Patient Preference for the Port Delivery System With Ranibizumab vs Intravitreal Injections: 1-Year Results From the Phase 3 Pagoda Trial in Patients With Diabetic Macular Edema

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Disclosures

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- KB, AD: None
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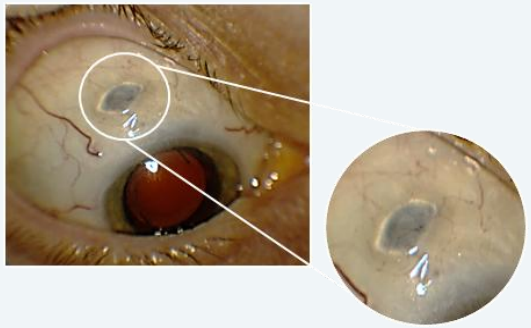
Study and Product Disclosures

- 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 of 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
- Funding was provided by F. Hoffmann-La Roche Ltd, Basel, Switzerland, for the study and third-party writing assistance, which was provided by Nibedita Gupta, PhD, CMPP, of Envision Pharma Group

nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; VEGF, vascular endothelial growth factor. 1. Susvimo [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2022.

Port Delivery System With Ranibizumab (PDS) Is an Innovative Drug–Device Combination for Continuous Drug Delivery



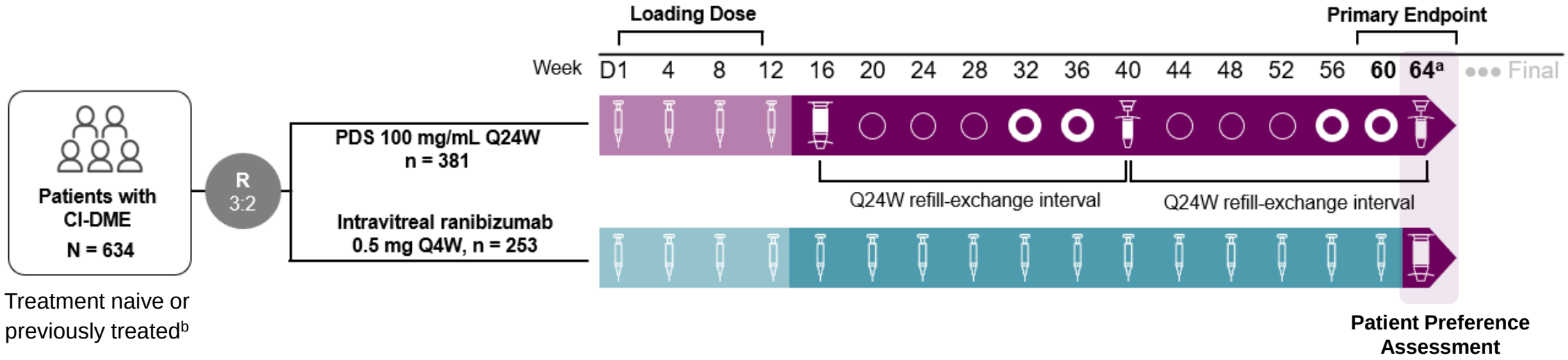
Implant

Refill Needle

- Refillable ocular implant for **continuous delivery** of a customized formulation of ranibizumab 100 mg/mL
  - In-clinic refill-exchange procedures 1 or 2 times a year
- Designed to **maintain clinical benefits** of monthly intravitreal anti-VEGF therapy while **reducing treatment burden** of retinal diseases
  - In Archway, **PDS was noninferior** to **monthly intravitreal** ranibizumab injections in nAMD
  - Real-world outcomes in DME reduced due to **undertreatment**
- The **patient voice** is becoming increasingly important for informing clinical decisions
- **Patient preference** for PDS vs intravitreal injections was evaluated in the Pagoda trial for DME

DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab, VEGF, vascular endothelial growth factor.

The Phase 3 Pagoda Trial Evaluated the Efficacy and Safety of PDS Q24W in DME



Pagoda met primary endpoint: PDS Q24W was **noninferior** to monthly ranibizumab in BCVA change from baseline averaged over weeks 60/64, with adjusted mean (95% CI) BCVA change of +9.6 (8.7–10.5) letters in the PDS Q24W arm vs +9.4 (8.3–10.5) letters in the monthly ranibizumab arm

Pagoda clinical trial [NCT04108156]. [a] Delayed PDS implantation and initial fill, if applicable. [b] Patients were treatment naïve for DR with or without DME in the study eye or previously treated, as long as no treatment was administered in the study eye up to 6 months before randomization. [c] If week 16 (PDS Q24W arm) or week 64 (ranibizumab 0.5 mg Q4W arm) is not possible, additional loading dose required at week 16 or week 64; implant insertion procedure must happen within 28 ± 7 days since last intravitreal injection; additional visits for safety assessments 1 and 7 days after implantation. [d] Patients were assessed for the need for supplemental intravitreal ranibizumab 0.5 mg treatment at study visits 16 and 20 weeks after implant insertion or each completed refill-exchange procedure. BCVA, best-corrected visual acuity; CI, confidence interval; CI-DME, center-involved diabetic retinopathy with diabetic macular edema; D, day; DME, diabetic macular edema; DR, diabetic retinopathy; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; R, randomization.

Baseline Demographics and Ocular Characteristics Were Generally Well Balanced Across Study Arms

Characteristic	PDS 100 mg/mL Q24W (n = 381)	Intravitreal Ranibizumab 0.5 mg Q4W (n = 253)
Age, mean (SD)	60.9 (9.40)	60.2 (9.99)
Male, n (%)	217 (57.0)	146 (57.7)
Ethnicity, n (%)		
Hispanic or Latino	78 (20.5)	41 (16.2)
Non-Hispanic or Latino	300 (78.7)	209 (82.6)
Race, n (%)		
White	289 (75.9)	200 (79.1)
Black or African American	60 (15.7)	33 (13.0)

Characteristic	PDS 100 mg/mL Q24W (n = 381)	Intravitreal Ranibizumab 0.5 mg Q4W (n = 253)
BCVA letter score, mean (SD)	65.4 (11.3)	65.1 (11.4)
CST, mean (SD) (µm)	484.9 (133.2)	483.7 (121.8)
ETDRS-DRSS status,[a] n (%)		
DRSS level ≤ 53 NPDR	354 (92.9)	234 (92.5)
DRSS level ≥ 60 PDR	20 (5.2)	12 (4.7)
Prior intravitreal anti-VEGF therapy for DR with/without DME, n (%)	87 (22.8)	55 (21.7)

Pagoda clinical trial [NCT04108156]. Efficacy population.
[a] 7 patients in each arm had baseline DRSS unable to be graded, so totals do not add up to 100%.
BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale; ETDRS, Early Treatment Diabetic Retinopathy Study; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks; VEGF, vascular endothelial growth factor.

The PDS Patient Preference Questionnaire (PPPQ)

PDS Patient Preference Questionnaire (PPPQ): a 3-item questionnaire that captures a patient's **preference for treatment**, the **strength** of their preference, and the **reasons** for their preference[1]

PPPQ

1 **Which method of administration did you prefer?**

- ☐ Intravitreal injections
- ☐ Port Delivery System
- ☐ No preference

2 **If you have a preference for one of the administration routes, how strong is this preference?**

- ☐ Very strong
- ☐ Fairly strong
- ☐ Not very strong

3 **If you have a preference for one of the administration routes, what are the main reasons for your preference? Please choose all that apply:**

- ☐ Less worry or nervousness
- ☐ Less discomfort
- ☐ Other reason
- ☐ Requires less time for treatment
- ☐ Fewer treatments

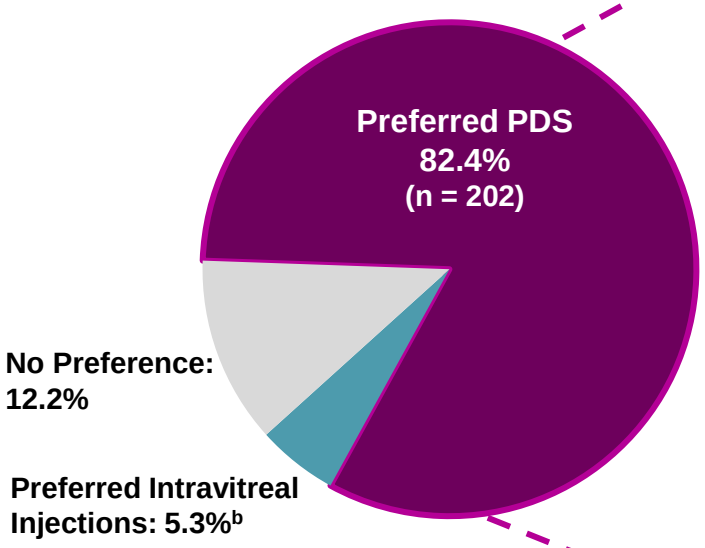
PDS, Port Delivery System with ranibizumab; PPPQ, PDS Patient Preference Questionnaire.

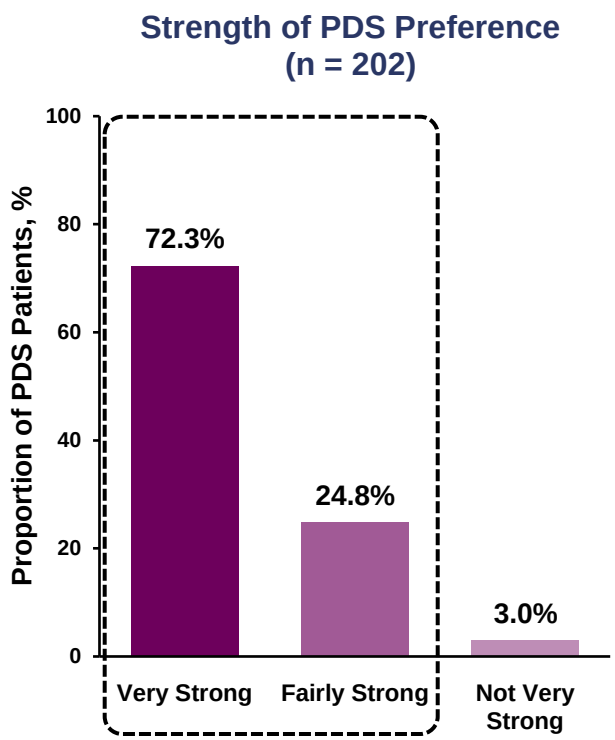
1. Beaulieu WT, Glassman AR. *JAMA Ophthalmol.* 2022;140:778–779.

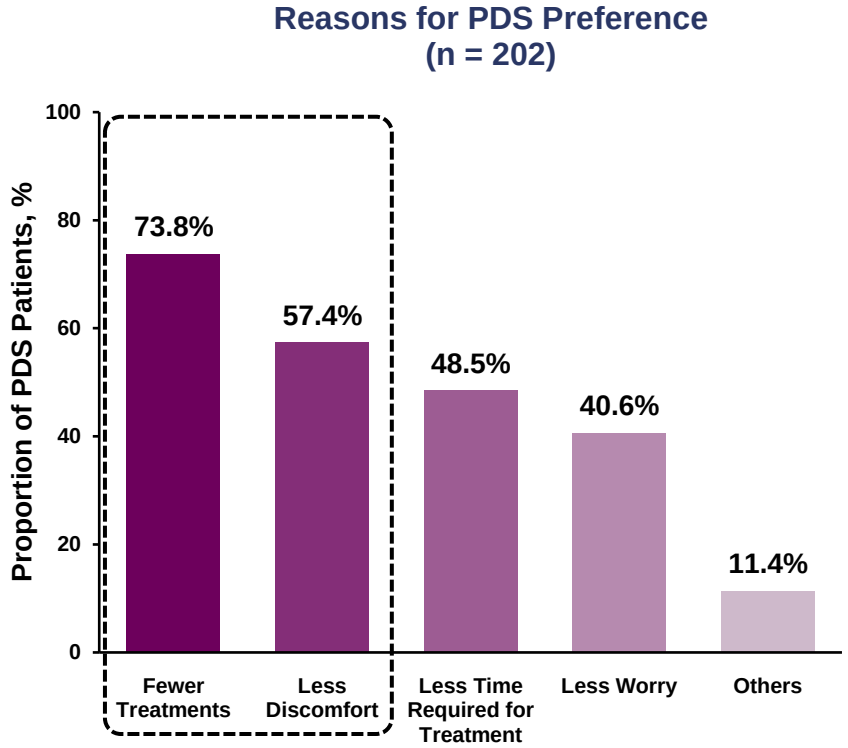
82% of PDS Patients Preferred PDS Over Intravitreal Injections

Response to PPPQ at Week 64

Patients who Completed the PPPQ, mITT Population (n = 245)[a]



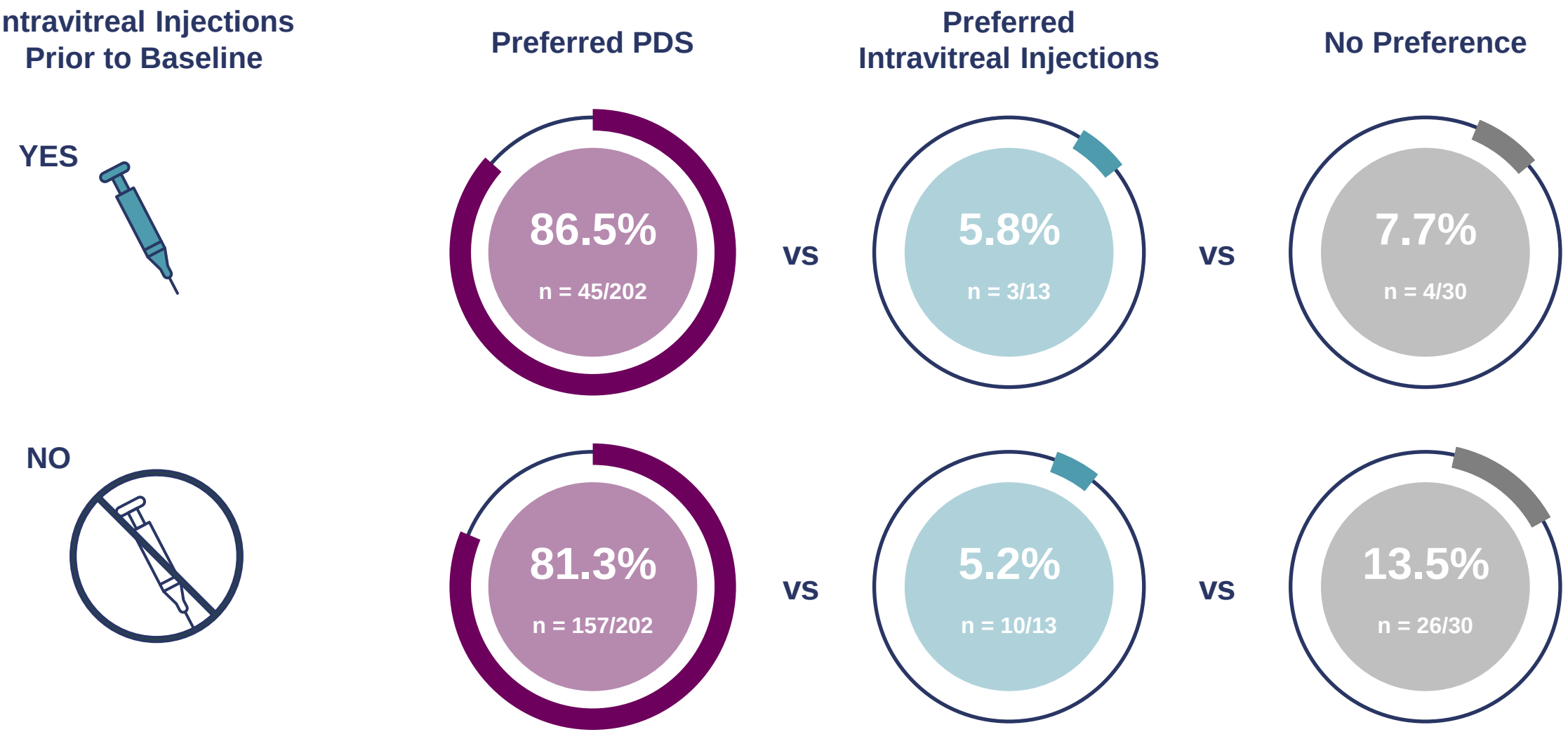




Pagoda clinical trial [NCT04108156]. Percentages may not add up to 100 due to rounding up. [a] mITT population comprised of all patients in the in the efficacy population with the exclusion of all patients in the randomization blocks consisting of PDS patients noncompliant to the protocol-defined PDS insertion schedule due to sponsor-initiated surgery pause. [b] Of the 13 patients who preferred intravitreal injections, only 4 experienced adverse events (cataract, n = 4; conjunctival bleb, n = 1; vitreous hemorrhage, n = 1). Of these 4 patients, 3 were NPDR and 1 was PDR.

IVI, intravitreal; mITT, modified intent-to-treat; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PDS, Port Delivery System with ranibizumab; PPPQ, PDS Patient Preference Questionnaire.

Majority of Patients Preferred PDS Regardless of Injections Prior to Baseline



Pagoda clinical trial [NCT04108156]. mITT population.
mITT, modified intent-to-treat; PDS, Port Delivery System with ranibizumab.

Majority of Patients Preferred PDS Regardless of the Number of Intravitreal Injections From Baseline Until Week 64

Number of Intravitreal Injections in Study Eye From Baseline to Week 64	Preferred PDS		Preferred Intravitreal Injections		No Preference
≤ 4 	80.7% n = 180/223	vs	5.8% n = 13/223	vs	13.5% n = 30/223
5 	100% n = 22/22	vs	0%	vs	0%

Pagoda clinical trial [NCT04108156]. mITT population.
mITT, modified intent-to-treat; PDS, Port Delivery System with ranibizumab.

Ocular AESIs Were Well Understood and Manageable

No Cases of Endophthalmitis or Retinal Detachment and 1 Case of Implant Dislocation Were Reported in the PDS Q24W Arm After Implantation Through Week 64

Ocular AESIs in the Study Eye Through Week 64

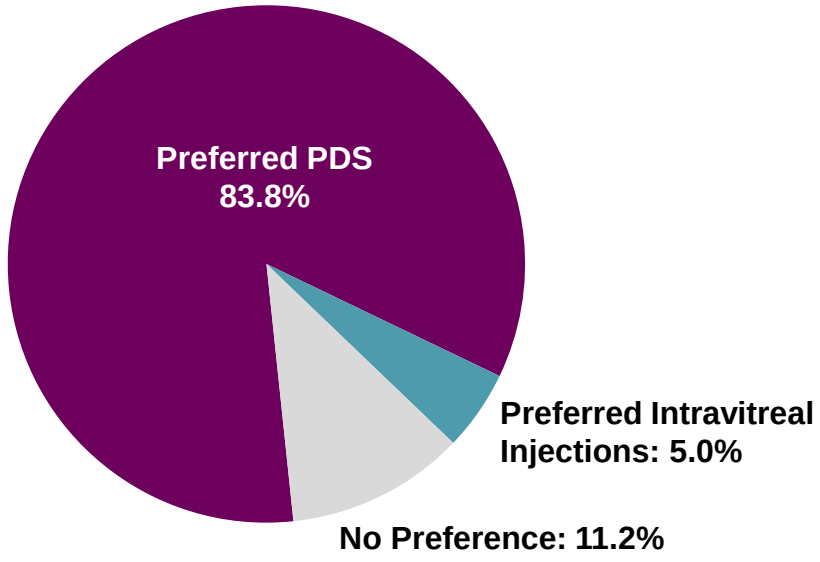
Patient Incidence, %[a]	PDS 100 mg/mL Q24W (n = 320) Overall		Intravitreal Ranibizumab 0.5 mg Q4W (n = 314) Overall	
	All	Serious	All	Serious
Total number of AE, n	110	12	34	2
Total number of patients with ≥ 1 AE, n (%)	88 (27.5)	9 (2.8)	28 (8.9)	2 (0.6)
Cataract[b]	35 (10.9)	1 (0.3)	23 (7.3)	1 (0.3)
Conjunctival bleb/conjunctival filtering bleb leak[c]	25 (7.8)	4 (1.3)	0	0
Conjunctival erosion	6 (1.9)	5 (1.6)	0	0
Conjunctival retraction	4 (1.3)	1 (0.3)	0	0
Implant dislocation[d]	**1 (0.3)**	**1 (0.3)**	0	0
Endophthalmitis	**0**	**0**	1 (0.3)	1 (0.3)
Hyphema	6 (1.9)	0	0	0
Retinal detachment[e]	**0**	**0**	0	0
Vitreous hemorrhage	31 (9.7)	1 (0.3)	5 (1.6)	0

One case of septum dislodgement was reported as a device deficiency in the PDS arm through week 64.

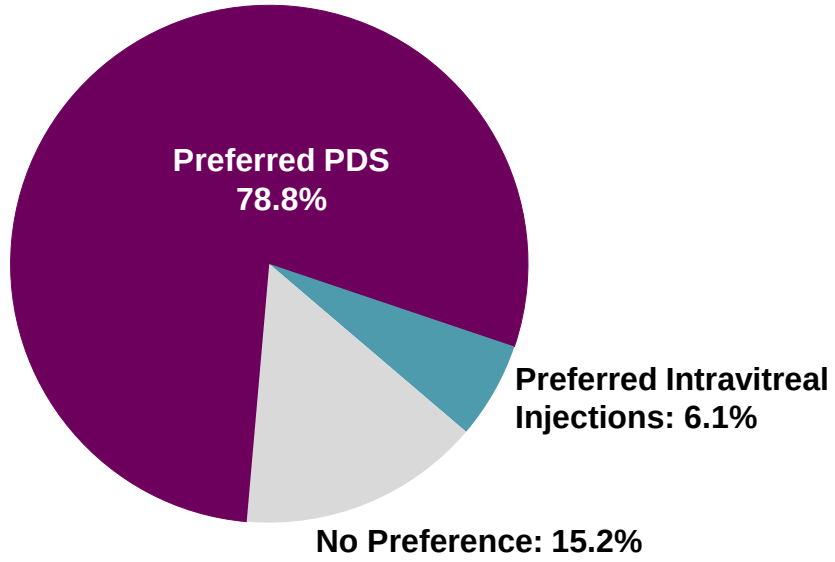
Pagoda clinical trial [NCT04108156]. Safety-evaluable population. [a] Frequency counts are by MedDRA Preferred Term. Multiple occurrences of the same adverse event in the same individual are counted only once per eye. [b] Includes cataract, cataract nuclear, cataract cortical, cataract subcapsular, and traumatic cataract. [c] Includes conjunctival bleb (defined as an elevation of the conjunctiva above the implant flange, which may be secondary to subconjunctival tissue thickening or transient fluid accumulation), conjunctival filtering bleb leak, conjunctival cyst, subconjunctival cyst, and implant site cyst. [d] Reported as "device dislocation." Case reported as a device deficiency. [e] Includes retinal detachment, rhegmatogenous retinal detachment, and tractional retinal detachment.
AE, adverse event; 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.

Majority of Patients Preferred PDS Regardless of the Number of Adverse Events Experienced Prior to Week 64

Patients Who Did Not Have Any AESI in the Study Eye Prior to Week 64 (N = 179)



Patients Who Had ≥ 1 AESI in the Study Eye Prior to Week 64 (N = 66)



Pagoda clinical trial [NCT04108156]. mITT population.
AESI, adverse events of special interest; mITT, modified intent-to-treat; PDS, Port Delivery System with ranibizumab.

Subgroup Analysis: Most PDS Patients Preferred PDS Regardless of Baseline Characteristics

	Preferred PDS (n = 202)	Preferred Intravitreal Injections (n = 13)	No Preference (n = 30)
Age group, n (%)			
< 65 years	136 (83.4)	11 (6.7)	16 (9.8)
65–≤ 75 years	56 (78.9)	2 (2.8)	13 (18.3)
≥ 75 years	10 (90.9)	0	1 (9.1)
Sex, n (%)			
Male	114 (80.9)	9 (6.4)	18 (12.8)
Female	88 (84.6)	4 (3.8)	12 (11.5)
Ethnicity, n (%)			
Hispanic	36 (80.0)	4 (8.9)	5 (11.1)
Non-Hispanic	164 (82.8)	9 (4.5)	25 (12.6)
Race, n (%)			
White	147 (80.8)	13 (7.1)	22 (12.1)
Black or African American	39 (86.7)	0	6 (13.3)
DR Severity, n (%)			
NPDR	191 (83.4)	9 (3.9)	29 (12.7)
PDR	10 (76.9)	3 (23.1)	0
Prior Intravitreal Injections, n (%)			
Yes	45 (86.5)	3 (5.8)	4 (7.7)
No	157 (81.3)	10 (5.2)	26 (13.5)

Pagoda clinical trial [NCT04108156]. mITT population.
DR, diabetic retinopathy; mITT, modified intent-to-treat; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; PDS, Port Delivery System with ranibizumab.

> 80% of Patients With DME Preferred the Continuous Delivery of Ranibizumab via PDS Over Intravitreal Injections

STRENGTH OF PREFERENCE

Among patients who preferred PDS, **97.0%** reported very strong or fairly strong preference

REASON OF PREFERENCE

Almost **three-quarters** of patients cited **reduction in treatment burden** as the reason for preferring PDS

CONSISTENCY OF PREFERENCE

PDS was **preferred regardless of baseline characteristics**, adverse events, DR severity, and prior intravitreal treatment

These findings, driven by the patient voice, provide further evidence for PDS as a meaningful alternative intervention that could fundamentally improve outcomes in patients with retinal diseases

Pagoda clinical trial [NCT04108156].
DME, diabetic macular edema; DR, diabetic retinopathy; PDS, Port Delivery System with ranibizumab.