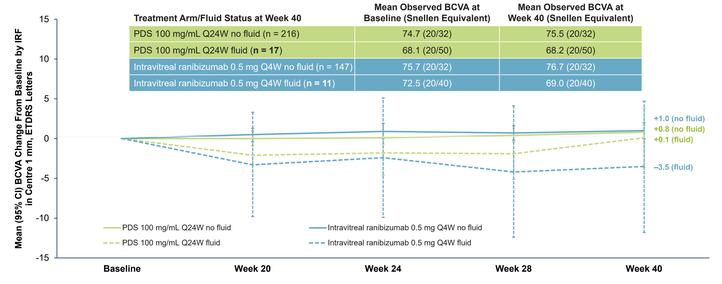
Treatment Arm/Fluid Status at Week 40	Mean Observed BCVA at Baseline (Snellen Equivalent)	Mean Observed BCVA at Week 40 (Snellen Equivalent)
PDS 100 mg/mL Q24W no fluid (n = 182)	73.6 (20/32)	74.5 (20/32)
PDS 100 mg/mL Q24W fluid (n = 51)	76.6 (20/32)	76.8 (20/32)
Intravitreal ranibizumab 0.5 mg Q4W no fluid (n = 137)	75.4 (20/32)	76.0 (20/32)
Intravitreal ranibizumab 0.5 mg Q4W fluid (n = 21)	76.1 (20/32)	77.1 (20/32)



Archway, NCT03677934.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; SRF, subretinal fluid.

6. Presence of IRF in the Centre 1 mm Was Associated With Worse Vision Outcomes

Treatment Arm/Fluid Status at Week 40	Mean Observed BCVA at Baseline (Snellen Equivalent)	Mean Observed BCVA at Week 40 (Snellen Equivalent)
PDS 100 mg/mL Q24W no fluid (n = 216)	74.7 (20/32)	75.5 (20/32)
PDS 100 mg/mL Q24W fluid (**n = 17**)	68.1 (20/50)	68.2 (20/50)
Intravitreal ranibizumab 0.5 mg Q4W no fluid (n = 147)	75.7 (20/32)	76.7 (20/32)
Intravitreal ranibizumab 0.5 mg Q4W fluid (**n = 11**)	72.5 (20/40)	69.0 (20/40)



Archway, NCT03677934.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; IRF, intraretinal fluid; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

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References

1. Susvimo [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2022.
2. Holekamp N et al; Archway Investigators. *Ophthalmology*. 2022;129(3):295-307.
3. Wykoff CC. Presented at: Bascom Palmer Eye Institute Angiogenesis, Exudation, and Degeneration Meeting; February 11-12, 2022; Virtual.

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- SB: Employee: Genentech, Inc.; Stockholder: Roche
- SG: Employee: Genentech, Inc.
- 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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