Updated Safety and Efficacy Results From the Archway Phase 3 Trial of the Port Delivery System With Ranibizumab (PDS) for Neovascular AMD

Presented at the 39th Annual Meeting of the American Society of Retina Specialists

Carl C. Awh, MD, FASRS[1] on behalf of Archway Investigators;

Giulio Barteselli, MD[2]; Anne E. Fung, MD[2]; Derrick Kaufman, PhD[2]; David Kardatzke, PhD[2]; Sneha Makadia, PharmD[2]; Merce Morral, MD[3]; Jeffrey Willis, MD, PhD[2]; and Shamika Gune, MD[2]

[1] Tennessee Retina, Nashville, TN; [2] Genentech, Inc., South San Francisco, CA; [3] F. Hoffmann-La Roche Ltd., Basel, Switzerland

Disclosures

Financial Disclosures

- CCA: Advisory Board: Allergan; Consultant: Bausch + Lomb, Genentech, Inc., Katalyst, Volk; Stockholder, Stock: ArcticDX; Katalyst; Research support: Investigator, Grants: Apellis, F. Hoffmann-La Roche Ltd., Genentech, Inc., GlaxoSmithKline, Merck, Ophthotech, PanOptica, Regeneron; Other, Honoraria: Allergan, Bausch + Lomb, Genentech, Inc., Volk.
- GB, AEF, DKaufman, DKardatzke, SM, JW, SG: Employee, Salary: Genentech, Inc.
- MM: Employee, Salary: F. Hoffmann-La Roche Ltd.

Study Disclosures

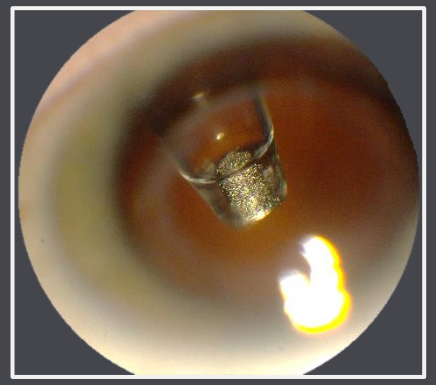
- PDS is an investigational medicine that is being studied for the treatment of neovascular age-related macular degeneration. Its efficacy and safety profile have not been established and it has not been approved by the health authorities
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by Genentech, Inc., a member of the Roche Group, for the study and third-party writing assistance, which was provided by Karlina J. Kauffman, PhD, of Envision Pharma Group

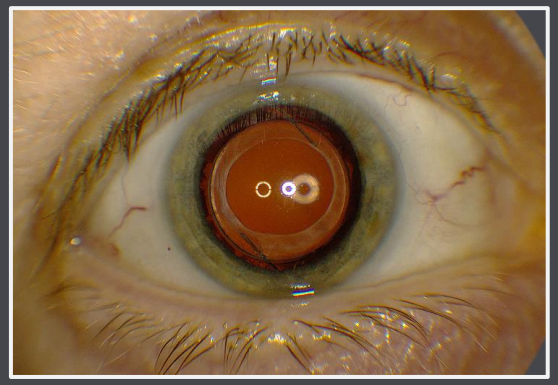
Acknowledgments

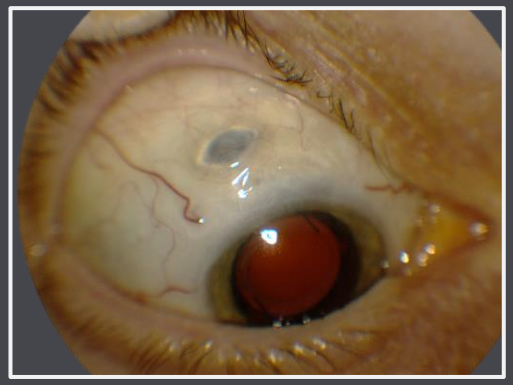
- Thanks to Nancy M. Holekamp, Peter A. Campochiaro, Margaret Chang, Daniel Miller, Dante Pieramici, Anthony P. Adamis, Christopher Brittain, Erica Evans, Katie F. Maass, Shienal Patel, Shrirang Ranade, Natalia Callaway, Cheryl Jones, and Varun Malhotra for additional support

The Port Delivery System With Ranibizumab (PDS)

Continuous intravitreal delivery of a customized formulation of ranibizumab







Innovative, Investigational Drug Delivery System

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

Ladder Phase 2 Trial of the PDS for nAMD

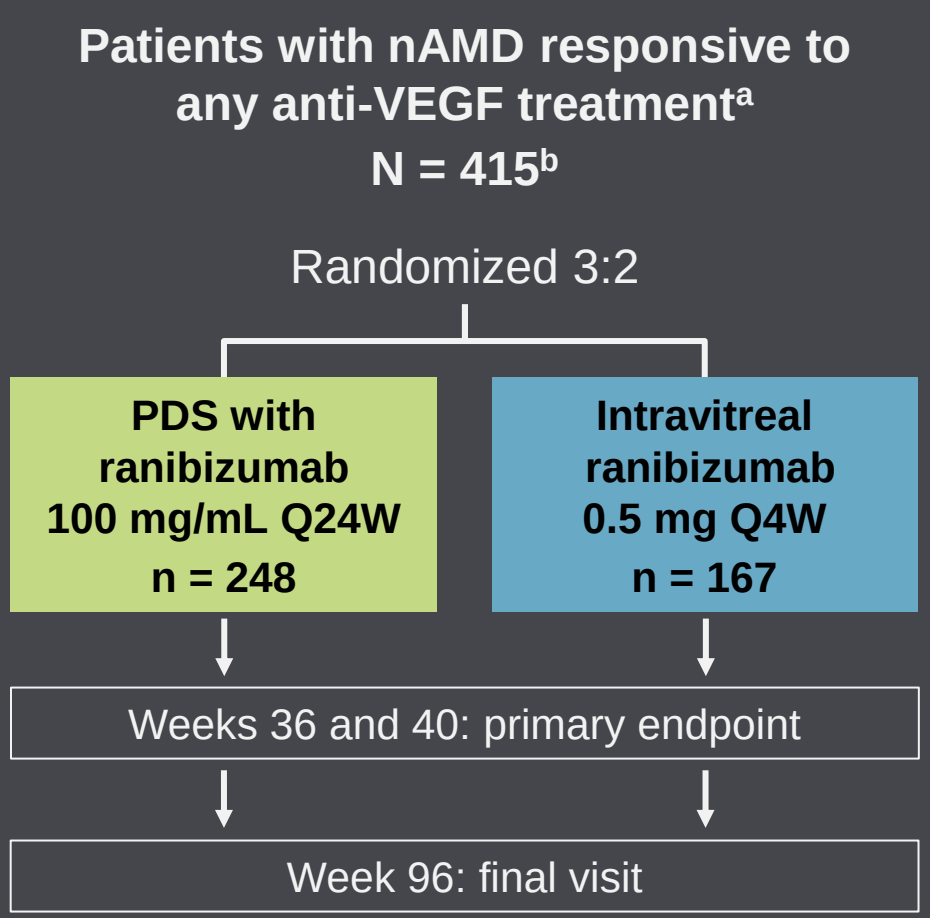
- PDS 100 mg/mL vision and anatomic outcomes comparable with monthly ranibizumab 0.5 mg
- PDS was generally well tolerated
- Supported evaluation in Archway phase 3 trial

Phase 3 Trials of the PDS

- Archway (nAMD): completed
- Portal (nAMD extension study): ongoing
- Velodrome (nAMD): enrollment initiated
- Pagoda (DME): ongoing
- Pavilion (DR): ongoing

Ladder, NCT02510794; Archway, NCT03677934; Portal, NCT03683251; Velodrome, NCT04657289; Pagoda, NCT04108156; Pavilion, NCT04503551.
Campochiaro PA et al. *Ophthalmology.* 2019;126(8):1141-1154. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016. Khanani AM et al. *Ophthalmol Retina*. 2021;5(8):775-787. DME, diabetic macular edema; DR, diabetic retinopathy; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab.

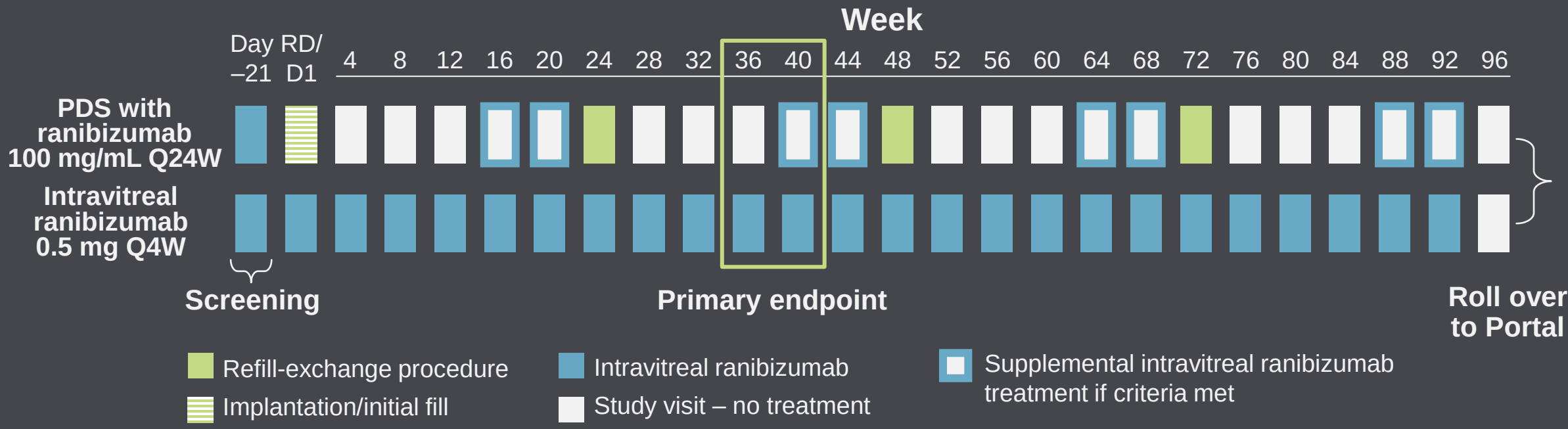
Archway: Designed to Evaluate the Efficacy and Safety of Continuous Drug Delivery With the PDS With Q24W Refill



Primary objective	Evaluate noninferiority and equivalence of PDS 100 mg/mL Q24W versus intravitreal ranibizumab 0.5 mg Q4W
Primary endpoint	Change in BCVA score from baseline averaged over weeks 36 and 40
Secondary endpoints	• Change in BCVA score from baseline over time • Change in CPT from baseline over time and at week 36 • Percentage of PDS-treated patients who received supplemental treatment during first refill-exchange interval • Incidence and severity of ocular and systemic AEs, SAEs, and ocular AEs of special interest

[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 randomized 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. Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016. AE, adverse event; BCVA, best-corrected visual acuity; CPT, center point thickness; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; SAE, serious adverse event; VEGF, vascular endothelial growth factor.

Archway Treatment Regimen: PDS With Fixed 24-Week Refill-Exchanges



Criteria for Supplemental Intravitreal Ranibizumab: Disease Activity Due to nAMD[a]				
CST + BCVA		**BCVA**		**CST**
Increase of ≥ 100 µm on SD-OCT from lowest measurement and decrease of ≥ 10 letters from best-recorded score	or	Decrease of ≥ 15 letters from best-recorded score	or	Increase of ≥ 150 µm on SD-OCT from lowest measurement

[a] Eligible for supplemental intravitreal ranibizumab treatment with open-label intravitreal ranibizumab at weeks 16 and 20 (after implant insertion) and at weeks 40, 44, 64, 68, 88, and 92 if any of the 3 criteria were met. Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016. BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; RD, randomization; SD-OCT, spectral-domain optical coherence tomography.

Baseline Demographics and Ocular Characteristics Were Well Balanced Across Treatment Arms

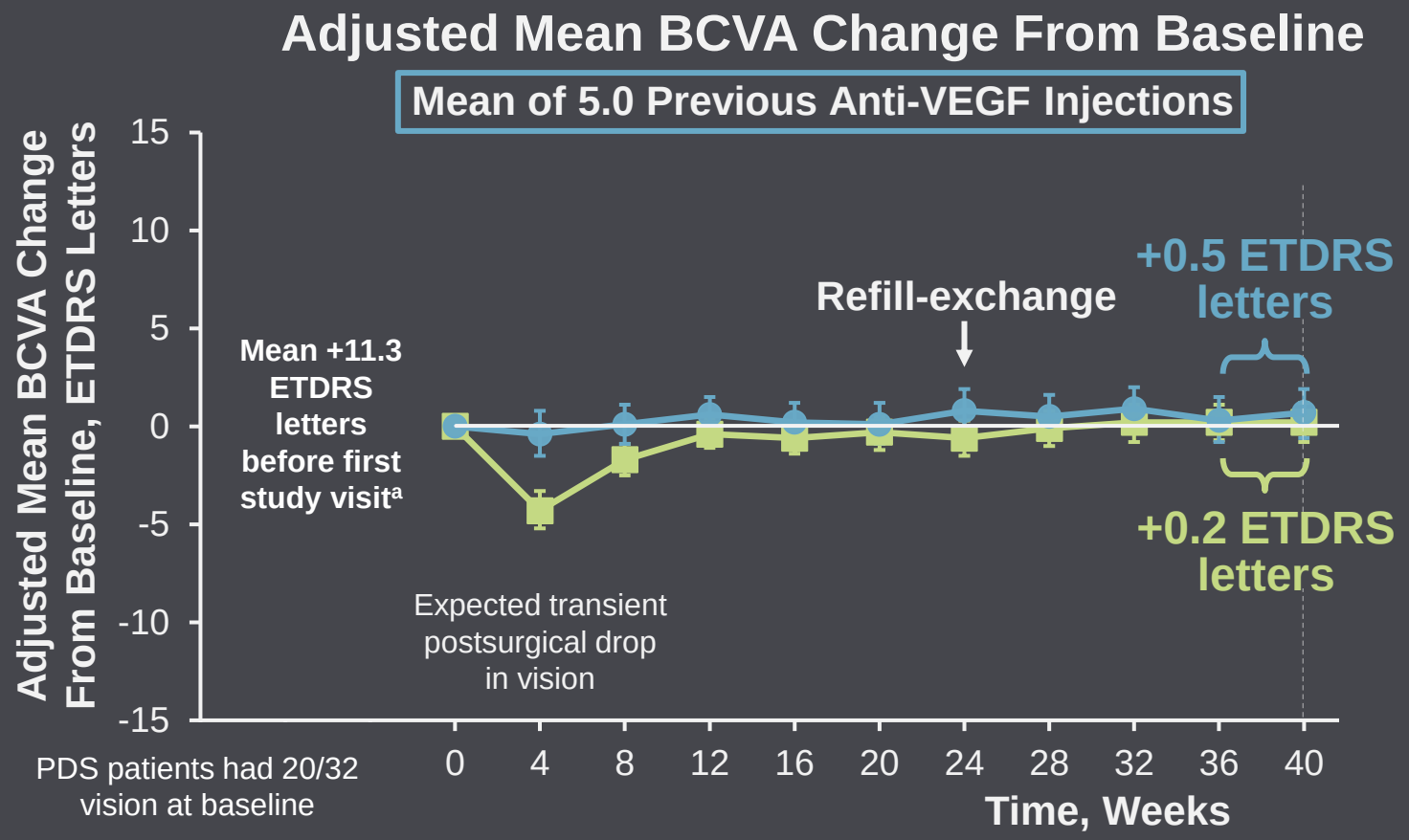
Characteristic	PDS 100 mg/mL Q24W (n = 248)	Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)
Age, years		
Mean (SD)	75.2 (8.1)	74.8 (7.6)
Range	51–96	54–89
Sex, n (%)		
Male	103 (41.5%)	67 (40.1%)
Baseline BCVA, ETDRS letter score		
Mean (SD)	74.4 (10.5)	75.5 (10.3)
Snellen equivalent	20/32	20/32
Baseline CPT, µm		
Mean (SD)	176.9 (54.8)	177.2 (49.1)
Time since nAMD diagnosis, months		
Mean (SD)	5.9 (9.5)	5.3 (2.0)
Number of prior anti-VEGF injections		
Mean (SD)	5.0 (2.1)	5.0 (1.5)

Impact of COVID-19 was low[a]

[a]2 cases of COVID-19 reported in Archway through the September 11, 2020 clinical cutoff date. Overall, 9 and 7 patients missed their study visit due to COVID-19 at weeks 44 and 48, respectively; none missed both visits. At week 48, 1 additional patient had missing certified examiner–assessed BCVA data. CPT measured from internal limiting membrane to the inner third of the retinal pigment epithelium. Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016 BCVA, best-corrected visual acuity; CPT, center point thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; 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.

Adjusted Mean BCVA Change From Baseline

PDS Q24W Was Noninferior and Equivalent to Monthly Ranibizumab at Primary Endpoint



Primary endpoint:
Change in BCVA from baseline averaged over weeks 36 and 40

Difference in adjusted means (95% CI)

–0.3 (–1.7, +1.1)

PDS equivalent to monthly treatment

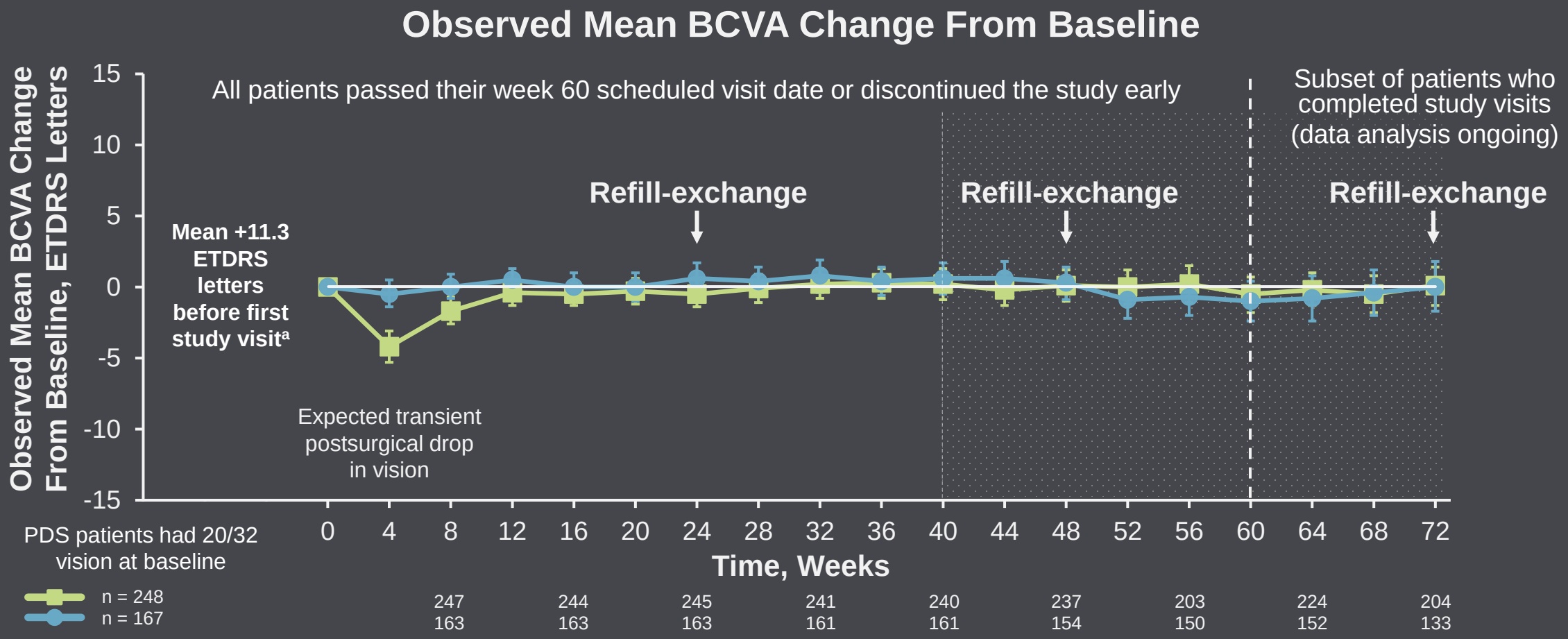
PDS 100 mg/mL Q24W (n = 248)

Intravitreal ranibizumab 0.5 mg Q4W (n = 167)

[a] Change in visual acuity from the last available visual acuity score assessed in the study eye before the start of anti-VEGF treatment and baseline. If ETDRS letters were not available, the Snellen value was converted to the ETDRS equivalent. Adjusted means from a mixed-effect model for repeated measures (MMRM) analysis through week 40. Vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. 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 ETDRS letters vs ≥ 74 ETDRS letters). Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016. 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; VEGF, vascular endothelial growth factor.

Observed Mean BCVA Change From Baseline

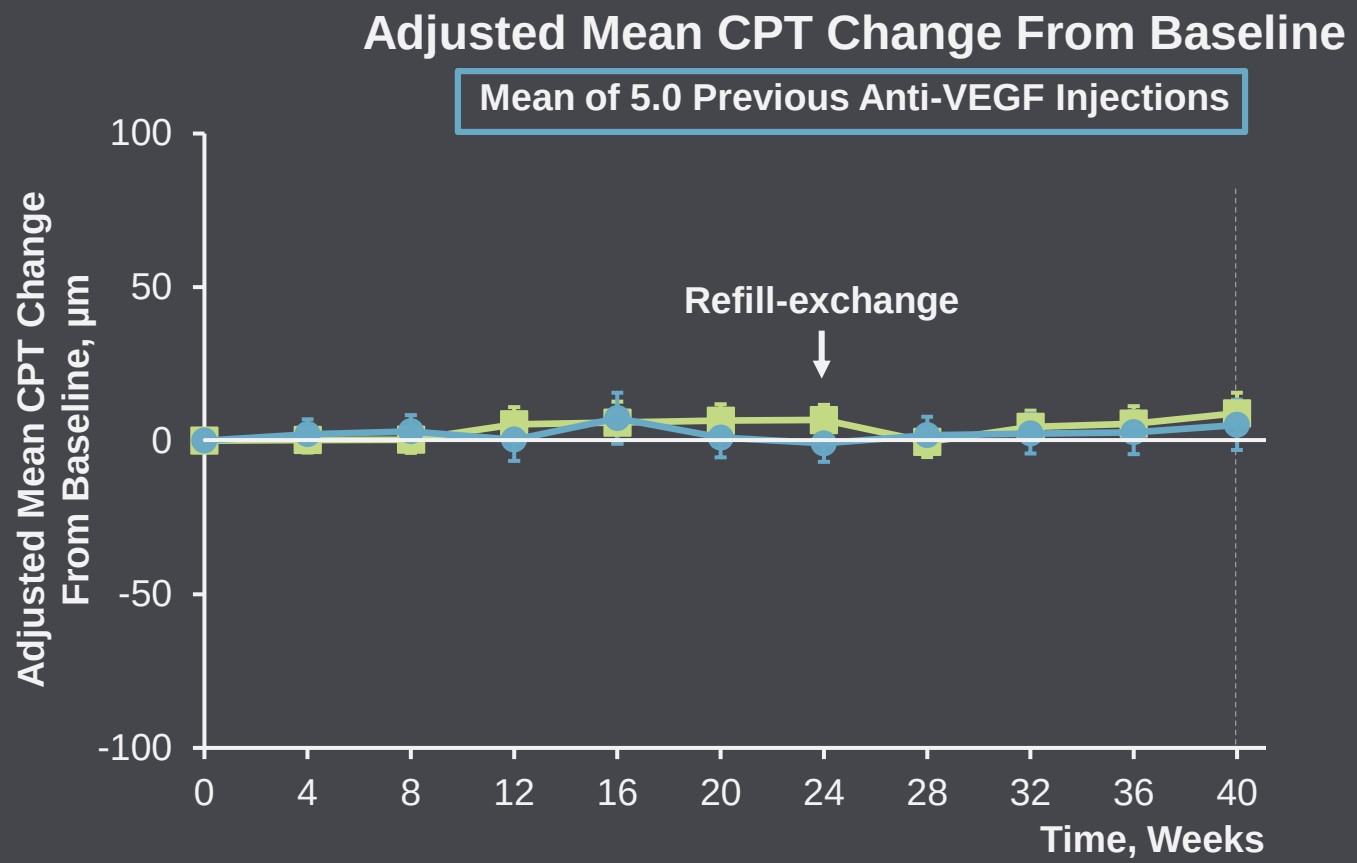
PDS Maintained Vision Through Week 72



[a] Change in visual acuity from the last available visual acuity score assessed in the study eye before the start of anti-VEGF treatment and baseline. If ETDRS letters were not available, the Snellen value was converted to the ETDRS equivalent. Observed data through the September 11, 2020 clinical cutoff date; data analysis ongoing. Vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016. 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; VEGF, vascular endothelial growth factor.

Adjusted CPT Outcomes

PDS Q24W and Monthly Ranibizumab Results Were Comparable Through Week 40



Secondary endpoint:
Change in CPT from baseline at week 36

Difference in adjusted means (95% CI)
2.8 (−6.2, +11.9)

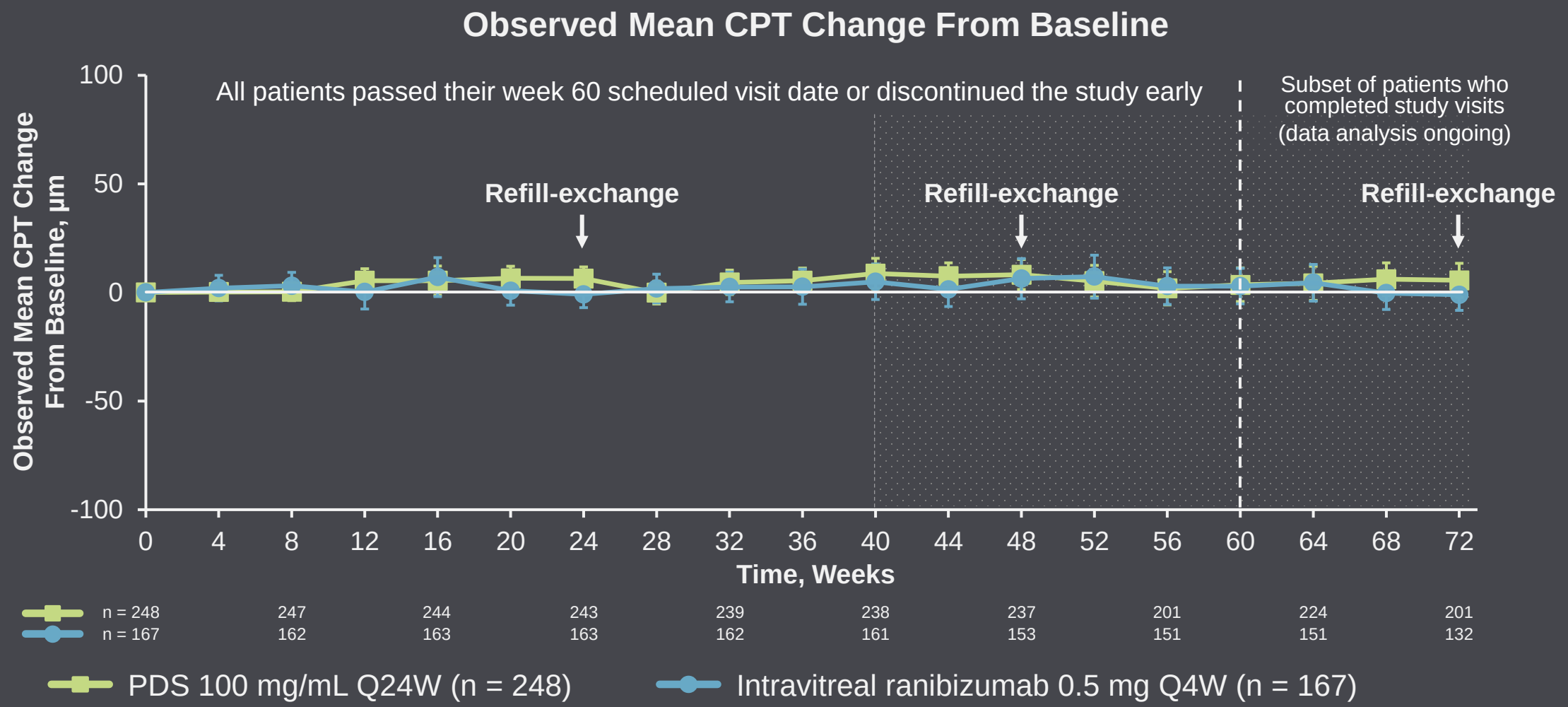
PDS 100 mg/mL Q24W (n = 248)

Intravitreal ranibizumab 0.5 mg Q4W (n = 167)

CPT defined as retinal thickness in the center of the fovea measured between the internal limiting membrane and the inner third of the retinal pigment epithelium layer. Adjusted means from a mixed-effect model for repeated measures (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 best-corrected visual acuity (< 74 Early Treatment Diabetic Retinopathy Study [ETDRS] letters 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. Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016. CPT, center point thickness; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

Observed Mean CPT Change From Baseline

PDS Q24W Controlled Retinal Thickness Through Week 72



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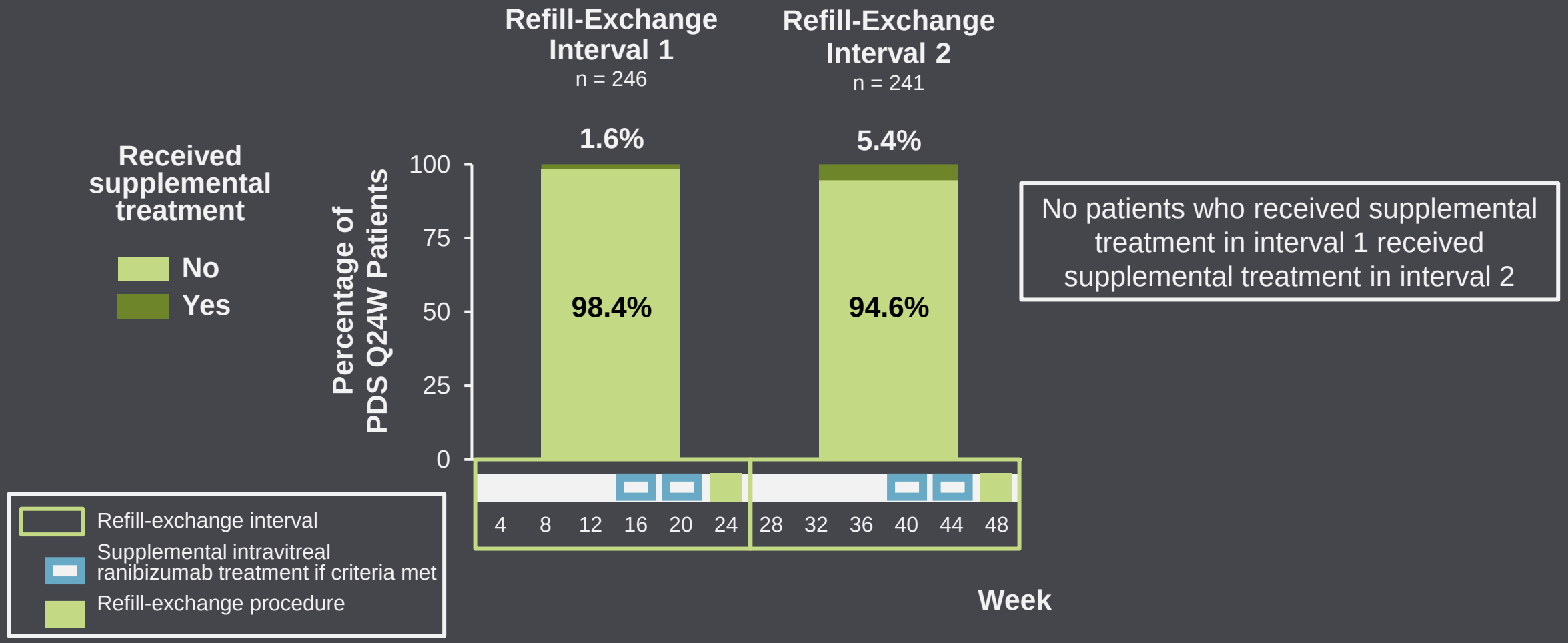
> 90% of Patients Did Not Receive Supplemental Treatment Before Each Refill-Exchange Procedure



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

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). Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016.
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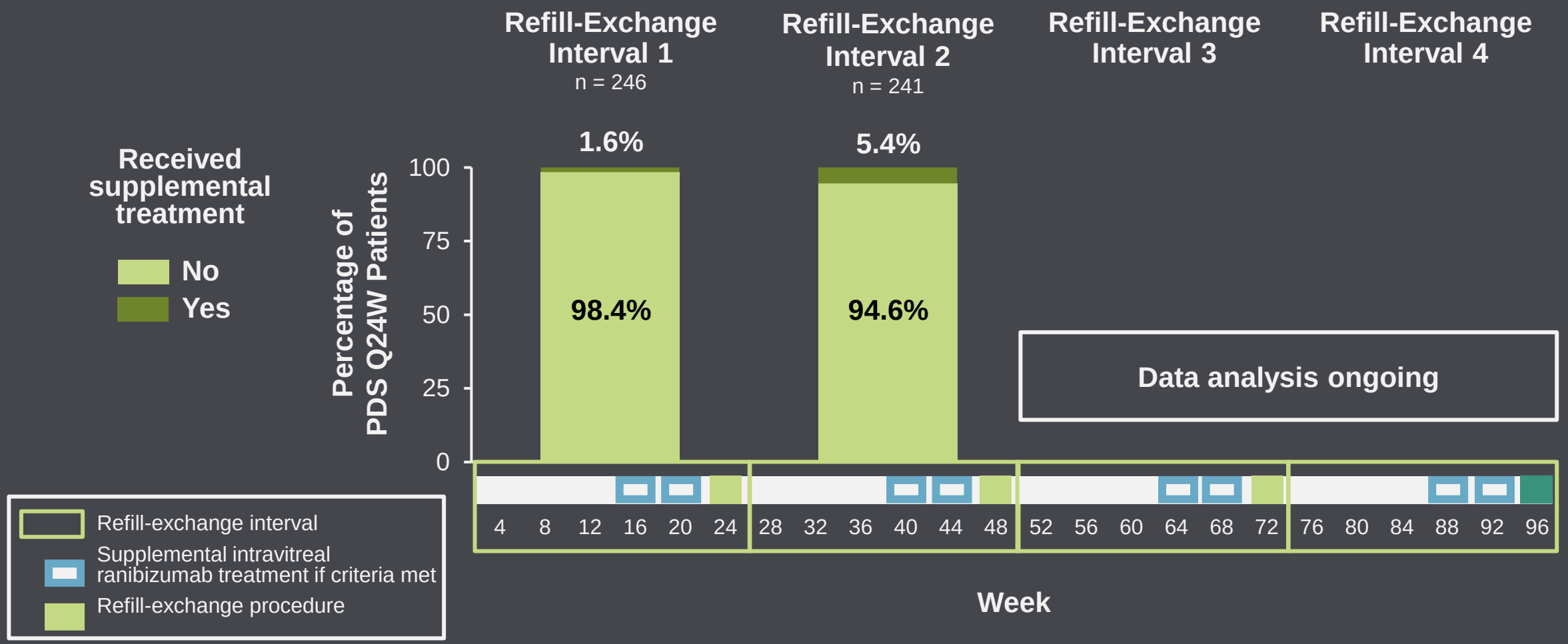

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Ocular Adverse Events of Special Interest[a] Through an Average of 79 Weeks of Follow-up

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

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

- 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 ocular AESIs 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 September 11, 2020 clinical cutoff date. [d] Includes the following terms: cataract, cataract nuclear, cataract cortical, cataract subcapsular. 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). Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016. AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

Ocular Adverse Events of Special Interest[a] Through an Average of 79 Weeks of Follow-up

PDS ocular safety profile generally unchanged from primary analysis, with an average of 38 additional weeks of follow-up per patient

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Tractional retinal detachment	0			
Vitreous hemorrhage	15 (6.0%)			

2 additional events of implant dislocation compared with primary analysis

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Summary of Endophthalmitis Cases

Patient	Event Onset	Case Details	Management	Patient Outcomes (Last Available Information)
PDS 100 mg/mL Q24W: 4/248 (1.6%) patients experienced endophthalmitis				

Archway, NCT03677934. Holekamp N et al. *Ophthalmology*. Published online September 28, 2021. doi:10.1016/j.ophtha.2021.09.016.
BCVA, best-corrected visual acuity; F, female; HLA-B27, human leukocyte antigen B27; M, male; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

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Patient 1 68/M	Week 23	• **Concurrent conjunctival retraction** • Patient reported cleaning a septic tank before event	• Study treatment withdrawn • Implant left in the eye • **Culture:** *E. faecalis*	Week 39: • Irreversible vision loss • No light perception

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Patient 2
85/F
	First event:
	week 40
	
	Second event:
	week 73
		• HLA-B27 positive with an underlying autoimmune condition
		• History of intraocular inflammation in fellow eye before study enrollment
		• The above information was not made available at the time of enrollment
			• **First event:** tap and inject, implant flush with vancomycin
			  • Patient recovered, continued refill-exchanges
			• **Second event:** tap and inject, implant flush
			  • Implant removed
			• **Culture:** both events negative
				Week 72:
				• BCVA 17 letters (20/500)
				  • –35 letters vs baseline

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Summary of Endophthalmitis Cases

Patient	Event Onset	Case Details	Management	Patient Outcomes (Last Available Information)
PDS 100 mg/mL Q24W: 4/248 (1.6%) patients experienced endophthalmitis				
Patient 1 68/M	Week 23	• **Concurrent conjunctival retraction** • Patient reported cleaning a septic tank before event	• Study treatment withdrawn • Implant left in the eye • **Culture:** *E. faecalis*	Week 39: • Irreversible vision loss • No light perception

Patient 2
85/F
	First event:
	week 40
	
	Second event:
	week 73
		• HLA-B27 positive with an underlying autoimmune condition
		• History of intraocular inflammation in fellow eye before study enrollment
		• The above information was not made available at the time of enrollment
			• **First event:** tap and inject, implant flush with vancomycin
			  • Patient recovered, continued refill-exchanges
			• **Second event:** tap and inject, implant flush
			  • Implant removed
			• **Culture:** both events negative
				Week 72:
				• BCVA 17 letters (20/500)
				  • –35 letters vs baseline

Patient 3 70/M	Week 8	• **Concurrent conjunctival retraction**	• Tap and inject, implant flushed with vancomycin • Patient recovered and resumed refills • **Culture:** negative	Week 44: • BCVA 81 letters (20/25) • +2 letters vs baseline

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Patient 3 70/M	Week 8	• **Concurrent conjunctival retraction**	• Tap and inject, implant flushed with vancomycin • Patient recovered and resumed refills • **Culture:** negative	Week 44: • BCVA 81 letters (20/25) • +2 letters vs baseline
Patient 4 82/M	Week 8	• **Preceded by conjunctival retraction** that was addressed with surgery • Retraction had not resolved at onset of endophthalmitis despite conjunctival revision	• Tap and inject • Implant removed soon after endophthalmitis event per investigator preference • **Culture:** *S. aureus*	Week 64: • BCVA 77 letters (20/32) • Same as baseline

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Intravitreal ranibizumab 0.5 mg Q4W: 1/167 (0.6%) patients experienced endophthalmitis				
Patient 1 69/F	Week 77		• Tap and inject • Drug interrupted • **Culture:** results not reported	Week 86: • BCVA 37 letters (20/200) • –11 letters vs baseline

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PDS Q24W Maintained Vision and Anatomic Outcomes Comparable With Monthly Ranibizumab Through a Mean Follow-up of 79 Weeks

Equivalent Vision, Controlled Retinal Thickness

- Primary endpoint: PDS Q24W was noninferior and equivalent for BCVA change at average of weeks 36/40
- Observed vision and anatomic results comparable with monthly ranibizumab through week 72

Q24W Treatment Durability, Reduced Treatment Burden

- Through 2 refill-exchange intervals, > 90% of PDS Q24W patients did not need supplemental ranibizumab treatment

Safety Profile Is Well Characterized and Manageable

- PDS ocular safety profile generally unchanged from the primary analysis, with an average of 38 additional weeks of follow-up per patient
- Continued experience with the PDS has led to procedural modifications that have the potential to decrease the risk of adverse events

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AE, adverse event; BCVA, best-corrected visual acuity; PDS, Port Delivery System with ranibizumab; Q24W, every 24 weeks.

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