Ophthalmic Practice Lessons Learned from the COVID-19 Pandemic

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Financial Disclosures

Consulting

- SomaLogic, ONL Therapeutics

Patents

- Clarvista Medical, Shapetech, 2C Tech

Equity, Co-Founder

- 2C Tech, Shapetech, Aurea Medical

Research

- SomaLogic, Genentech

Objectives

- Identify changes implemented in our Ophthalmology clinics due to the COVID-19 pandemic
- Impact of the pandemic on eye disease and eye care quality
- Lessons learned
- Focus on the future direction given what we have learned

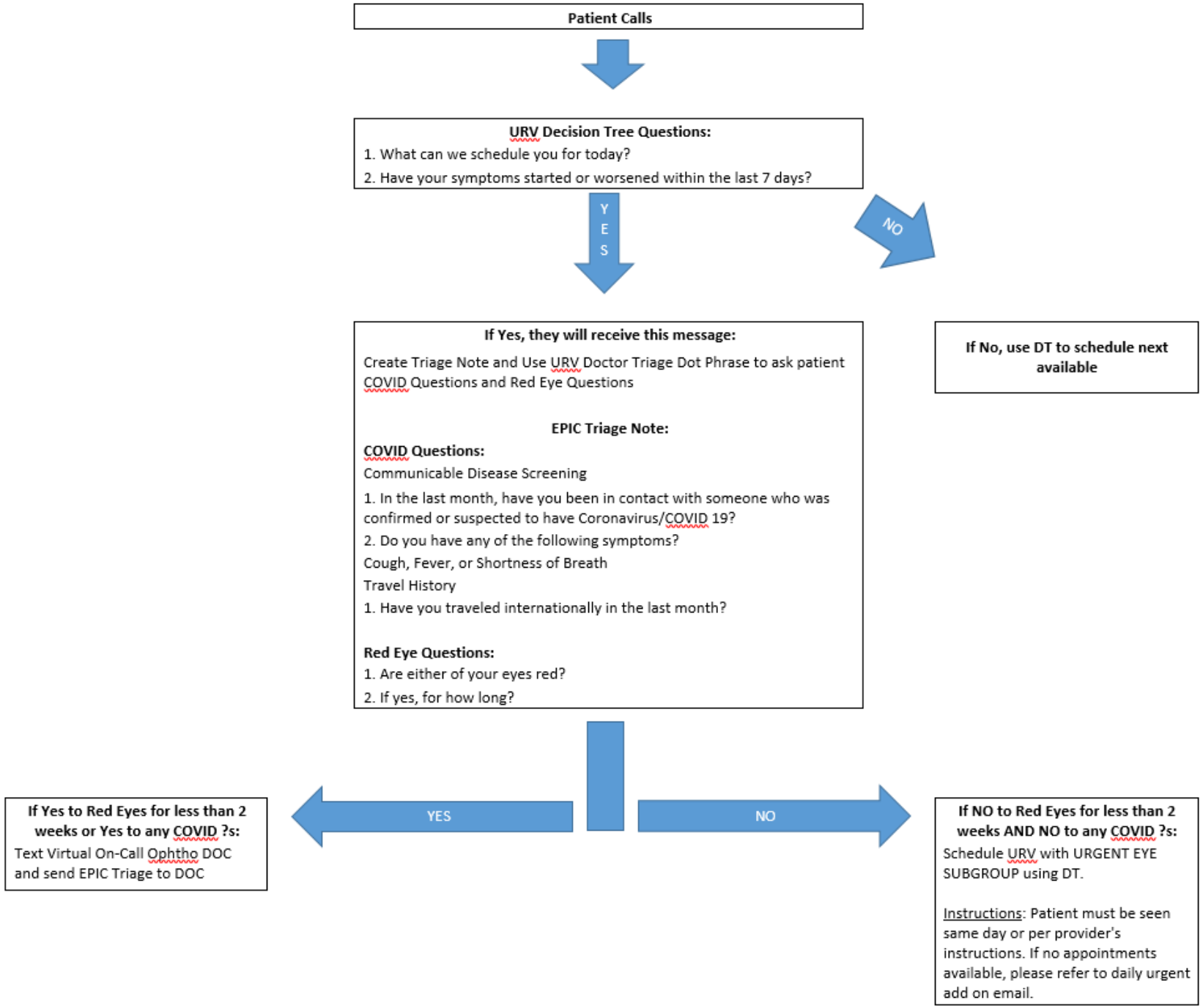
Barriers encountered

- Rapidly evolving information coming from federal, state, and local sources
- CU Anschutz, UCH, DH, CHC and VA recommendations were not always aligned
- Shortages of everything: PPE, sanitizing wipes, COVID tests, staff, information
- Explaining the particular needs of Ophthalmology and Optometry providers/staff to UCH leadership
    - Eye/face shields don’t fit at an operating scope, slitlamp, or indirect

Changes we implemented

- PPE:
  - Shortages → cloth caps, ‘reusable’ gowns, masks, and eye/face shields; scrub racks removed from eye OR
  - UV resterilizing; limits on mask distribution imposed
  - Healthgrade vs. industrial N95 masks
  - Eye Center response:
    - Early inventory of all PPE and redistribution across locations
    - Secured surgical mask stocks sufficient to support our needs
    - Multi-faculty review of available data to inform PPE best-practices
    - Rationale to UCH Ambulatory Leadership to explain in detail why healthgrade N95s must be made available to Ophthalmology providers and staff
    - Established Eye-specific PPE protocols for staff and faculty
    - Handing patients masks when deemed necessary; taping for diagnostics
- Cleaning protocols
  - PDI wipes → bleach solution; impact on room turnover and patient volume
  - Signage on waiting room chairs
  - Disinfection visibility for patients: EVS, waiting room attendants
  - Disposable applanator tips; I-care
  - Extended sanitizing of imaging equipment

- Distancing measures
  - Restrictions on group gatherings/break rooms
  - Social distancing: signage, floor/wall stickers
  - Plexiglass barriers
  - Slitlamp breath shields
- Pivoted staff to remote work; reassigned/modified roles
  - Waiting room attendant; clinic runners/patient escorts; patient calls; VV assistants
- Urgent patient workflow created


Patient Calls
URV Decision Tree Questions:
1. What can we schedule you for today?
2. Have your symptoms started or worsened within the last 7 days?
YES
NO
If Yes, they will receive this message:
Create Triage Note and Use URV Doctor Triage Dot Phrase to ask patient COVID Questions and Red Eye Questions
EPIC Triage Note:
COVID Questions:
Communicable Disease Screening
1. In the last month, have you been in contact with someone who was confirmed or suspected to have Coronavirus/COVID 19?
2. Do you have any of the following symptoms?
Cough, Fever, or Shortness of Breath
Travel History
1. Have you traveled internationally in the last month?
Red Eye Questions:
1. Are either of your eyes red?
2. If yes, for how long?
If No, use DT to schedule next available
YES
NO
If Yes to Red Eyes for less than 2 weeks or Yes to any COVID ?s:
Text Virtual On-Call Ophtho DOC and send EPIC Triage to DOC
If NO to Red Eyes for less than 2 weeks AND NO to any COVID ?s:
Schedule URV with URGENT EYE SUBGROUP using DT.
Instructions: Patient must be seen same day or per provider's instructions. If no appointments available, please refer to daily urgent add on email.

Reactivation: April 2020

- Much of our structure for protection established
- Patient safety/flow measures
  - **Centralized check-in**
  - Symptom and temperature screening
  - Visitor limitations
  - Physical barriers (distancing in waiting rooms; plexiglass at check-in
  - Visible distancing signage, waiting room staff to monitor/disinfect
  - Runners/escorts
  - **Reconfigured check-out** (in-room, exit halls)

Tele-ophthalmology at CU

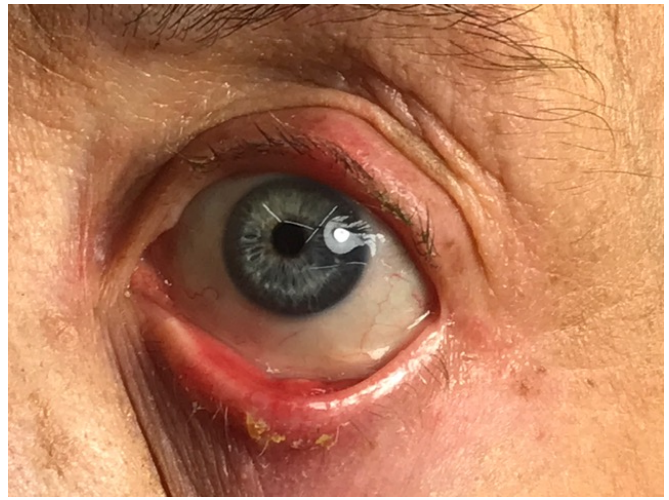
- 3/2/20: Halted our tele-ophthalmology initiative (intent: diabetic retinopathy screening
  - across UCH, VV only available for select urgent care PCP/ED indications
- 3/6/20: CMS telehealth clause signed
- 3/11/20: Eye clinic telehealth efforts revived
  - UCH-wide rolled out to 700+ clinics in 2 weeks
- 3/18/20: EPIC Virtual Visit environment went live

Types of VVs offered

- Video
- Telephone
- Hybrid in-person and video/phone visits
- E-messaging
- Image encounters

Appropriate visits

- Urgent visits
- Hybrid visits
  - Glaucoma, N-Ophth, OCP: diagnostic testing f/b Video/Phone provider visit
- Oculoplastic new and return patients:
  - Postop visits
  - Lesions (patient upload photo via MHC prior to visit)
  - Select follow-up visits
- Neuro-ophthalmology – return patients
  - Ex. MG follow up, postop strab, triage acute issues
- Retina- none (technology for home OCT etc.)
- Cataract- second eye (one week postop visit)



Things that helped with efficiency

- Take-home vision charts for patients at time of surgery (or link to website)
- Scribes/techs pre-charting
- IACs contacting patients to check them in for visits and troubleshoot technology
- Ability to use multiple video/phone platforms VidyoConnect, Zoom, FT, Doximity
- AAO Virtual Health resources

Things that were tough

- Navigating coding and billing – changed several times
- Unclear expiration date for reimbursement
- Unclear out-of-state policies early on
- Tech barriers

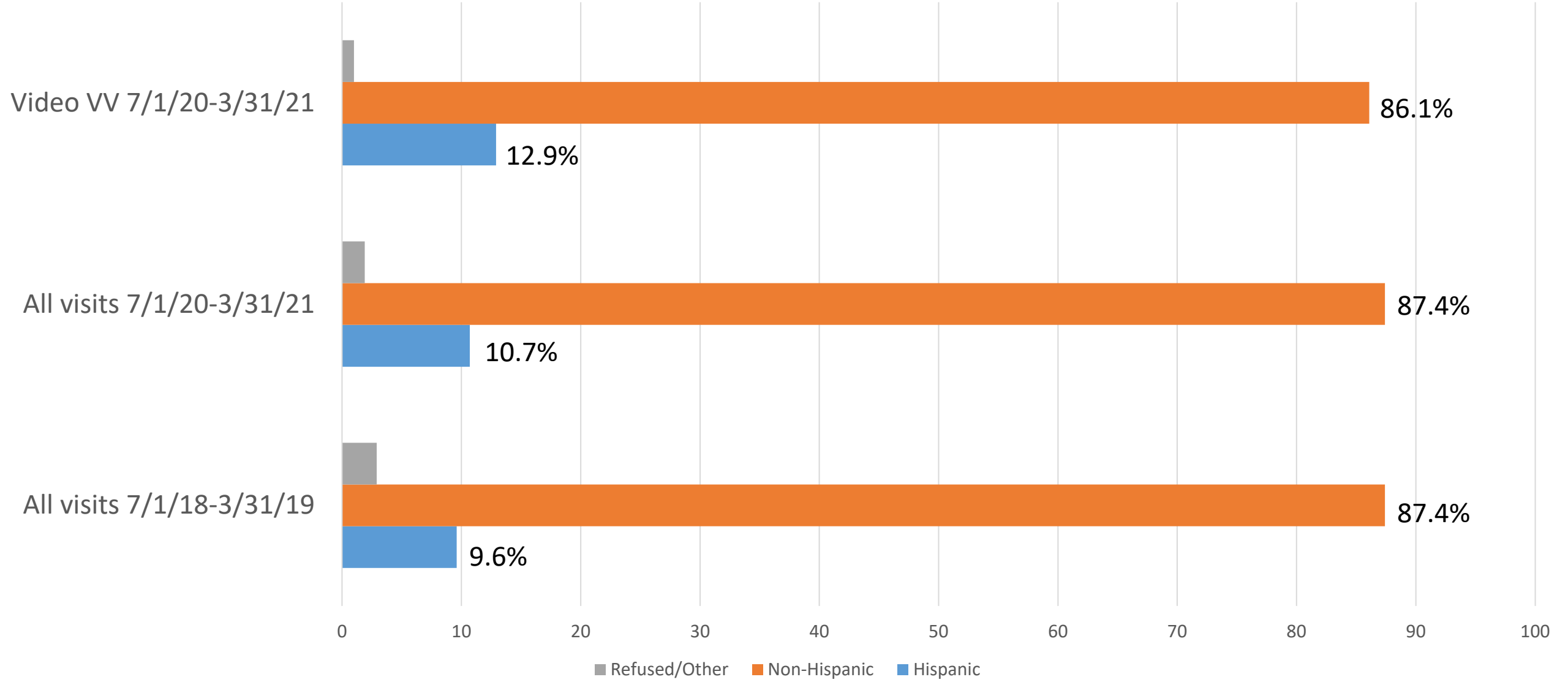
Virtual Health: are we doing enough?

- Most Ophthalmology patients can't be treated virtually
- Access to care affected by:
  - Demographics
  - Access to technology (elderly, rural, poor, disabled, low vision)
  - Location (out of state patients: legal and Site of Practice limitations)
- Who aren't we reaching?

Video visits in the eye clinic population

- 112 Telehealth visits total between July 2020-March 2021
- 101 video visits
- Spanish video interpreter services available starting 3/30/20
  - Ethnicity breakdown of VVs

% Eye clinic visits by ethnicity



EPIC Slicer Dicer: Base, All Oph Department, Slice: Ethnicity. Base, All Oph Department and All Video Visits, Slice: Ethnicity.

VV access: differences bv race?

Journal of the American Medical Informatics Association, 27(12), 2020, 1949–1954
doi: 10.1093/jamia/ocaa216
Advance Access Publication Date: 31 August 2020
Brief Communications

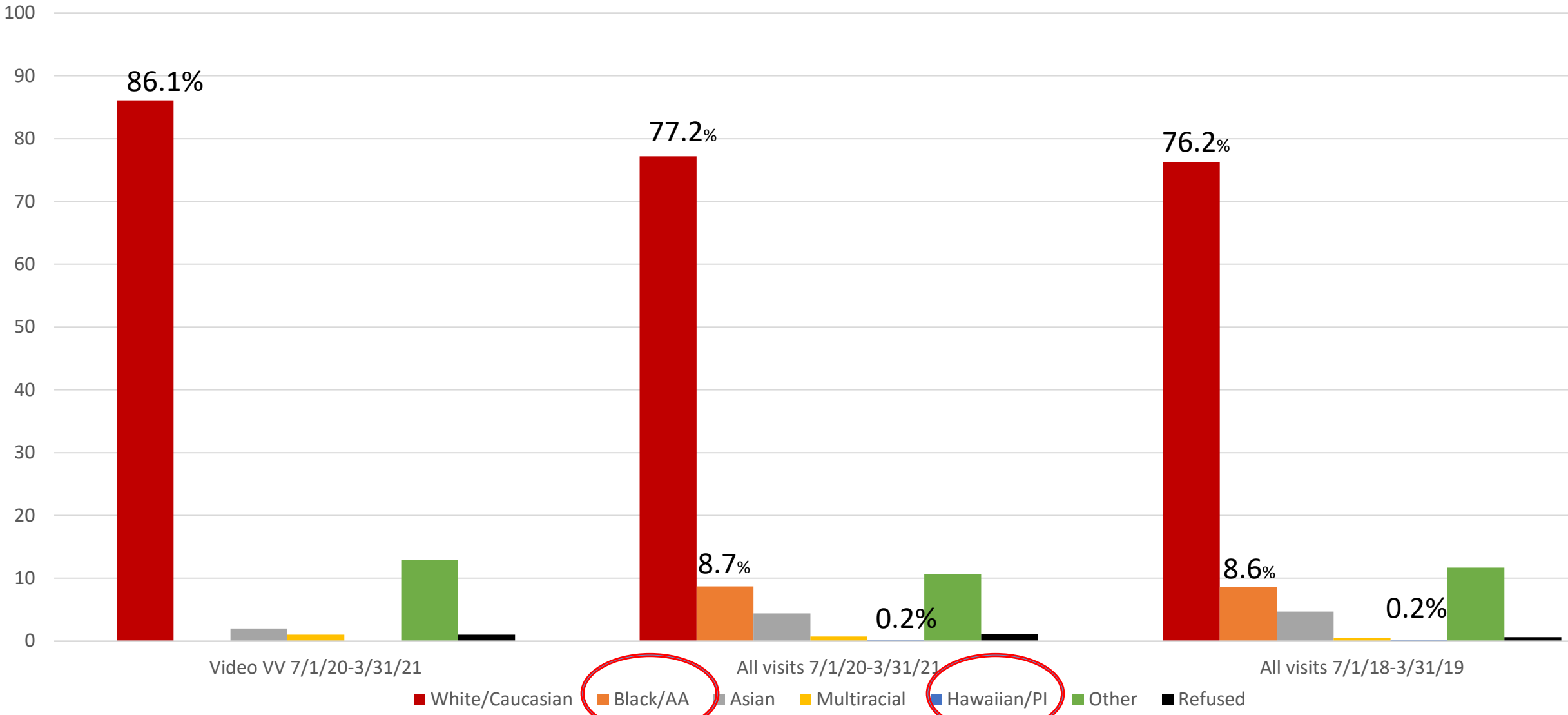
Brief Communications

Characteristics of telehealth users in NYC for COVID-related care during the coronavirus pandemic

Ellerie Weber *, Sarah J. Miller, Varuna Astha, Teresa Janevic, and Emma Benn

- Race, age predictive of telehealth use
  - AA vs. white patients: adjusted OR 4.3 use of ER instead of telehealth; 1.4 in-person visit vs. telehealth
  - Hispanic vs. white patients: OR 2.5/1.2

% Eye clinic visits by race



EPIC Slicer Dicer: Base, All Oph Department, Slice: Race. Base, All Oph Department and All Video Visits, Slice: Race.

Technology Access

- Concerted effort to sign up patients for MHC:
  - Feb 2020: 64% of our clinic patients had a MHC account
  - Feb 2021: 83% have MHC (vaccine scheduling drove increase)
- Technology problems
  - Review of patient satisfaction surveys informative but problems aren't quantified
  - Issues mitigated by provider access to multiple platforms
  - Room for improvement

Eye clinic OOS Virtual Visits

- Site of practice approvals
  - VA, MD, IL, WY, NE, CO, NV
- **22 of 518** total Video VVs since 3/2020
  - WY: 11
  - AZ, CA, KS: 3 each
  - MT: 2
  - MD, MN, NY, NE, MO, NM: 1 each

- 96% of telehealth visits were in-state

Tele-ophthalmology: worth the effort?

- Scheduling barriers:
  - lack of dedicated blocks
  - Manual review of candidates often required
  - Time-consuming to troubleshoot calls
- Financial barriers:
  - Additional analysis needed to compare time/resources spent on VV vs. in-person visits, and factoring in reimbursement
- Demographic barriers:
  - Aren't reaching some minority populations well – widening the disparity gap?
- Those who utilize VVs → overwhelmingly positive response
  - Continuity of care while saving patients money, time, travel and exposures
  - Multiple platforms and support staff are key to patient/provider satisfaction

Areas for future study

- Are inequities in ophthalmic care widening?
- Are there geographical/demographic differences in who seeks care (economically advantaged)?
- Other impacts on ophthalmic care

How has the pandemic affected ophthalmic care?

- **Changing prevalence of disease**

Disease case study: orbital cellulitis

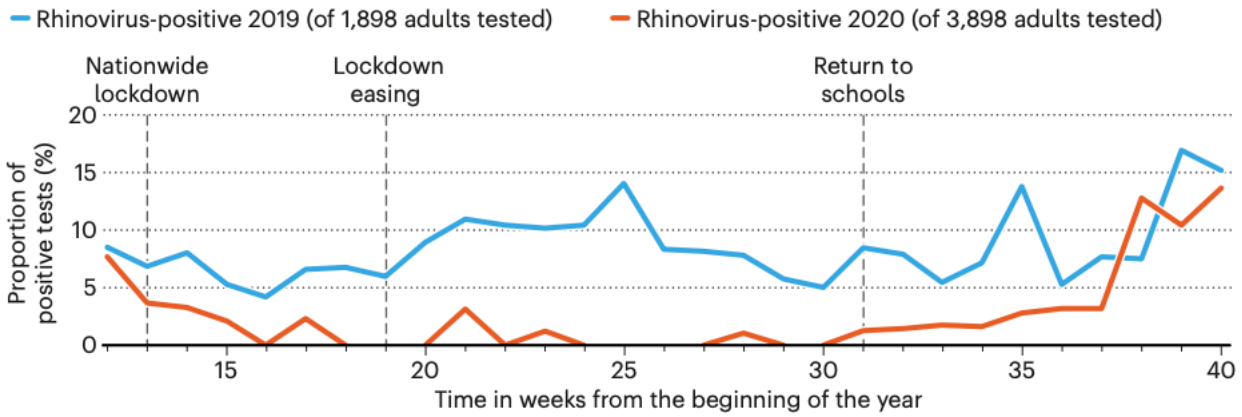
- Stay-at-home orders, masking, virtual schooling → decrease in infectious agent transmission among children
- Expect a decrease in infectious diseases as well
- Impact on cases of orbital cellulitis?

HOW COVID-19 IS CHANGING THE COLD AND FLU SEASON

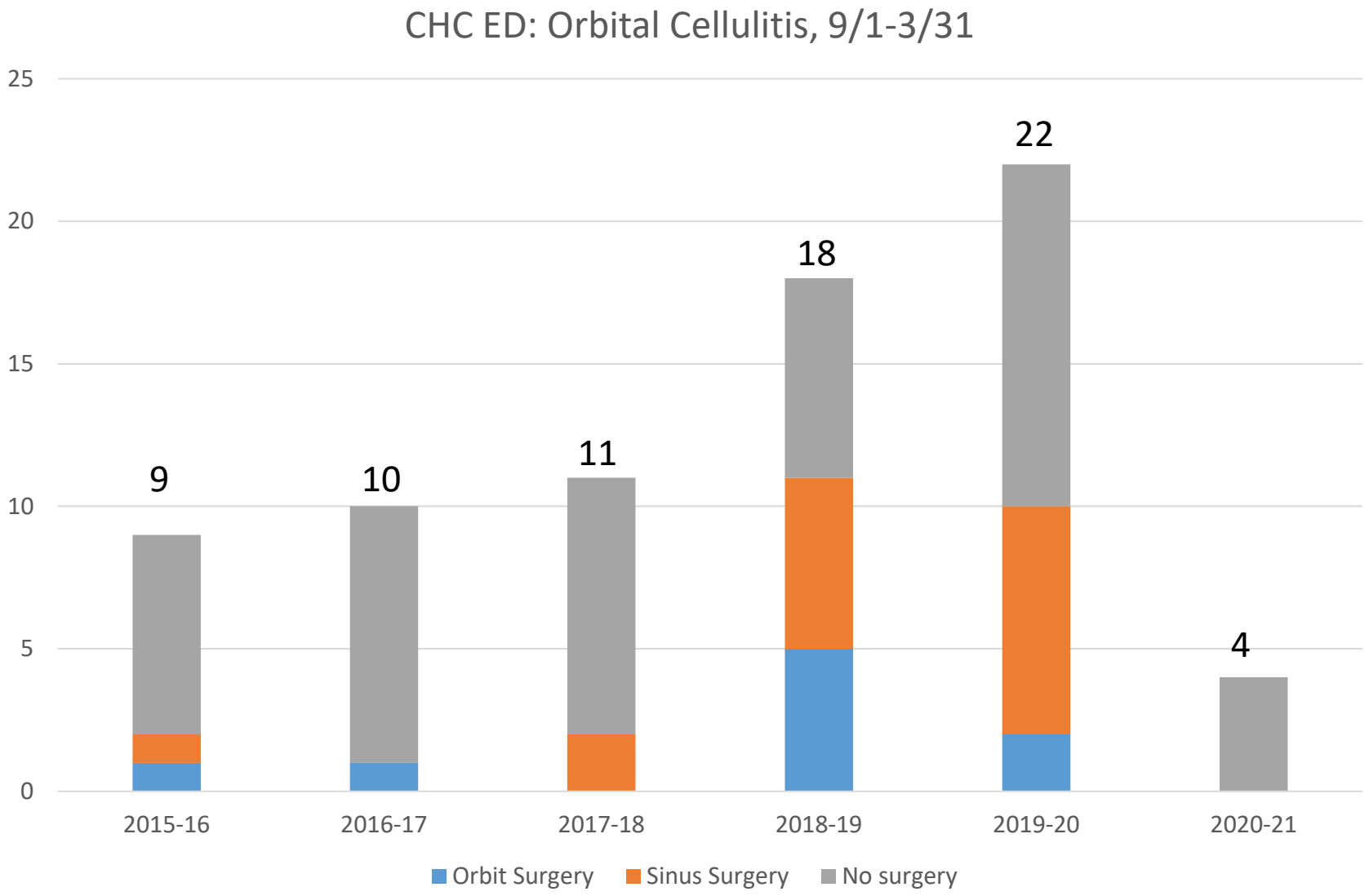
Measures meant to tame the coronavirus pandemic are quashing influenza and most other respiratory diseases, which could have wide-ranging implications.
By Nicola Jones

SHIFTING PATTERNS OF COLDS AND FLU

Following the United Kingdom's national lockdown in March 2020, there was a drop in detection of most common respiratory viruses, including rhinovirus. Infections didn't rise when lockdown eased, but they did rise rapidly after schools started again in September.



Nature **588**, 388-390 (2020)


CHC ED: Orbital Cellulitis, 9/1-3/31
25
20
15
10
5
0
9
10
11
18
22
4
2015-16
2016-17
2017-18
2018-19
2019-20
2020-21
Orbit Surgery
Sinus Surgery
No surgery

Prevalence of disease- access to care

Acta Ophthalmologica

Acta Ophthalmologica 2021

References

Bilgic E, Turkdogan S, Watanabe Y, Madani A, Landry T, Lavigne D, Feldman LS & Vassiliou MC (2017): Effectiveness of telementoring in surgery compared with on-site mentoring: a systematic review. Surg Innovat **24**: 379–385.

El-Sabawi B & Magee W (2016): The evolution of surgical telementoring: current applications and future directions. Ann Trans Med **4**: 391.

Erridge S, Yeung DKT, Patel HRH & Purkayastha S (2019): Telementoring of surgeons: a systematic review. Surg Innovat **26**: 95–111.

Table 1. Total retinal detachment repairs and total retinal tear/holes requiring laser in the COVID-19 lockdown period at the University of Colorado Sue Anschutz-Rogers Eye Center from 3/13/2020 to 5/8/2020 as compared with the same time period in 2019.

Characteristics	2019	2020
Total # retinal detachment repairs	25	11
Sex (Female/Male)	9/16	3/8
Mean age ± SD	56.8 ± 16	57.8 ± 8.1
Macula On	14 (56%)	4 (36.4%)
Macula Off	11 (44%)	7 (63.6%)
Total # retinal tear/hole laser procedures	16	8
Sex (Female/Male)	9/7	3/5
Mean age ± SD	61.1 ± 12.9	63.0 ± 14.0

How has the pandemic affected ophthalmic care?

- Changing prevalence of disease
- **Decreased access to technology**

Disruption of care: case study

- Operation Warp Speed took "steps to require contractors to prioritize vaccine production"
- Starting 12/17/20, production of teprotumumab, an orphan drug for TAO, was halted
- Facilities redirected to produce COVID19 vaccine

https://ows.gaoinnovations.gov/vaccine-tracker

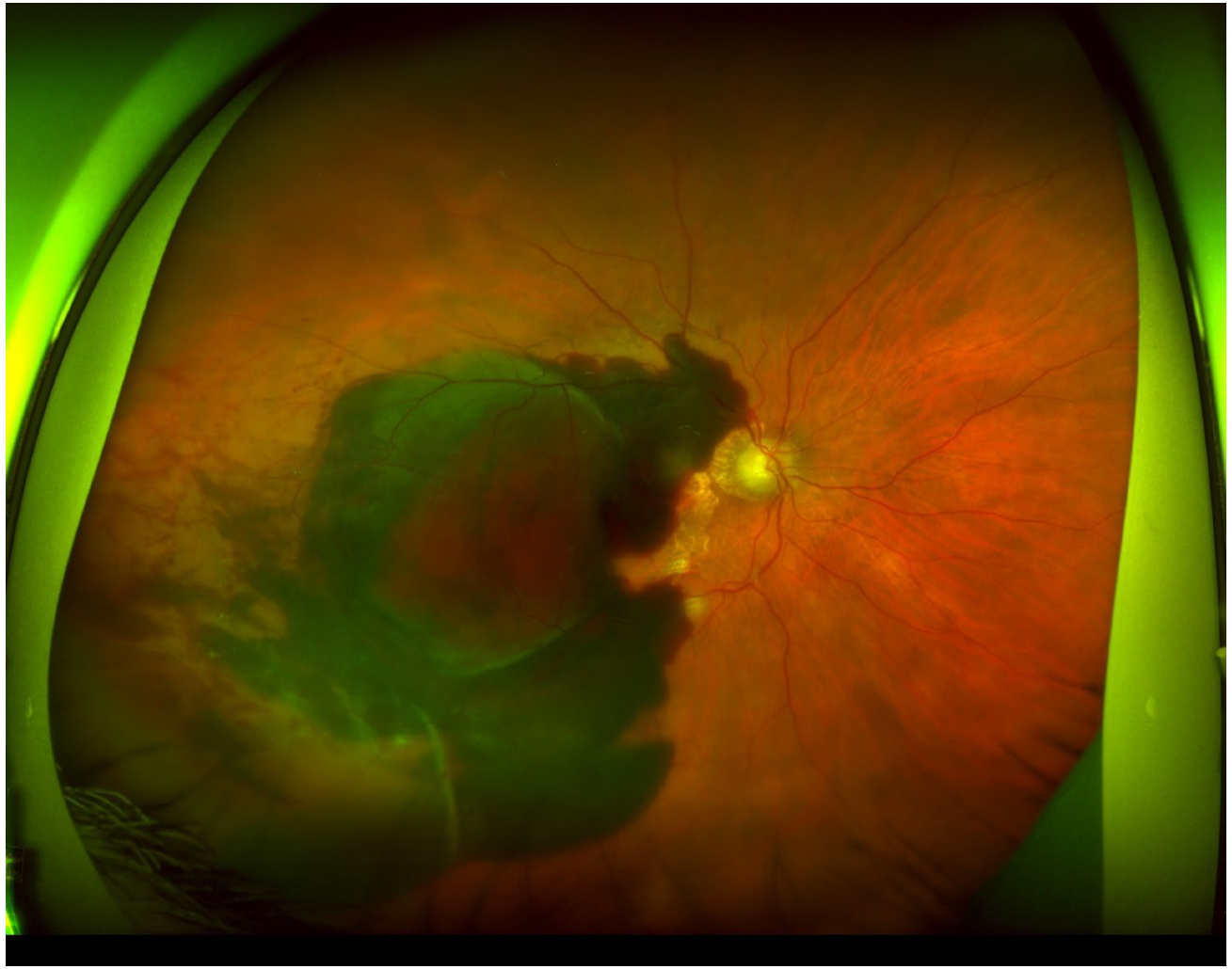
Teprotumumab “Hunger Games”

- 8 infusions, 24 weeks
- 22 total doses available
- 15 patients being actively infused that required prioritization
- Patients required q1-2 month followup
  - Data to be reviewed, including additional patients waitlisted since December: at least 3 forced to seek alternative
- Alternatives: High-dose steroid, off-label tocilizumab, rituximab
- Production restarted as of 3/30/21

How has the pandemic affected ophthalmic care?

- Changing prevalence of disease
- Decreased access to technology
- **Decreased adherence to treatment plans**

Missed Intravitreal injections



Intravitreal injections

- Bilateral injections when at all possible
- Separate injection setups
- Different drug lot for each eye

How has the pandemic affected ophthalmic care?

- Changing prevalence of disease
- Decreased access to technology
- Decreased adherence to treatment plans
- **New complications**

Intravitreal injections

- Strep Mitis endophthalmitis case
- Mask taping vs. Pulling mask down

Effect of Taping Face Masks on Quantitative Particle Counts Near the Eye: Implications for Intravitreal Injections in the COVID-19 Era

WILLIAM G. SCHULTHEIS, JAMES E. SHARPE, QIANG ZHANG, SAMIR N. PATEL, AJAY E. KURIYAN, ALLEN CHIANG, SUNIR J. GARG, AND JASON HSU

How has the pandemic affected ophthalmic care?

- Changing prevalence of disease
- Decreased access to technology
- Decreased adherence to treatment plans
- New complications
- **Driving the value proposition of technologies that decrease office visits or procedures**

Home Testing

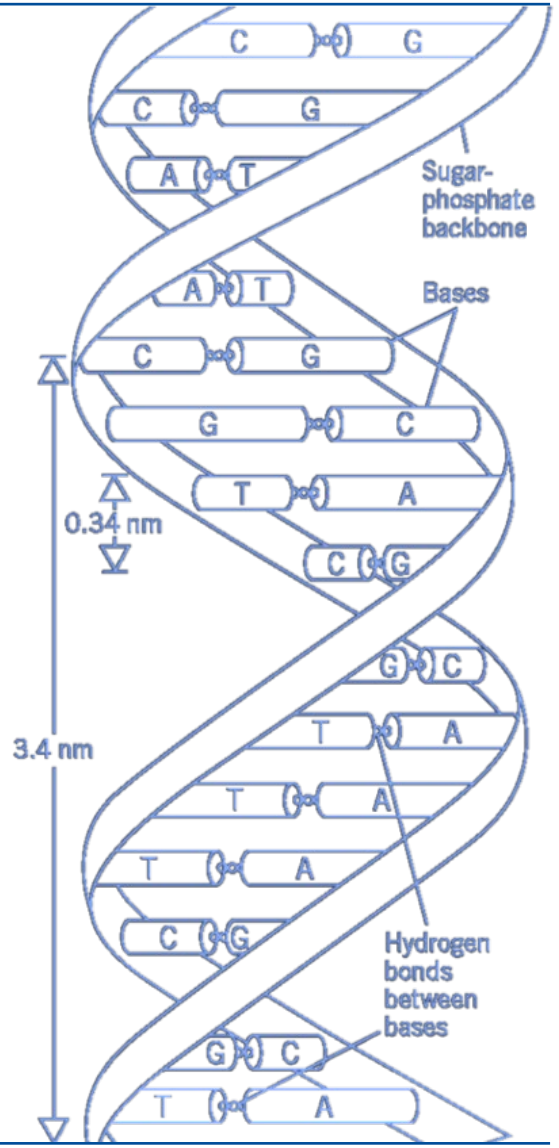
Notal Vision is developing a first-of-its-kind Artificial Intelligence-enabled digital diagnostic for patients with neovascular retina diseases using our patient-operated Home Optical Coherence Tomography device. The first disease in the Notal Home OCT Program pipeline is neovascular Age-related Macular Degeneration (AMD)

Investigational device not cleared for clinical use.

Intravitreal Injection Treatment Burden

- Sustained delivery technology
- New drugs with longer duration of efficacy

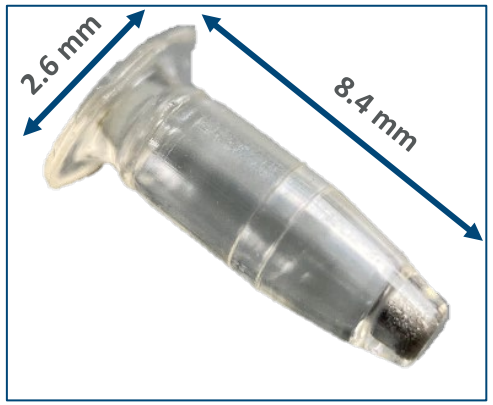
PORT DELIVERY SYSTEM IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION (nAMD)

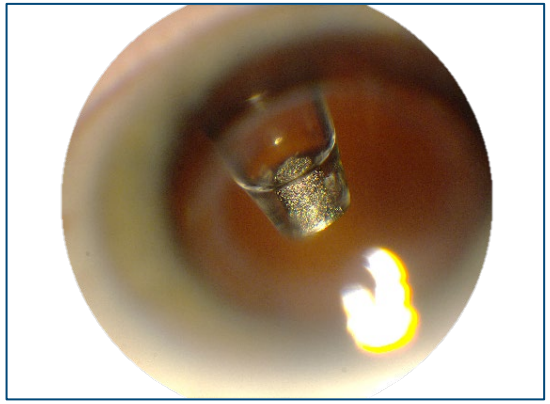


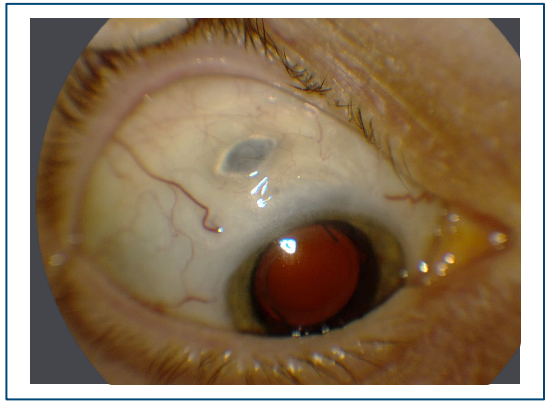
Genentech
A Member of the Roche Group

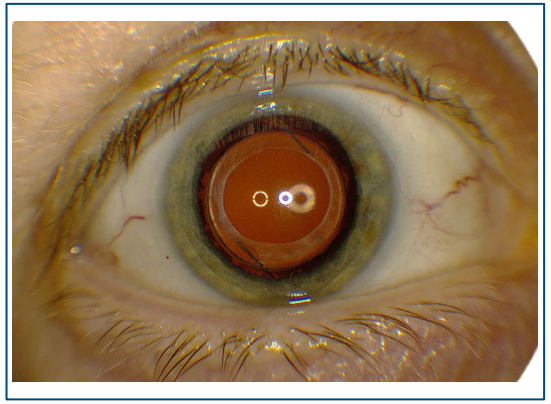
THE PORT DELIVERY SYSTEM WITH RANIBIZUMAB (PDS)

Continuous intravitreal delivery of a customized formulation of ranibizumab







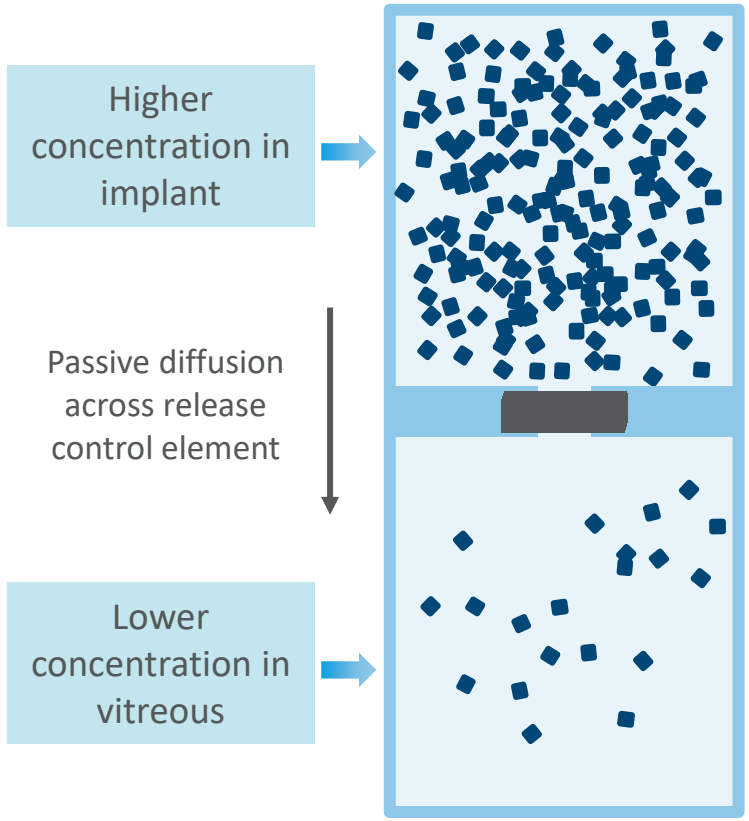


Innovative, investigational drug delivery system

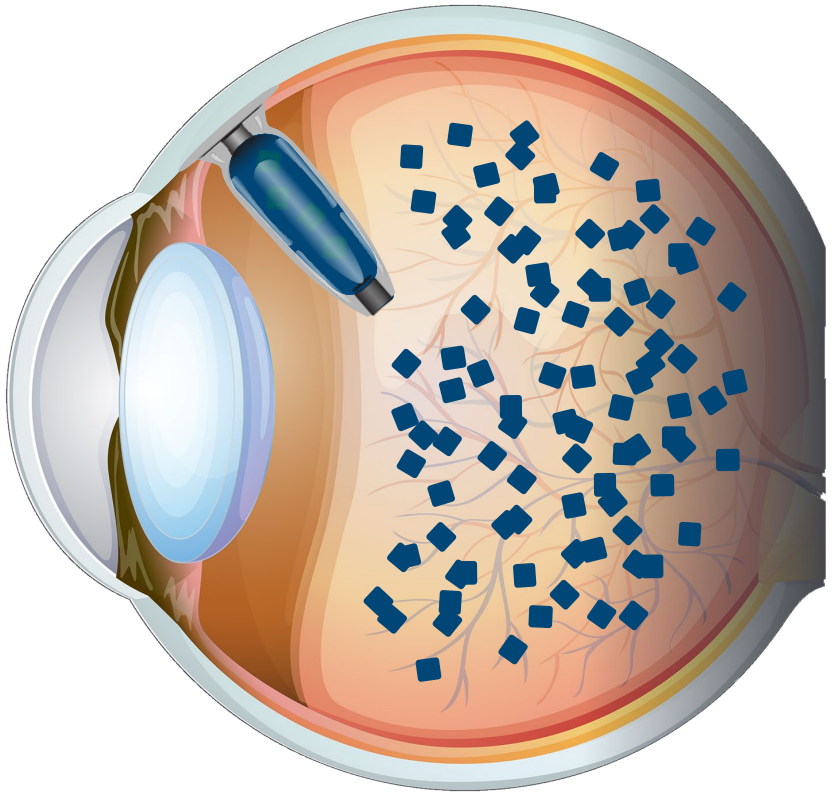
- Permanent, refillable ocular implant
- Customized formulation of ranibizumab
- Implant surgically placed at the pars plana in operating theater
- In-clinic refill-exchange procedures

PDS, Port Delivery System with ranibizumab.

RANIBIZUMAB RELEASE FROM THE PDS IMPLANT IS MEDIATED BY PASSIVE DIFFUSION



- Pars plana implant is a refillable ocular reservoir for ranibizumab
- Enables continuous drug delivery into the vitreous
- Mediated by passive diffusion along a concentration gradient
- PDS serum PK profile reflects implant release rate because implant release is the rate-limiting step



PDS, Port Delivery System with ranibizumab; PK, pharmacokinetic.

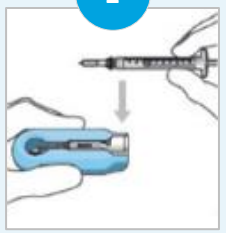
THE PDS SURGICAL PROCEDURES HAVE EVOLVED TO SUPPORT OPTIMAL OUTCOMES

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

Critical steps for surgical success

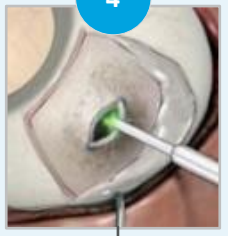
1. **Peritomy**

2. **Implant prep**



3. **Scleral dissection**

4. **Pars plana laser ablation**



5. **Pars plana incision**

6. **Implant insertion**

7. **Conjunctival and Tenon's closure**

To ensure the implant is seated securely

Ensure a final incision length of 3.5 mm during scleral dissection. A final incision length > 3.5 mm may result in an improperly seated implant and will require additional suturing. A final incision length < 3.5 mm may increase risk of vitreous hemorrhage

To ensure postoperative hemostasis

- Apply edge-to-edge laser ablation of the pars plana
- Be careful to apply laser only to the choroidal tissue in the exposed pars plana

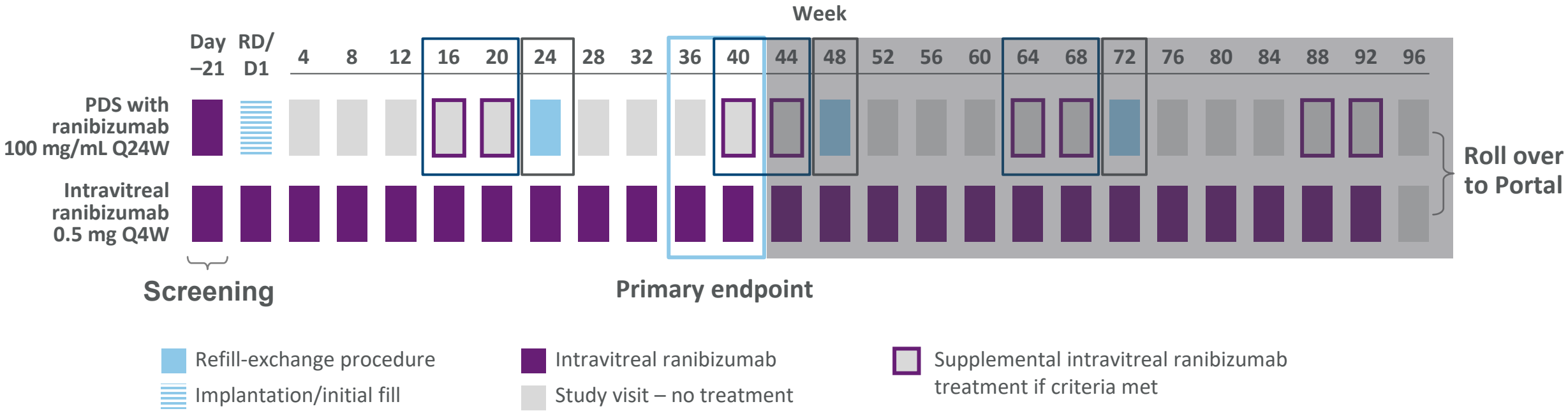
Perform precise pars plana incision

To ensure preservation of the conjunctiva and Tenon's capsule integrity

Proper dissection and closure of the conjunctiva and Tenon's capsule over the flange are essential for preventing early and late complications

PDS, Port Delivery System with ranibizumab.

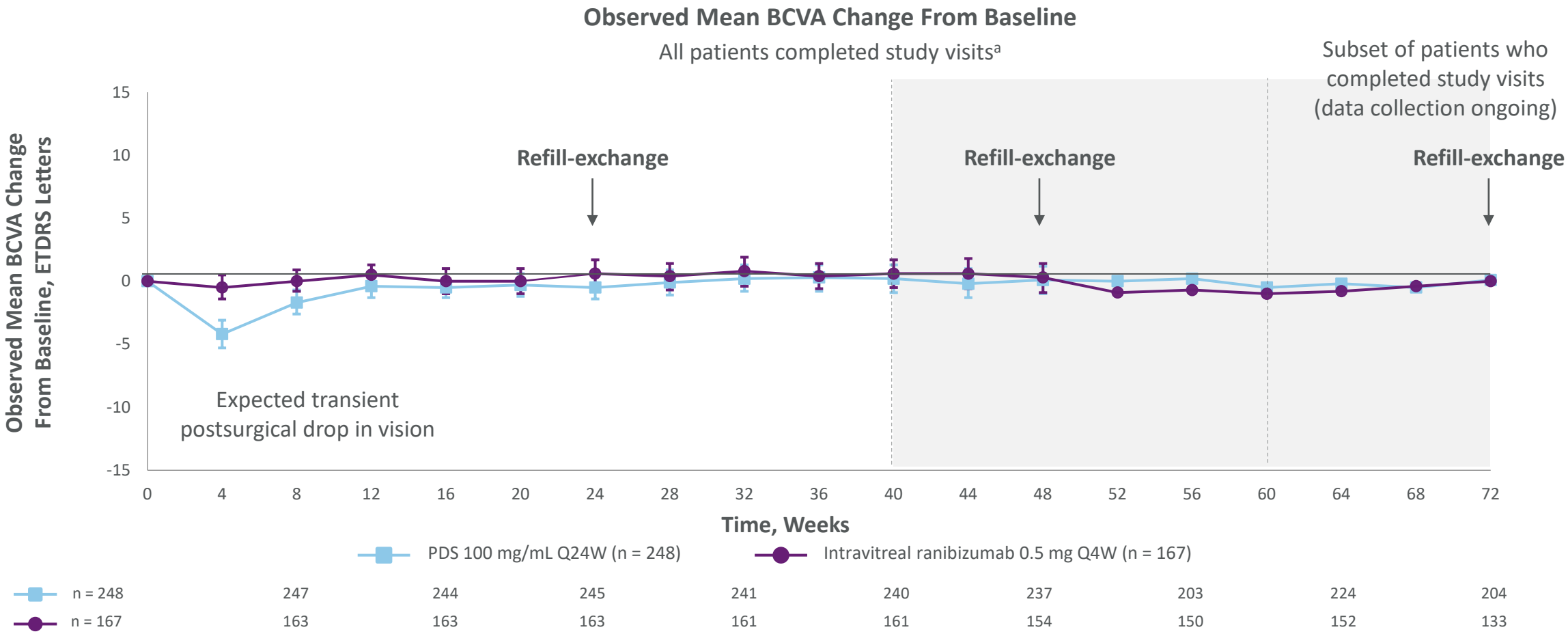
ARCHWAY TREATMENT REGIMEN: PDS WITH FIXED 24-WEEK REFILL-EXCHANGES



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

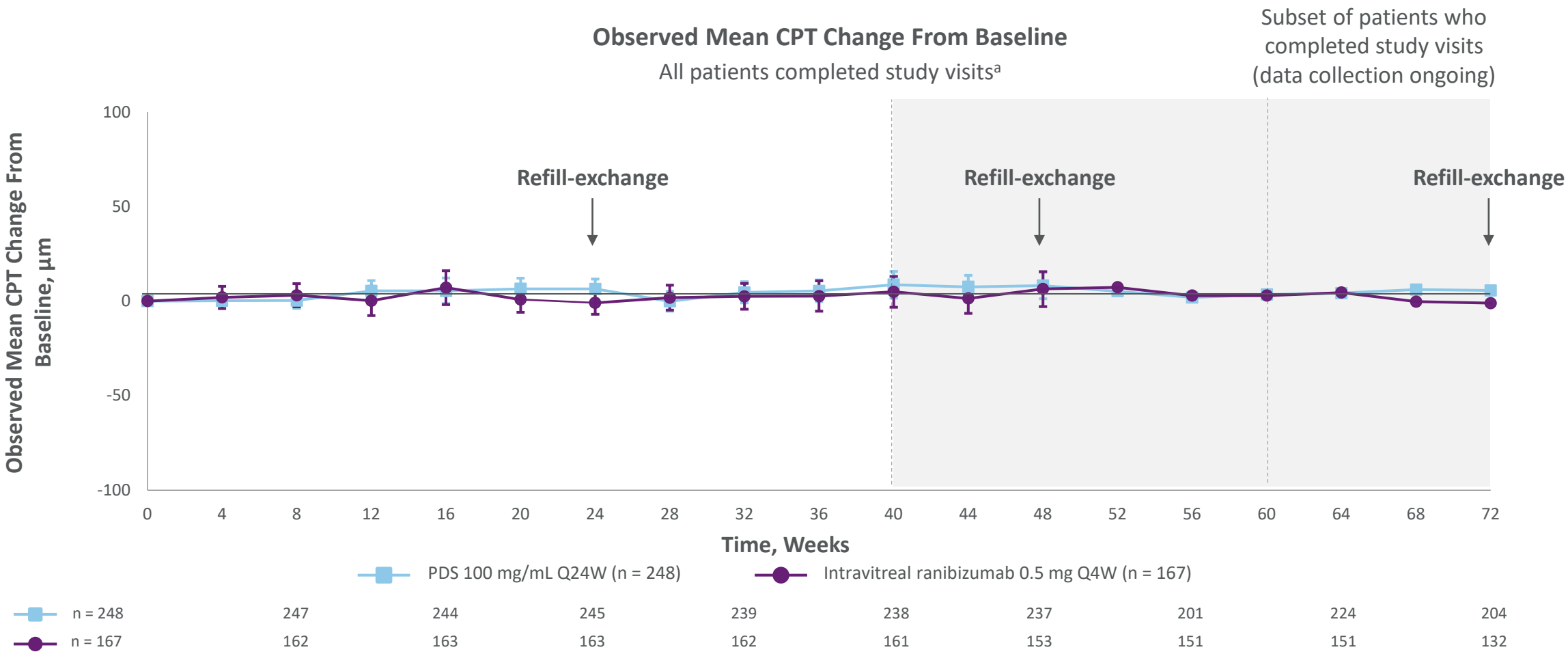
[a] Eligible for supplemental intravitreal ranibizumab treatment with open-label intravitreal ranibizumab at weeks 16 and 20 (after implant insertion) and at weeks 40, 44, 64, 68, 88, and 92 if any of the 3 criteria were met. BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; nAMD, neovascular age-related macular degeneration; PDS, Port Delivery System with ranibizumab; Q 4W, every 4 weeks; Q24W, every 24 weeks; RD, randomization; SD-OCT, spectral domain optical coherence tomography.

PDS Q24W MAINTAINED VISION THROUGH WEEK 72



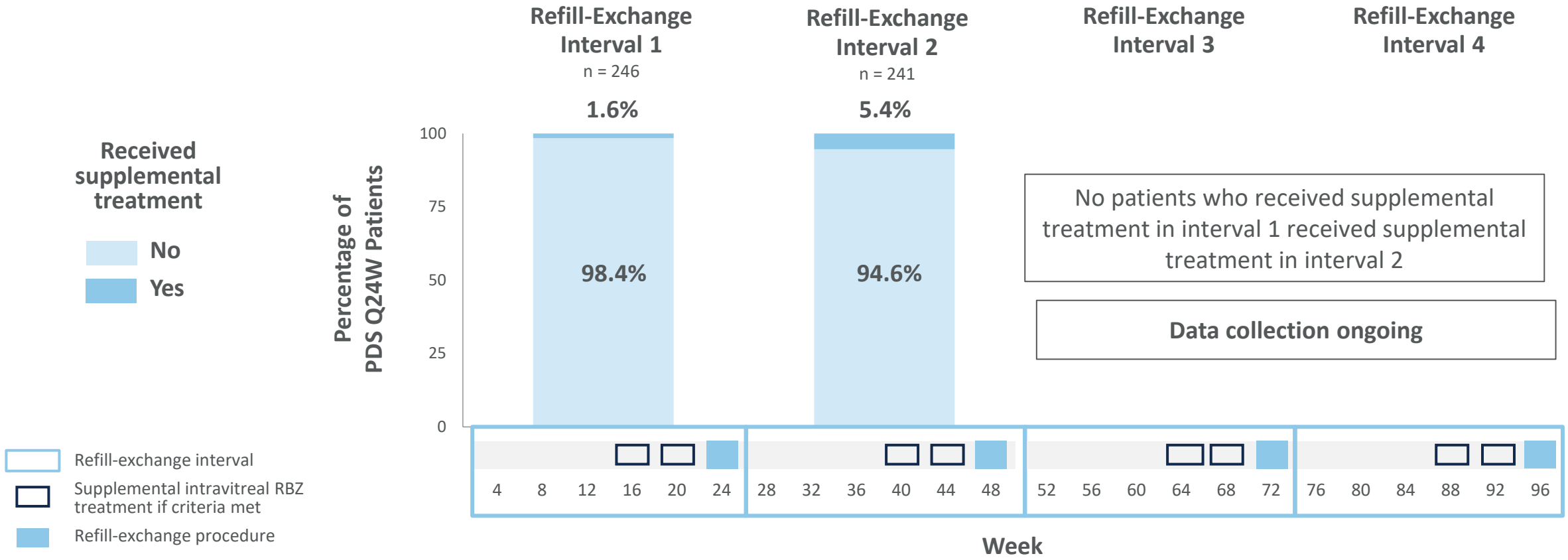
[a] All patients have passed their week 60 scheduled visit date or have discontinued the study early.
Observed data through the September 11, 2020 clinical cutoff date; data collection ongoing. Vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. 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.

OBSERVED MEAN CPT CHANGE FROM BASELINE



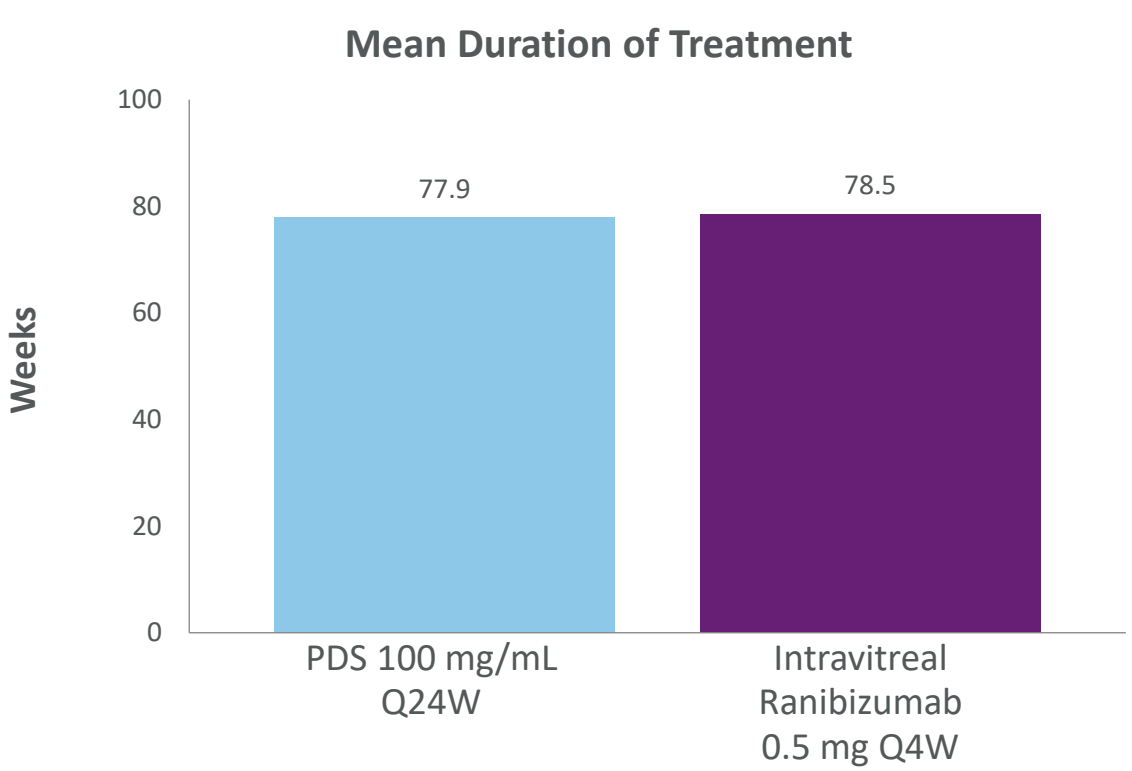
[a] All patients have passed their week 60 scheduled visit date or have discontinued the study early. Observed data through the September 11, 2020 clinical cutoff date; data collection ongoing. Vertical bars represent 95% CI. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. 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.CPT, center point thickness; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

> 90% OF PATIENTS DID NOT RECEIVE SUPPLEMENTAL TREATMENT BEFORE EACH REFILL-EXCHANGE PROCEDURE

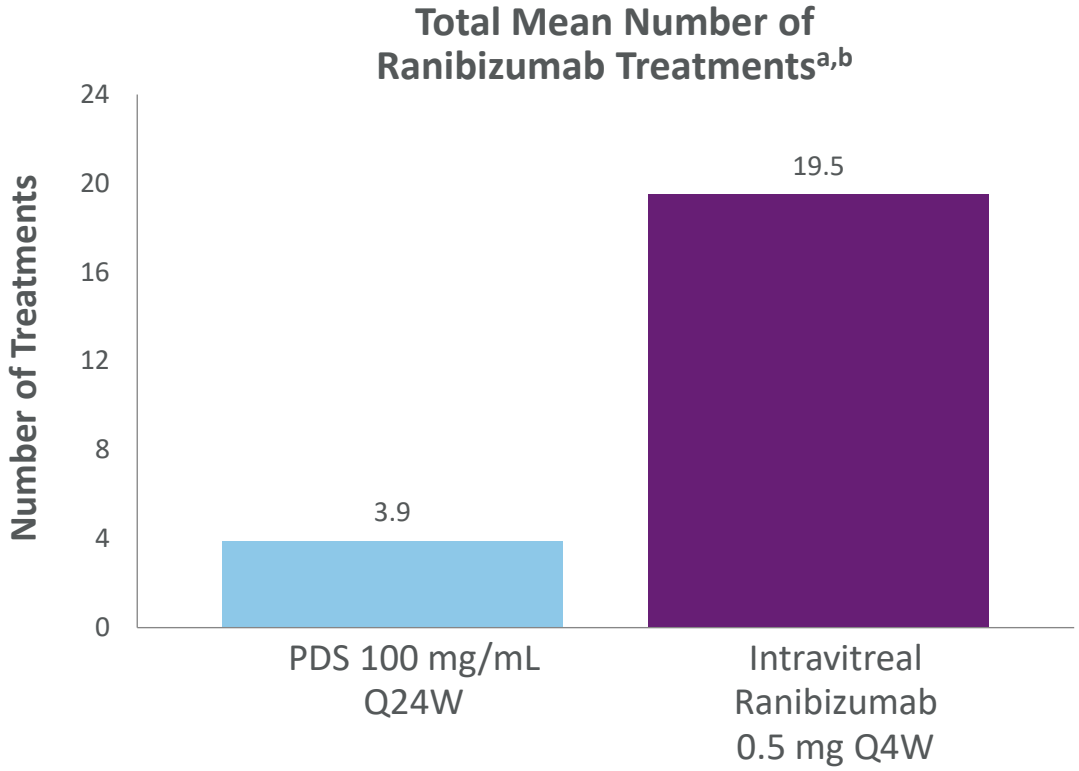


For each interval, percentages of patients who did/did not receive supplemental treatment were calculated out of the number of patients who were on treatment and assessed for supplemental treatment for ≥ 1 visit (interval 1, week 16 or 20; interval 2, week 40 or 44).
PDS, Port Delivery System with ranibizumab; RBZ, ranibizumab.

TREATMENT BURDEN THROUGH SEPTEMBER 2020: ~5X TIMES FEWER TREATMENTS IN PDS Q24W ARM OVER A MEAN DURATION OF 78 WEEKS



~80% of patients had data through the week 72 visit



Includes initial fill, refill-exchanges, and supplemental injections

Data through the September 11, 2020 clinical cutoff date; data collection ongoing. [a] Total number of ranibizumab treatments includes initial fill, refill-exchanges, and supplemental intravitreal ranibizumab 0.5 mg injections in PDS-treated patients and all intravitreal ranibizumab 0.5 mg injections in patients in the intravitreal ranibizumab 0.5 mg Q4W arm. [b] Includes PDS patients who received supplemental treatment.
PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

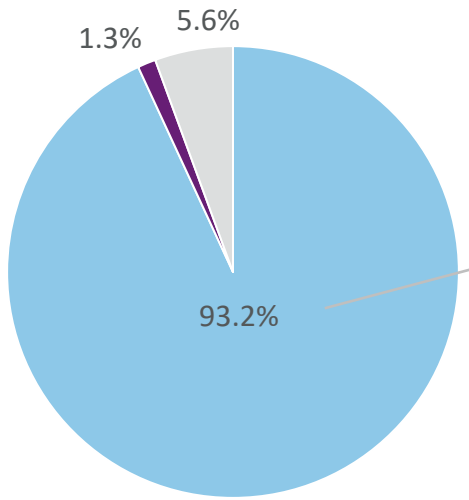
93% OF PDS PATIENTS PREFERRED PDS OVER INTRAVITREAL INJECTIONS

PDS Patient Preference Questionnaire

- The PPPQ is a 3-item questionnaire that captures a patient's preference for treatment, the strength of their preference, and the reasons for their preference
- The PPPQ was administered to all patients in the PDS arm at week 40

Responses to the PPPQ at Week 40[a]

Preference Among PDS Patients
(n = 234)[b]



90.2% indicated a very strong or fairly strong preference for PDS

Top 3 reasons for preference[c]:
- Fewer treatments
- Less discomfort
- Less worry/nervousness

PDS (n = 218)
Intravitreal injections (n = 3)
No preference (n = 13)

[a] For patients with missing week 40 values, the last postbaseline observation was imputed. [b] Percentages are based on total number of patients who completed the measure. [c] Results for patients with a very strong or fairly strong preference for PDS treatment.
PDS, Port Delivery System with ranibizumab; PPPQ, PDS Patient Preference Questionnaire.

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

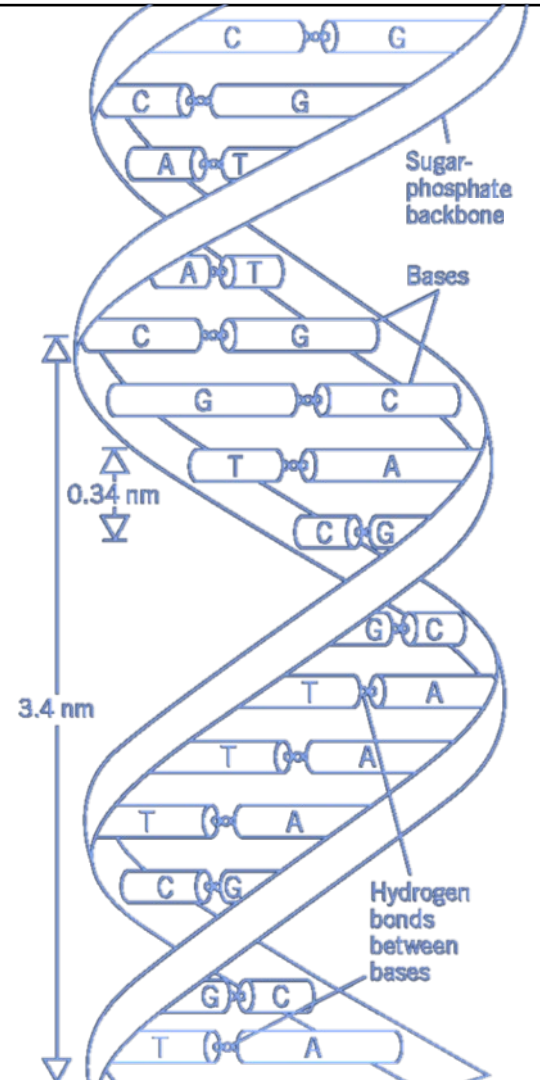
MedDRA Preferred Term, n (%)[b]	PDS 100 mg/mL Q24W (n = 248)		Intravitreal Ranibizumab 0.5 mg Q4W (n = 167)	
	Onset After Week 40	Overall[c]	Onset After Week 40	Overall[c]
Cataract[d]	11 (4.4%)	20 (8.1%)	2 (1.2%)	8 (4.8%)
Conjunctival bleb/ conjunctival filtering bleb leak	1 (0.4%)	17 (6.9%)	0	0
Conjunctival 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 hemorrhage	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

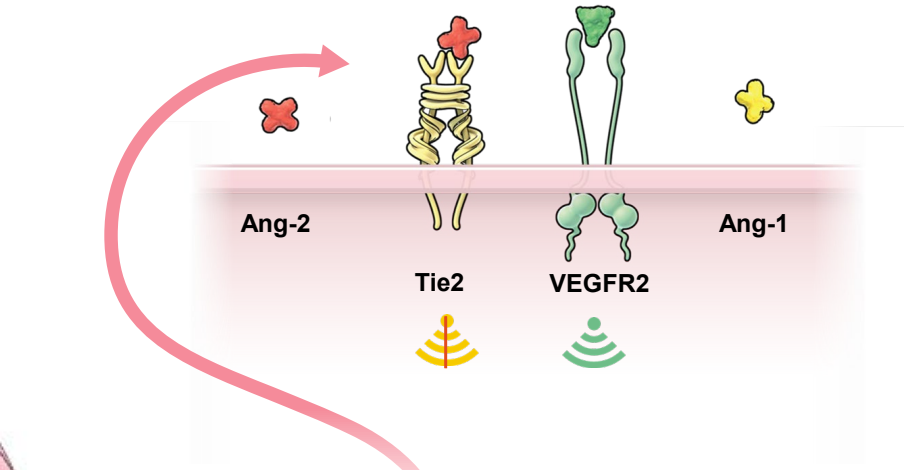
[a] Protocol-defined ocular adverse events of special interest potentially related to the PDS implant or implant insertion procedure. [b] Frequency counts by Preferred Term. Multiple occurrences of the same adverse event in an individual are counted only once for each column. [c] All data through the 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). HLA-B27, human leukocyte antigen B27; MedDRA, Medical Dictionary for Regulatory Activities; PDS, Port Delivery System with ranibizumab; Q4W, every 4 weeks; Q24W, every 24 weeks.

Dual Inhibition of Ang-2 and VEGF-A With Faricimab: Advances in Understanding and Treatment of Retinal Diseases

Presented at Angiogenesis 2021



Ang-2 Promotes Vascular Instability in Disease by Blocking Ang-1–Tie2 Signaling



1 Endothelial tight junctions weaken, leading to vascular leakage…

2 …and increased inflammation due to leukocyte migration

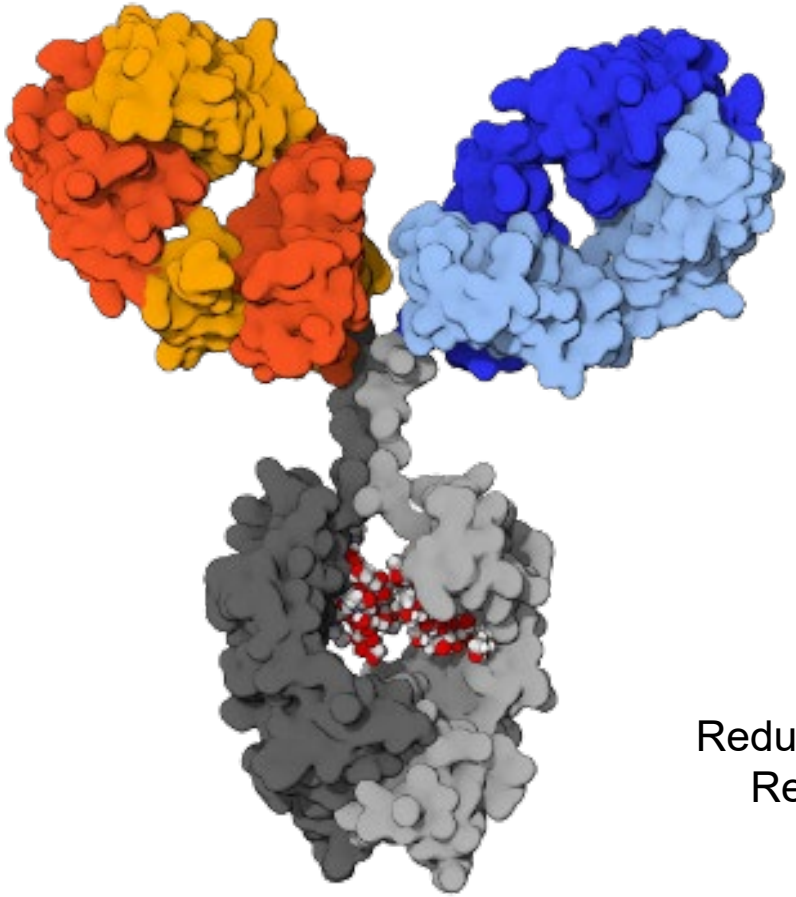
3 Pericyte dropout and loss further destabilizes vessels

4 Vascular sprouting and neovascularization occur

5 Immature, leaky vessels contribute to fibronectin deposition, which may cause vision loss

Faricimab Is the First Bispecific Antibody Designed for Intraocular Use: 1 Molecule, 2 Targets

Anti–Ang-2 Fab
Enhances vascular stability
Reduces inflammation and vascular leakage



Anti–VEGF-A Fab
Inhibits vascular leakage and neovascularization

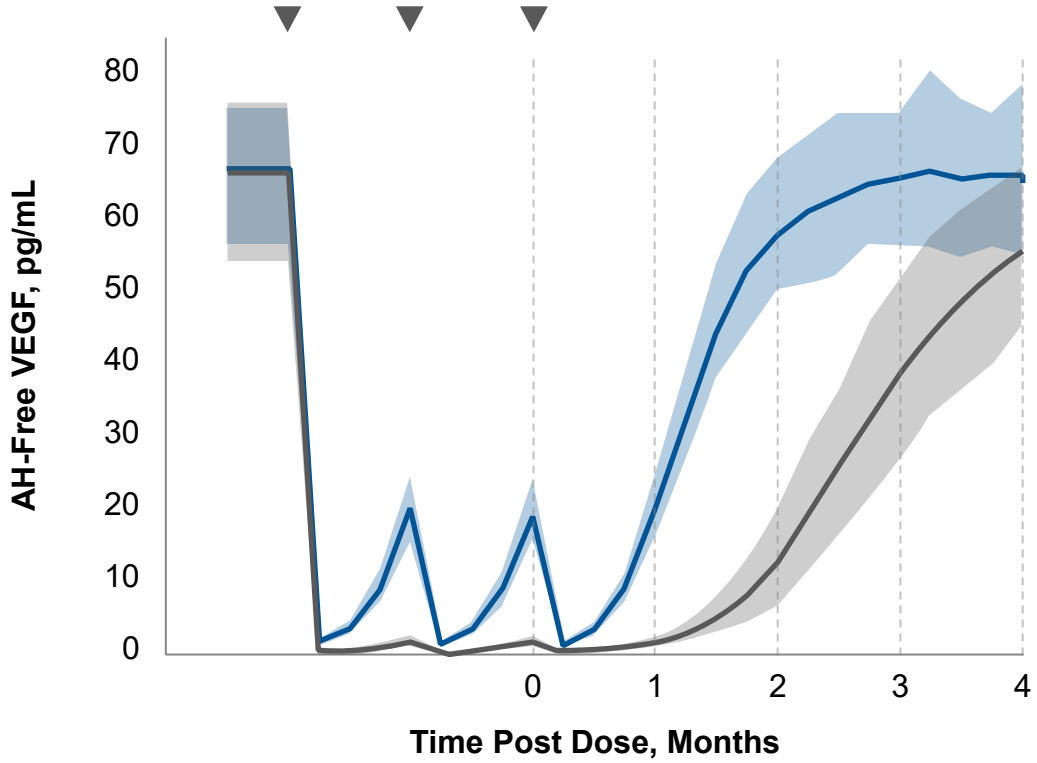
Modified Fc
Reduces systemic exposure
Reduces inflammatory potential

CrossMAb molecule representative of faricimab.
Regula JT et al. *EMBO Mol Med.* 2016;8(11):1265-1288, with correction in Regula JT et al. *EMBO Mol Med.* 2019;11(5):e10666.
Ang-2, angiopoietin-2; Fab, fragment antigen binding; Fc, fragment crystallizable; VEGF-A, vascular endothelial growth factor-A.

Faricimab Demonstrates Durable Intraocular Ang-2 and VEGF Suppression in Humans

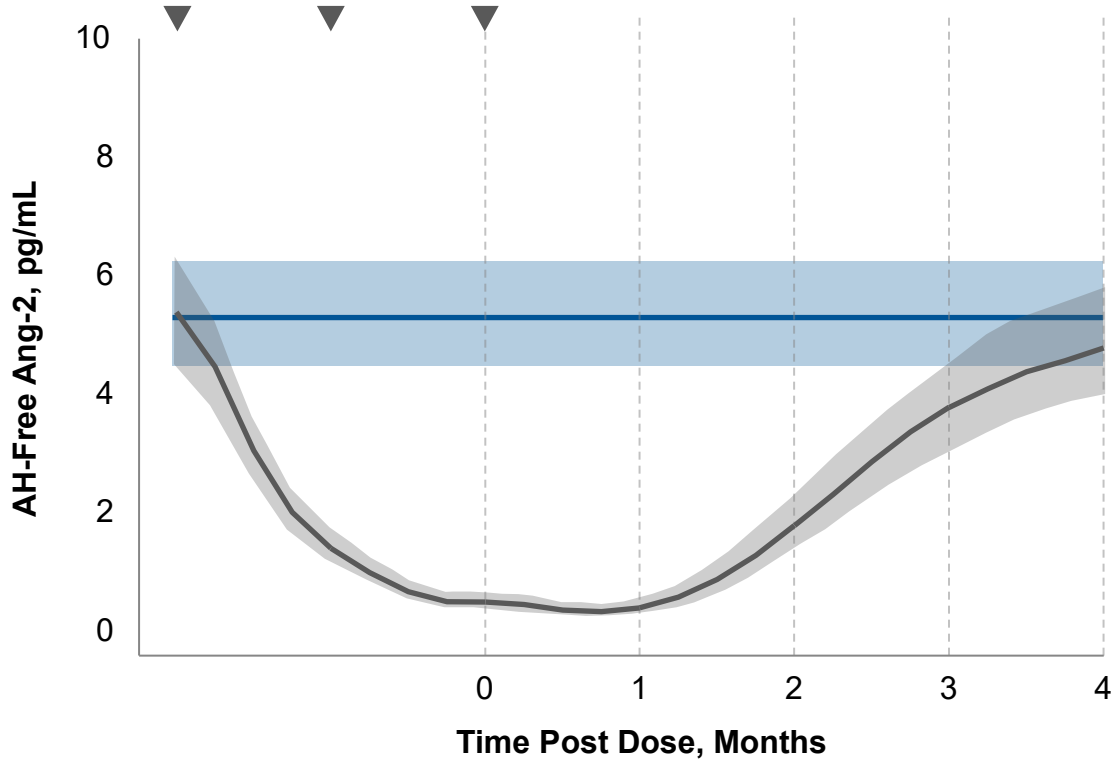
VEGF

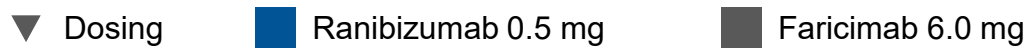
Predicted AH-free VEGF–time profile after ranibizumab 0.5 mg Q4W or faricimab 6.0 mg dosing



Ang-2

Predicted AH-free Ang-2–time profile after ranibizumab 0.5 mg Q4W or faricimab 6.0 mg dosing



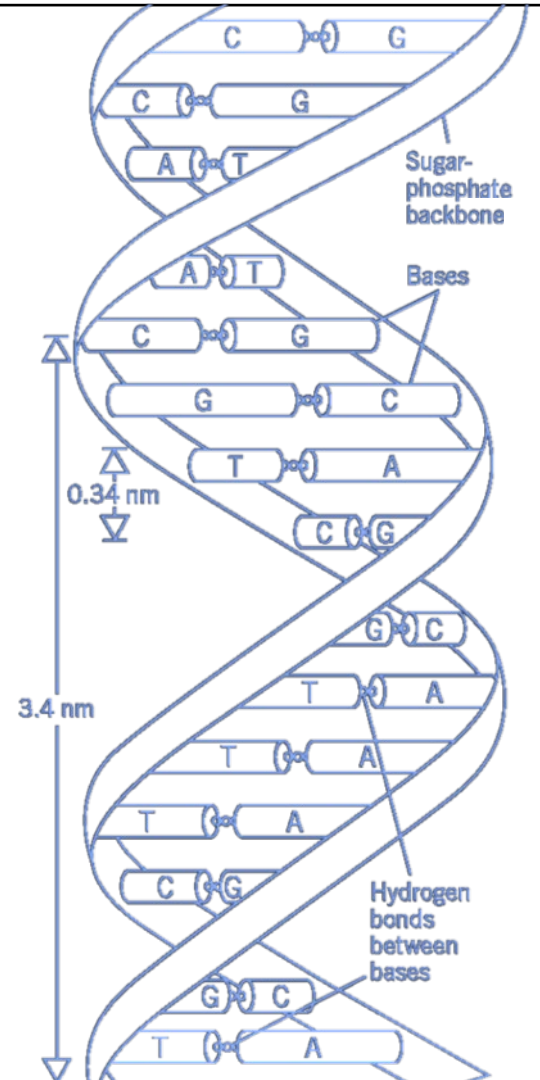


Roche and Genentech, Inc. data on file. AVENUE clinical trial (NCT02484690).
AH, aqueous humor; Ang-2, angiopoietin-2; Q4W, every 4 weeks; VEGF, vascular endothelial growth factor.

Faricimab in Neovascular Age-Related Macular Degeneration TENAYA and LUCERNE Study Results

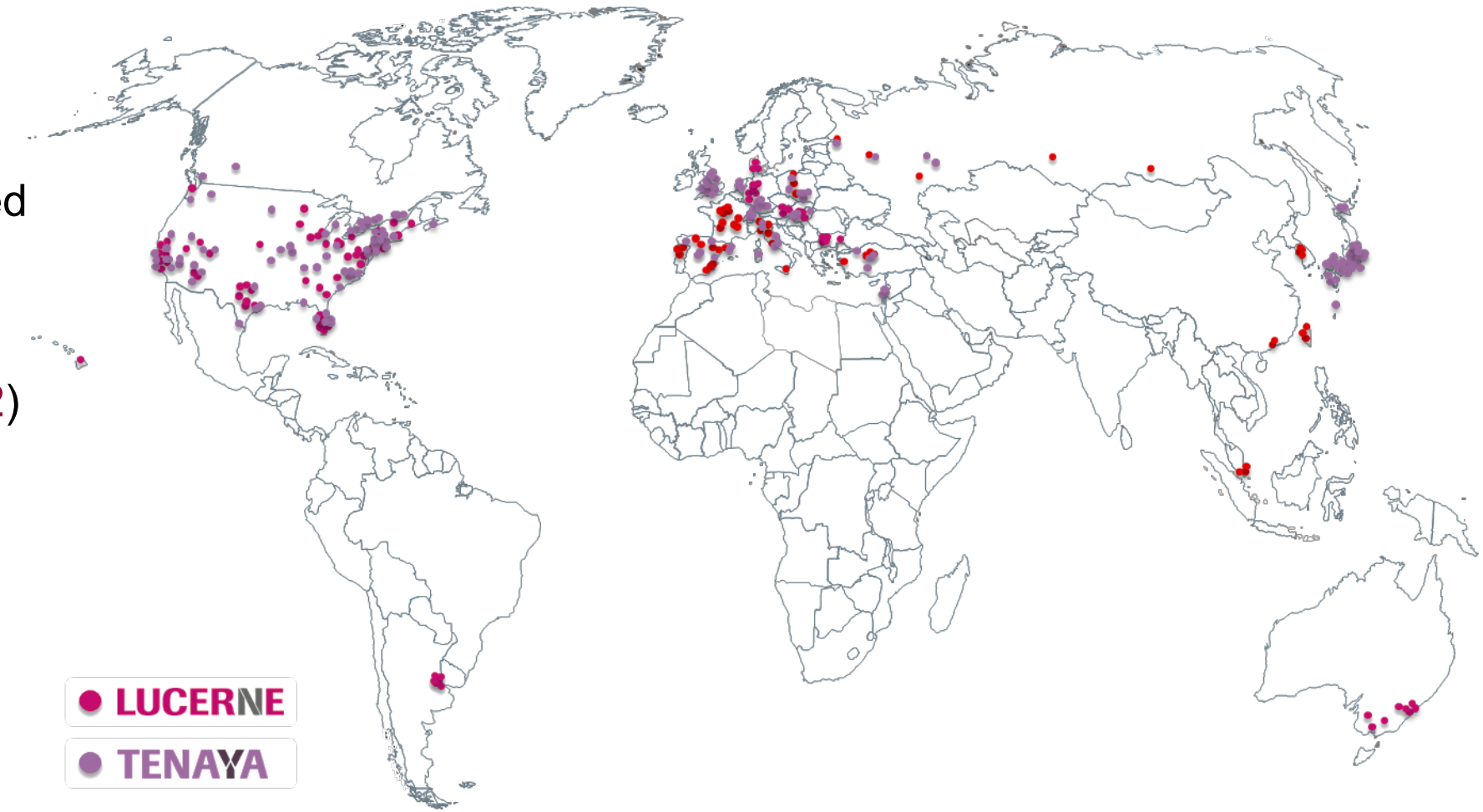
Phase 3, Multicenter, Randomized, Double-Masked, Active Comparator–Controlled Studies to Evaluate the Efficacy and Safety of Faricimab in Patients With Neovascular Age-Related Macular Degeneration

Presented at Angiogenesis 2021



TENAYA and LUCERNE Are Global Studies Enrolling > 1300 Patients Across 271 Study Sites

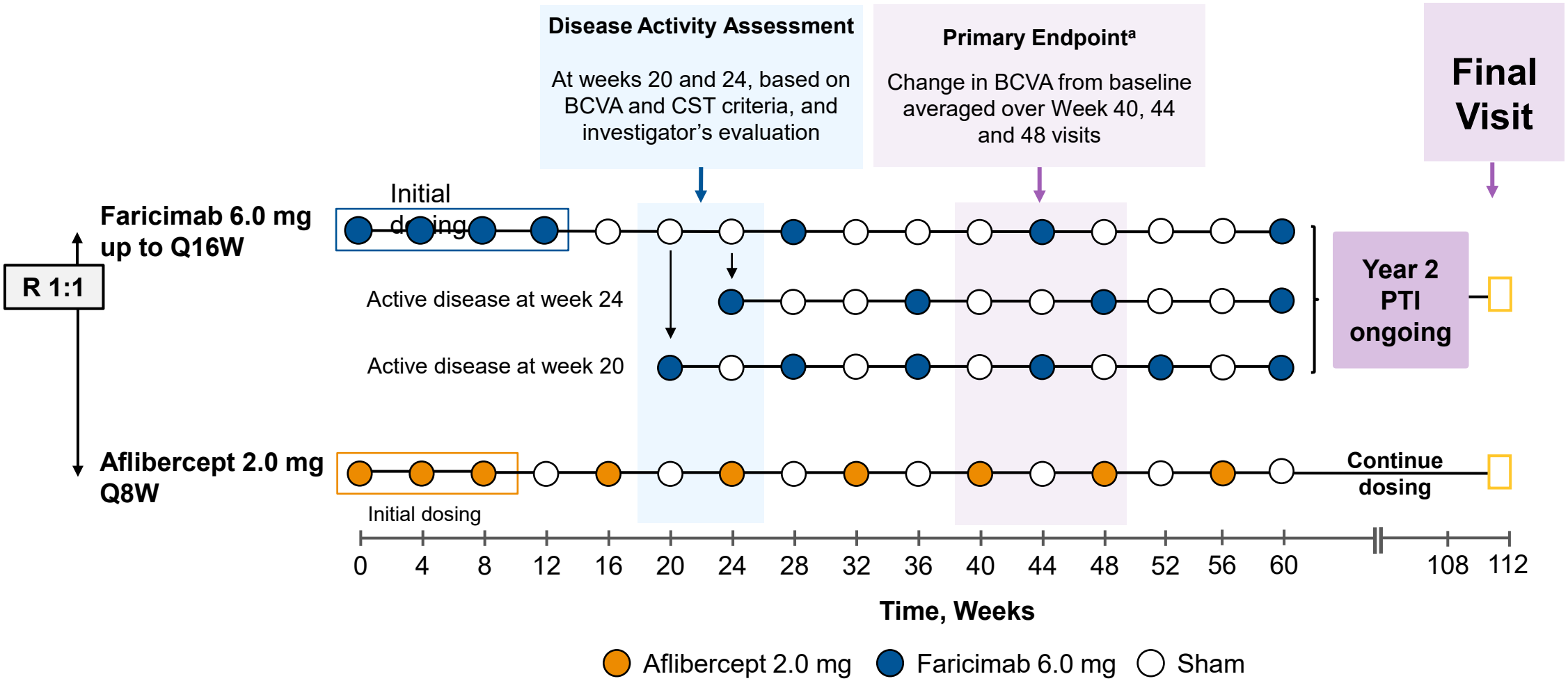
- **1329 patients** enrolled (671 and 658)
- **271 sites** enrolled patients (149 and 122)



ClinicalTrials.gov identifiers: NCT03823287 (TENAYA); NCT03823300 (LUCERNE).

TENAYA and LUCERNE

Randomized, Double-Masked, Multicenter Studies Designed to Evaluate the Efficacy and Safety of Faricimab Versus Aflibercept



ClinicalTrials.gov identifiers: NCT03823287 (TENAYA); NCT03823300 (LUCERNE).

[a] BCVA was measured using the Early Treatment Diabetic Retinopathy Study visual acuity chart at a starting distance of 4 m.

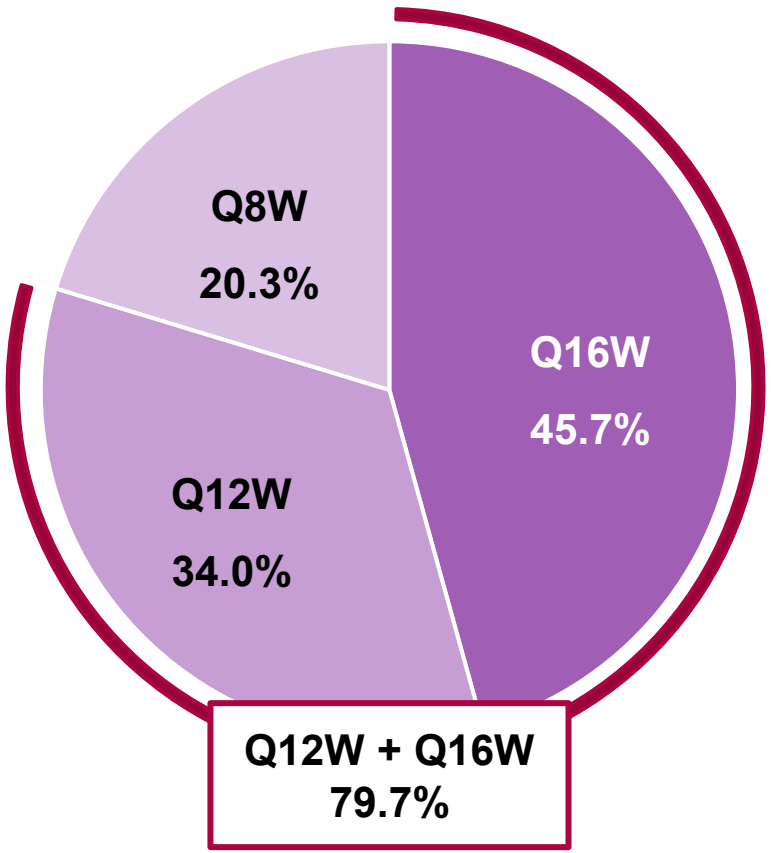
BCVA, best-corrected visual acuity; CST, central subfield thickness; Q8W, every 8 weeks; Q16W, every 16 weeks; R, randomized.

Durability With Faricimab: ~45% of Patients on Q16W and Almost 80% on ≥ Q12W Dosing at Week 48

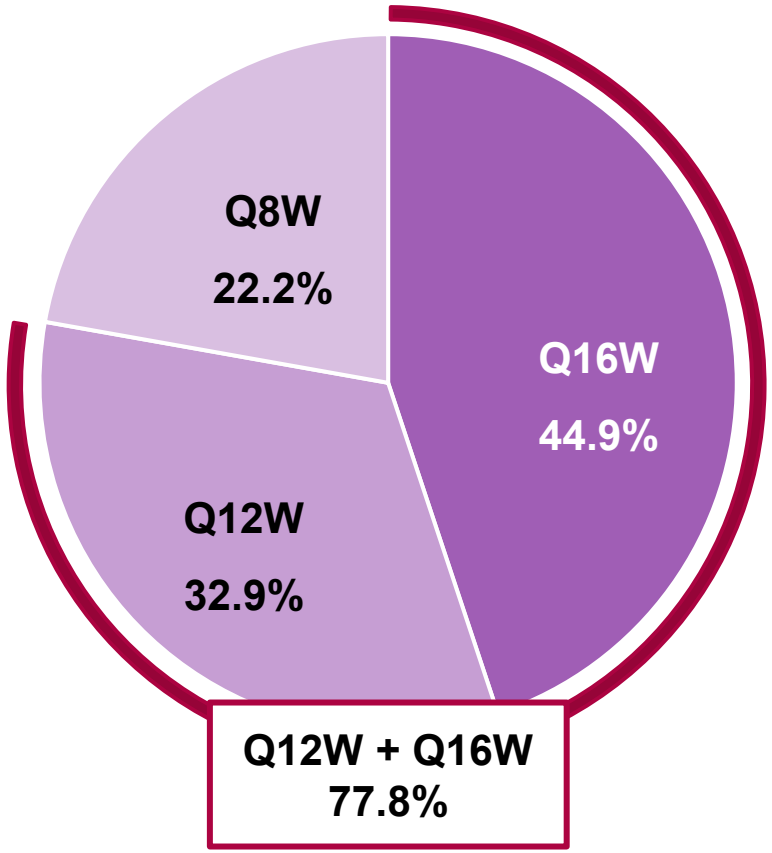
Proportion of patients in the faricimab arm on each treatment interval among those completing Week 48

ITT Population

TENAYA (n = 334)



LUCERNE (n = 331)



Median number of injections:

Faricimab – 6

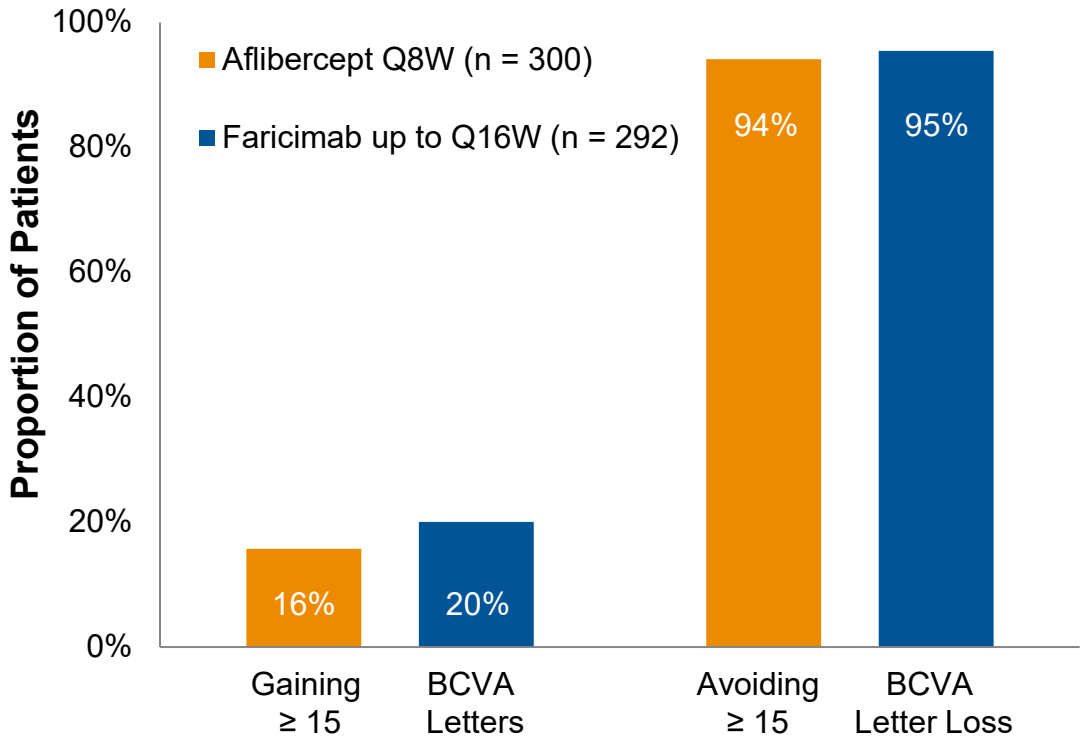
Aflibercept – 8

Percentages are based on number of patients randomized to the faricimab arm who have not discontinued the study at Week 48. Treatment interval at Week 48 is defined as the treatment interval decision followed at that visit
ITT, intent to treat; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

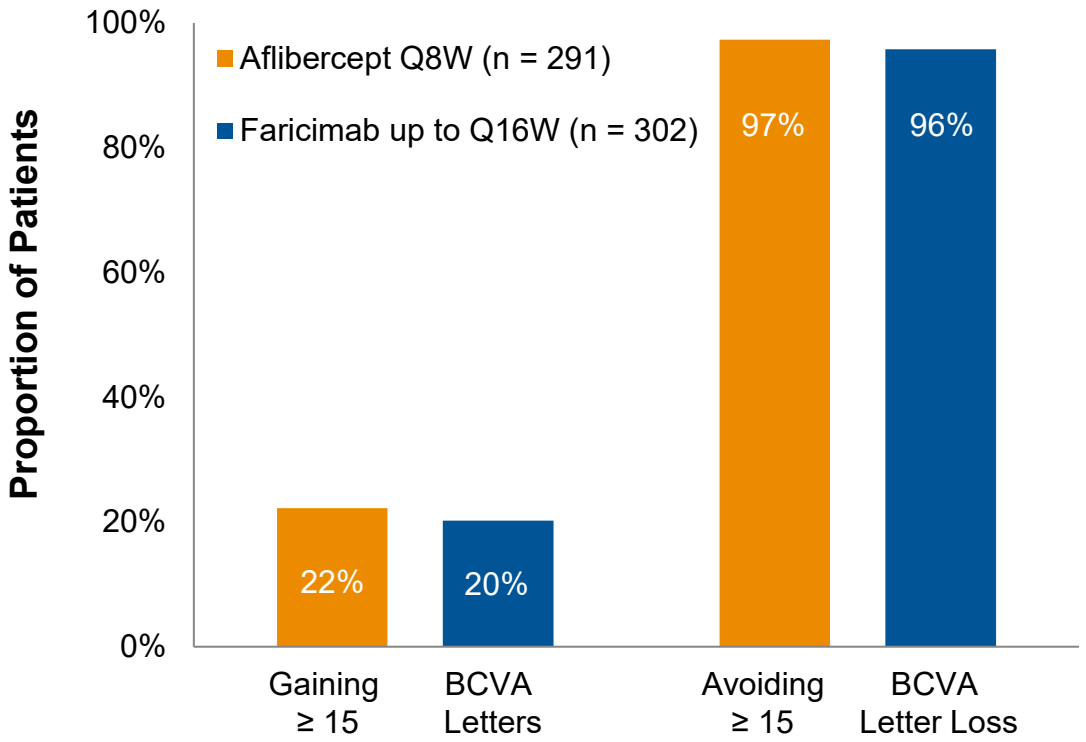
Comparable Proportion of Patients Gaining or Maintaining Vision[a] With Faricimab up to Q16W and Aflibercept Q8W

ITT population

TENAYA



LUCERNE

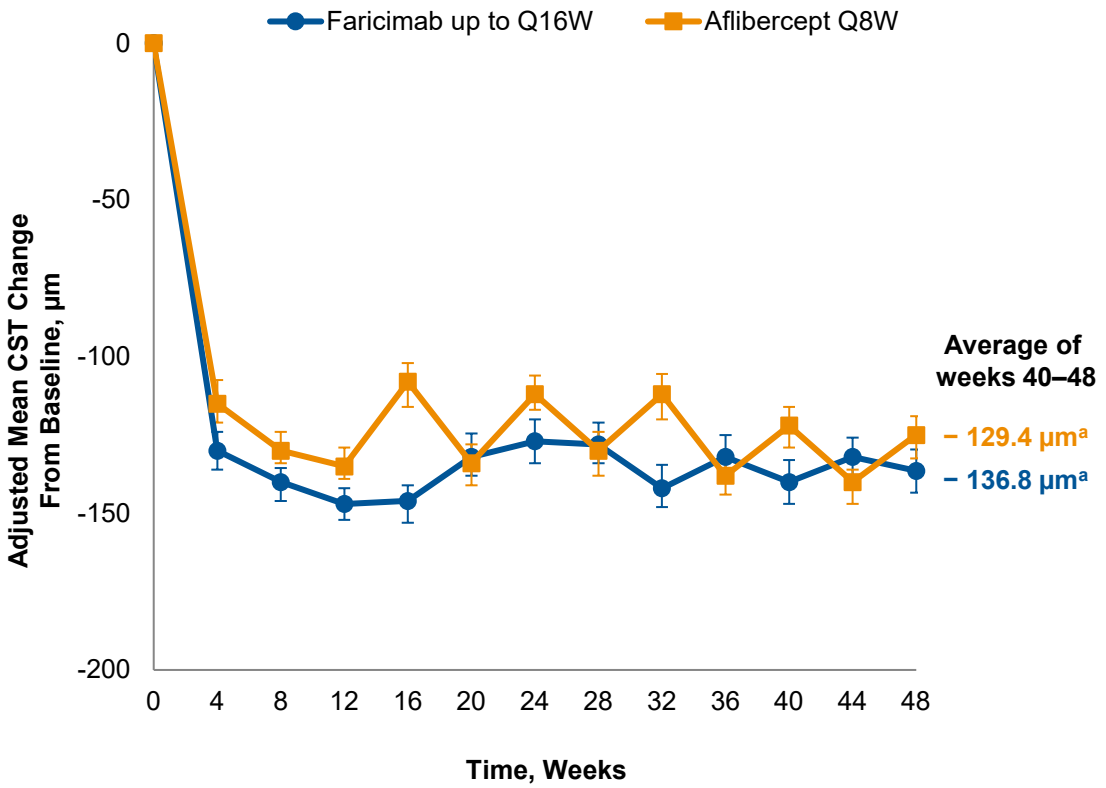


n represents patients with at least one non-missing assessment at Weeks 40, 44, 48. Proportion of patients in each group was estimated using the Cochran-Mantel Haenszel method.
[a] Proportion of patients who gained or avoided a loss of ≥ 15 ETDRS letters at 1 year, averaged over weeks 40, 44, and 48.
BCVA, best-corrected visual acuity; ITT, intent to treat; Q16W, every 16 weeks.

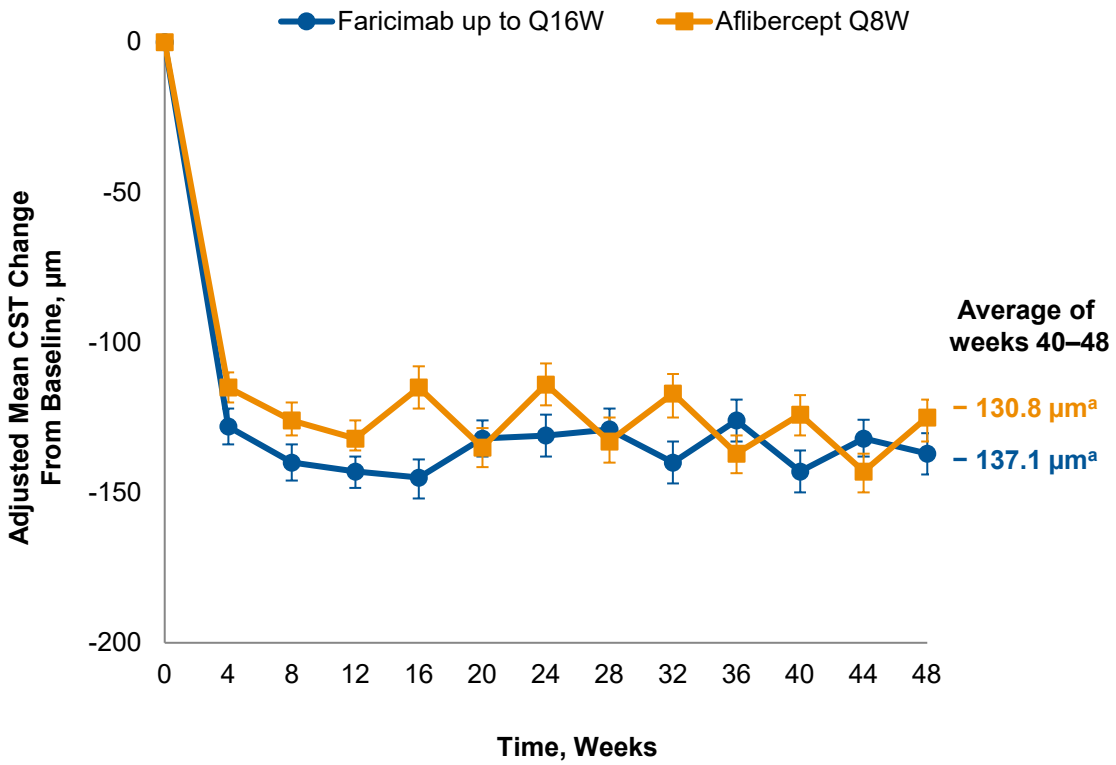
Meaningful and Comparable Reductions in CST From Baseline Through Week 48 With Faricimab up to Q16W and Aflibercept Q8W

ITT population

TENAYA



LUCERNE



[a]Adjusted mean CST change from baseline at 1 year, averaged over weeks 40, 44, and 48
Results are based on a mixed model for repeated measures analysis. 95% CIs are shown.
CST is measured as ILM-RPE, as graded by central reading center.
CST, central subfield thickness; ILM, internal limiting membrane; ITT, intent-to-treat; Q8W, every 8 weeks; Q16W, every 16 weeks; RPE, retinal pigment epithelium.

Rates of AEs of Intraocular Inflammation Were Low

IOI Events Were on Average Reported in 2.0% and 1.2% of Patients for Faricimab and Aflibercept, Respectively

Intraocular Inflammation (IOI) Through Week 48	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (N=326)
Patients with any AEs of IOI (excluding endophthalmitis), n (%)	5 (1.5%)	2 (0.6%)	8 (2.4%)	6 (1.8%)
Number of patients with events, n (%)				
Iritis	2 (0.6%)	1 (0.3%)	1 (0.3%)	1 (0.3%)
Uveitis	1 (0.3%) **S**	1 (0.3%)	1 (0.3%) **S**	1 (0.3%) **S**
Keratic precipitates	1 (0.3%)	0	0	0
Vitritis	1 (0.3%)	0	2 (0.6%)	1 (0.3%)
Iridocyclitis	0	0	3 (0.9%)	2 (0.6%)
Chorioretinitis	0	0	1 (0.3%) **S**	0
Postprocedural inflammation	0	0	0	1 (0.3%)

	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (N=326)
Endophthalmitis, n (%)	0	0	0	1 (0.3%)

Results are presented based on the Safety Evaluable Population. All events are investigator-reported. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once. Includes AEs with onset up to Day 349 (last day of Week 48 analysis visit window). S: Severe events are called out; all other events were mild or moderate. AE, adverse event; Q8W, every 8 weeks; Q16W, every 16 weeks.

No Cases of Retinal Vasculitis in Either Study

Retinal Vasculitis Events Through Week 48	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 326)
Number of patients with events	0	0	0	0

Retinal Occlusive Events Through Week 48	TENAYA		LUCERNE	
	Faricimab up to Q16W (n = 333)	Aflibercept Q8W (n = 336)	Faricimab up to Q16W (n = 331)	Aflibercept Q8W (n = 326)
Patients with any events, n (%)	0	0	1 (0.3%)	0
Number of patients with events, n (%)				
Retinal vein occlusion	0	0	0	0
Retinal artery occlusion	0	0	0	0
Retinal artery embolism	0	0	1 (0.3%)	0

Results are presented based on the Safety Evaluable Population. All events are investigator-reported. For frequency counts by preferred term, multiple occurrences of the same AE in an individual are counted only once.
Q8W, every 8 weeks; Q16W, every 16 weeks.