NASDAQ: KOD KODIAK.COM

KODIAK

THE OPHTHALMOLOGY MEDICINES COMPANY

R&D Day
October 14, 2019

JOHN BORGESON

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CFO

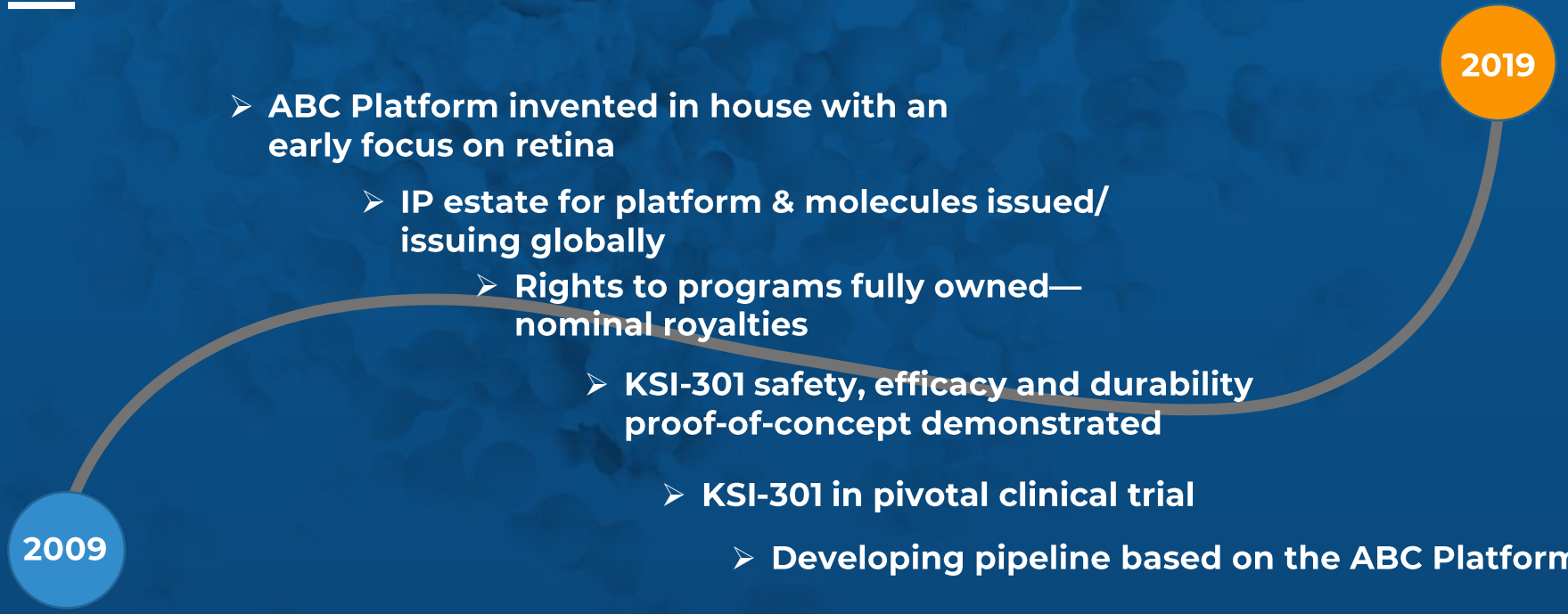
SPECIAL NOTE REGARDING

FORWARD-LOOKING STATEMENTS

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements we make regarding the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our regulatory strategy, our ability to advance product candidates into, and successfully complete, clinical studies, and the timing or likelihood of regulatory filings and approvals are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties that are described in our most recent quarterly report on Form 10-Q, as well as our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

KODIAK'S JOURNEY

BUILDING BLOCKS OF AN OPHTHALMOLOGY FRANCHISE



KSI-301+

A PIPELINE OF ABCs FOR RETINA

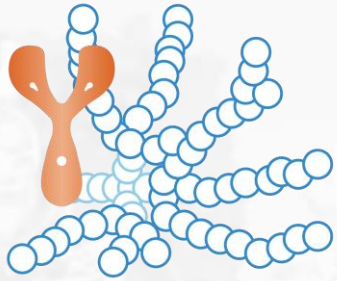
Kodiak's deepening pipeline of mono-, bi-specific and triplet inhibitors that merge biologics with small molecules to address major causes of vision loss beyond retinal vascular disease.

MONOSPECIFIC

1 Molecule, **1 Target**

Antibody conjugated to phosphorylcholine biopolymer

KSI-301 inhibits VEGF—In clinical development

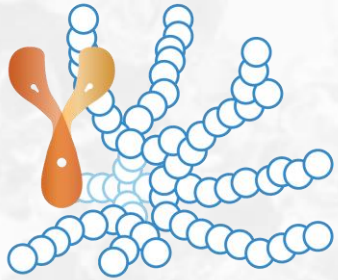


BISPECIFIC

1 Molecule, **2 Targets**

Bispecific antibody conjugated to phosphorylcholine biopolymer

KSI-501 inhibits VEGF and IL-6 for retinal diseases with inflammatory component—In GMP manufacturing

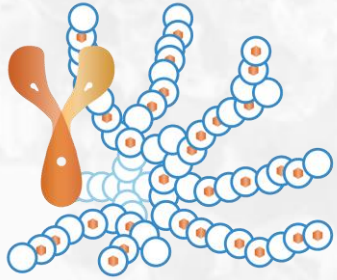


TRIPLET

1 Molecule, **3 Targets**

Bispecific antibody conjugated to phosphorylcholine biopolymer embedded with 100's of copies of small-molecule drug

For high-prevalence multifactorial diseases, such as dry AMD and glaucoma—In research



TODAY'S AGENDA

John Borgeson Chief Financial Officer—Kodiak	**Welcome**
Victor Perlroth, M.D. Chief Executive Officer—Kodiak	**About Kodiak and ABC Platform**
Jason Ehrlich, M.D., Ph.D. Chief Medical & Development Officer—Kodiak	**Putting Phase 1b Data in Context**
Charles C. Wykoff, M.D., Ph.D. Director of Research, Retina Consultants of Houston	**Latest Data on KSI-301**
Carl Regillo, M.D. Chief, Retina Service, Wills Eye Hospital	**Wet Age-Related Macular Degeneration**
Charles C. Wykoff, M.D., Ph.D. Director of Research, Retina Consultants of Houston	**Diabetic Eye Disease**
Arshad Khanani, M.D. Director of Clinical Research, Sierra Eye Associates	**Retinal Vein Occlusion**
Max Cambras, M.A. Managing Director & Partner, LEK Consulting	**Commercial Opportunity**
Nancy Holekamp, M.D. Director of Retina Services, Pepose Vision Institute	**Synthesis & Reflections**
Panel	**Discussion and Q & A**

Our Speakers

Carl Regillo, M.D.

Chief of Retina Service, Wills Eye Hospital

—

Professor of Ophthalmology, Thomas Jefferson University School of Medicine

Arshad Khanani, M.D.

Director of Clinical Research, Sierra Eye Associate

—

Clinical Associate Professor, University of Nevada, Reno

Nancy Holekamp, M.D.

Director of Retina Services, Pepose Vision Institute

—

Professor of Clinical Ophthalmology & Visual Sciences

Washington University School of Medicine, St. Louis

Charles Wykoff, M.D., Ph.D.

Director of Research, Retina Consultants of Houston & Greater Houston Retina Research Foundation

—

Deputy Chair of Ophthalmology, Blanton Eye Institute, Houston Methodist Hospital

Max Cambras, M.A.

Managing Director & Partner, L.E.K. Consulting

VICTOR PERLROTH, M.D.

—

CEO

THE OPHTHALMOLOGY MEDICINES COMPANY

OUR MISSION

1 TRAILBLAZING SCIENCE

Our creative and thoughtful foundation

2 "GO-TO" MEDICINES

Our challenge to the status quo

3 SINGULAR FOCUS IN OPHTHALMOLOGY

Our 24 / 7 / 365

OUR 2022 VISION

WET AMD

2021 DAZZLE top-line data
2022 wAMD confirmatory pivotal top-line data
2022 supplemental BLA

Diabetic Macular Edema

Diabetic Retinopathy

RETINAL VEIN OCCLUSION

2021 BRVO pivotal top-line data
2021 CRVO pivotal topline data
2022 BLA filing
2022 Potential U.S. approval

KSI-501 anti-VEGF/IL-6

2021 IND submitted
2022 Phase 1 data DME, uveitic macular edema, +/- wAMD

1	BLA submitted	1	Supplemental BLA submitted	2	Clinical programs	1	IND per year beginning 2021

PROGRAM ACCELERATION

Potential milestones

2019

KSI-301

- ✓ Safety, efficacy
- ✓ Durability proof-of-concept established
- ✓ Initiation of DAZZLE wAMD pivotal

2020

KSI-301

- Quarterly readouts of Phase 1b data
- Initiate RVO Phase 3 trials
- Initiate confirmatory wAMD Ph3 trial
- DAZZLE interim: % patients on 3, 4, 5 month dosing

2021

KSI-301

- Three pivotal study readouts:
  - CRVO
  - BRVO
  - DAZZLE wAMD

KSI-501

- Submit IND

2022

KSI-301

- Submit BLA for RVO
- Confirmatory wAMD pivotal data readout
- Submit sBLA for wAMD

KSI-501

- Phase 1 data in inflammatory retinal diseases

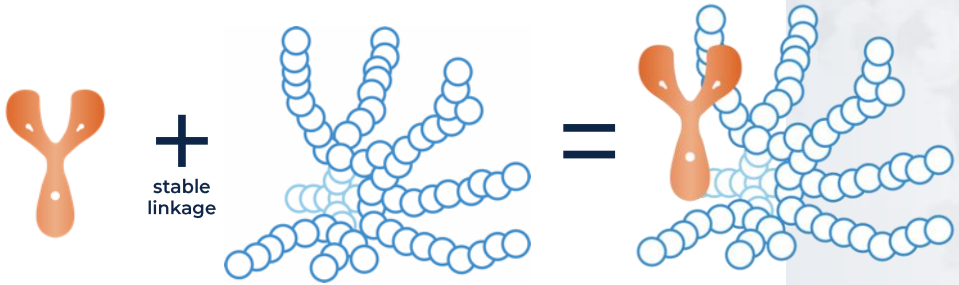
Additional ABC

- Submit IND

ANTIBODY BIOPOLYMER CONJUGATE

ABC PLATFORM™

A new scientific approach and design platform for intravitreal medicines



ANTIBODY

IgG1 with inert immune effector function

BIOPOLYMER

Optically clear, high molecular weight phosphorylcholine polymer

CONJUGATE

Antibody and biopolymer covalently bound via single site-specific linkage

Kodiak has designed ophthalmic antibody biopolymer conjugates for increased durability and efficacy.

SAME WHERE IT MATTERS

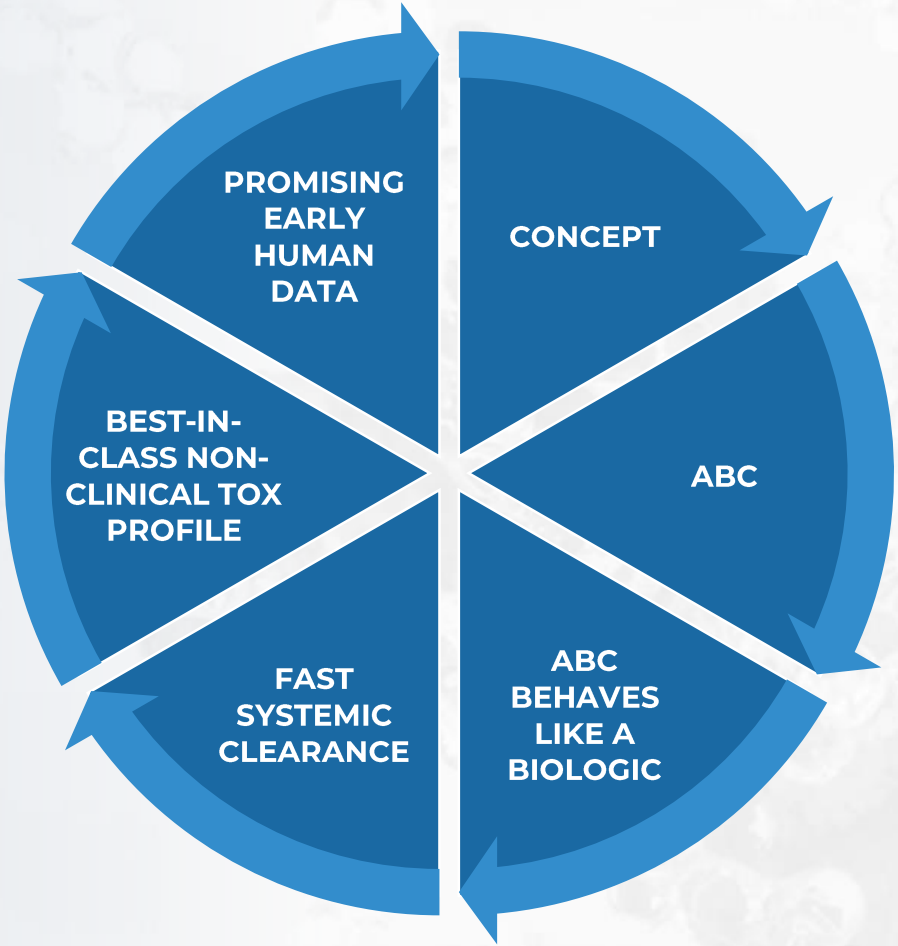
- Clinically proven targets
- Antibody-based biologic
- Intravitreal: safest method of administration
- Optically clear, no residues
- Fast and potent clinical responses

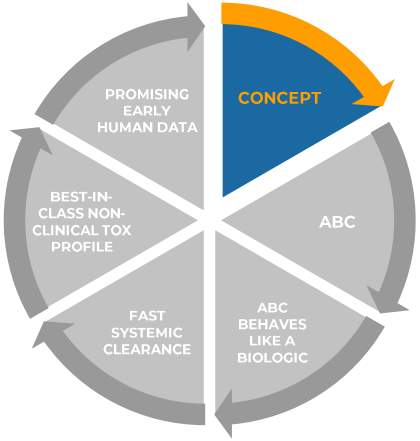
DIFFERENT WHERE IT COUNTS

- Designed-in ocular durability
- Designed-in rapid systemic clearance
- Improved bioavailability
- Improved biocompatibility
- Improved stability

KSI-301

DEEP DIVE: WHAT SETS US APART

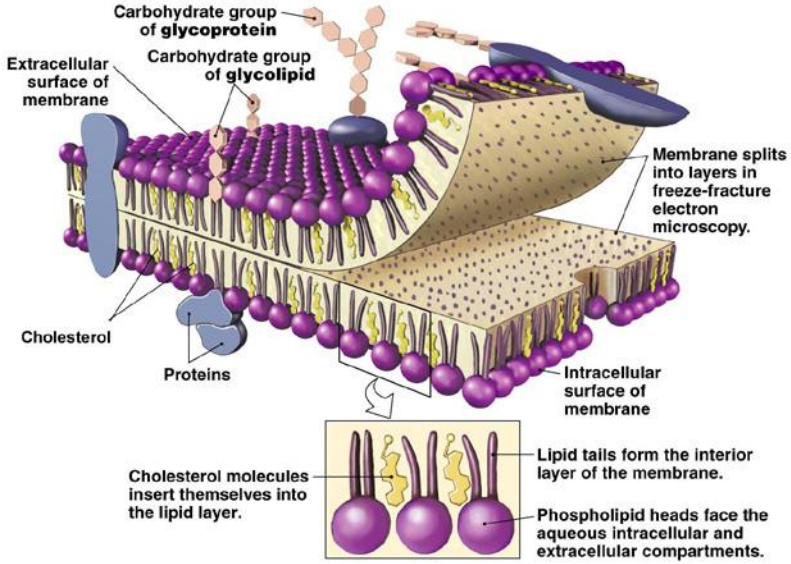


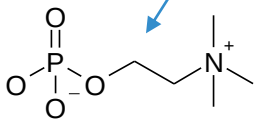


CONCEPT

Phosphorylcholine-based biopolymer is naturally biocompatible

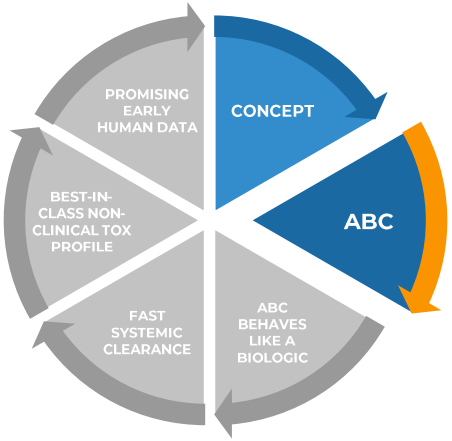
1. Phosphorylcholine is the primary lipid head group (>95%) on the external surface of all human cells
2. A zwitterion that tightly binds and structures many times of its weight of water, forms “structure water” or “macromolecular water”
3. Reduces local non-specific protein-protein interactions, and directs stereospecificity of ligand-receptor interactions
4. Demonstrated long term safety and effectiveness in increasing biocompatibility, reduce nonspecific protein absorption, and reduce cell adhesion when coated on surface of medical devices





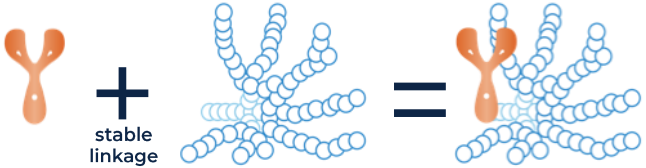
Phosphorylcholine

Zhang et al, Effect of Salt on Phosphorylcholine-based Zwitterionic Polymer Brushes, Langmuir 2016, 32, 5048−5057
Ishihara et al, Why do phospholipid polymers reduce protein adsorption? J. Biomed. Mater. Res. 1998, 39, 323−330.
Schlenoff, Zwitteration: coating surfaces with zwitterionic functionality to reduce nonspecific adsorption. Langmuir 2014, 30, 9625−9636.
Yang et al, Salt-responsive zwitterionic polymer brushes with tunable friction and antifouling properties Langmuir 2015, 31, 9125−9133.



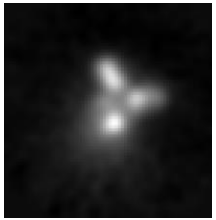
Antibody Biopolymer Conjugate (ABC)

is a stable linkage of one antibody to one branched, optically clear, high molecular-weight phosphorylcholine-based biopolymer

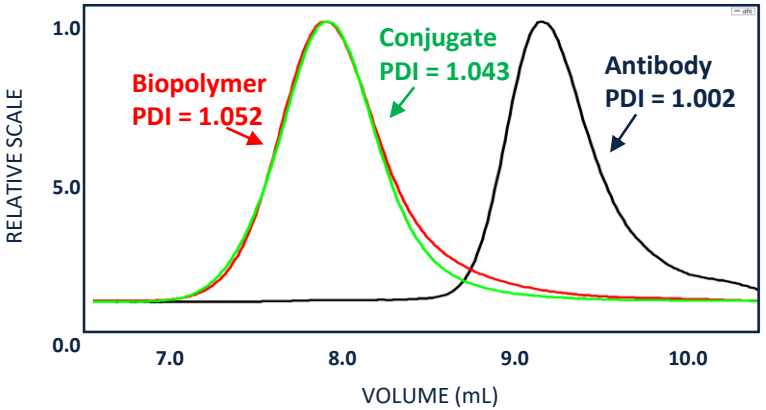


ANTIBODY 150kD + **BIOPOLYMER** 800KD = **CONJUGATE** 950KD

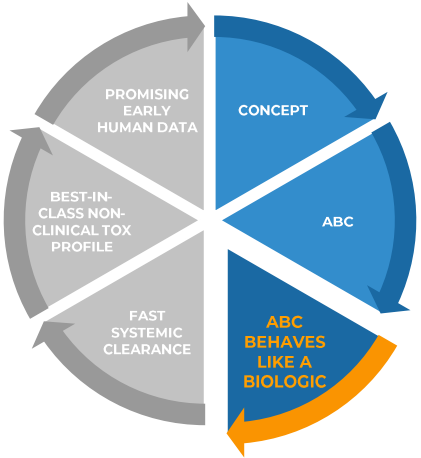
MW of ABC conjugate is the sum of MW of one antibody with one biopolymer



Electron microscope image of ABC



Biopolymer and ABC conjugate are manufactured to high quality with tight molecular weight distribution as shown by PDI

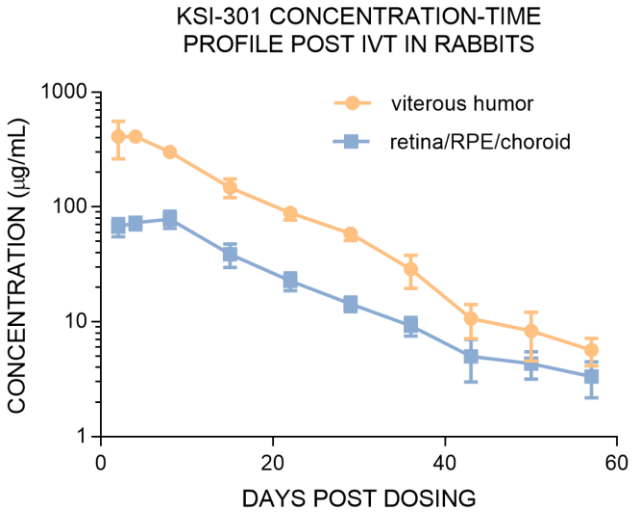


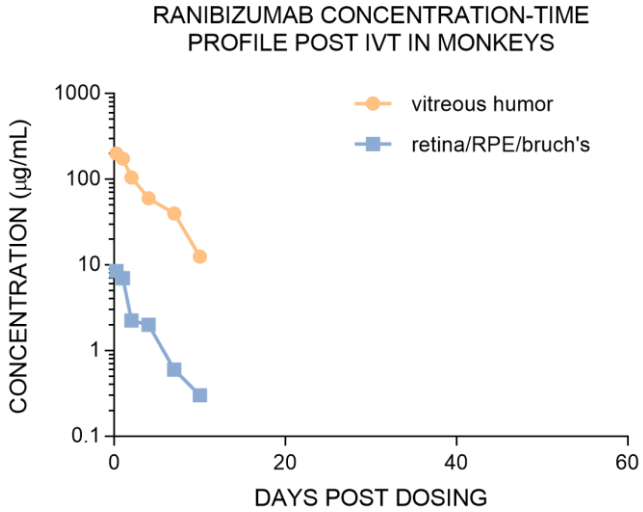
ABC BEHAVES LIKE A BIOLOGIC

After IVT, ABC traverses from vitreous to the retina/choroid and aqueous, exits to systemic similar to predicate anti-VEGF biologics, albeit with flatter curves

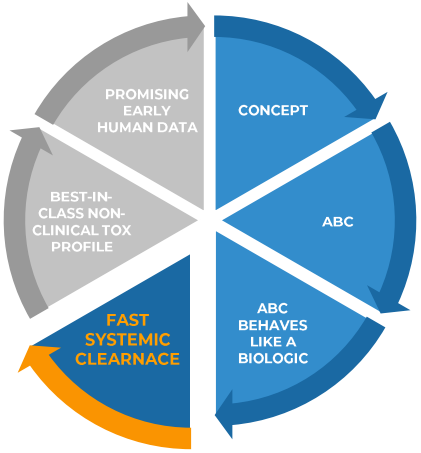
ABC is formulated in an optically clear, aqueous solution.

ABC is administered via intravitreal injection (IVT) like other anti-VEGF biologics.



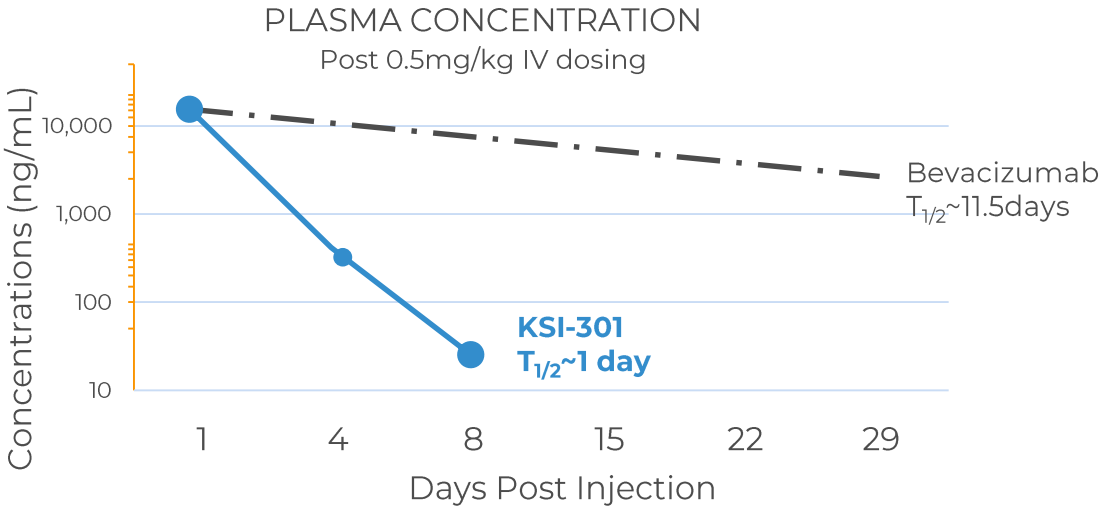


Ranibizumab profile was adapted from Gaudreault et al, Invest Ophthalmol Vis Sci. 2005 46(2):726-33
KSI-301 profile was adjusted from 725µg/eye dose to 500µg/eye dose to match that of ranibizumab

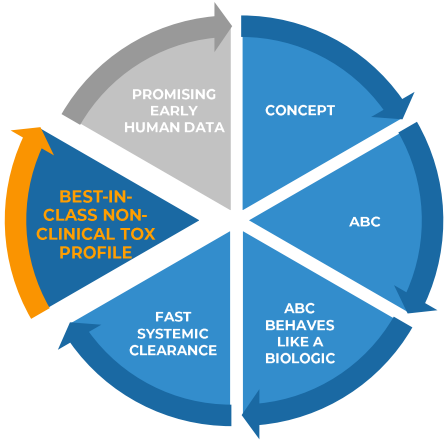


FAST SYSTEMIC CLEARANCE

Despite its large size (MW), ABC has fast systemic clearance



Yeung et al 2010 cancer research



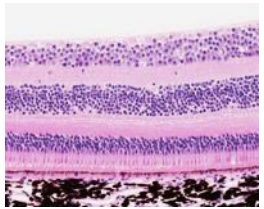
BEST-IN-CLASS NON-CLINICAL TOX PROFILE

Unlike predicate marketed anti-VEGF agents, the starting human dose in KSI-301 clinical trials was not limited by non-clinical toxicology findings.

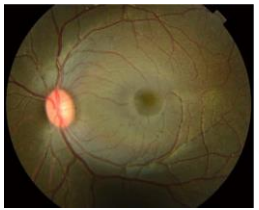
Repeat-dose GLP toxicology studies with 4-week dosing intervals in monkeys demonstrated KSI-301 was well tolerated up to the highest doses tested after ocular (intravitreal, 5 mg/eye, up to 7 doses) and systemic (intravenous, up to 5 mg/kg, 3 doses) administration.

No significant KSI-301 treatment related changes were reported in all studies.

Hematology

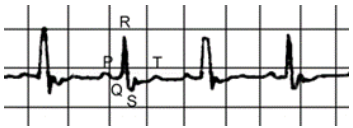


Ocular and systemic histology

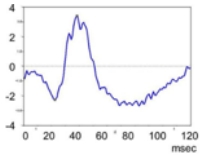


Fundus imaging

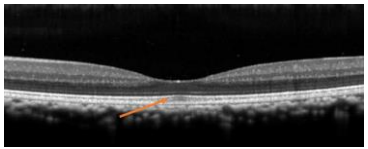
IOP



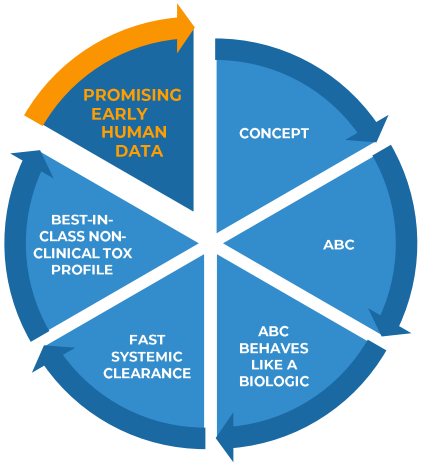
ECG



ERG

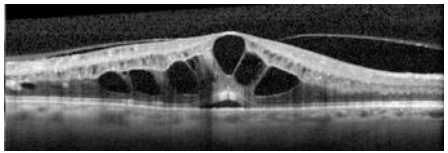


OCT imaging

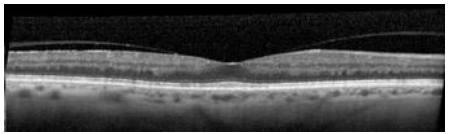


PROMISING EARLY HUMAN DATA

- 300+ doses -
- No inflammation -
- 9+ months ; multiple injections -
- No drug related adverse events -
- Fast onset, durable effect -

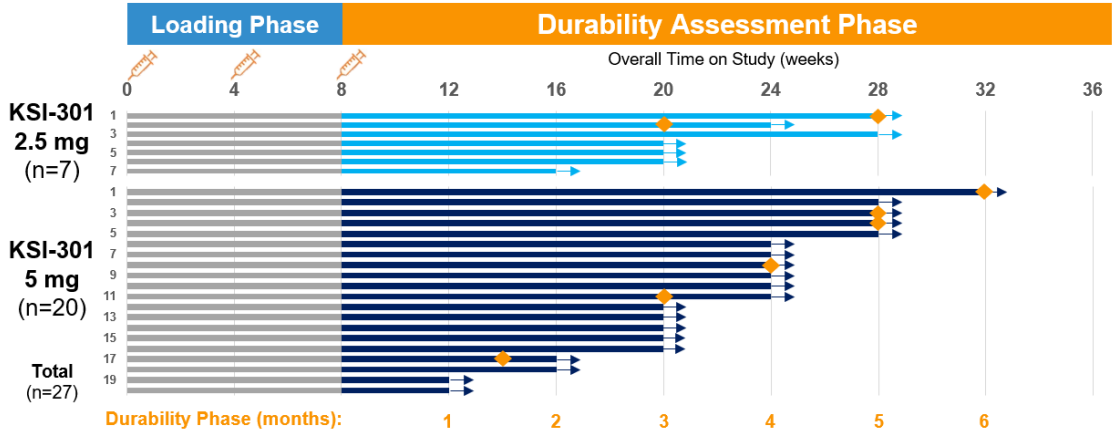


KSI-301 (5 mg)



KSI-301 in wAMD: Durability Assessment

Emerging data support 3 to 5+ month durability



◆ Retreatment with KSI-301

→ Continuing follow-up

Interim data. Includes patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019. Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

JASON EHRLICH, M.D., PH.D.

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CMO & CDO

THE NEXT FIRST-LINE ANTI-VEGF

We are developing KSI-301 to have a meaningfully differentiated profile in the 4 major retinal vascular disease

Wet AMD

CURRENT BEST

Aflibercept
once every 2 months[1]
after 3 monthly loading doses

Brolucizumab
once every 2 – 3 months[2]
after 3 monthly loading doses

—

KODIAK PIVOTAL STUDY DESIGN

KSI-301
once every 3, 4 or 5 months
after 3 monthly loading doses

Diabetic Macular Edema

CURRENT BEST

Aflibercept
once every 2 months[1]
after 5 monthly doses

—

KODIAK VISION FOR KSI-301

KSI-301
once every 3, 4, 5 or 6 months
after 3 monthly loading doses

Retinal Vein Occlusion

CURRENT BEST

Aflibercept
once every month[1]
after 3 monthly loading doses

—

KODIAK VISION FOR KSI-301

KSI-301
once every 2 months or longer
after 2 monthly loading doses

Non-Proliferative Diabetic Retinopathy

CURRENT BEST

Aflibercept
once every 2 months[1]
after 5 monthly doses

—

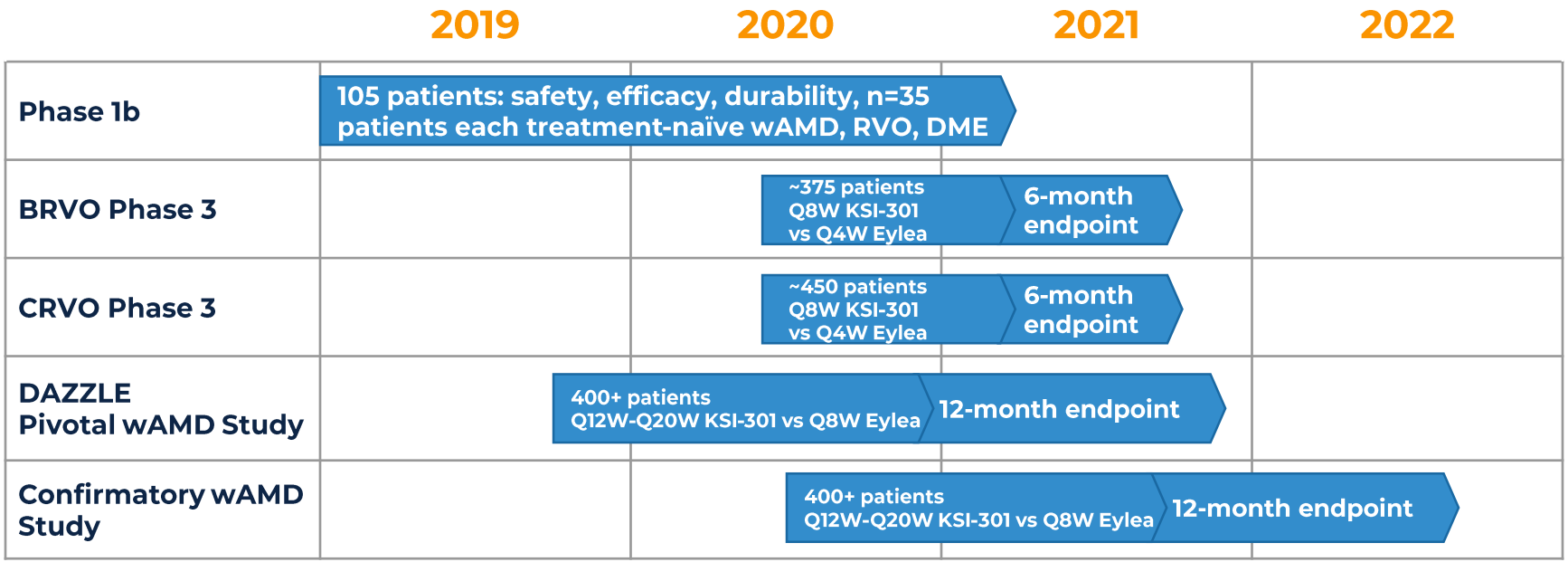
KODIAK VISION FOR KSI-301

KSI-301
once every 3, 4 or 6 months
no loading doses

Each has different treatment needs

1. Source: Aflibercept US Prescribing Information as of August 2019
2. Source: Brolucizumab US Prescribing Information as of October 2019

2022 Vision: Clinical/Regulatory Timeline



CHARLES WYKOFF, M.D., PH.D.

Director of Research
Retina Consultants of Houston

Extended Durability in Exudative Retinal Diseases Using the Novel Intravitreal Anti-VEGF Antibody Biopolymer Conjugate KSI-301

First-time Results from a Phase 1b Study in Patients with wAMD, DME and RVO

Charles C. Wykoff, MD, PhD
Retina Consultants of Houston
Houston, TX

AAO Annual Meeting – Retina Subspecialty Day
October 11, 2019

Disclosures

- **Financial:**

  Adverum (C, R); Aerpio (C, R); Alimera Sciences (C); Allegro (C); Allergan (C, R); Apellis (C, R); Bayer (C); Clearside Biomedical (C, R); Chengdu Kanghong (R); DORC (C); EyePoint (C); Fosun (C); Genentech/Roche (C, R); Iveric Bio (formerly Ophthotech) (C, R); Kodiak Sciences (C, R); Neurotech (R), Novartis (C, R); ONL Therapeutics (C); Opthea (R); PolyPhotonix (C); Recens Medical (C, R); Regeneron (C, R, S); Regenxbio (C, R); Samsung (R), Santen (C, R), Takeda (C).

- **Study Disclosures:**

  This study includes research conducted on human subjects. Institutional Review Board (IRB) approval was obtained prior to study initiation.

Investigational Treatments for Exudative Retinal Diseases
aimed at improving efficacy & durability

Aflibercept

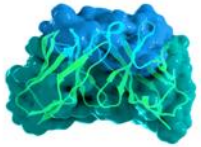
Bevacizumab

Ranibizumab

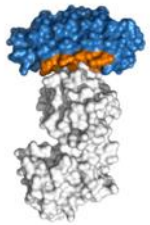
Dexamethasone

Triamcinolone

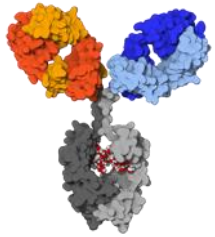
Fluocinolone acetonide



Brolucizumab

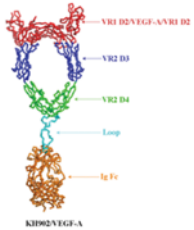


Abicipar

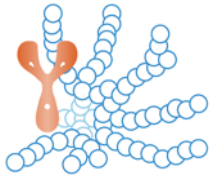


Faricimab

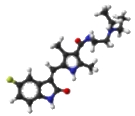
PDS



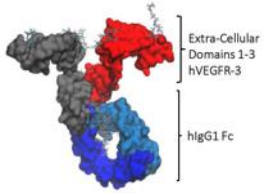
Conbercept



KSI-301



Sunitinib



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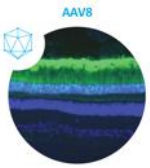
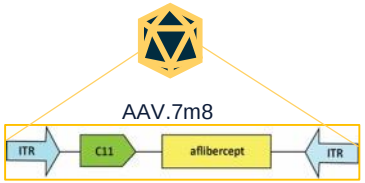


RGX-314

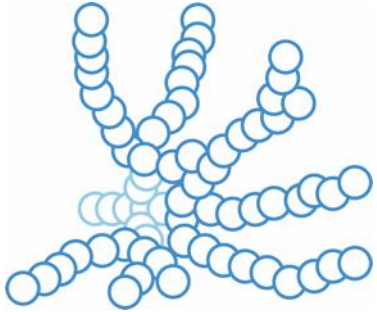


ADVM-022

Antibody Biopolymer Conjugates (ABC)

biologics engineered for increased durability and efficacy

Single
Site-Specific
+
Stable
(Covalent)
Linkage



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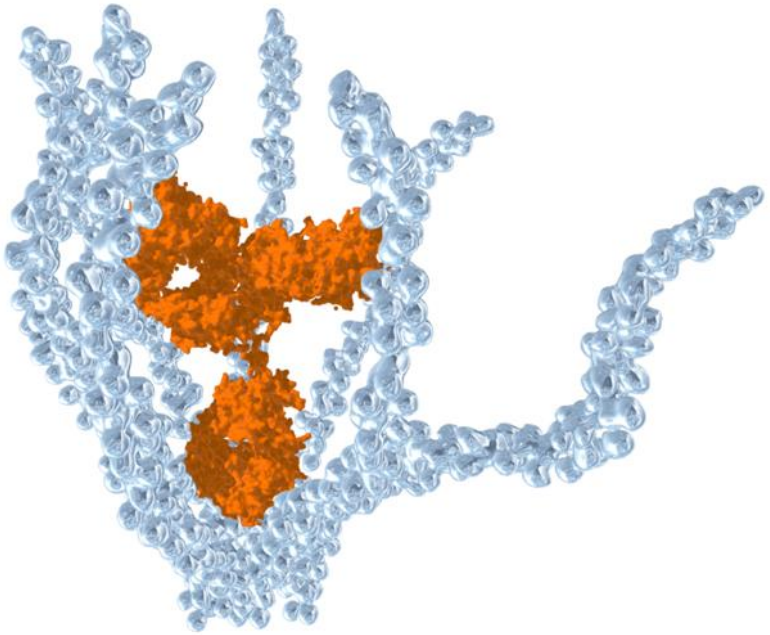


ANTIBODY

IgG1 Antibody
Inert Immune
Effector Function

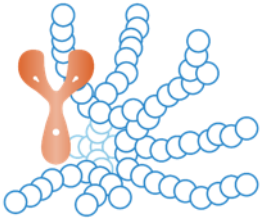
BIOPOLYMER

Branched
High Molecular Weight
Optically Clear
Phosphorylcholine Polymer

ANTIBODY BIOPOLYMER CONJUGATE
KSI-301 is an intravitreally injected anti-VEGF ABC

Go Bigger to Last Longer

KSI-301: ABC designed to block all VEGF-A Isoforms

	Brolucizumab	Ranibizumab	Bevacizumab	Aflibercept	KSI-301
Molecule type	Single-chain antibody fragment	Antibody fragment	Antibody	Recombinant fusion protein	**Antibody Biopolymer Conjugate (ABC)**
Molecular structure					
Molecular weight	26 kDa	48 kDa	149 kDa	115 kDa	**950 kDa**
Clinical dose	6 mg	0.3-0.5 mg	1.25 mg	2 mg	**5 mg** (by weight of antibody)
Equivalent molar dose	11	0.5	0.9	1	**3.5**
Equivalent ocular PK	< 0.7	0.7	1	1	**3**
Equivalent ocular concentration at 3 months	< 0.1	0.001	NA[1]	1	**1,000**

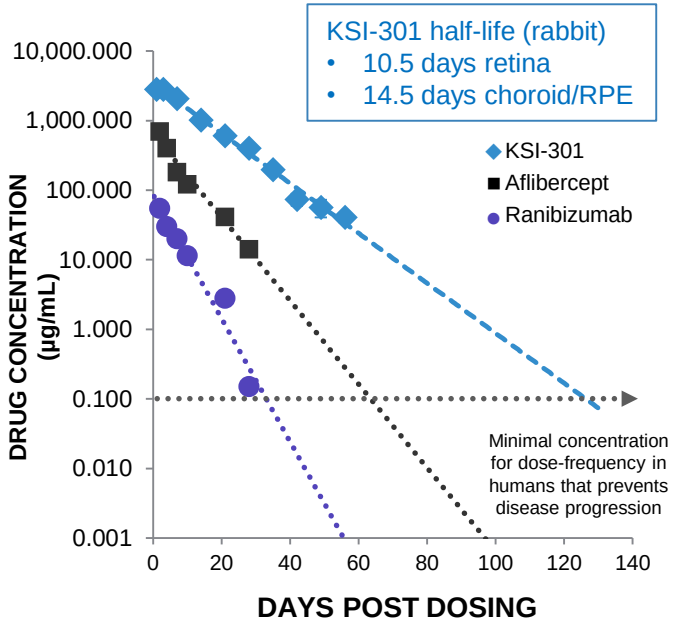
Equivalent values are shown as (approximate) fold difference relative to aflibercept. kDa= kilodalton

1. Lower affinity of bevacizumab precludes a useful comparison

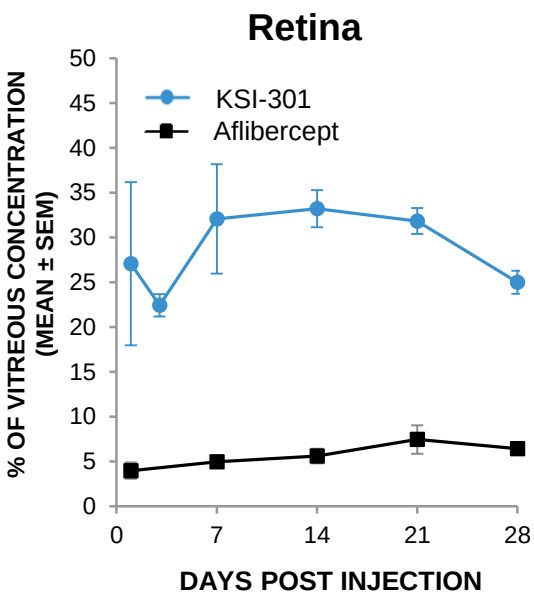
KSI-301 Properties: Preclinical Data

Special features from the ultra-hydrophilic phosphorylcholine biopolymer

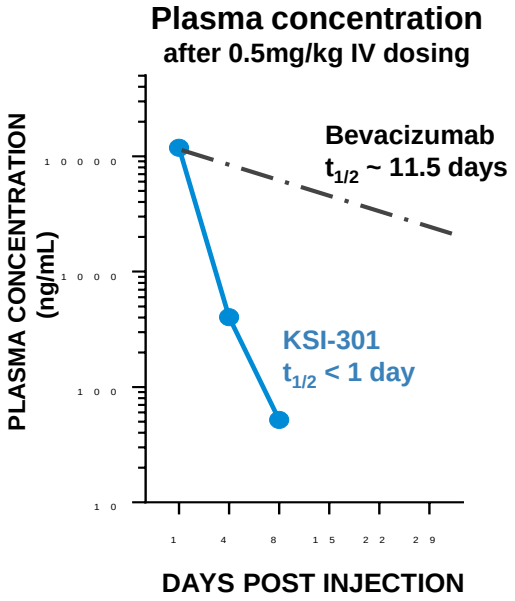
Remarkable Intraocular Durability[1]



Excellent Retinal Bioavailability[2]



Fast Systemic Clearance[3]



1. Data from rabbit model. Ranibizumab data: Gaudrealt et al (2007) IOVS 46(2) 726 Gaudrealt et al (2007) Retina 27(9) 1260 Bakri et al (2007) Ophthalmol 114(12) 2179 || Aflibercept data: EVER Congress Portoroz Slovenia (2008) Struble (Covance) Koehler-Stec (Regeneron). Aflibercept data adjusted arithmetically to reflect 2,000µg dose administered (based on rabbit in vivo dosing of 500 µg) || KSI-301 data on file, adjusted arithmetically to reflect 5,000 µg dose administered (based on rabbit in vivo dosing of 725 µg). Error bars reflects standard error of the mean
2. Covance rabbit ADME (absorption, distribution, metabolism, elimination) model: Aflibercept data (2008): EVER Congress Portoroz Slovenia Struble (Covance), Koehler-Stec (Regeneron). KSI-301 data (2017): Covance study, data on file. Error bars reflects standard error of the mean
3. KSI-301 data: Non-human primate toxicology study, data on file; Bevacizumab data: Yeung et al 2010 Cancer Research.

KSI-301

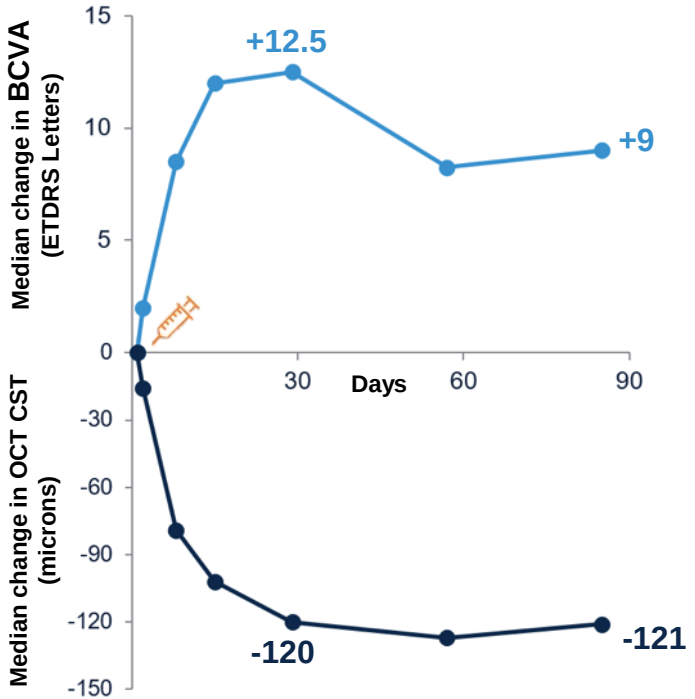
Clinical Data

113 patients dosed to date

KSI-301 Phase 1a

well-tolerated with rapid anatomic & visual response

- Diabetic macular edema (DME) patients with severe disease (n=9)
- Incompletely responsive to previous anti-VEGF treatment (8/9 previously treated) (median 3, range 0-7 in the year prior)
- A single injection of KSI-301 resulted in rapid, high-magnitude responses durable to 12 weeks
  - n=3 patients per dose level (1.25mg, 2.5mg, 5mg)
- No intraocular inflammation and no drug-related adverse events



Median changes from baseline to week 12 pooled across 3 dose groups (n=9 patients total)

Do DV, Angiogenesis 2019; Patel et al., ARVO 2019

KSI-301 Phase 1b

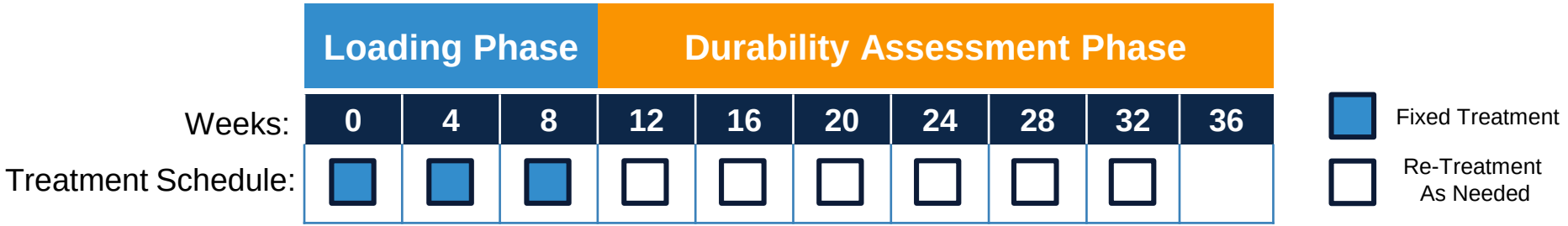
insight into durability among treatment naïve subjects

Randomized, open label study to evaluate multidose safety, efficacy & durability (n=105)

wAMD (n=35) | **DME** (n=35) | **RVO** (n=35)

Randomized 1:3

KSI-301 2.5 mg (50 μL) | KSI-301 5 mg (100 μL)



wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion;
Clinicaltrials.gov ID: NCT03790852

KSI-301 Phase 1b Retreatment Criteria
prespecified by disease state

- **wAMD**
  - Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12, *OR*
  - Decrease in BCVA of > 5 letters compared to Day 1, due to worsening wAMD activity, *OR*
  - Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening wAMD activity
- **DME and RVO**
  - Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12 or the prior visit, *OR*
  - Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening DME/RVO disease activity

For all subjects, investigators can retreat at their discretion if significant disease activity is present that does not meet the above criteria

wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion; CST = central subfield retinal thickness; BCVA = best corrected visual acuity.
Clinicaltrials.gov ID: NCT03790852

KSI-301 Phase 1b Baseline Characteristics

Variable	wAMD Cohort (n=35)	DME Cohort (n=34)	RVO Cohort (n=35)
Age, mean (SD), years	77.2 (11.0)	60.7 (10.4)	63.6 (12.6)
Gender, n (%), female	25 (71.4)	13 (38.2)	13 (37.1)
Race, n (%), White	32 (91.4)	28 (82.4)	31 (88.6)
BCVA, mean (SD), ETDRS letters	64.5 (11.1)	66.8 (10.3)	54.9 (15.4)
BCVA, Snellen 20/40 or better, n (%)	14 (40.0)	16 (47.1)	6 (17.1)
OCT CST, mean (SD), microns	426 (176)	449 (109)	675 (237)

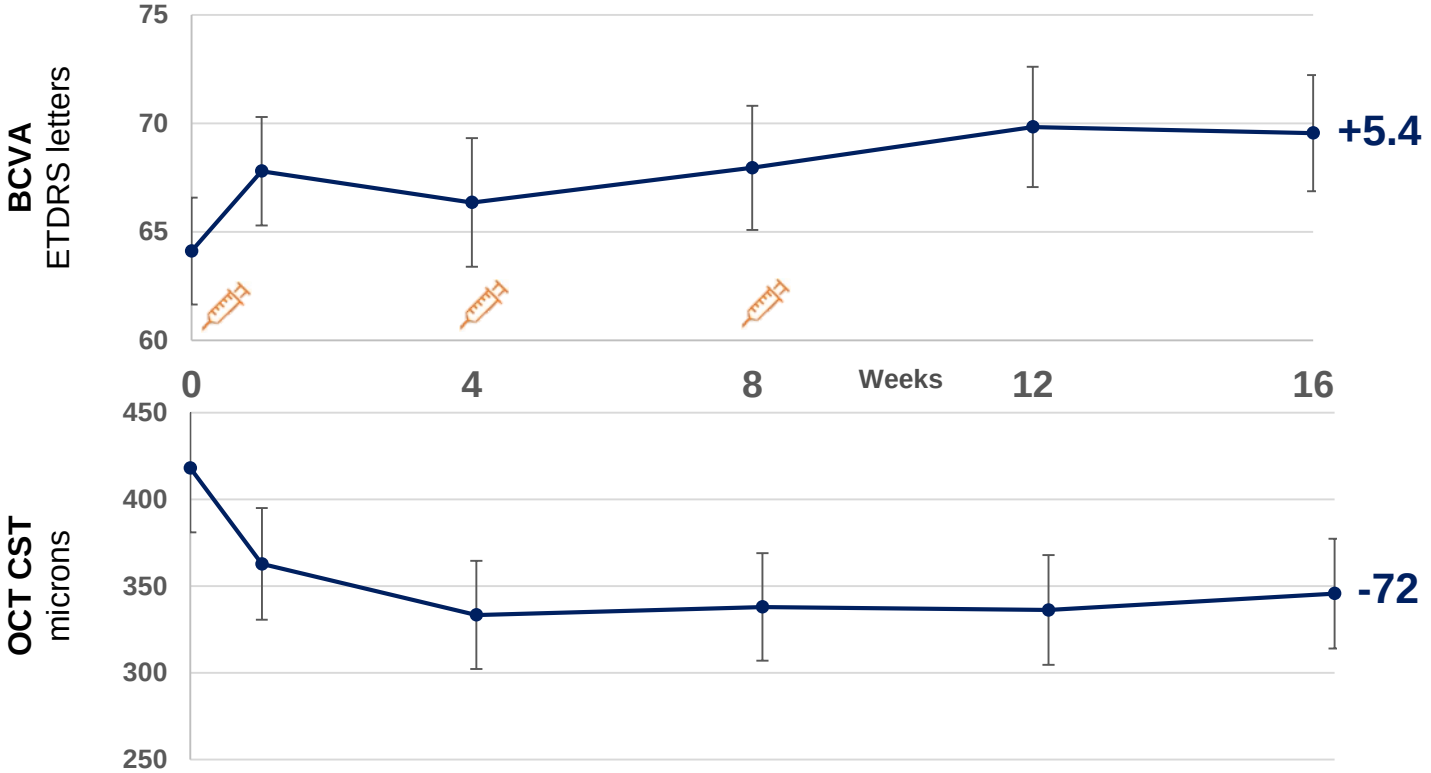
Includes all patients randomized as of 10 October 2019. SD= standard deviation; BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

KSI-301 Phase 1b

First Time Results

Efficacy of KSI-301 in Wet AMD

change from baseline to week 16 in mean BCVA & OCT

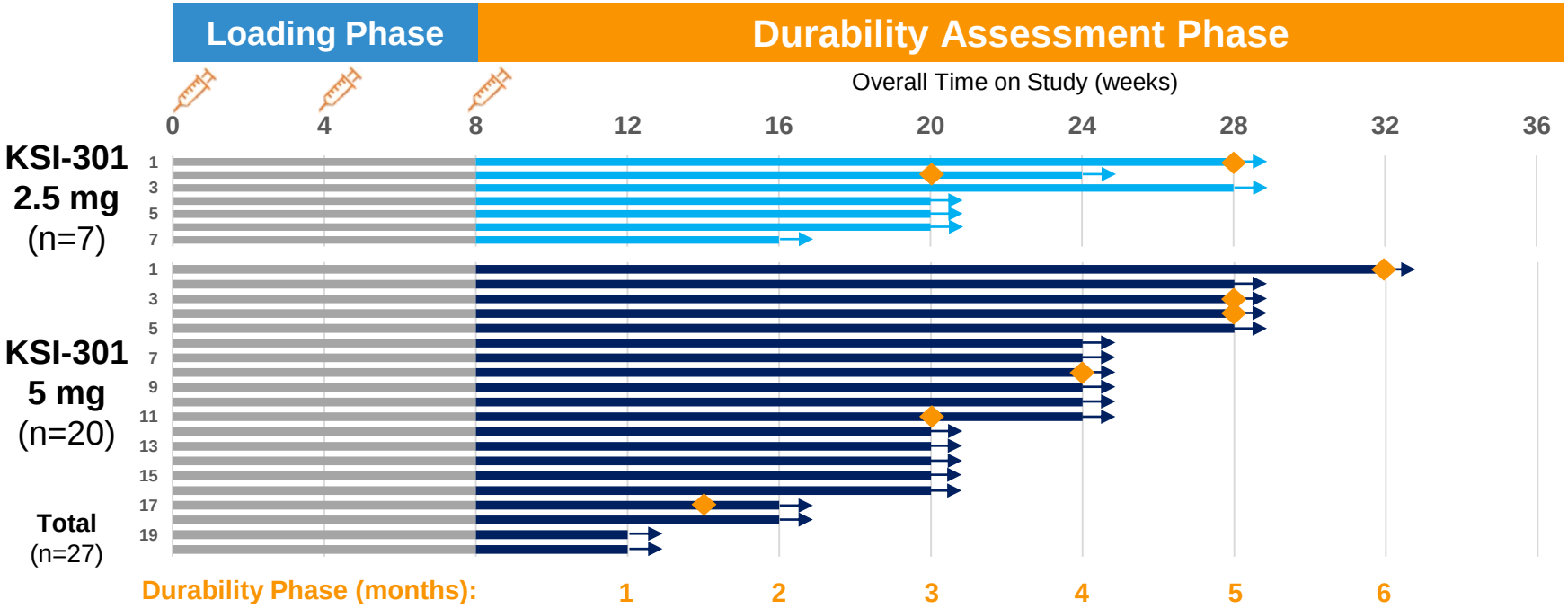


Interim data. Includes only randomized patients that reached Week 16 visit by the data cutoff date of 10 Oct 2019; 2.5 & 5 mg doses pooled. Error bars represent standard error of the mean. OCT CST values are site reported.
BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

n= 25 **Patients reaching Week 16 visit by data cutoff**

KSI-301 in wAMD: Durability Assessment

Emerging data support 3 to 5+ month durability



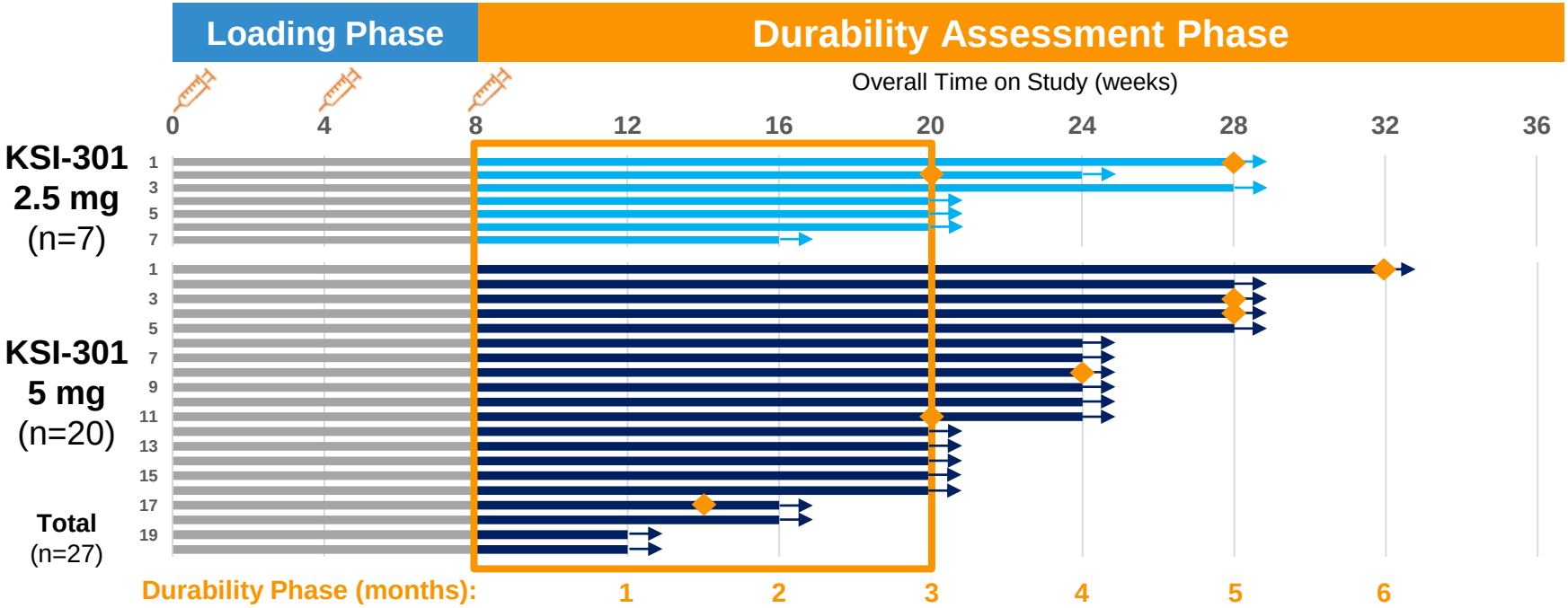
◆ Retreatment with KSI-301

→ Continuing follow-up

Interim data. Includes patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

KSI-301 in wAMD: Durability Assessment

Emerging data support 3 to 5+ month durability



◆ Retreatment with KSI-301

→ Continuing follow-up

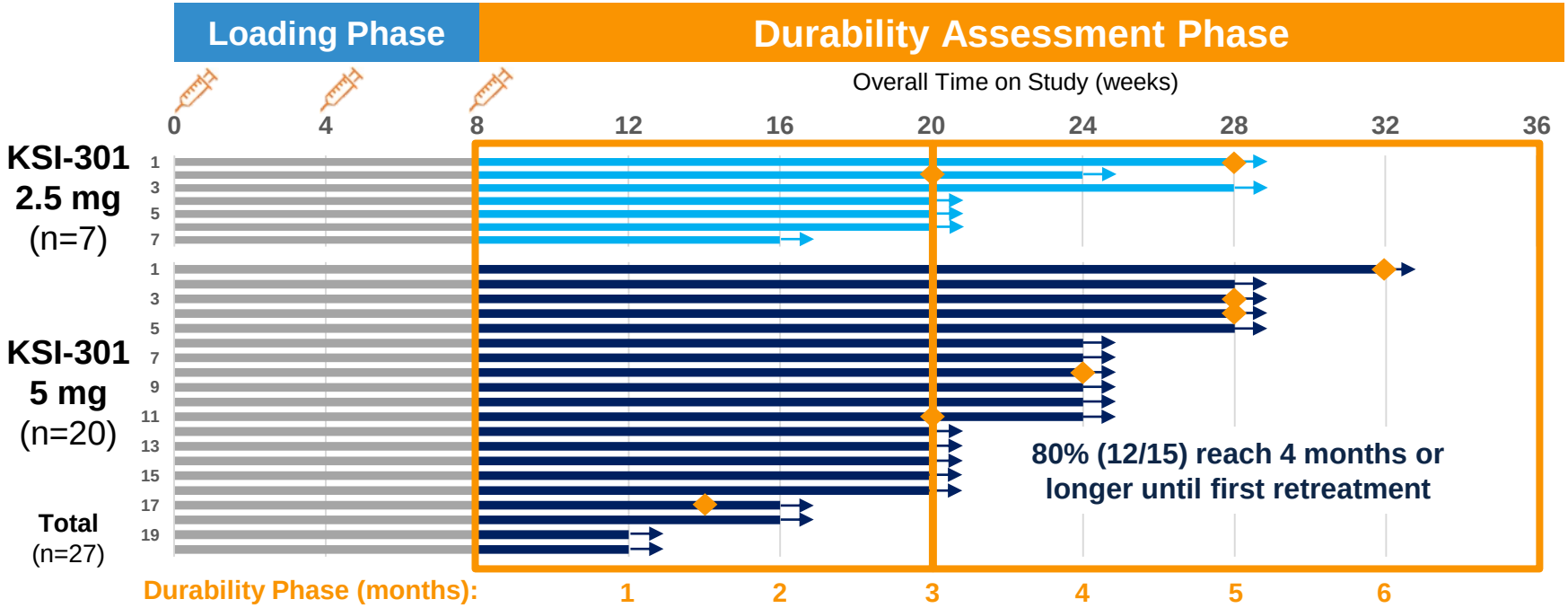
4% (1/25) retreated before 3 months

10% (2/20) retreated at 3 months

Interim data. Includes patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

KSI-301 in wAMD: Durability Assessment

Emerging data support 3 to 5+ month durability



Retreatment with KSI-301

Continuing follow-up

4% (1/25) retreated before 3 months

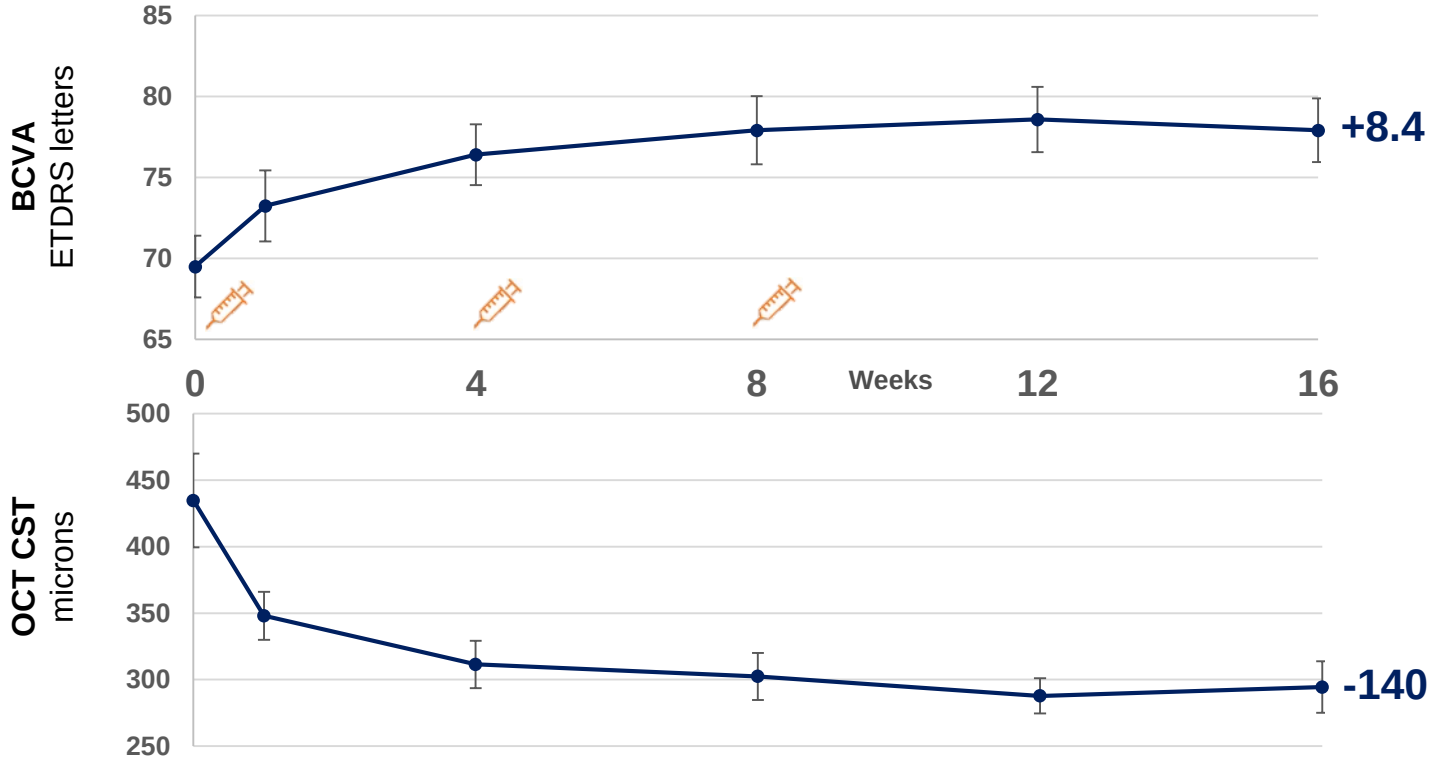
10% (2/20) retreated at 3 months

87% (20/23) have gone longer than 3 months after the last loading dose

Interim data. Includes patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

Efficacy of KSI-301 in DME

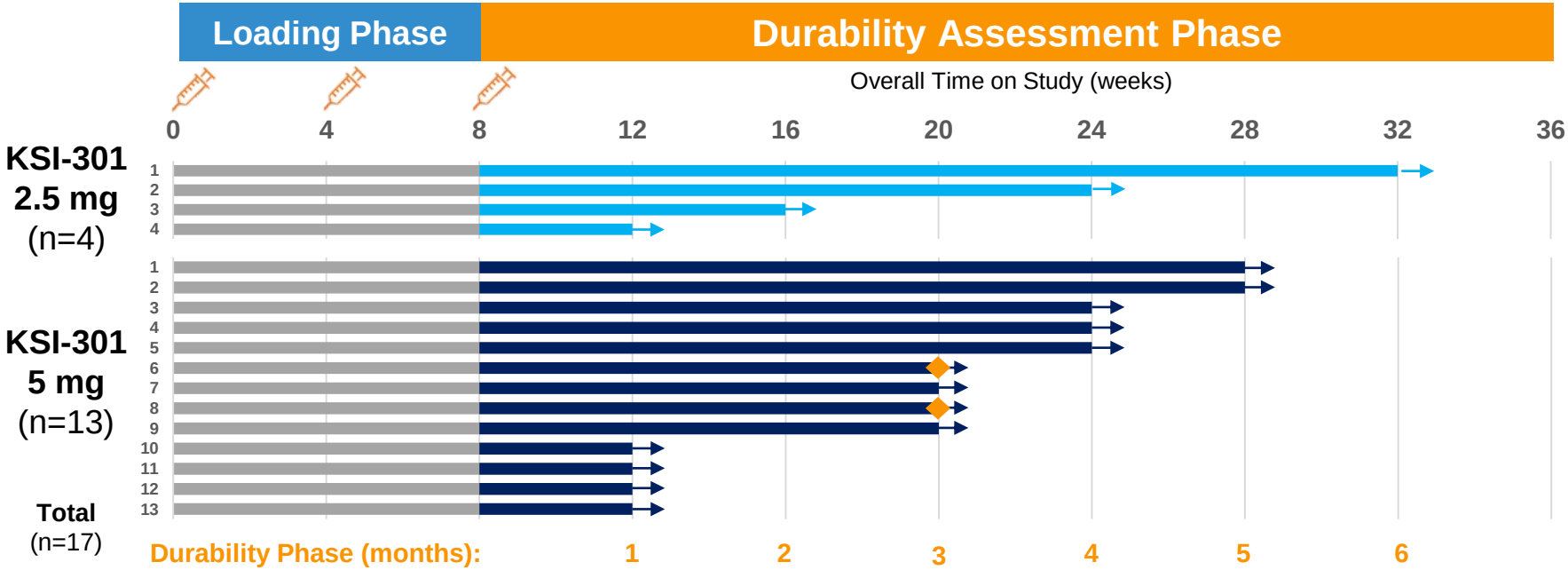
change from baseline to week 16 in mean BCVA & OCT



Interim data. Includes only randomized patients that reached Week 16 visit by the data cutoff date of 10 Oct 2019; 2.5 & 5 mg doses pooled. Error bars represent standard error of the mean. OCT CST values are site reported.
BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

n= 12 **Patients reaching Week 16 visit by data cutoff**

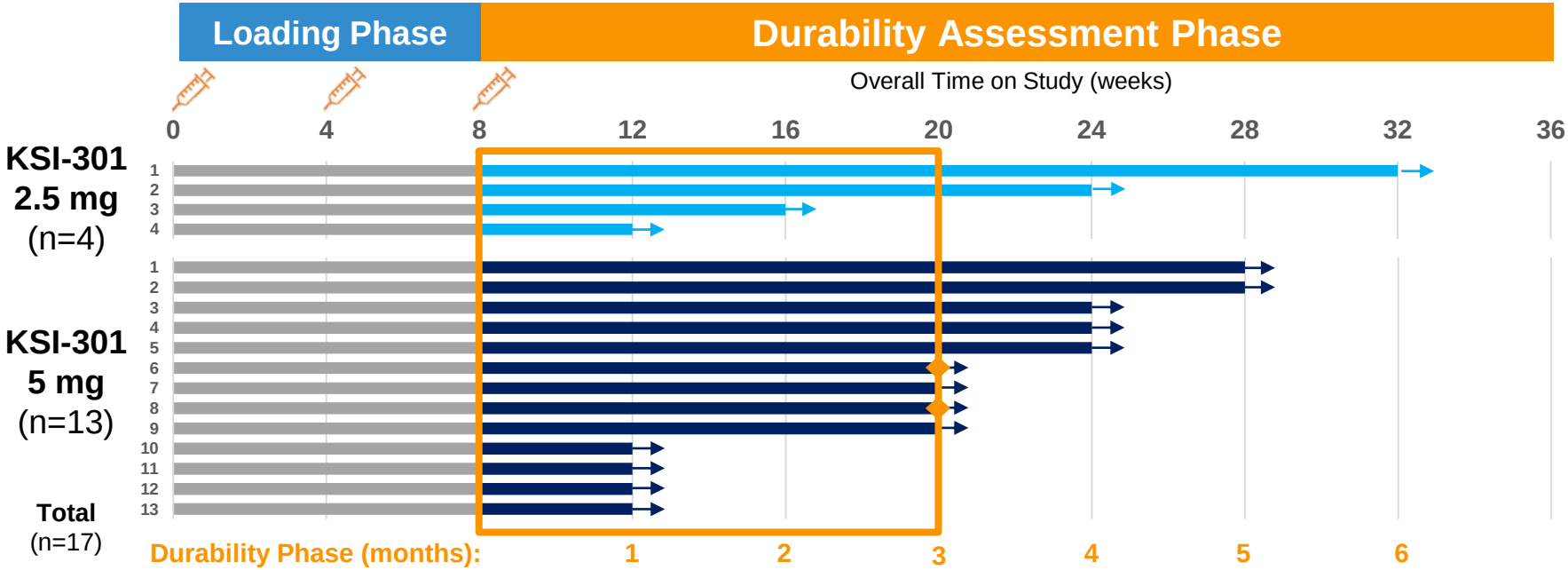
KSI-301 in DME: *3 loading doses can provide sustained disease control of 3 months or longer*



◆ Retreatment with KSI-301
→ Continuing follow-up

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

KSI-301 in DME: *3 loading doses can provide sustained disease control of 3 months or longer*



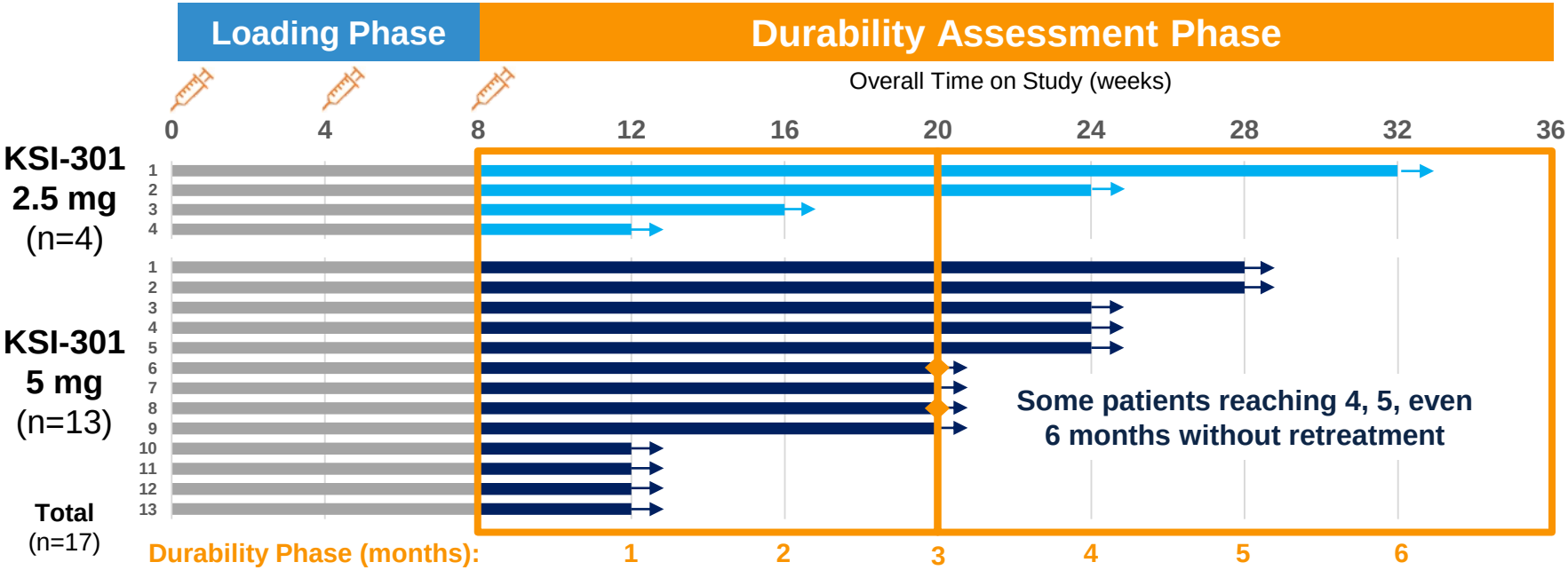
No patient has been retreated yet before 3 months

18% (2/11) retreated at 3 months

◆ Retreatment with KSI-301
→ Continuing follow-up

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

KSI-301 in DME: *3 loading doses can provide sustained disease control of 3 months or longer*



No patient has been retreated yet before 3 months

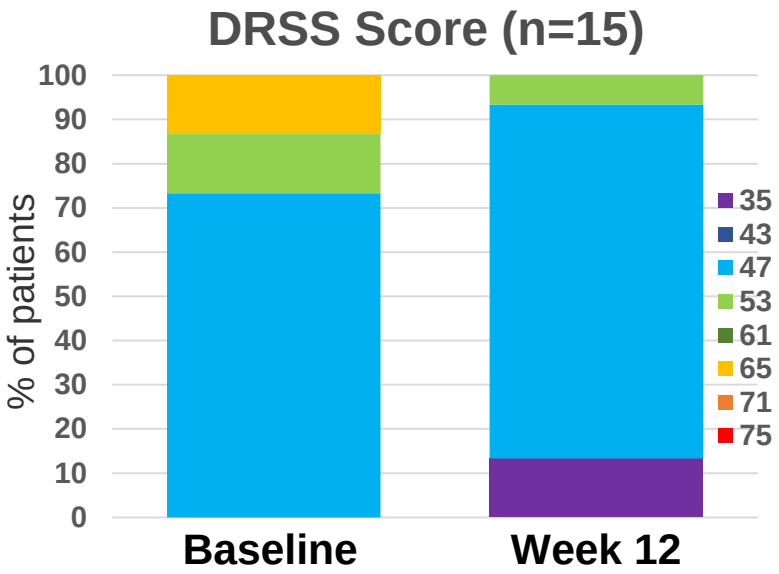
18% (2/11) retreated at 3 months

82% (9/11) have gone longer than 3 months after the last loading dose

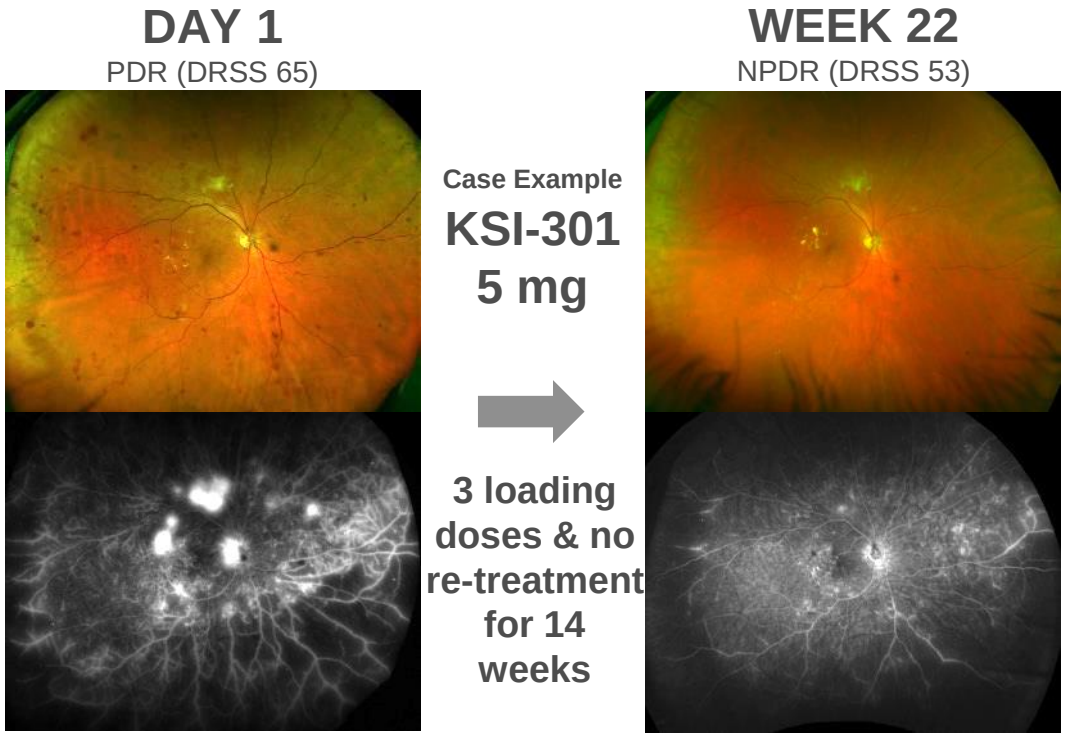
◆ Retreatment with KSI-301
→ Continuing follow-up

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

KSI-301 in DR: *signs of disease modification seen within 12 weeks*



- **All patients have improved (40%) or maintained (60%) DR severity level**
- **No patient developed a PDR event**

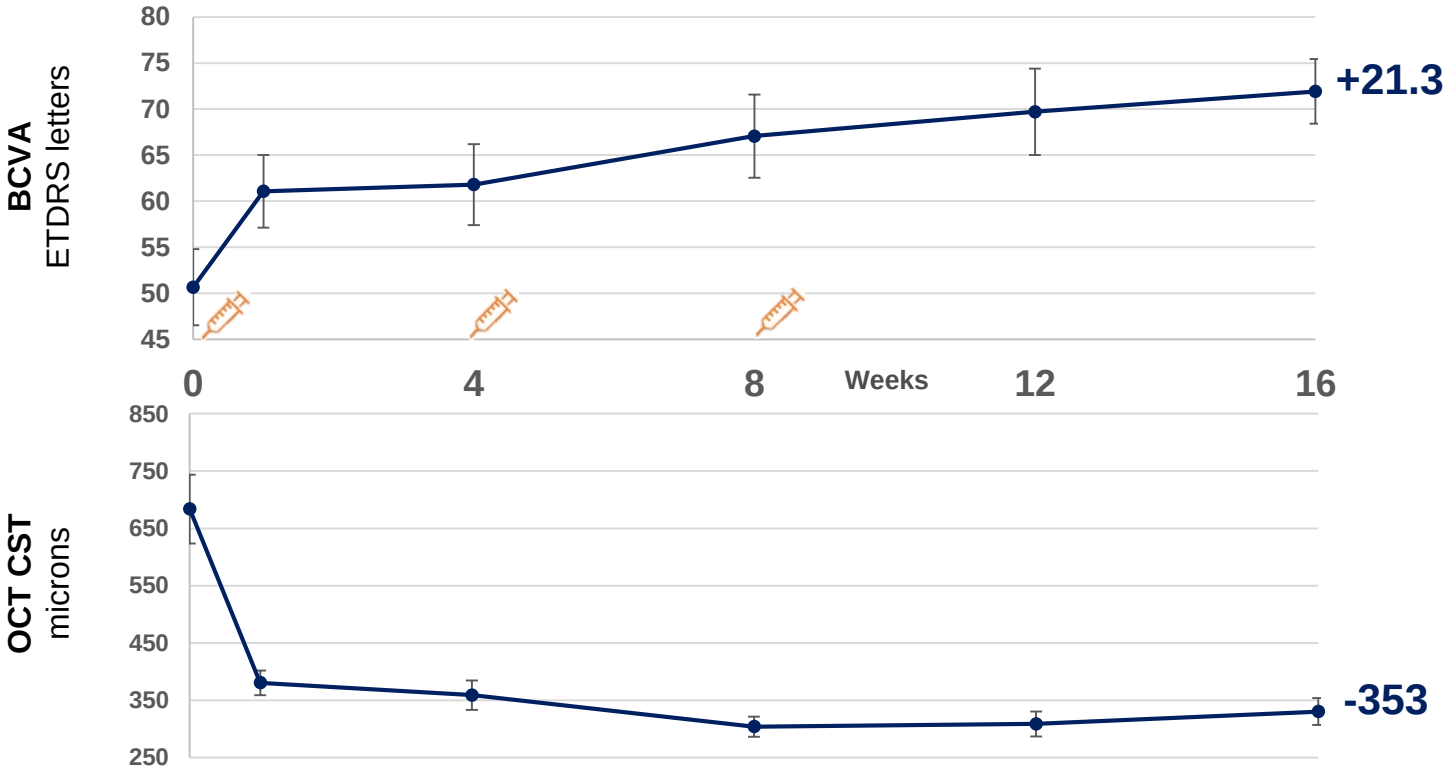


Meaningful DRSS score improvement (PDR to NPDR; 2-steps) sustained 14 weeks after last loading dose

Includes only randomized patients that reached Week 12 and have gradable color fundus photos by the data cutoff date of 10 Oct 2019 DR= Diabetic Retinopathy; PDR= Proliferative DR; NPDR= Non-Proliferative DR; DRSS = DR Severity Scale; DRSS 53 = Severe NPDR; DRSS 65 = Moderate PDR; need for panretinal photocoagulation or vitrectomy

Efficacy of KSI-301 in RVO

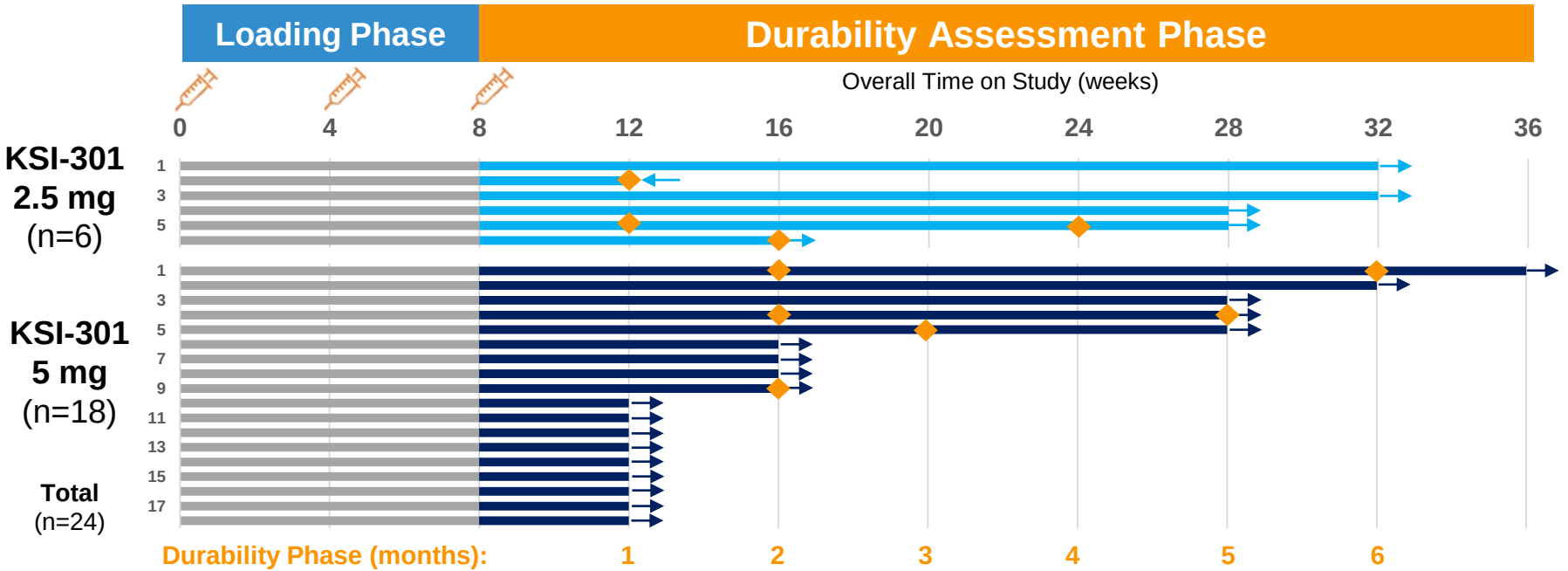
change from baseline to week 16 in mean BCVA & OCT



Interim data. Includes only randomized patients that reached Week 16 visit by the data cutoff date of 10 Oct 2019; 2.5 & 5 mg doses pooled. Datapoints include one subject that discontinued after Week 12. Error bars represent standard error of the mean. OCT CST values are site reported. BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

n= 15 **Patients reaching Week 16 visit by data cutoff**

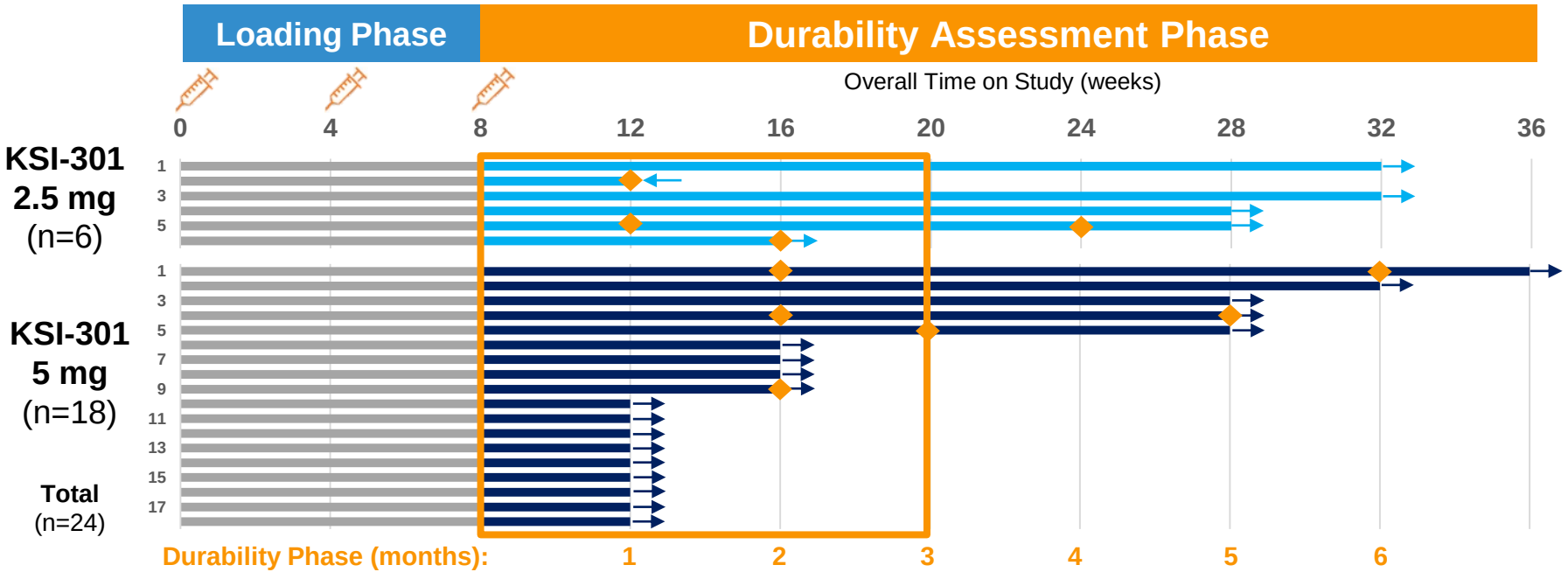
KSI-301 in RVO: *emerging durability data show potential for 2 to 3 month or longer dosing*



Retreatment
Continuing follow-up
Discontinuation

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019. Each bar represents an individual patient.

KSI-301 in RVO: *emerging durability data show potential for 2 to 3 month or longer dosing*

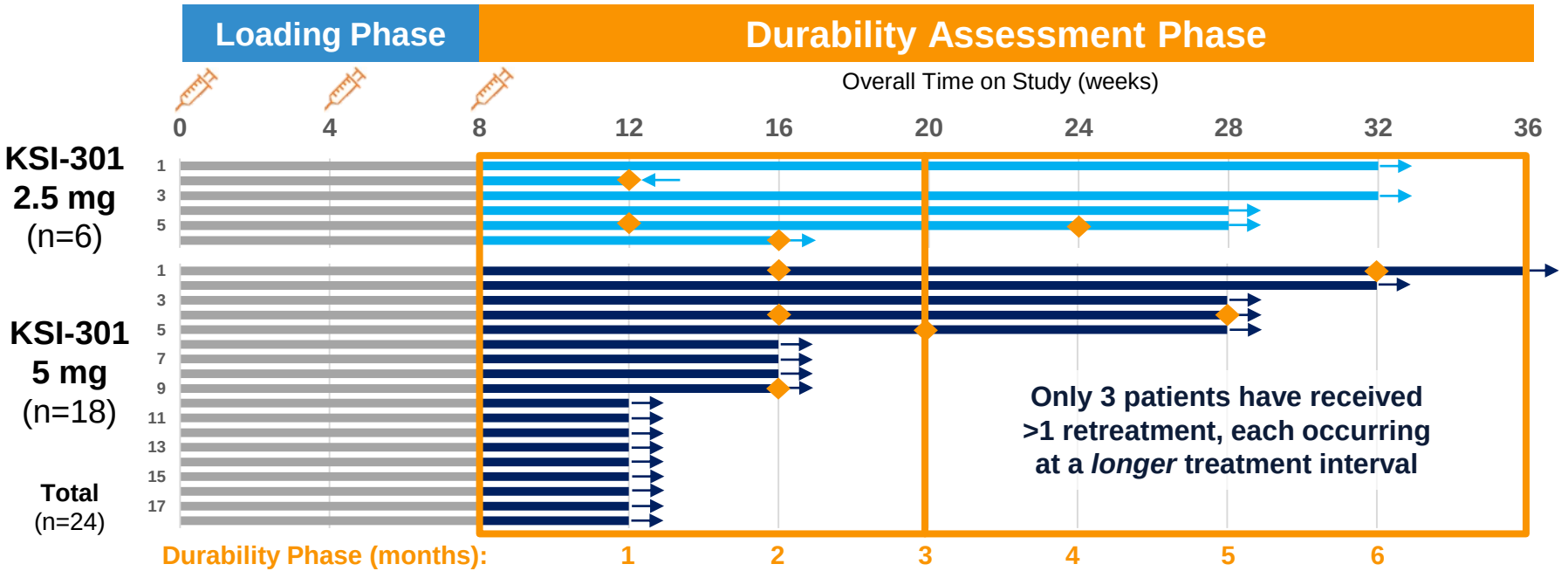


8% (2/24), 28% (4/14) & 11% (1/9) received first retreatment at 1, 2 & 3 months respectively

Retreatment
Continuing follow-up
Discontinuation

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019. Each bar represents an individual patient.

KSI-301 in RVO: *emerging durability data show potential for 2 to 3 month or longer dosing*



8% (2/24), 28% (4/14) & 11% (1/9) received first retreatment at 1, 2 & 3 months respectively

56% (5/9) have gone longer than 3 months after the last loading dose

◆ Retreatment
→ Continuing follow-up
← Discontinuation

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019. Each bar represents an individual patient.

Safety of KSI-301: *multiple-dose exposure is well-tolerated with no intraocular inflammation*

113
Subjects dosed in Phase 1a+1b

316
Total doses given in Phase 1a+1b

104
At Day 1

99
At Week 4

86
At Week 8

Phase 1b subjects with # of loading doses received

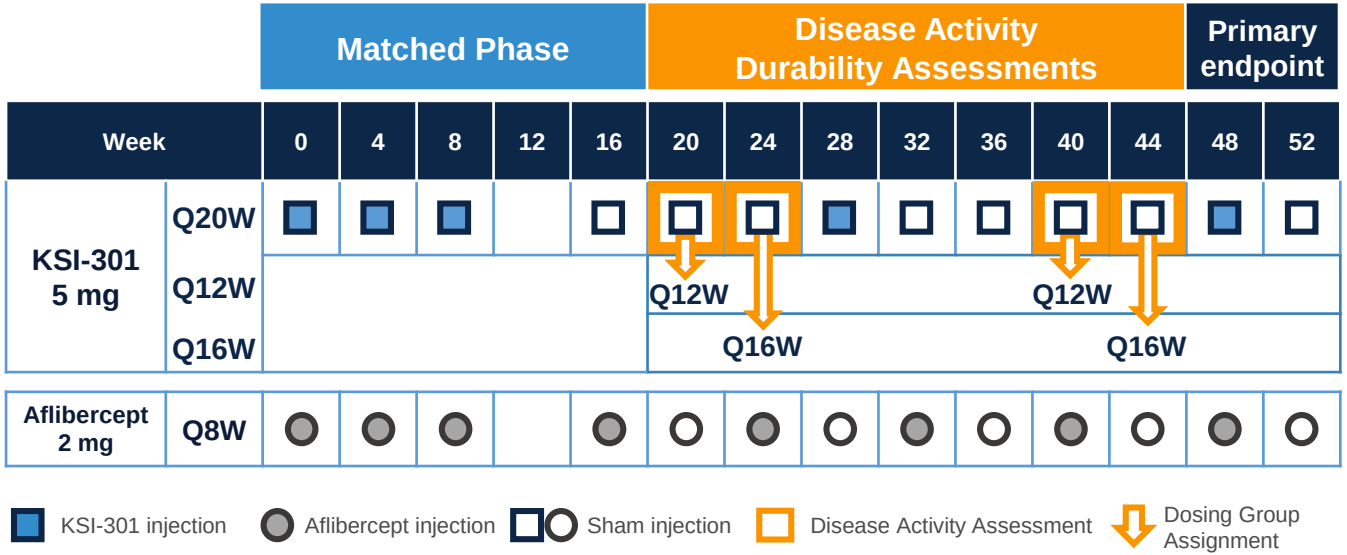
- No intraocular inflammation or ocular SAEs in the study eye reported to date
- No drug-related AEs or drug-related SAEs reported to date
- Most AEs were assessed as mild and are consistent with profile of intravitreal anti-VEGFs
- 8 non-ocular SAEs that were not drug-related have been reported in 4 subjects:
  - One 92 y/o RVO subject with hospitalization related to a pre-existing condition that resulted in death
  - One 66 y/o RVO subject with hospitalization related to dizziness
  - One 43 y/o DME subject with hospitalization related to a pre-existing condition
  - One 56 y/o DME subject with hospitalization related to a pre-existing condition

Includes all patients randomized as of 10 Oct 2019, all doses administered across cohorts
Interim safety data as of 10 Oct 2019; AE: adverse event; SAE: serious adverse event

Now Recruiting: Pivotal Phase 2 DAZZLE Study

Dosing with KSI-301 in wet AMD as infrequently as every 20 weeks

- ~400 treatment naïve wAMD patients
- Randomized study vs aflibercept
- US & EU study sites
- KSI-301 dosing: every 12, 16, or 20 weeks depending on pre-specified disease activity assessments*



*After the loading phase
Clinicaltrials.gov ID NCT04049266

Conclusion: KSI-301 is Demonstrating Promising Safety, Efficacy and Durability

- Antibody Biopolymer Conjugates (ABCs) are a new design platform for long durability intravitreal medicines
- KSI-301 (anti-VEGF ABC) has achieved important development milestones
  - **Excellent Safety:** zero cases of intraocular inflammation after 300+ doses
  - **Strong Efficacy:** across 3 major phenotypically variable retinal diseases wet AMD, DME/DR & RVO
  - **Remarkable Biological Durability:** majority of treated eyes extended to 4 months or beyond without retreatment after 3 loading doses. Potential is being demonstrated for:
    - 3 to 5+ month interval in wAMD
    - 3 to 5+ month interval in DME
    - 2 to 3+ month interval in RVO
- Next steps
  - Phase 1b study has been extended to 18 months to collect additional durability outcomes
  - Pivotal ‘DAZZLE’ study of KSI-301 vs aflibercept in treatment-naïve wet AMD now recruiting

Acknowledgements

Principal Investigators

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- Bryce Miller, MPA
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- Jason Ehrlich, MD, PhD
- Victor Perlroth, MD

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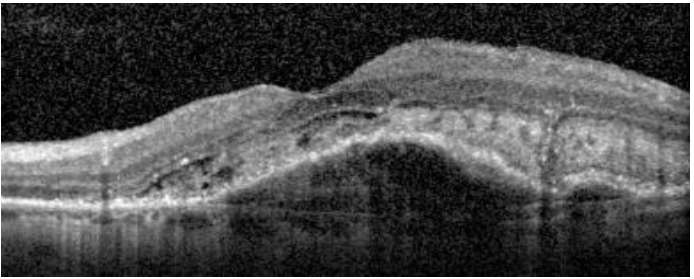
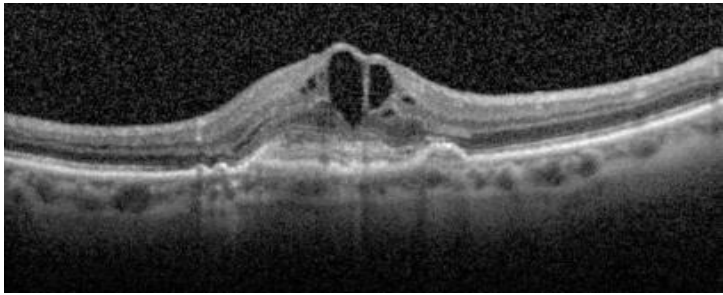
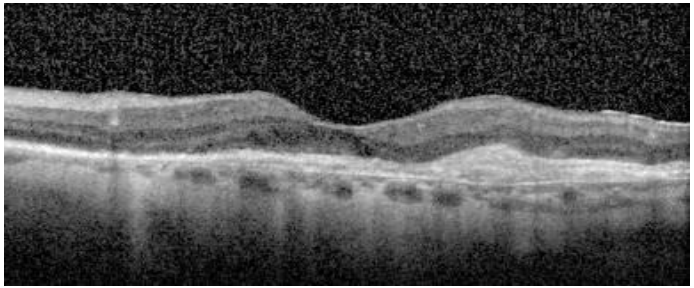
Chief, Retina Service
Wills Eye Hospital

Current Neovascular AMD Treatment
Intravitreal VEGF Inhibition

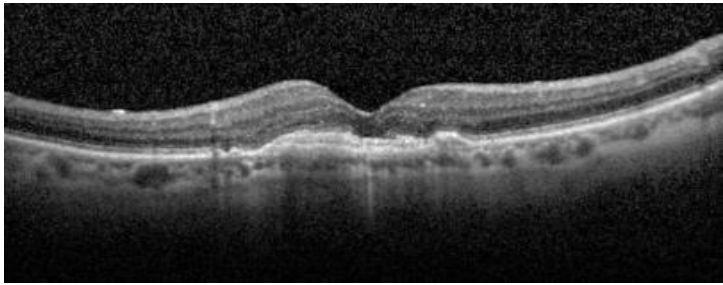


Before
anti-VEGF





After
anti-VEGF



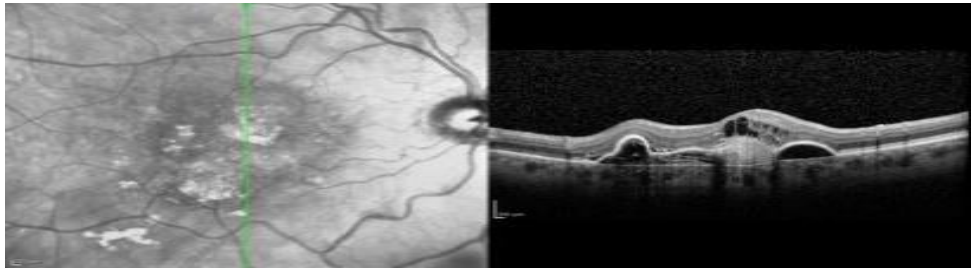
Optimizing Outcomes in nAMD

- Goal: Achieve & maintain best vision
- Disease control
  - Obtaining and maintaining a dry macula
    - Minimizing signs of exudation
    - Preventing CNV growth
  - Least amount of anti-VEGF treatments (and visits)

Neovascular AMD Therapy Induction-Maintenance

Before

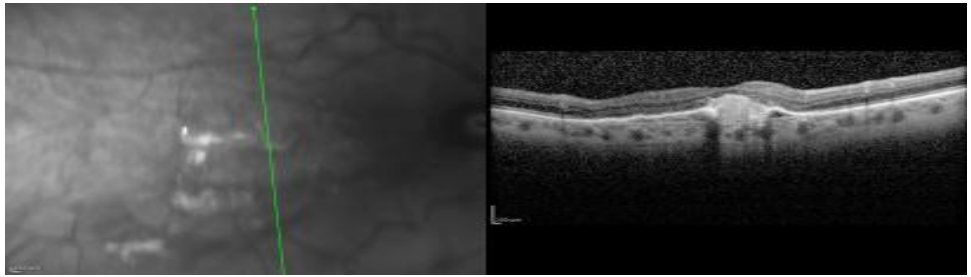
Anti-VEGF Rx



Induction (1-3 Injections)

On

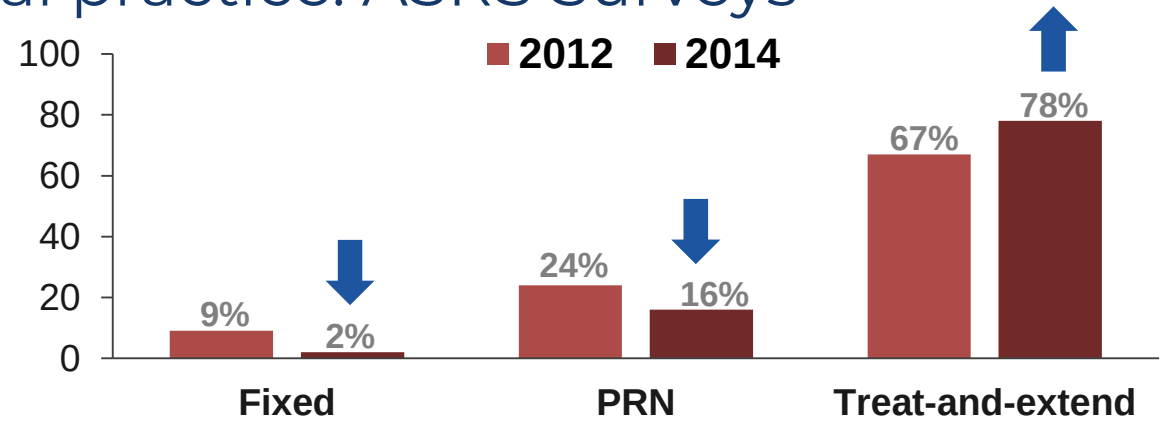
Anti-VEGF Rx



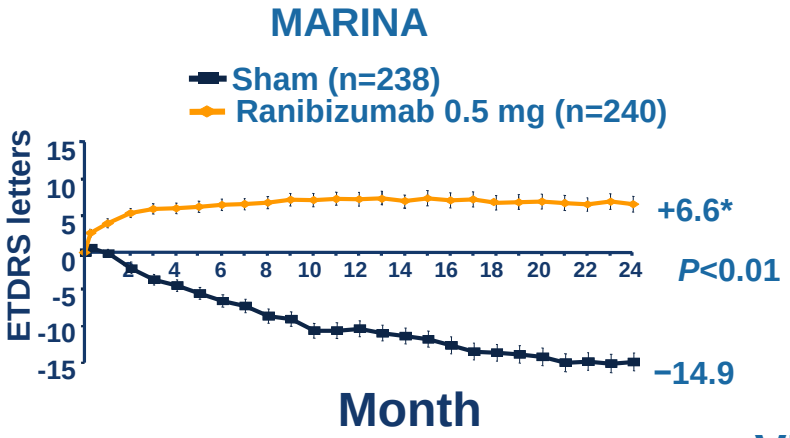
Maintenance (Disease Control)

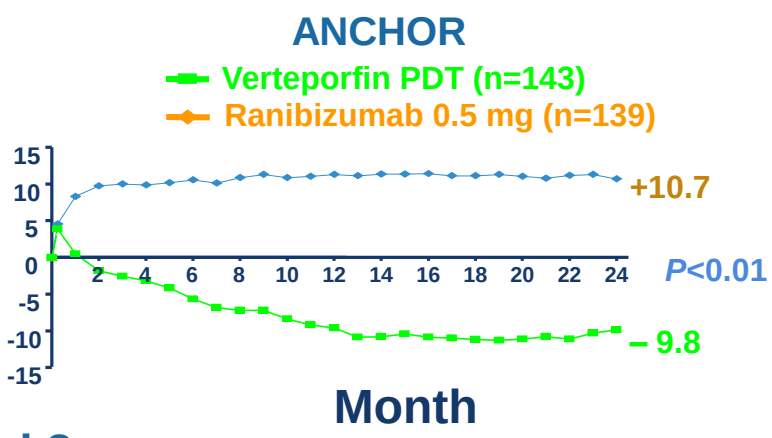
Maintenance Dosing Regimens

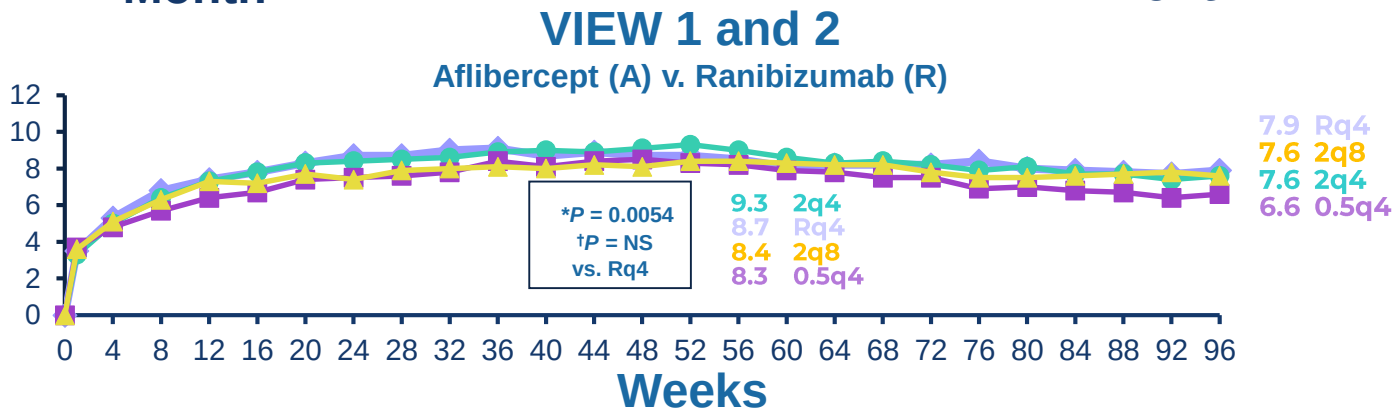
- Regimens:
  - Continuous-Fixed (“Monthly/bimonthly”)
  - Discontinuous-Variable (“Pro Re Nata”: PRN)*
  - Continuous-Variable (“Treat & Extend”: TAE)*
- Clinical practice: ASRS Surveys



Fixed Frequent Dosing







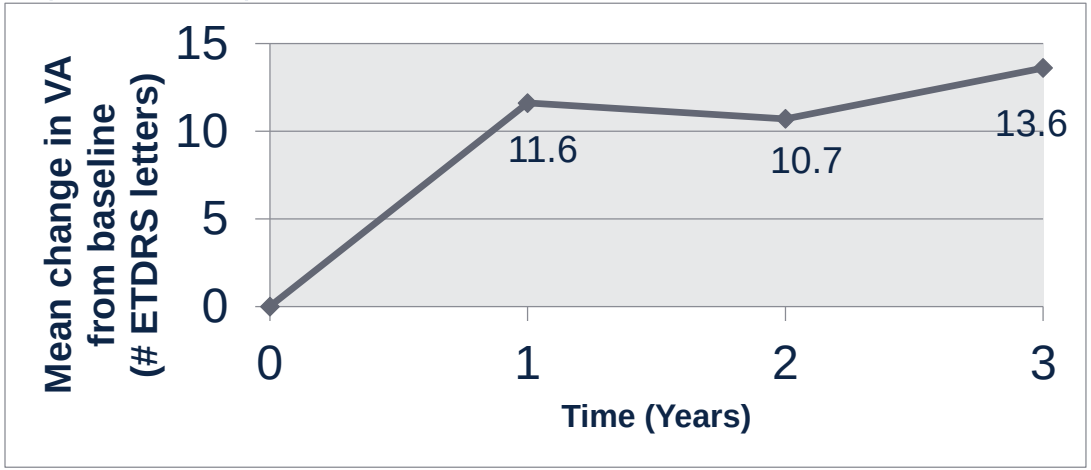
Rosenfeld et al *N Engl J Med* 2006;355:1419-1431; Brown et al *N Engl J Med* 2006;355:1432-1444; Heier et al. *Ophthalmology* 2012;119:2537-2548; Schmidt-Erfurth et al. *Ophthalmology* 2014;121:193-201

Individualized Anti-VEGF Therapy

- **Why:**
  - Avoid over treatment
  - Safer and more cost effective
- **How:**
  - Pro Re Nata (PRN) “As needed”
  - “Treat and Extend”
- **Goal:**
  - Suppress CNV growth and secondary exudation
  - Frequent OCT imaging to assess disease control

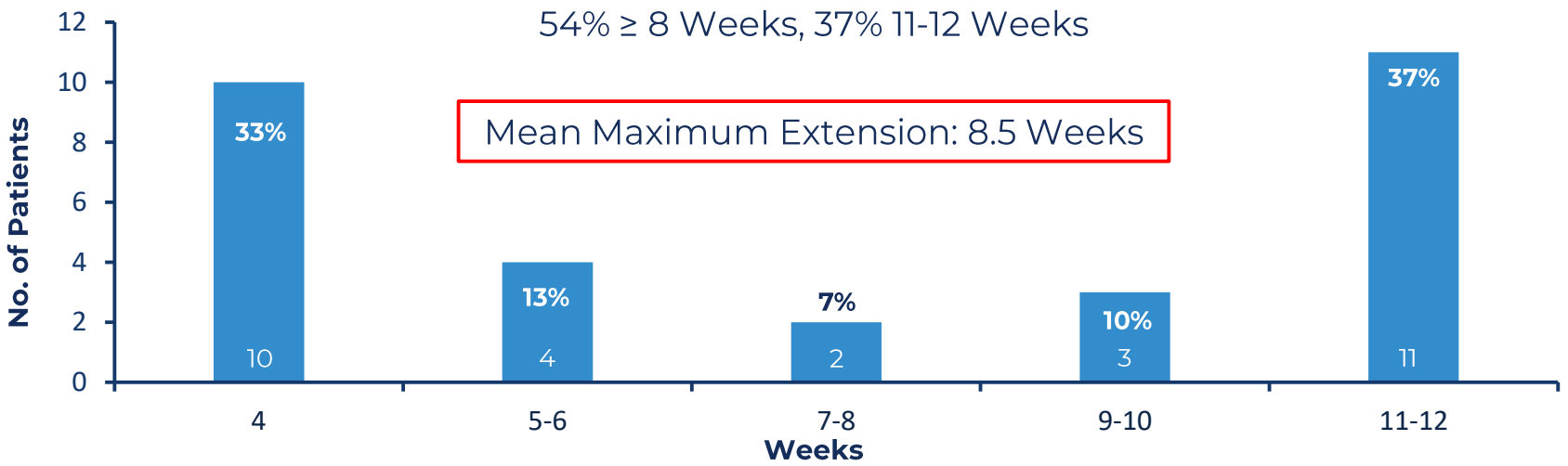
Wills Eye Long-term TAE Study

- Treatment naïve neovascular AMD (N=212)
- Treat and extend regimen: Ranibizumab or bevacizumab
- Results (1-3 yrs):
  - Mean visual acuity change: 10.7-13.6 letters gained
  - Proportion eyes > 3 lines gained: 30.6 – 36.3 %
  - Mean # injections (yrs 1/2/3): 7.6 /5.7/5.8



* Rayess et al. *Am J Ophthalmol* 2015;159:3-8

TREX Extension Interval at 2 Years



Mean maximum extension interval calculated using LOCF

	No. of Injections	
	Mean* (Range)	Median
Monthly	25.5 (22-27)	26.0
TREX*	18.6 (10-25)	17.5

* P<.001

Approximate No. of Rx: 10 in Year 1 and 8 in Year 2 (with monthly X 3 load in Year 1)

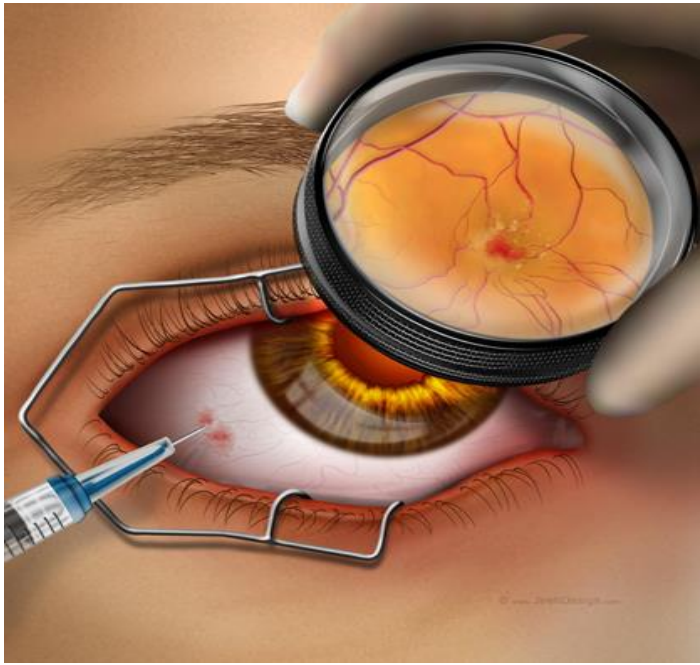
Wykoff et al. *Ophthalmology* 2015;122(12):2514-2522
Wykoff et al. *Ophthalmol Retina* 2017;1(4):314-321

Abbreviation LOCF: Last Observation Carried Forward

Real World Data

Most Patients With Wet AMD Receive ~5 Injections per Year

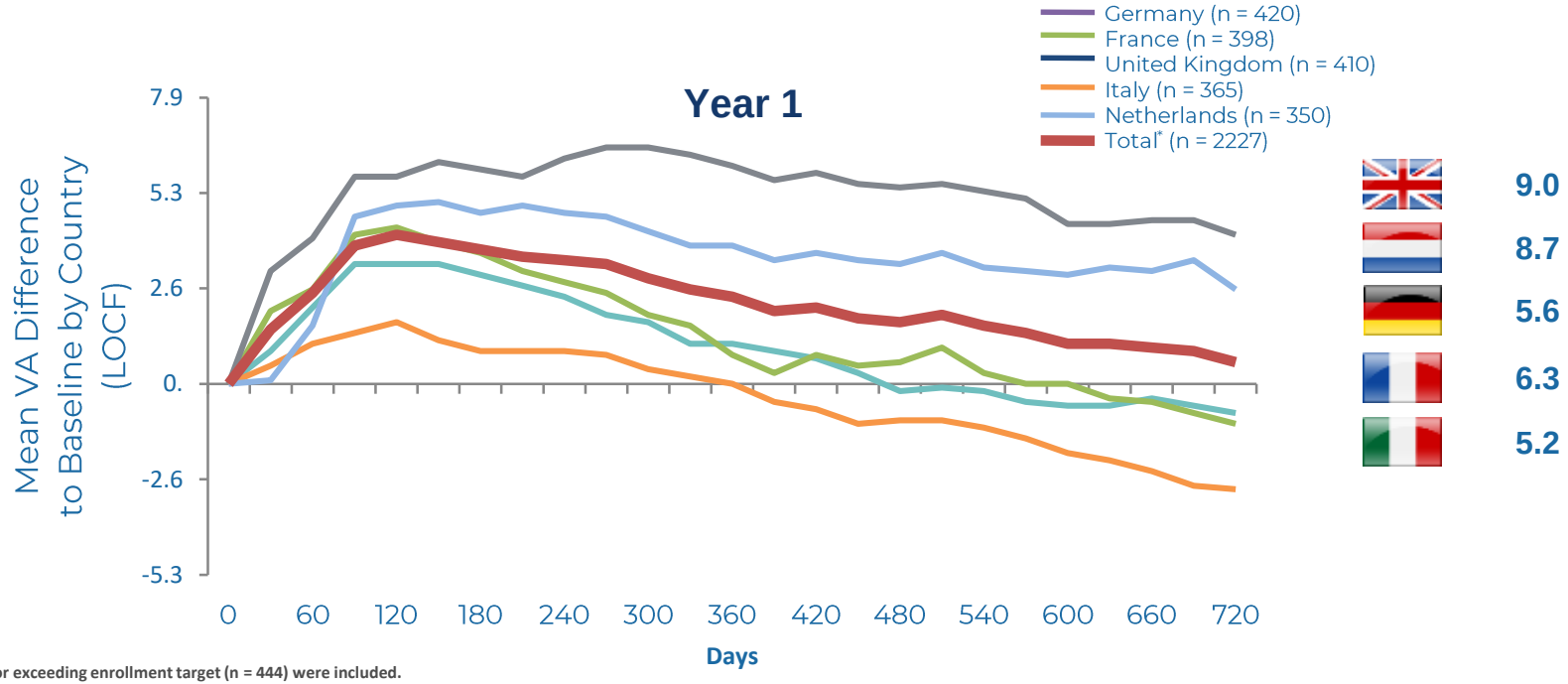
	Study Population	Injection Duration, Year	Mean Injection Rate
Medicare analysis[1]	459,237	1	4.3
LUMINOUS[2]	4,437	1	4.3-5.5
Retrospective claims analysis[3]	11,688	1	4.5-6.8
Retrospective claims analysis[4]	53,621	1	4.6-6.9



1. Lad EM, et al. *Am J Ophthalmol*. 2014;158(3):537-543.e2.
2. Holz FG, et al. *Br J Ophthalmol*. 2013;97(9):1161-1167.
3. Kiss S, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2014;45(4):285-291.
4. Holekamp NM, et al. *Am J Ophthalmol*. 2014;157(4):825-833.e1.

AURA Study

Real-life use of anti-VEGF therapy is associated with poorer visual outcomes compared with clinical trial outcomes



*Only countries meeting or exceeding enrollment target (n = 444) were included.

Holz FG, et al. *Br J Ophthalmol.* 2015;99(2):220-226.

Neovascular AMD Management 2019

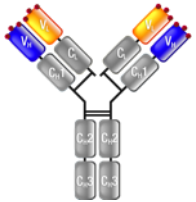
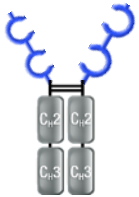
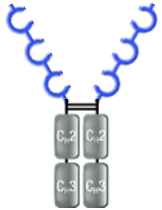
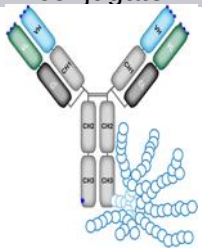
- Individualized anti-VEGF A therapy
  - Available agents: Ranibizumab, aflibercept, bevacizumab
    - Similar efficacy, safety & durability (Mean 8-9 wks, range 1-3 months)
    - All requires indefinite, frequent treatment/evaluations
  - Treat and Extend most common and non-inferior to monthly Rx
  - Real world
    - Relative under treatment still prevalent
    - Suboptimal outcomes beyond 2 years in most studies
  - Early detection = better vision but not less treatment
- Major unmet need = More durable anti-VEGF
  - Decreased burden: Treatment, evaluations, risk
  - Better long-term visual outcomes

Extending Anti-VEGF Durability

- **New anti-VEGF agents:**
  - Brolucizumab
  - Abicipar*
  - Conbercept*+
  - KSI-301*

* Not FDA approved
+ Approved in China; Phase 3 in US underway

Current and Emerging Anti-VEGF Agents

Drug	bevacizumab	aflibercept	ranibizumab	conbercept	brolucizumab	abicipar pegol	KSI-301
Format[1-5]	Full antibody (IgG1)	VEGFR1/2-[SEP]Fc fusion protein	Fab fragment	VEGFR1/2-[SEP]Fc fusion protein	Single-chain antibody fragment	DARPIN	Antiody biopolymer conjugate
Molecular structure							
Molecular weight[1-5]	149 kDa	97-115 kDa[a]	48 kDa	143 kDa	26 kDa	34 kDa	950 kDa
Clinical dose[2,3,5-7]	1.25 mg	2.0 mg	0.3-0.5 mg	0.5-2.0 mg	6.0 mg	2.0 mg	5.0 mg
Equivalent molar dose	0.4	Reference	0.5	1.0	11.2	2.9	14
Dissociation Constant	1100 pM	1 pM	192 pM	0.1 pM	104 pM	4 pM	6.75 pM

1. Avastin [package insert]. South San Francisco, CA: Genentech, Inc.; 2016; 2. Eylea [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; 2017; 3. Lucentis [package insert]. South San Francisco, CA: Genentech, Inc.; 2017; 4. Holz FG, et al. *Ophthalmology*. 2016;123(5):1080-1089; 5. Dugel PU, et al. *Ophthalmology*. 2017;124(9):1296-1304; 6. CATT Research Group. *N Engl J Med*. 2011;364(20):1897-1908; 7. IVAN Study Investigators. *Ophthalmology*. 2012;119(7):1399-1411

Brolucizumab was recently approved in US

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use BEOVU safely and effectively. See full prescribing information for BEOVU.

BEOVU® (brolucizumab-dbll) injection, for intravitreal injection
Initial U.S. Approval: 2019

----------INDICATIONS AND USAGE----------
BEOVU is a human vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of Neovascular (Wet) Age-Related Macular Degeneration (AMD) (1).

----------DOSAGE AND ADMINISTRATION----------
BEOVU is administered by intravitreal injection. The recommended dose for BEOVU is 6 mg (0.05 mL of 120 mg/mL solution) monthly (approximately every 25-31 days) for the first three doses, followed by one dose of 6 mg (0.05 mL) every 8-12 weeks (2.2).

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 6 mg/0.05 mL solution for intravitreal injection in a single-dose vial (3).

----------CONTRAINDICATIONS----------
- Ocular or periocular infections (4.1).
- Active intraocular inflammation (4.2).
- Hypersensitivity (4.3).

----------WARNINGS AND PRECAUTIONS----------
- Endophthalmitis and retinal detachments may occur following intravitreal injections. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay (5.1).
- Increases in intraocular pressure (IOP) have been seen within 30 minutes of an intravitreal injection (5.2).
- There is a potential risk of arterial thromboembolic events (ATE) following intravitreal use of VEGF inhibitors (5.3).

----------ADVERSE REACTIONS----------
The most common adverse reactions (≥ 5%) reported in patients receiving BEOVU are vision blurred (10%), cataract (7%), conjunctival hemorrhage (6%), eye pain (5%), and vitreous floaters (5%) (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

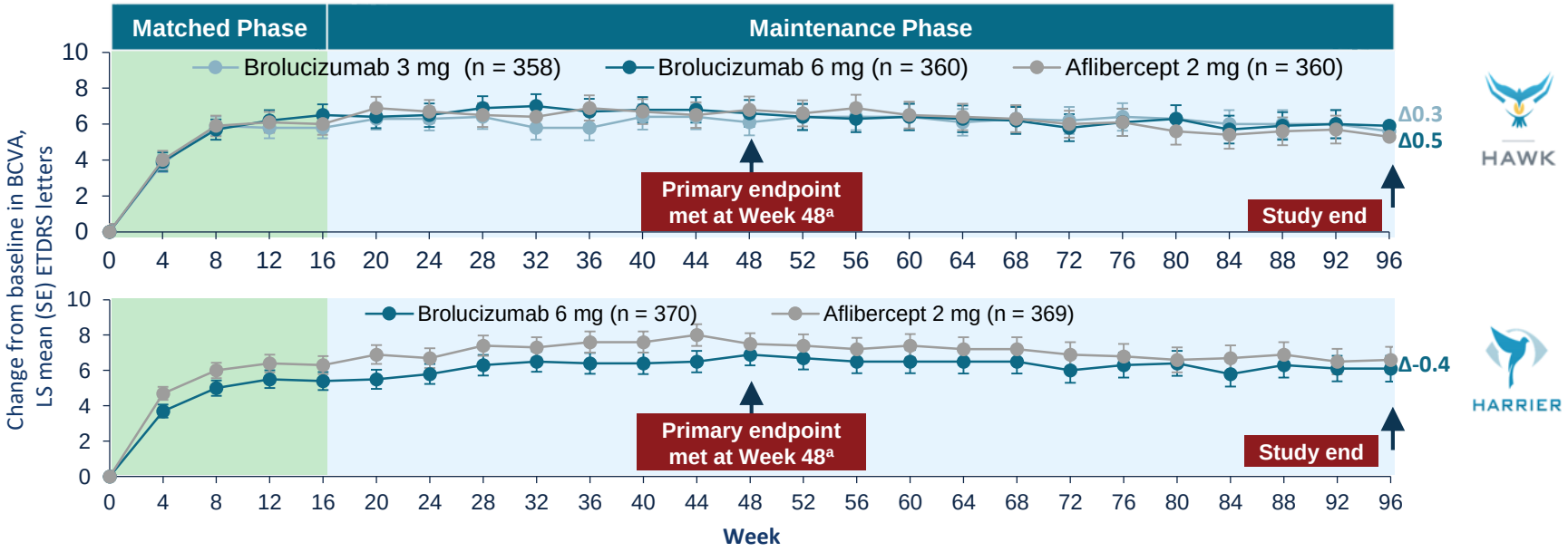
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 10/2019

- **~50% on q12w at Year 1, ~40% at Year 2**

BCVA Change From Baseline to Wk 96

Brolucizumab vs Aflibercept

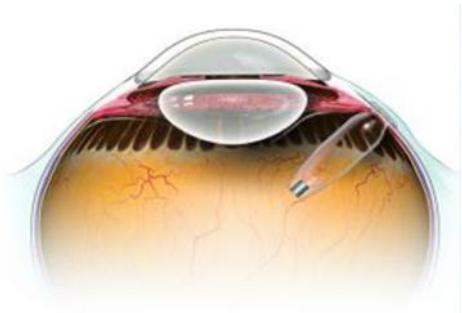


Full analysis set LOCF. Mean differences in BCVA (brolucizumab–aflibercept, Δ). [a] Non-inferiority (NI) margin = 4 letters. Analyzed using ANOVA model with baseline BCVA categories (<=55, 56-70, >=71 letters), age categories (<75,≥75 years) and treatment as fixed effect factors. LS, least squares

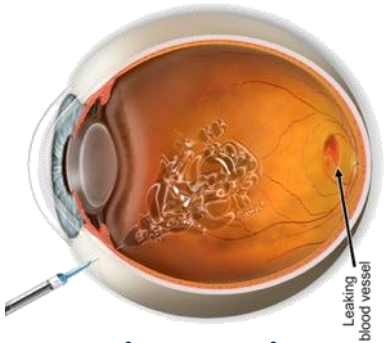
Dugel PU et al. Presented at: The Annual Meeting of the American Academy of Ophthalmology 2018; Chicago, IL; October 27-30, 2018.

Extending Anti-VEGF Durability

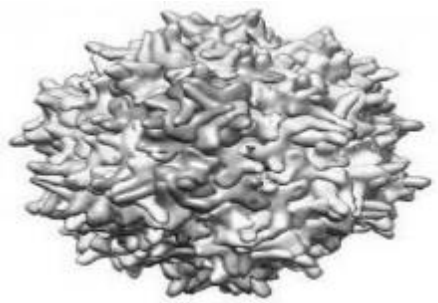
- Sustained Release Implants
- Microparticles (biodegradeable polymers or hydrogels)
  - GB-102 (Sunitinib TKI)
  - Others: OTX TKI/OTX-IVT, AXT 107
- Gene therapy



Reservoir-based Port Delivery



Microparticles



Viral Vector Delivery

Extending Anti-VEGF Durability

- Current agents:
  - All require frequent anti-VEGF injections
    - Mean durability 8-9 weeks (maintenance phase)
    - Range 1-3 months
- Promise:
  - Decreased burden: Patients, care givers, providers
  - Better long-term visual outcomes

DISCUSSION

—

Wet AMD

KSI-301 Phase 1b

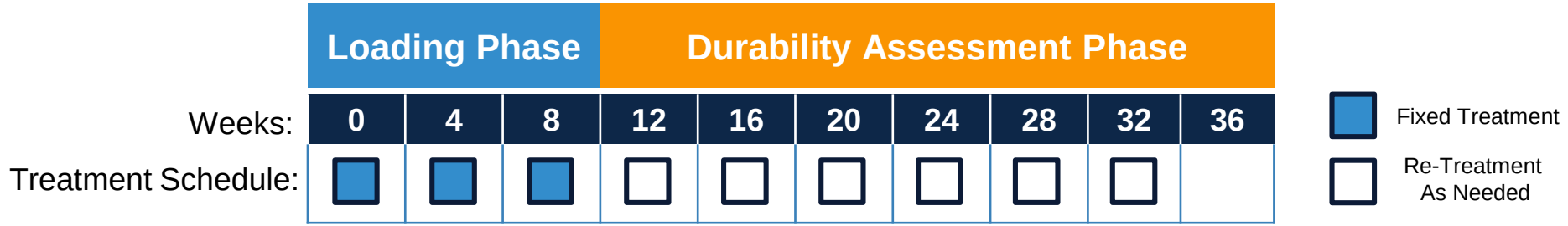
insight into durability among treatment naïve subjects

Randomized, open label study to evaluate multidose safety, efficacy & durability (n=105)

wAMD (n=35) | **DME** (n=35) | **RVO** (n=35)

Randomized 1:3

KSI-301 2.5 mg (50 μL) | KSI-301 5 mg (100 μL)



wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion;
Clinicaltrials.gov ID: NCT03790852

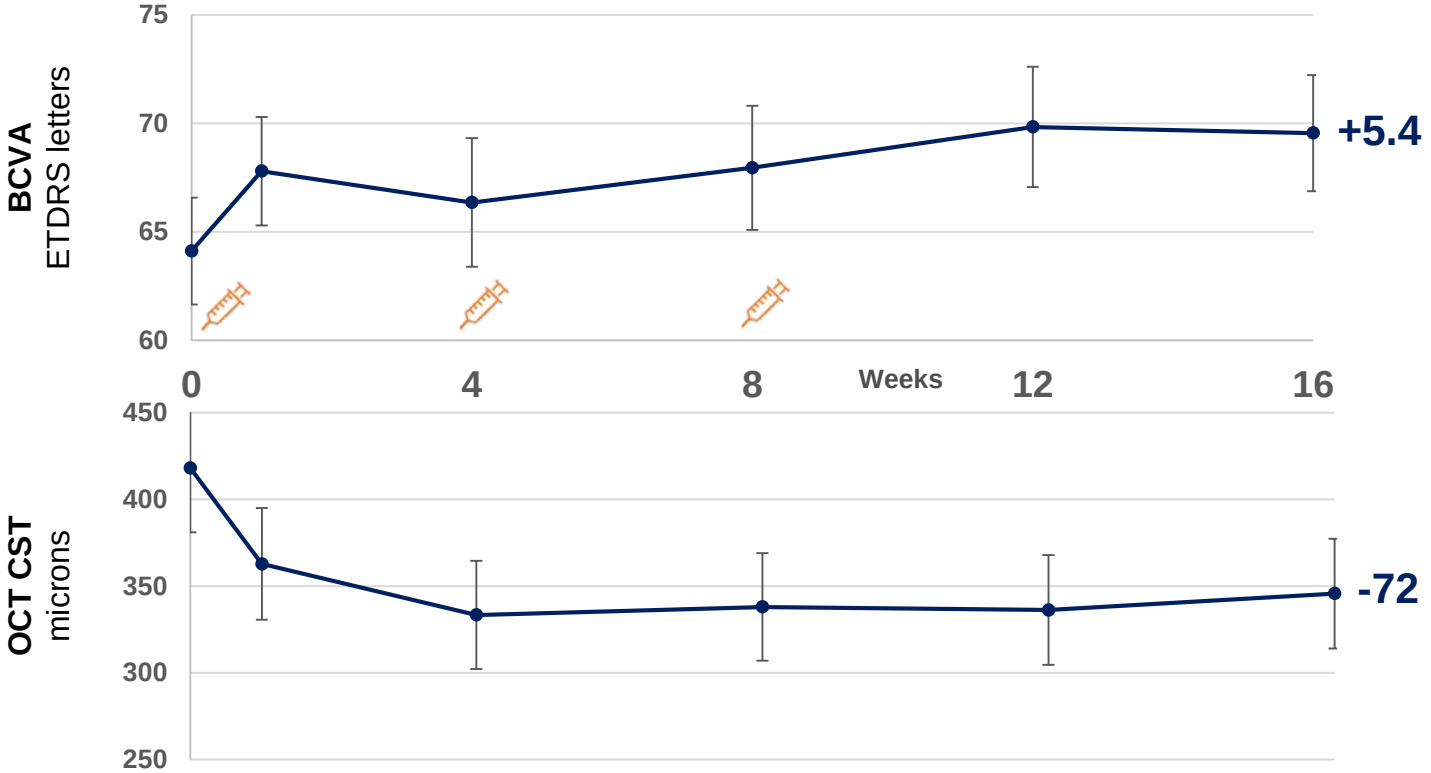
KSI-301 Phase 1b Baseline Characteristics

Variable	wAMD Cohort (n=35)
Age, mean (SD), years	77.2 (11.0)
Gender, n (%), female	25 (71.4)
Race, n (%), White	32 (91.4)
BCVA, mean (SD), ETDRS letters	64.5 (11.1)
BCVA, Snellen 20/40 or better, n (%)	14 (40.0)
OCT CST, mean (SD), microns	426 (176)

Includes all patients randomized as of 10 October 2019. SD= standard deviation; BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

Efficacy of KSI-301 in Wet AMD

change from baseline to week 16 in mean BCVA & OCT



Interim data. Includes only randomized patients that reached Week 16 visit by the data cutoff date of 10 Oct 2019; 2.5 & 5 mg doses pooled. Error bars represent standard error of the mean. OCT CST values are site reported.
BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

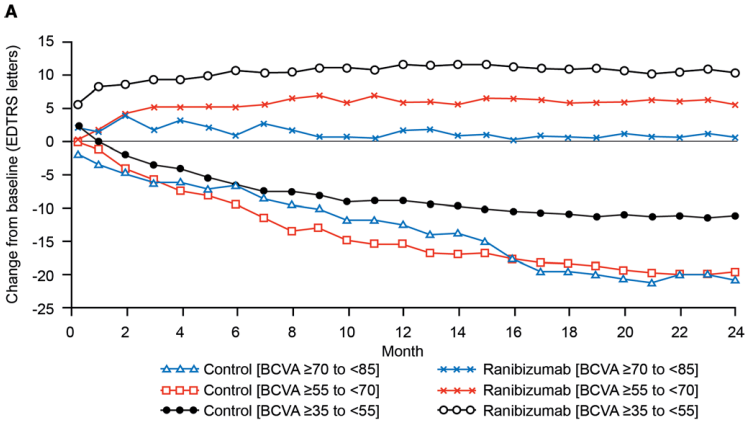
n= 25 **Patients reaching Week 16 visit by data cutoff**

Visual Acuity Improvements
Impact of Baseline BCVA

Study	Arm	N	Mean Baseline BCVA	Mean ΔBCVA at Week 16
KSI-301 Ph1b	KSI-301	25	64.5 ± 11.1	5.4
HAWK	Brolu 3mg	358	61.0 ± 13.6	5.7
	Brolu 6mg	360	60.8 ± 13.7	6.5
	Eylea 2mg	360	60.0 ± 13.9	6
HARRIER	Brolu 6mg	370	61.5 ± 12.6	5.4
	Eylea 2mg	370	60.8 ± 12.9	6.3

Visual benefit versus visual gain: what is the effect of baseline covariants in the treatment arm relative to the control arm? A pooled analysis of ANCHOR and MARINA

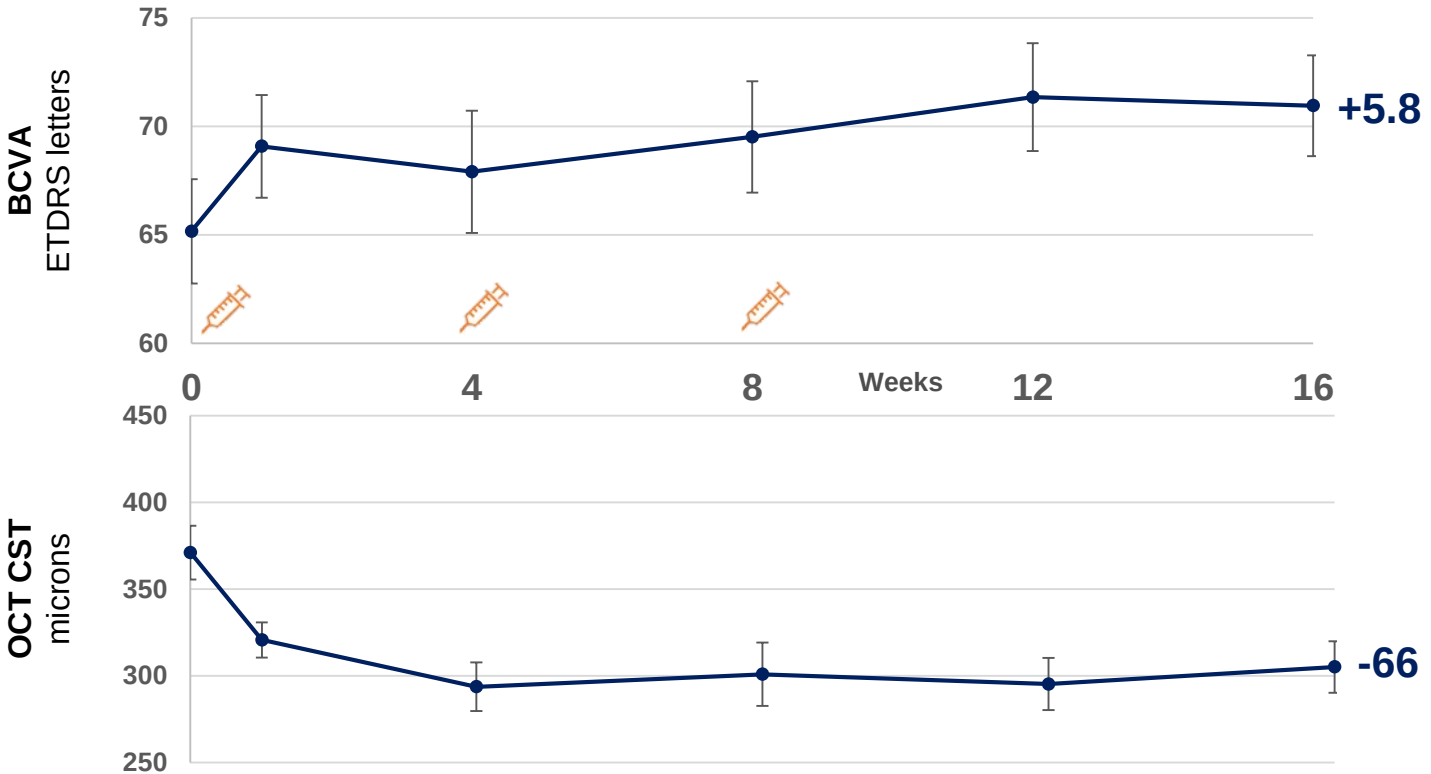
Adnan Tufail [1], Philippe Margaron,[2] Tadhg Guerin,[3] Michael Larsen[4]



Tufail et al, BJO 2019

Efficacy of KSI-301 in Wet AMD in 23/25 subjects <u>without high PEDs</u>

change from baseline to week 16 in mean BCVA & OCT

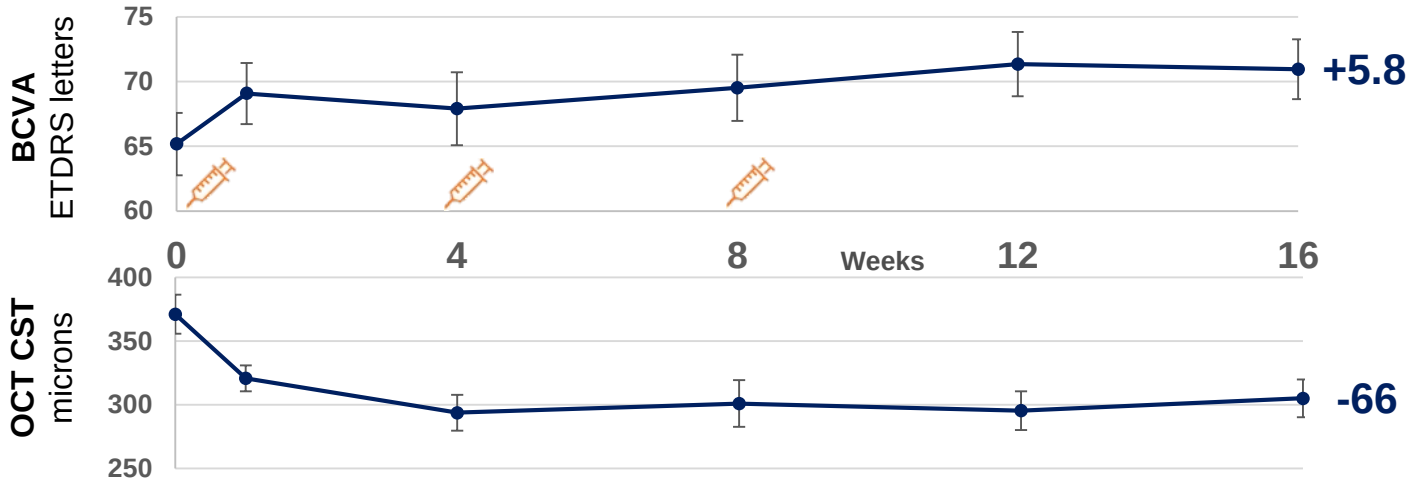


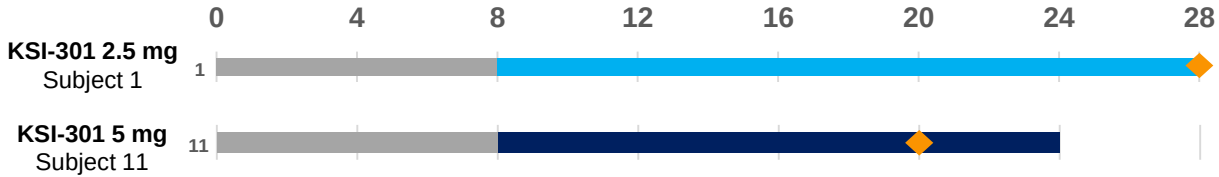
Interim data. Includes only randomized patients that reached Week 16 visit by the data cutoff date of 10 Oct 2019; 2.5 & 5 mg doses pooled. Error bars represent standard error of the mean. OCT CST values are site reported. BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness. High PED defined as presence of a PED with baseline CST ≥500 microns.

n= 23 **Patients without high PEDs reaching Week 16 visit by data cutoff**

Efficacy of KSI-301 in Wet AMD in 23/25 subjects without high PEDs

change from baseline to week 16 in mean BCVA & OCT





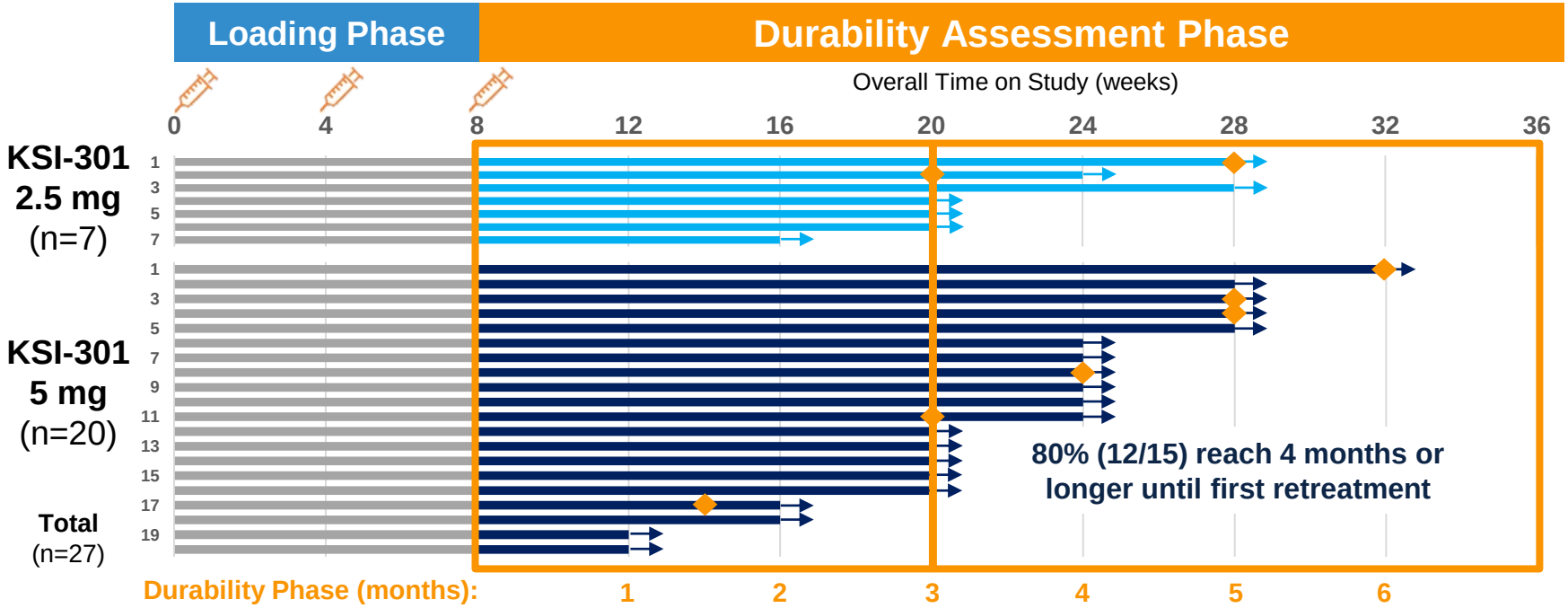
The two subjects with high PEDs received retreatment 20 and 12 weeks after the last loading dose, respectively

Interim data. Includes only randomized patients that reached Week 16 visit by the data cutoff date of 10 Oct 2019; 2.5 & 5 mg doses pooled. Error bars represent standard error of the mean. OCT CST values are site reported.
BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

n= 23 **Patients without high PEDs reaching Week 16 visit by data cutoff**

KSI-301 in wAMD: Durability Assessment

Emerging data support 3 to 5+ month durability



Retreatment with KSI-301

Continuing follow-up

4% (1/25) retreated before 3 months

10% (2/20) retreated at 3 months

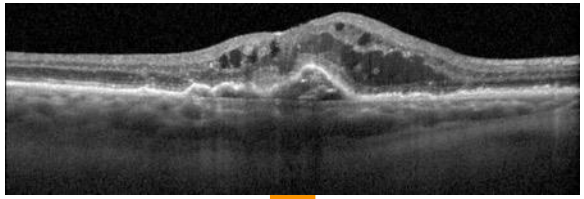
87% (20/23) have gone longer than 3 months after the last loading dose

Interim data. Includes patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

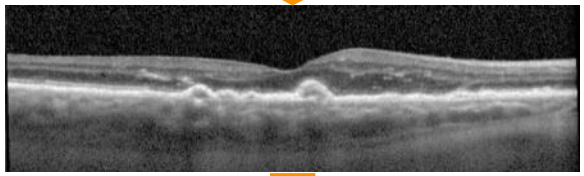
Is it realistic to dose KSI-301 every 5 months after the loading phase in wAMD?

Case Example of KSI-301 5 mg in the Phase 1b Study

DAY 1

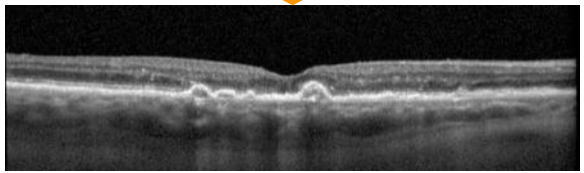


WEEK 1



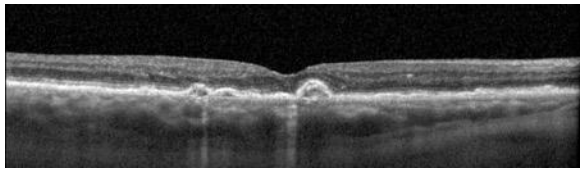
After 1 dose

MONTH 3



1 month after 3 loading doses

MONTH 7

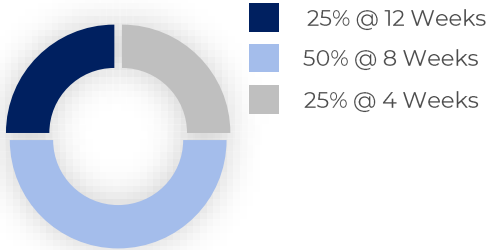


No retreatment required for 5 months

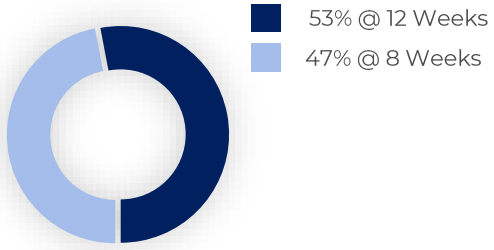
Extended durability continues to be an unmet need in anti-VEGF therapy

	Maintenance Phase				
	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks
Aflibercept					
Brolucizumab					

Aflibercept[1]



Brolucizumab[2]

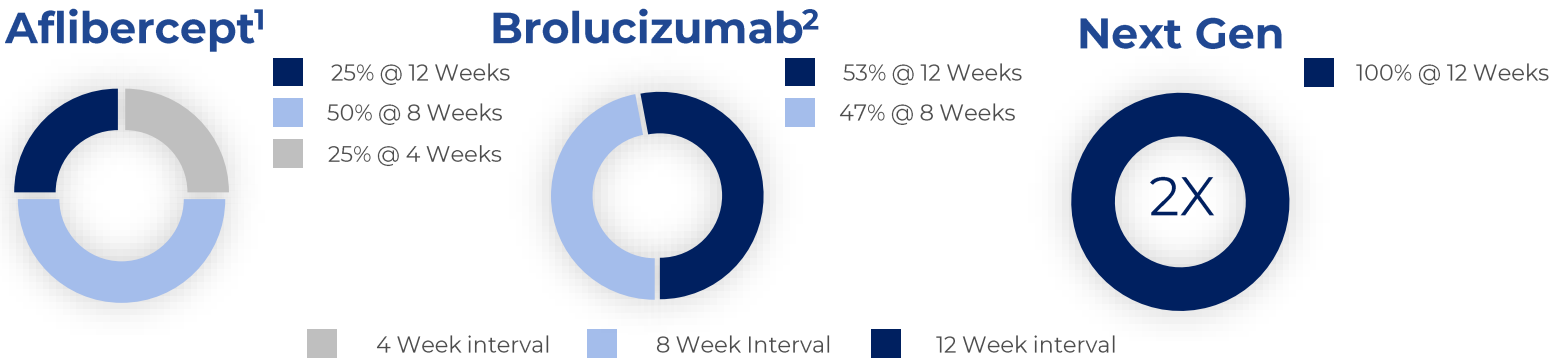


4 Week interval 8 Week Interval 12 Week interval

1. According to current clinical practice
2. According to the interval results used from the Phase 3 wAMD trials HAWK and HARRIER

A next generation biologic should bring nearly all patients to a 12-week interval

	Maintenance Phase				
	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks
Aflibercept					
Brolucizumab					
Next Gen					



1. According to current clinical practice
2. According to the interval results used from the Phase 3 wAMD trials HAWK and HARRIER

A biologic bringing nearly all patients to 12 weeks *and* a majority to 4- and 5- months would be potentially disruptive

	Maintenance Phase				
	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks
Aflibercept					
Brolucizumab					
Next Gen					

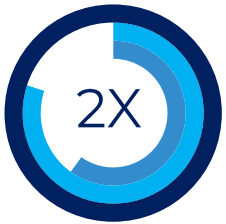
Aflibercept

- 25% @ 12 Weeks
- 50% @ 8 Weeks
- 25% @ 4 Weeks

Brolucizumab[2]

- 53% @ 12 Weeks
- 47% @ 8 Weeks

Next Gen



- 100% @ 12 Weeks
- 80% @ 16 Weeks
- 60% @ 20 Weeks

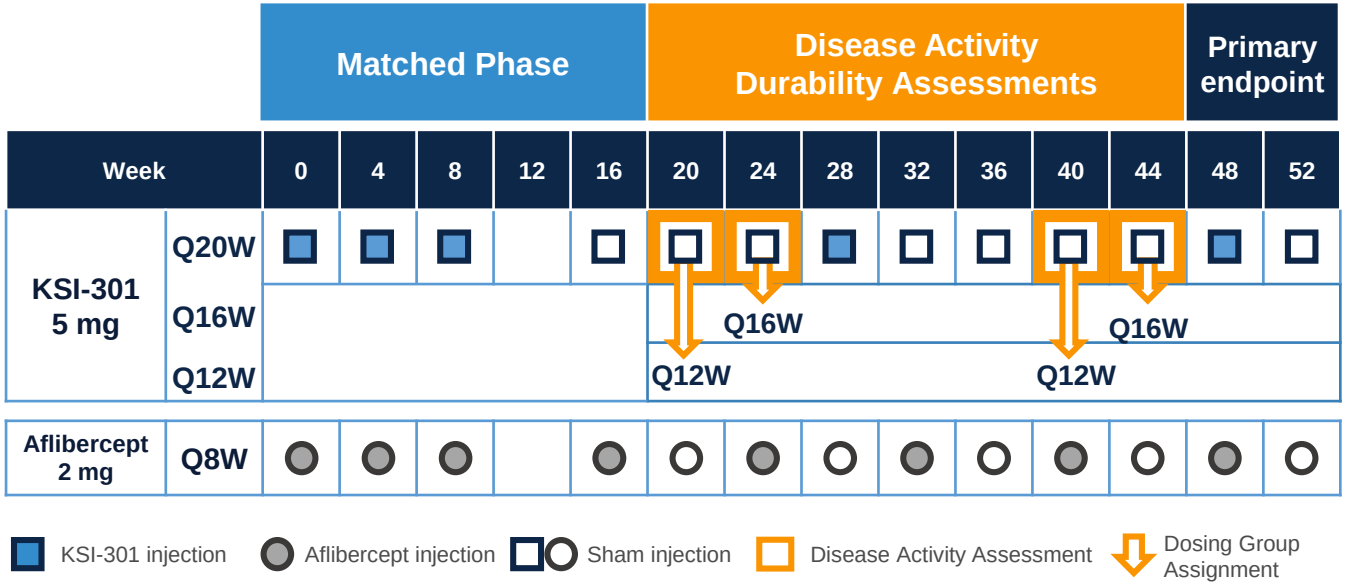
4 Week interval | 8 Week Interval | 12 Week interval | 16 Week Interval | 20 Week interval

1. According to current clinical practice
2. According to the interval results used from the Phase 3 wAMD trials HAWK and HARRIER

Now Recruiting: Pivotal DAZZLE wAMD Study

Dosing with KSI-301 as infrequently as every 20 weeks

- ~400 treatment naïve wAMD patients
- Randomized study vs aflibercept
- US & EU study sites
- KSI-301 dosing: every 12, 16, or 20 weeks depending on pre-specified disease activity assessments*



*After the loading phase
Clinicaltrials.gov ID NCT04049266

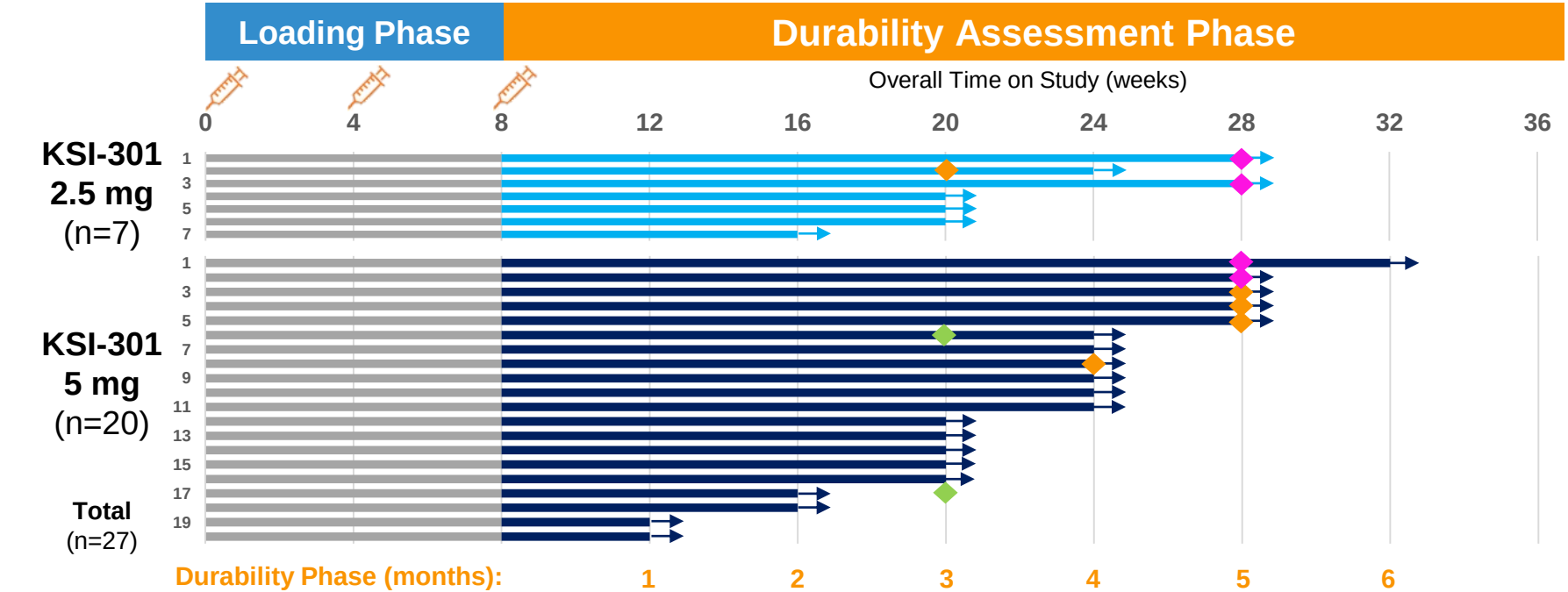
How do DAZZLE Study Disease Activity Assessment Criteria Compare to Phase 1b?

Parameters	Phase 1b Study	DAZZLE study	Change
Visual *and* anatomical	Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12, *OR*	Increase in CST ≥50 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12, *OR*	Tighter CST control (25 microns)
Visual only	Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening wAMD activity, *OR*	Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening wAMD activity, *OR*	No change
	Decrease in BCVA of > 5 letters compared to Day 1, due to worsening wAMD activity	N/A	Eliminated for simplicity (not needed)
Anatomical only	N/A	Increase of ≥ 75 microns compared to Week 12, *OR*	Added two anatomical-only criteria
	N/A	New Macular Hemorrhage	

wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion; CST = central subfield retinal thickness; BCVA = best corrected visual acuity.
Clinicaltrials.gov ID: NCT03790852

KSI-301 in wAMD: Durability Assessment

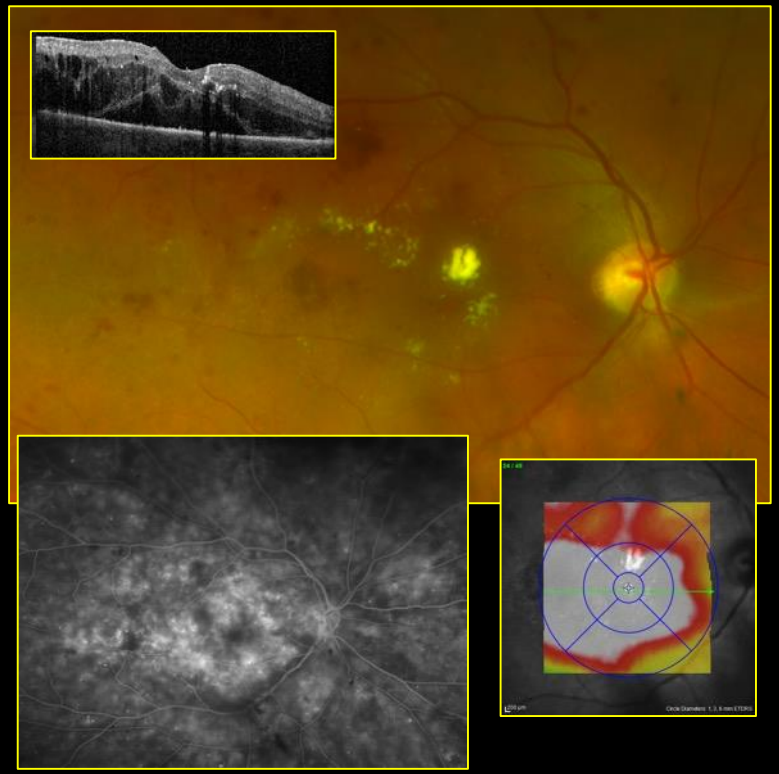
Ph1b patient hypothetical retreatments based on DAZZLE criteria

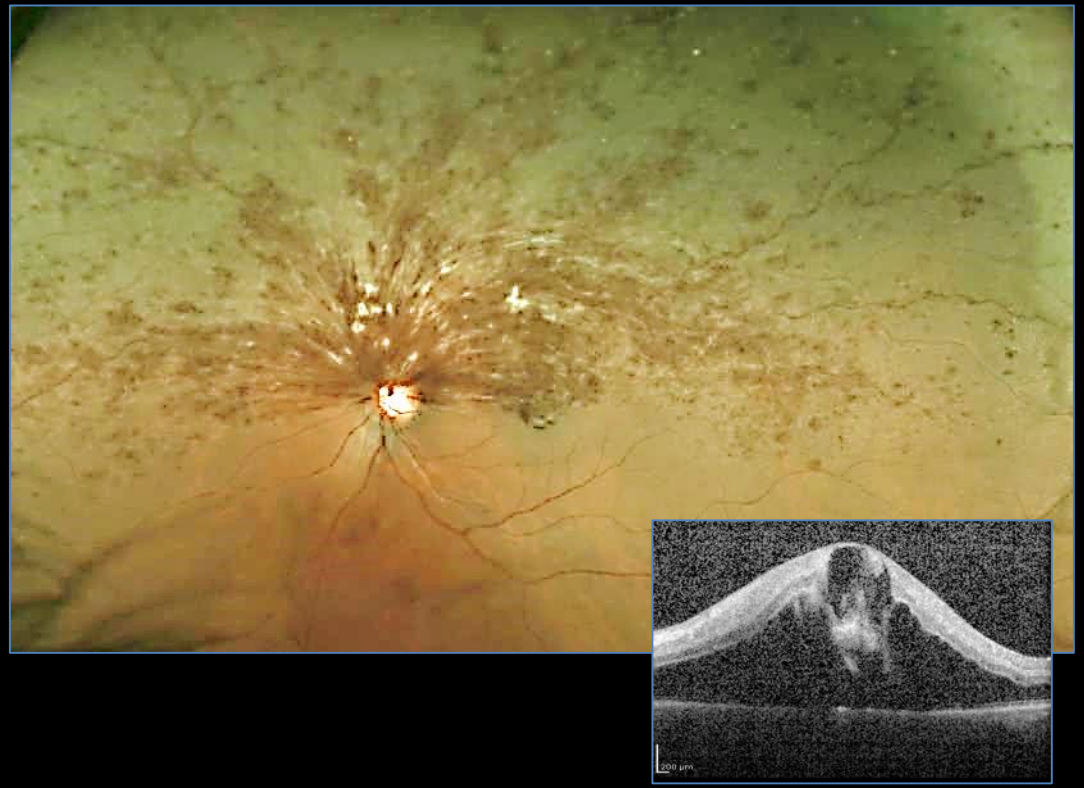


CHARLES WYKOFF, M.D., PH.D.

Director of Research
Retina Consultants of Houston

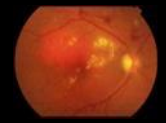
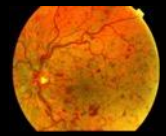
Retinal Vascular Diseases





Scope of the Problem

Exudative Retinal Diseases

	Avg age of onset	Prevalence* (MM)	Disease overview	
Wet AMD	70 yrs	1.9	A leading cause of blindness in the elderly	
Diabetic Macular Edema	60 yrs	1.9	Most frequent cause of blindness in middle aged adults	
Retinal Vein Occlusion	55 yrs	2.5	Second most common cause of vision loss due to vascular disease	
Diabetic Retinopathy w/o DME	45-50 yrs	5.1	Common cause of vision loss among diabetics classified as NPDR vs PDR	

wAMD = wet AMD; DME = Diabetic Macular Edema; BRVO = Branch Retinal Vein Occlusion; CRVO = Central Retinal Vein Occlusion; NPDR = Non-Proliferative Diabetic Retinopathy; PDR = Proliferative Diabetic Retinopathy

Note: Numbers may be rounded; Source: epidemiology data based on multiple literature sources, diagnosis rates based on Datamonitor Report, DRG Market Forecast Assumptions; other sources: Regeneron USA: 230k anti-VEGF treated patients, Roche USA: 200k patients under ophtha care https://www.gene.com/stories/retinal-diseases-fact-sheet and DRG Market Forecast Assumptions

*US, EU5, Japan

Global Report on Diabetes (2016)

World Health Organization

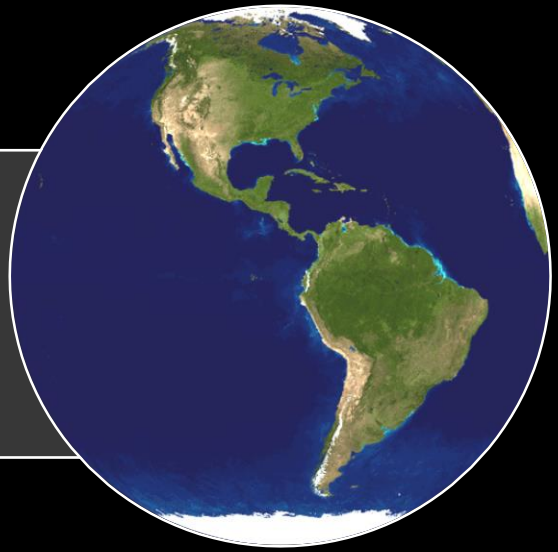
1990s
2.8%

↑ 79%

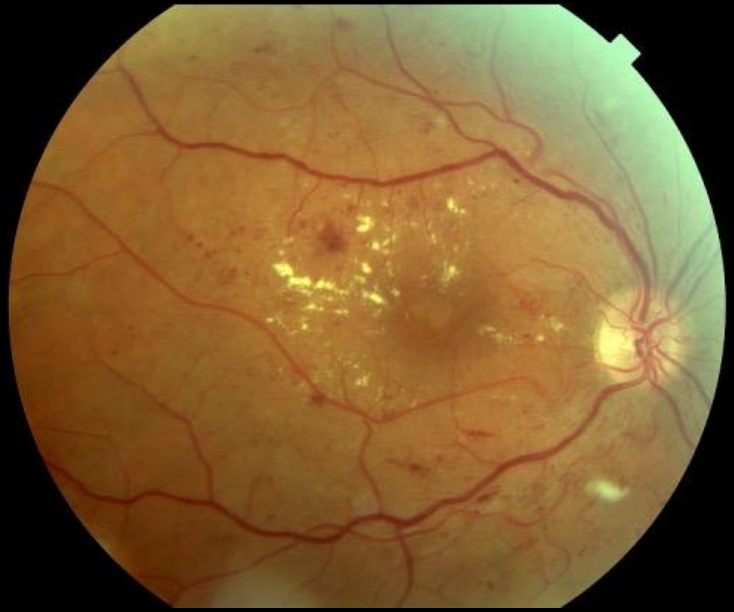
2010
5.0%

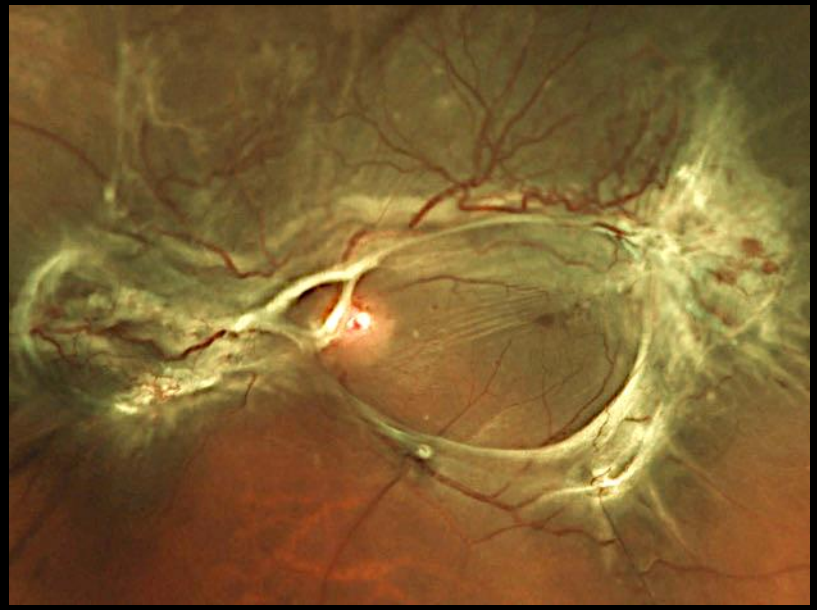
↑ 60%

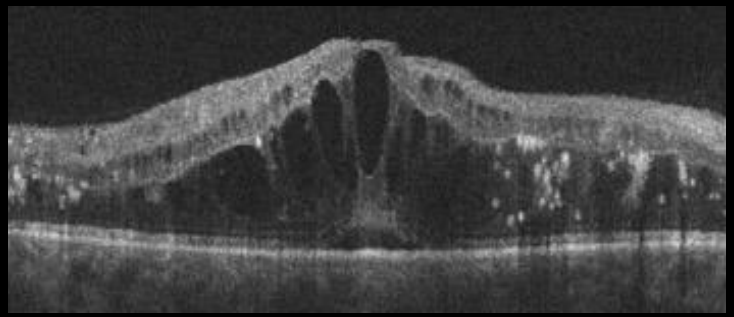
2016
8.0%

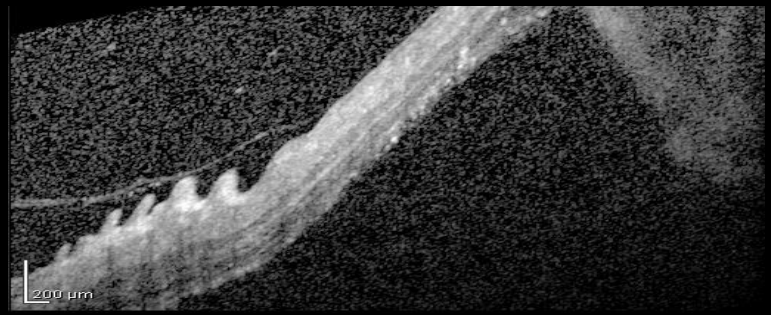



DR = When Not If



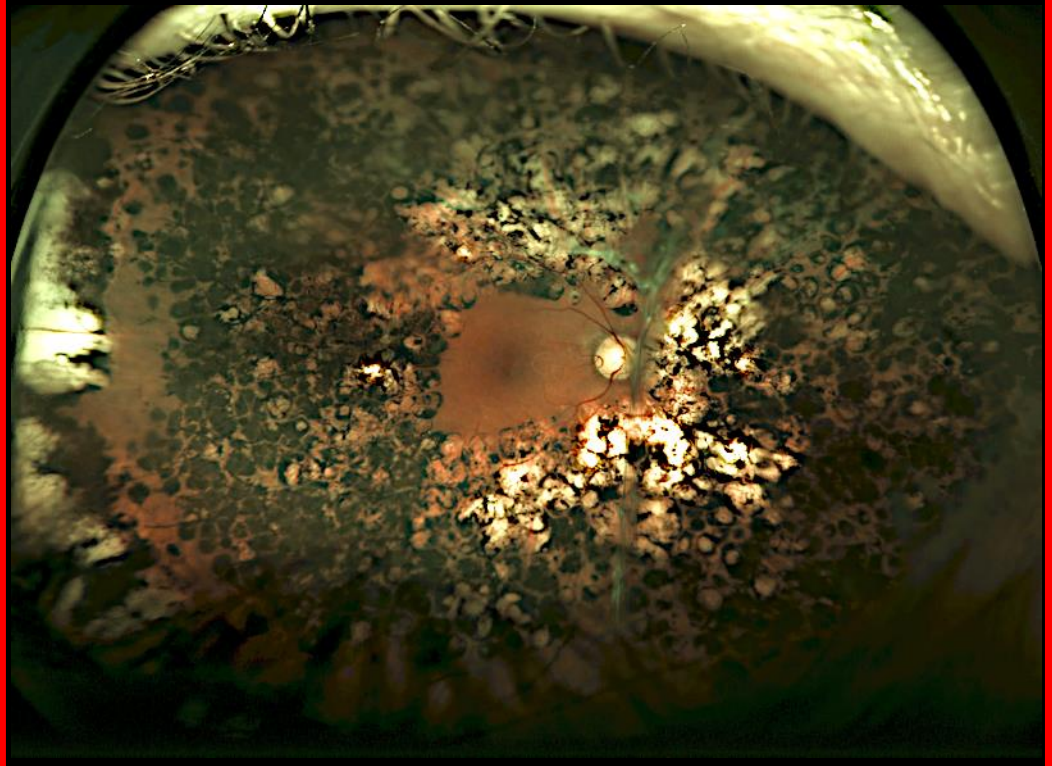





200 µm

Treatment Options

Laser



Injections

Aflibercept

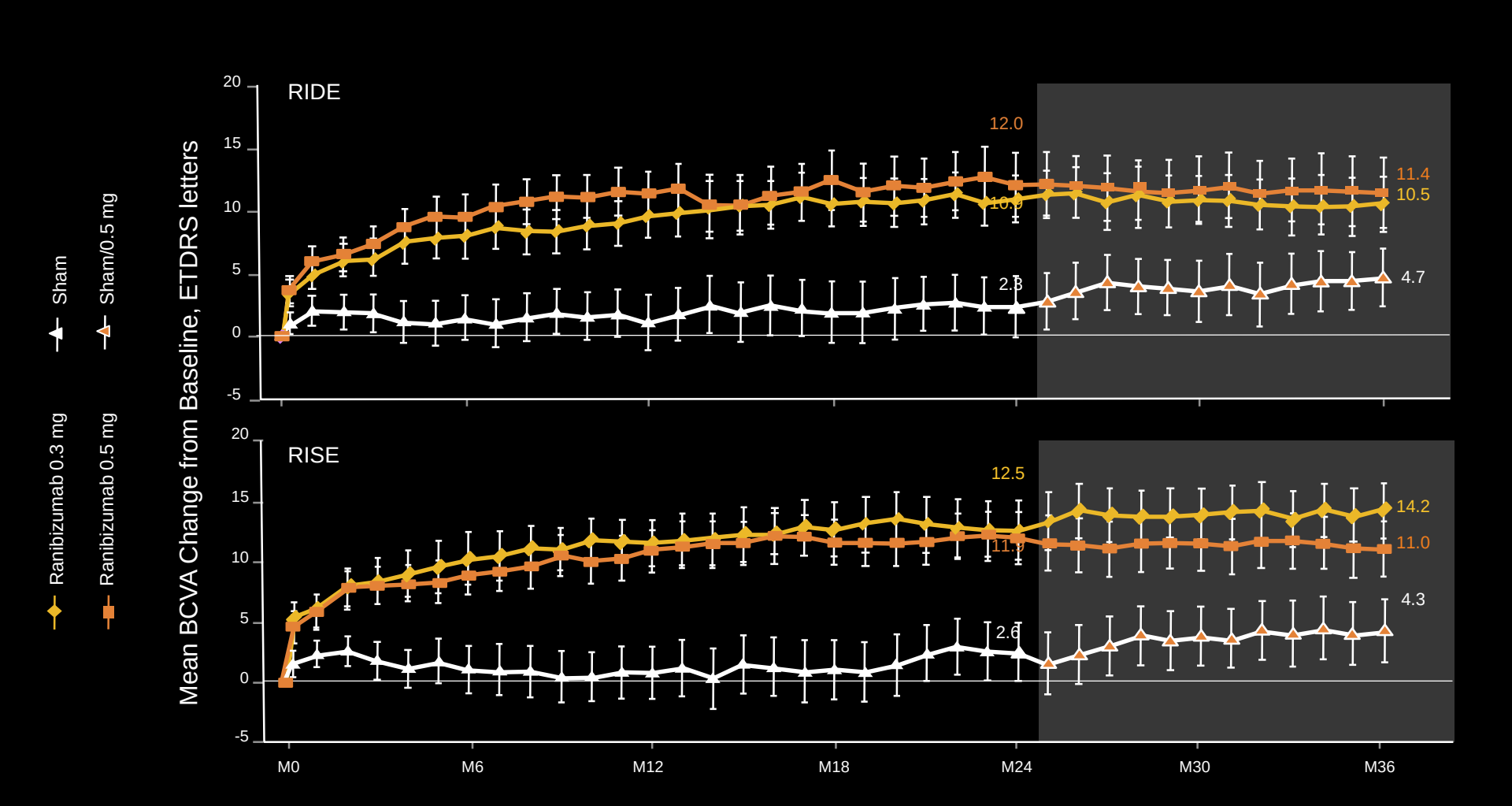
Bevacizumab

Ranibizumab

Dexamethasone

Fluocinolone acetonide

Triamcinolone

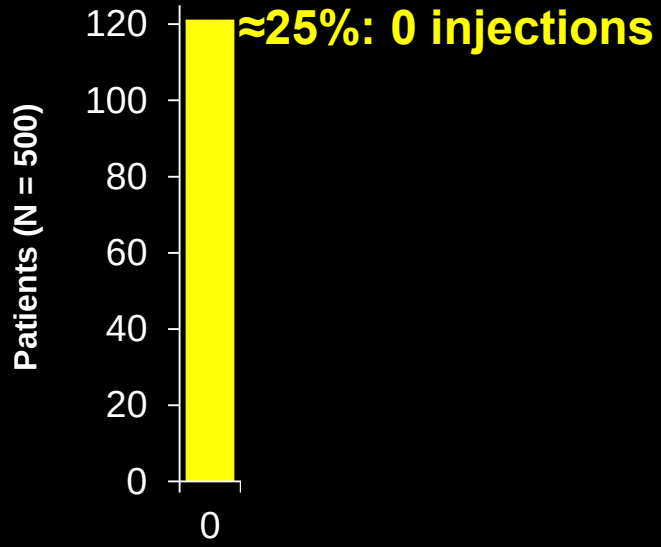


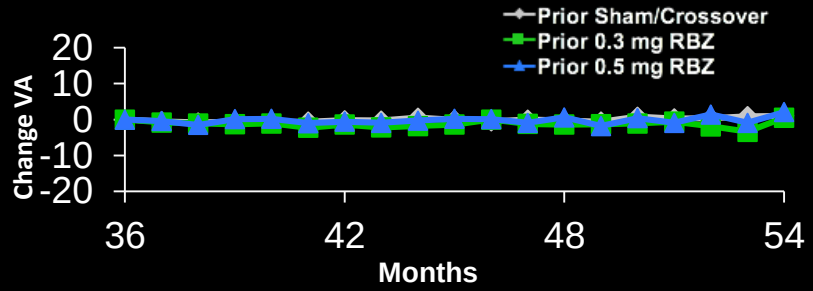
RIDE/RISE Phase 3 Trials

Outcomes with As-Needed Ranibizumab after Initial Monthly Therapy

Long-Term Outcomes of the Phase III RIDE and RISE Trials

Boyer *et al. Ophthalmology* 2015



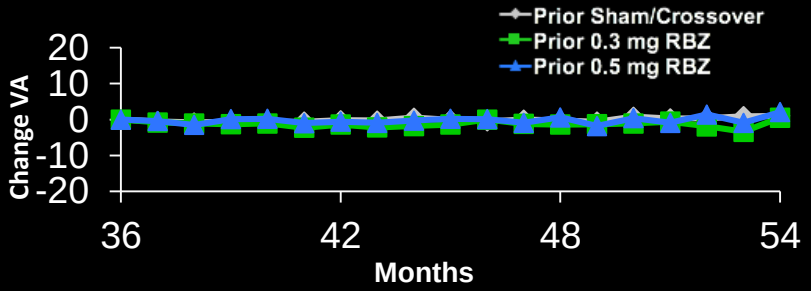


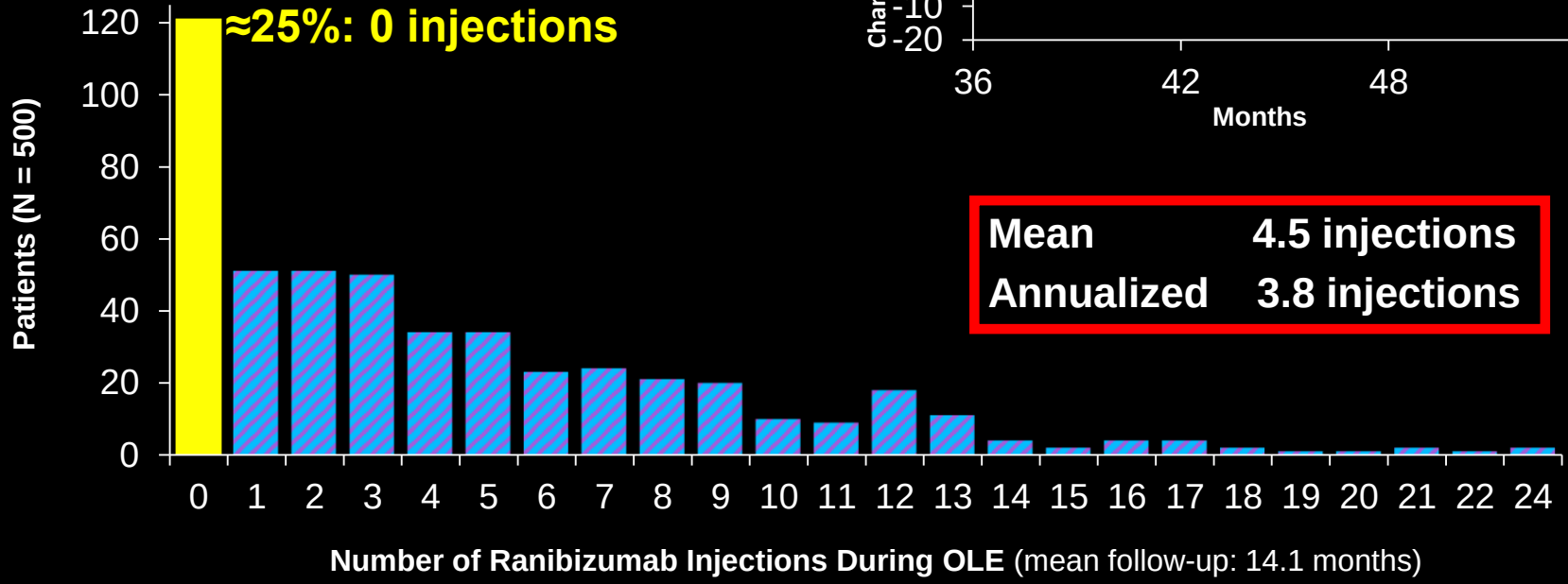
Number of Ranibizumab Injections During OLE (mean follow-up: 14.1 months)

Outcomes with As-Needed Ranibizumab after Initial Monthly Therapy

Long-Term Outcomes of the Phase III RIDE and RISE Trials

Boyer *et al. Ophthalmology* 2015

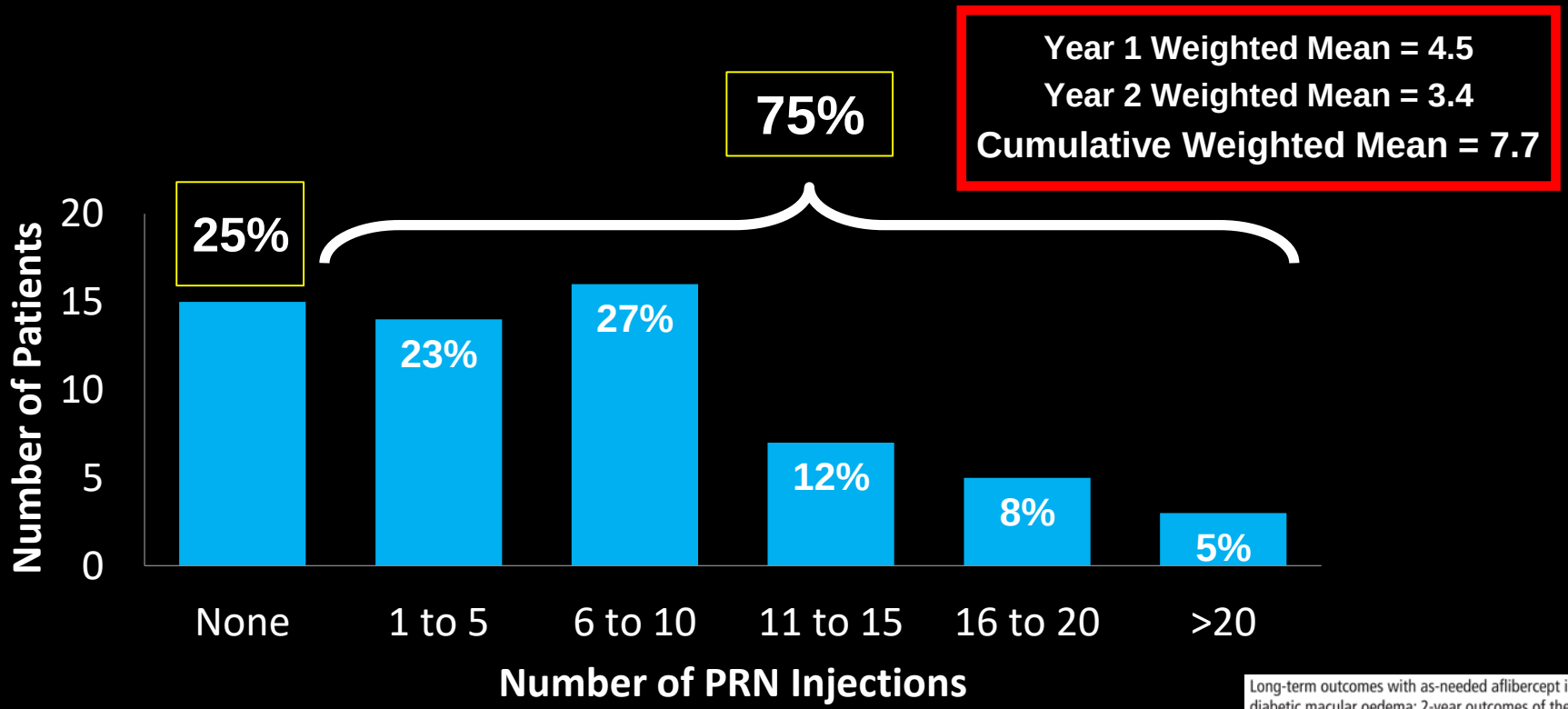




Mean	**4.5 injections**
Annualized	**3.8 injections**

Long-Term Management of DME & DR

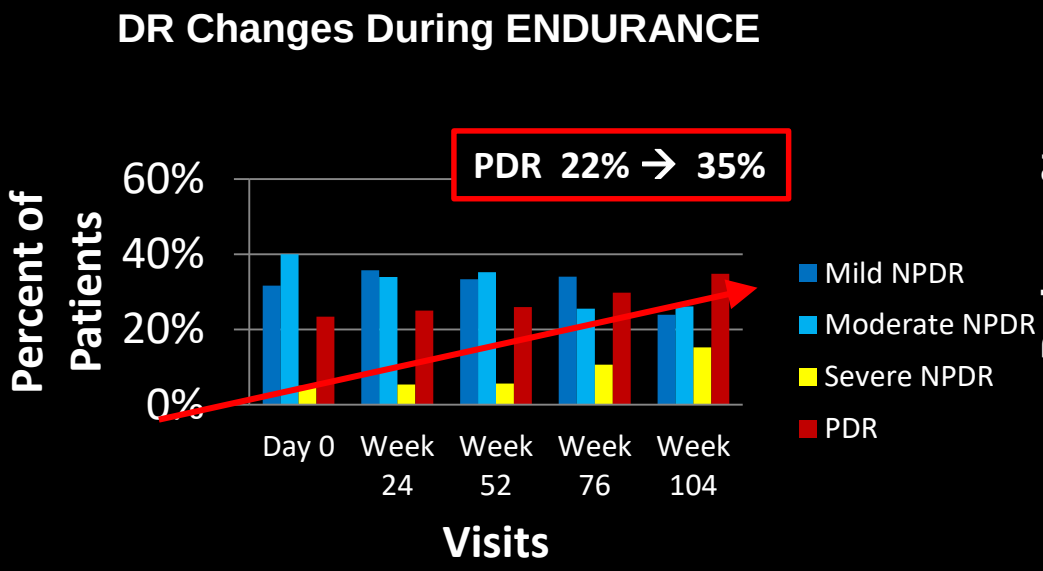
Treatment Burden in Years 4-5 of Management



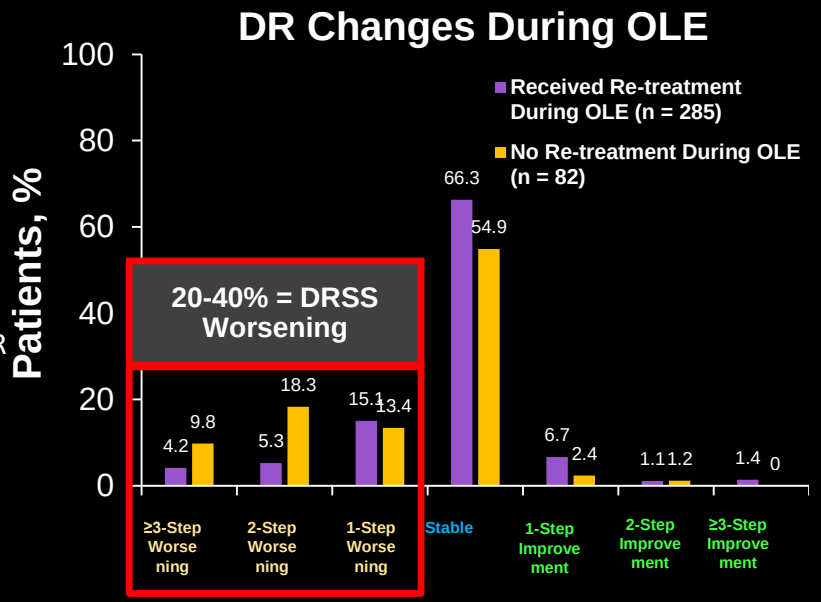
Long-term outcomes with as-needed aflibercept in diabetic macular oedema: 2-year outcomes of the ENDURANCE extension study BJO 2017

Charles C Wykoff,[1,2] William C Ou,[1] Rahul N Khurana,[3,4] David M Brown,[1,2] W Lloyd Clark,[5] David S Boyer,[6] for the ENDURANCE Study Group

Long-Term DR Outcomes

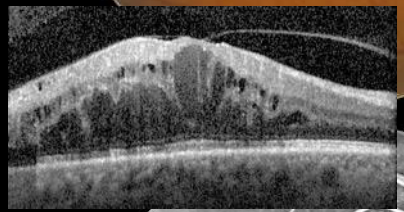


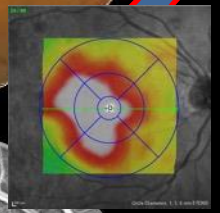
Wykoff *et al.* BJO 2018

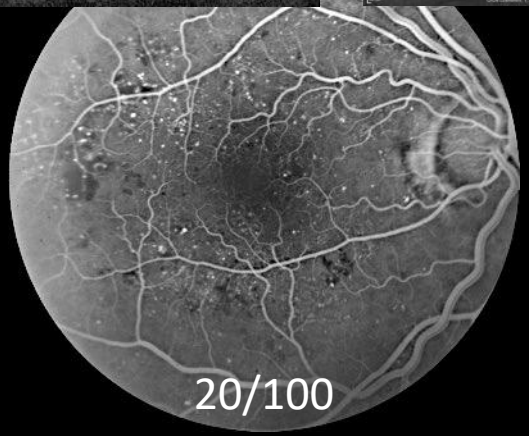


Sun *et al.* Ophthalmology *2019*

64yo WM

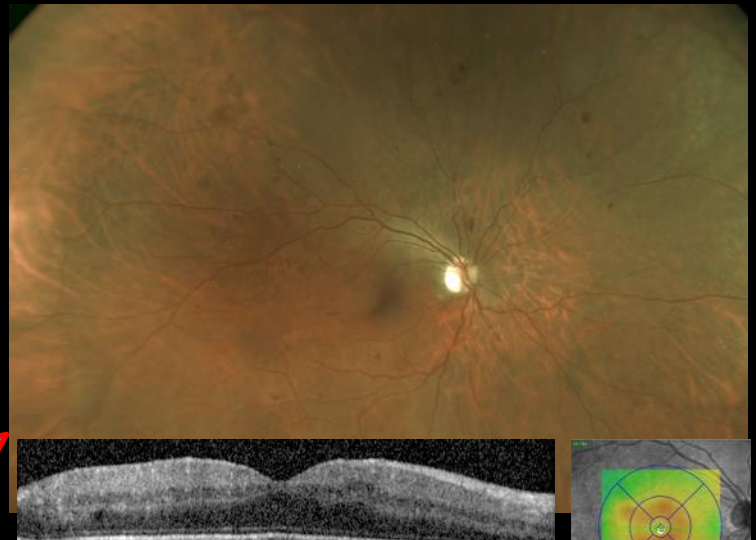


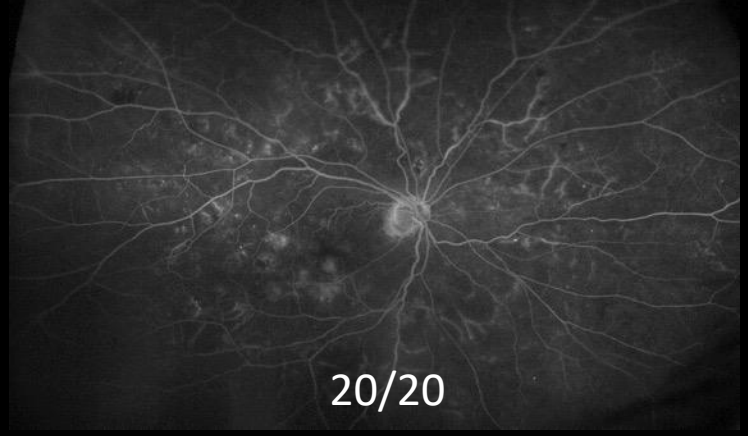




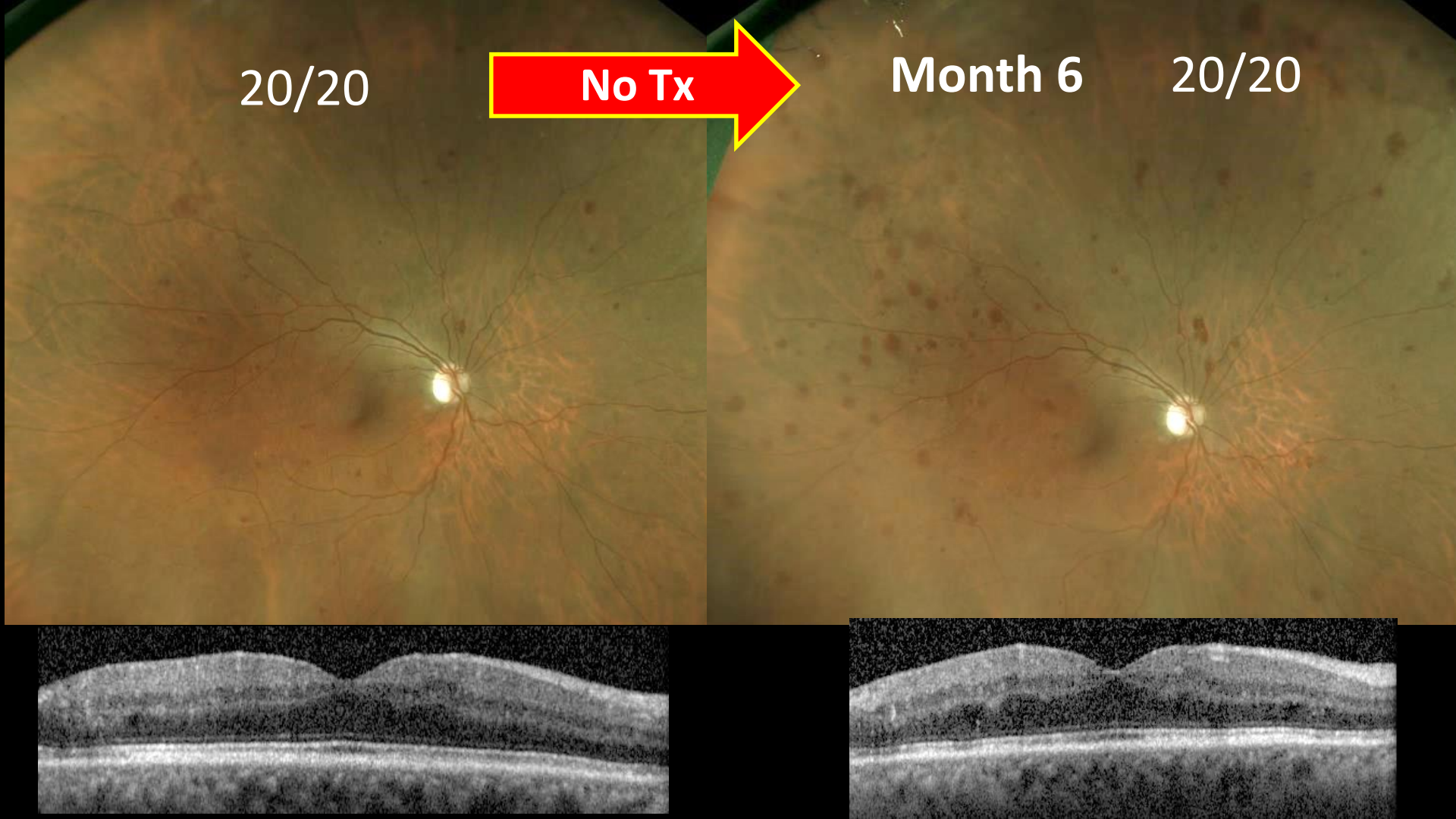
20/100

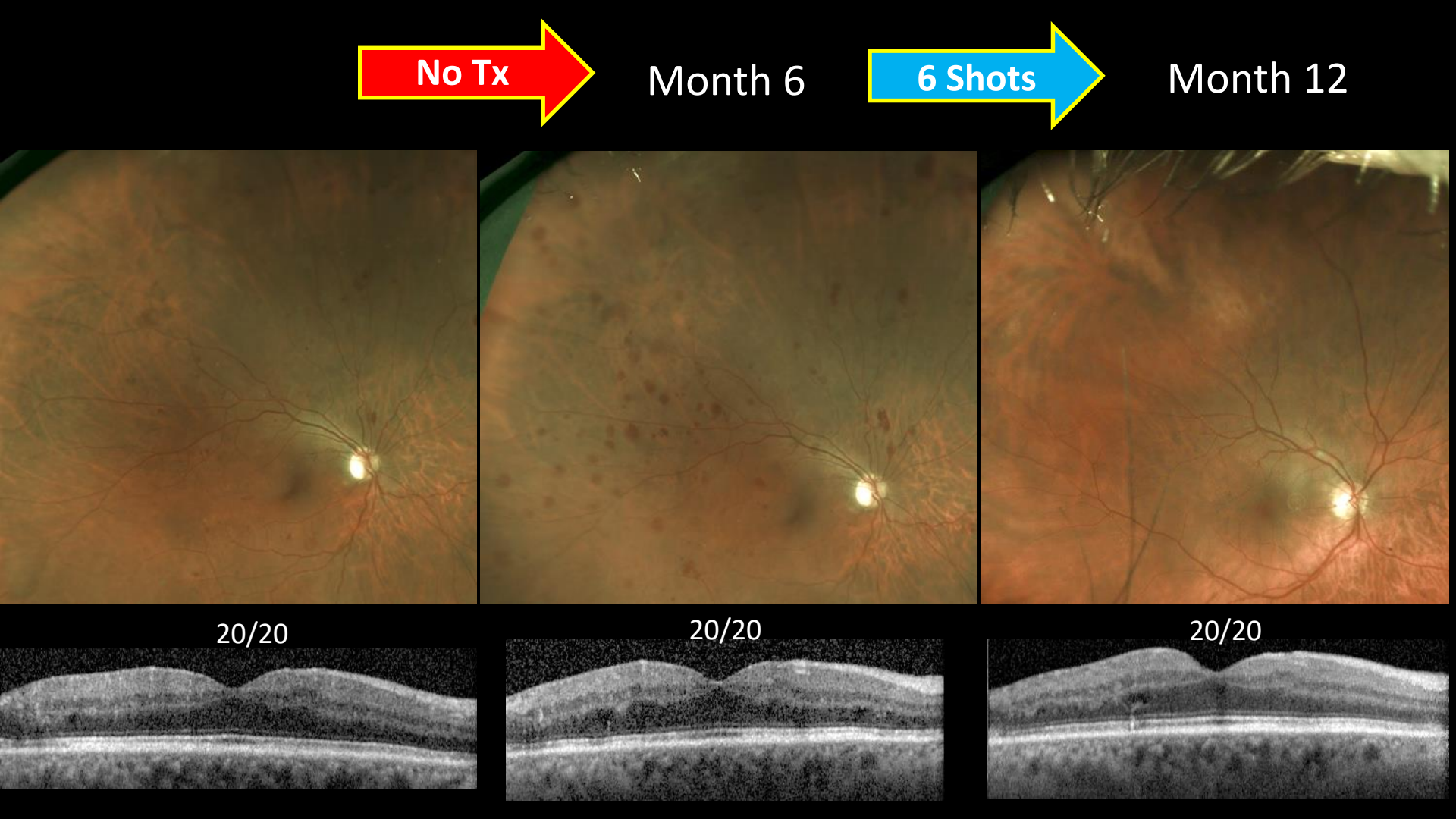
3 years
Q4-12 Week
Anti-VEGF
Dosing





20/20


20/20
No Tx
Month 6
20/20


No Tx
Month 6
6 Shots
Month 12
20/20
20/20
20/20

Protocol S

PRP Arm

- 49% = single PRP session
- Years 3-5: 11% additional PRP
- Mean 5.4 ranibizumab injections
- Median visits = 21

Anti-VEGF Arm

- 19.2 mean injections through 5-years
  - Year (mean # IVI)
  - 1 (7.1) 2 (3.3) 3 (3.0) 4 (2.9) 5(2.9)
- Years 3-5: 63-73% required injections
- Median visits = 43

JAMA Ophthalmology | Original Investigation

Five-Year Outcomes of Panretinal Photocoagulation vs Intravitreous Ranibizumab for Proliferative Diabetic Retinopathy
A Randomized Clinical Trial

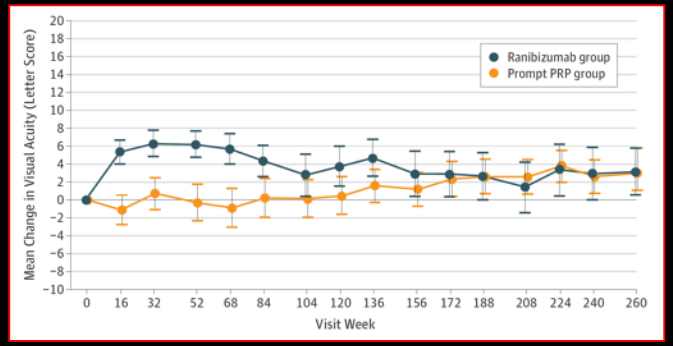


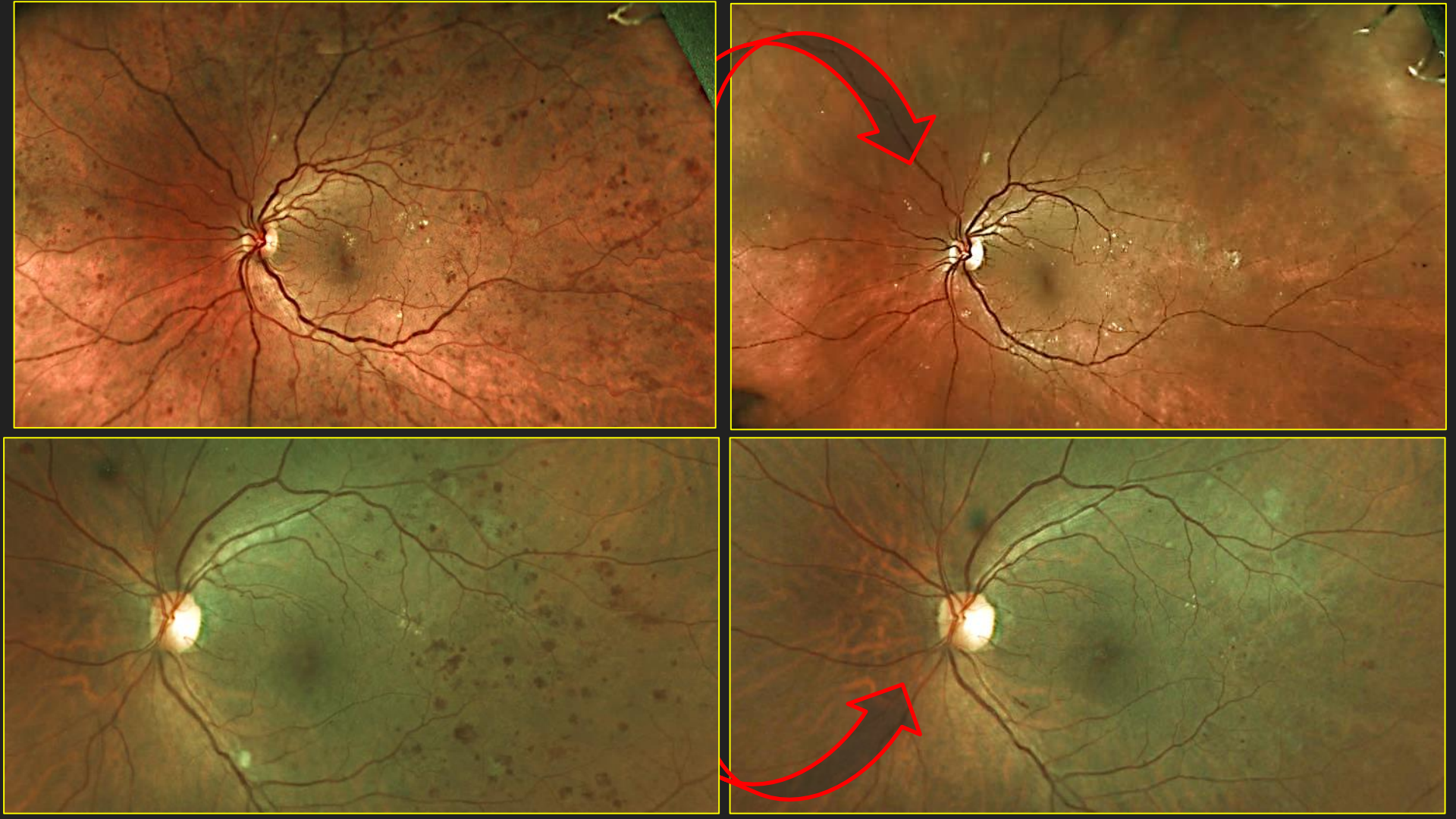
Table 2. Change in Diabetic Retinopathy

Variable	No. (%) Ranibizumab Group	No. (%) PRP Group	Adjusted Difference, % (95% CI)[a]
Diabetic Retinopathy on Fundus Photographs at 5 y[b]			
No. of eyes	90	93	NA
Eyes without PDR (≤level 60)	39 (43)	34 (37)	NA
Eyes with regressed NV (level 61A)	25 (28)	31 (33)	NA
Eyes with active NV (≥level 61B)	26 (29)	28 (30)	NA
Eyes improving from PDR (≥level 61) to NPDR (≤level 53)	30 (33)	NA	NA
Eyes without retinopathy (≤level 20)	9 (10)	NA	NA
Eyes improving ≥2 steps in diabetic retinopathy severity on fundus photographs at 5 y[c]	41 (46)	NA	NA

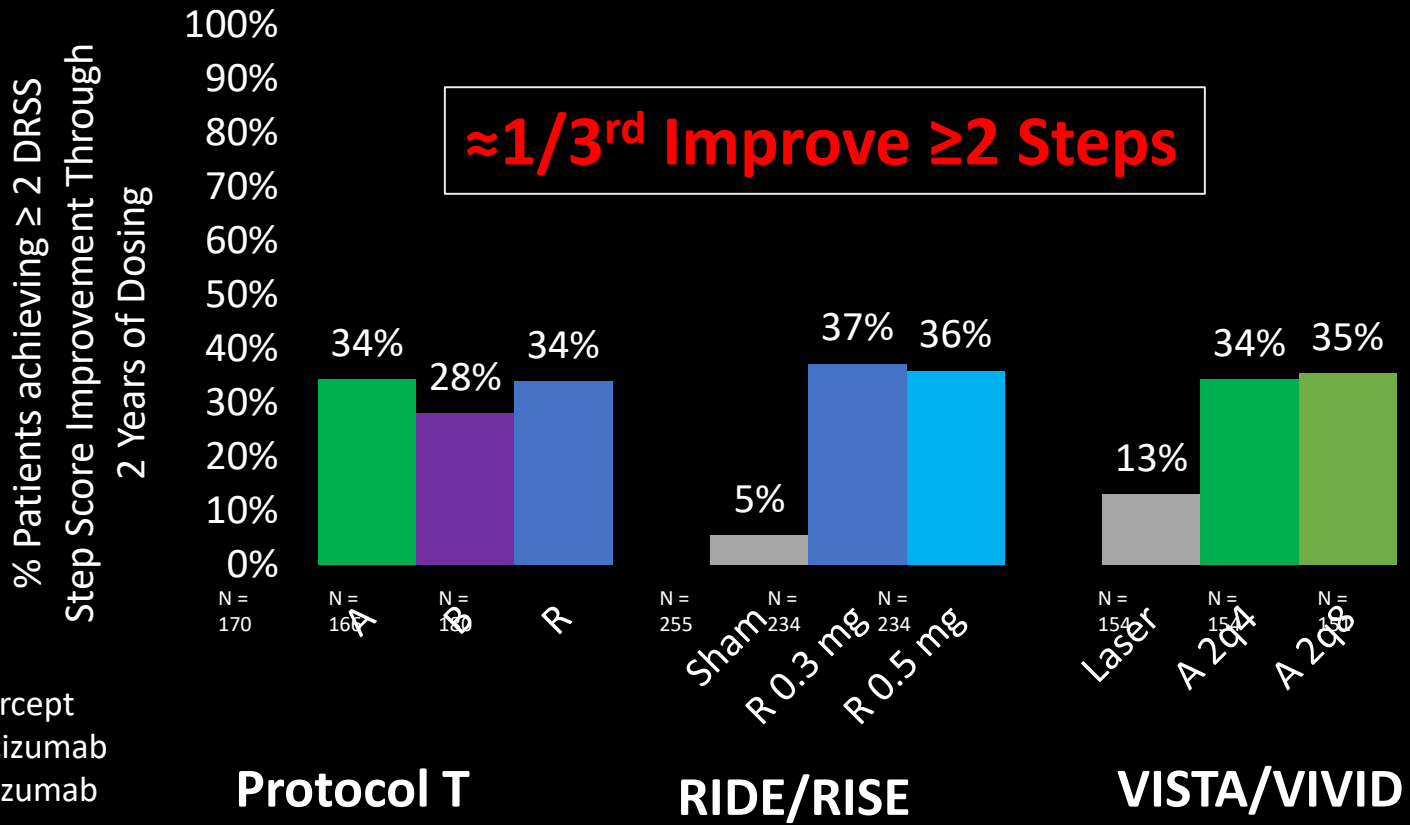
Patients with active NV at year 5 = identical in both arms

Protocol S 5-Year Data. *JAMA Ophthalmology*. 2018

Shift Towards DR

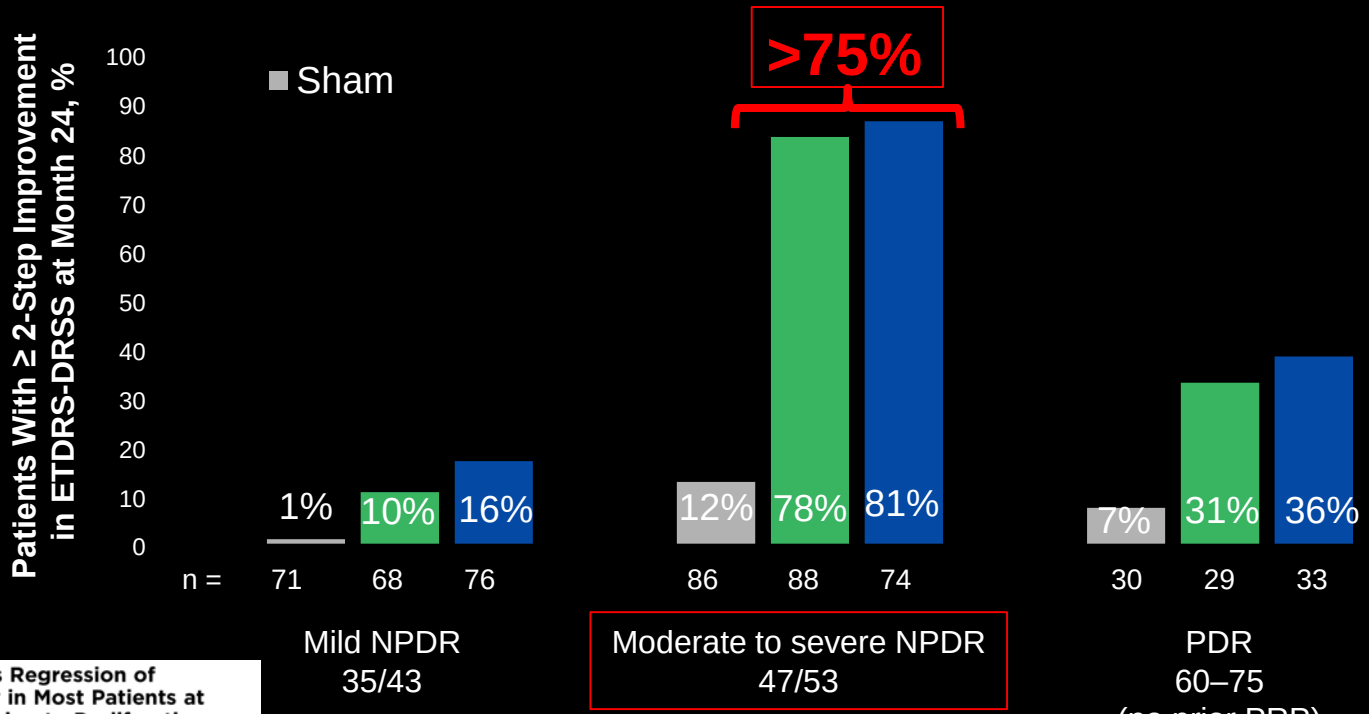


DRSS Improvements with Anti-VEGF Dosing



A = aflibercept
B = bevacizumab
R = ranibizumab

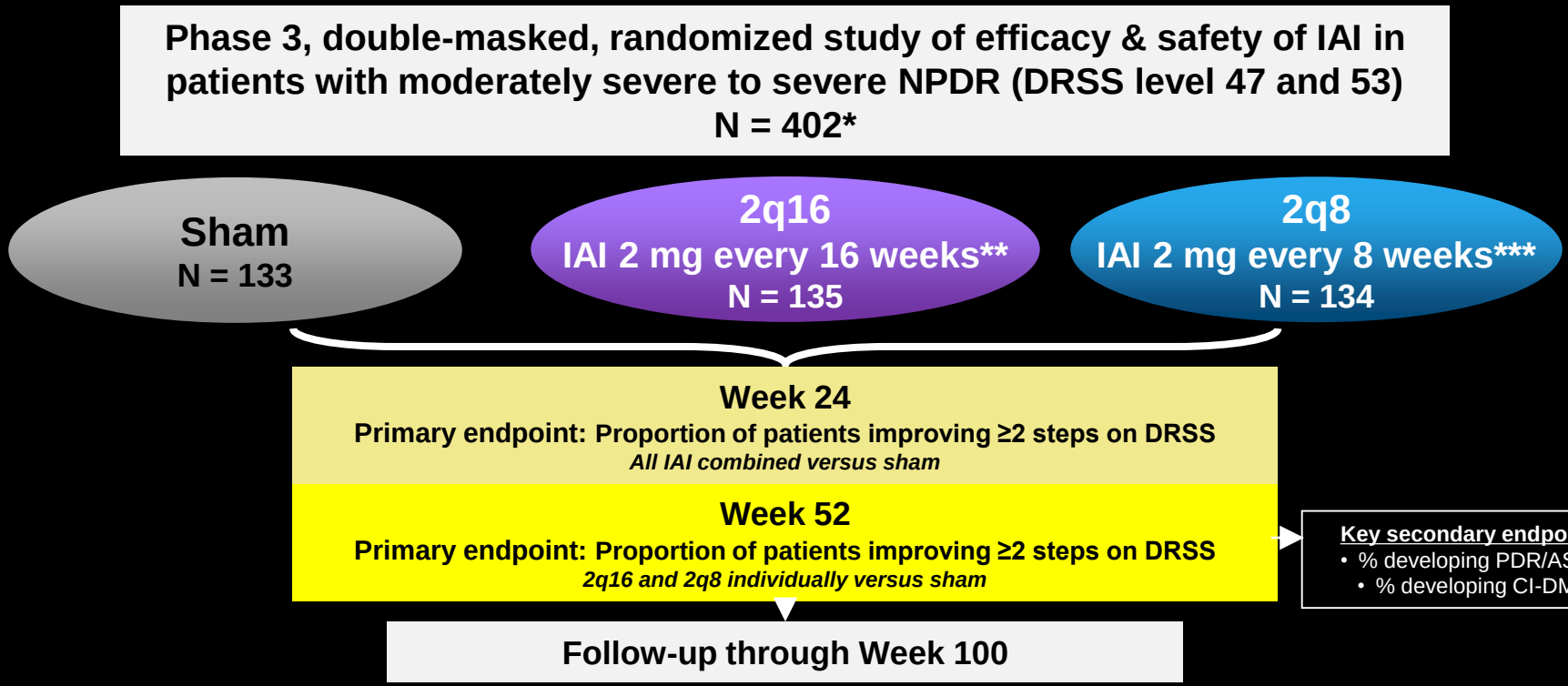
DR Improvements by Baseline DR Severity



Ranibizumab Induces Regression of Diabetic Retinopathy in Most Patients at High Risk of Progression to Proliferative Diabetic Retinopathy

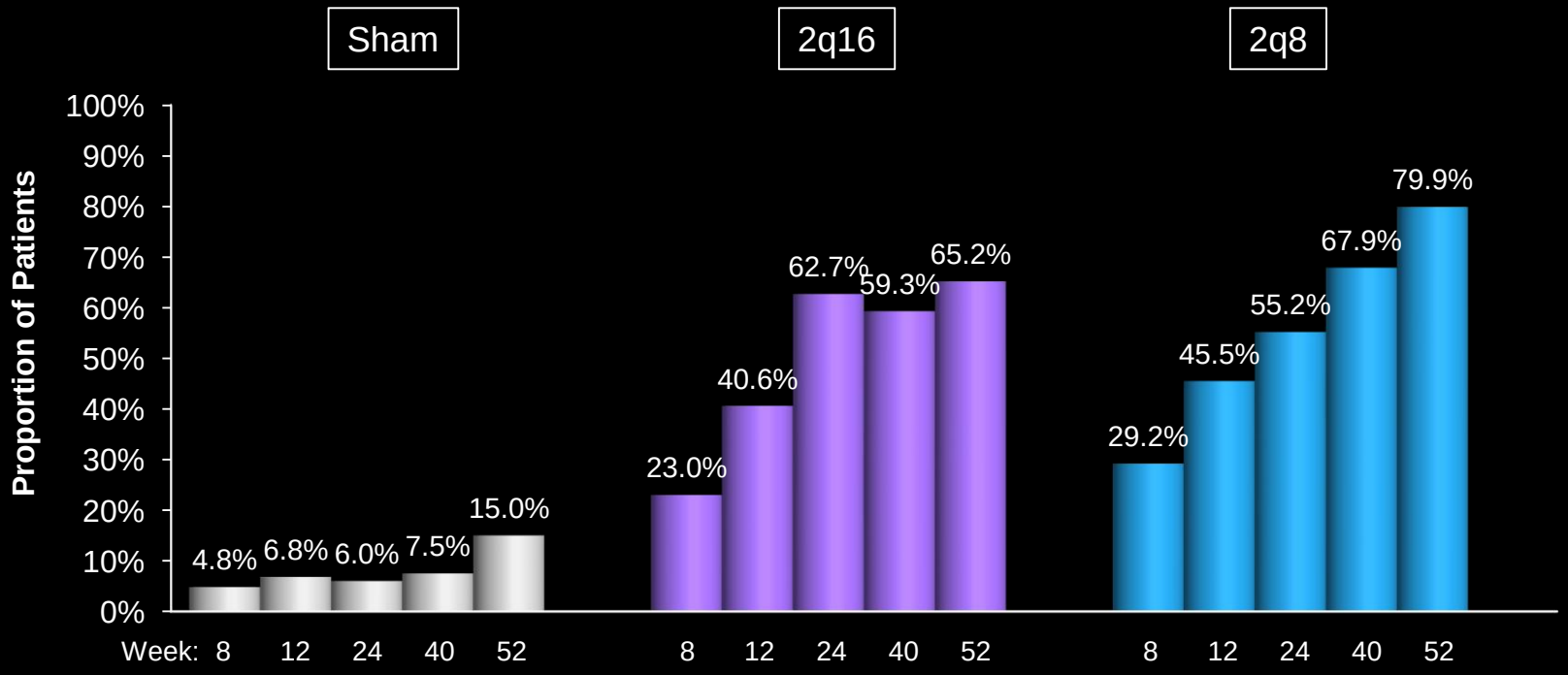
Charles C. Wykoff, MD, PhD,[1] David A. Eichenbaum, MD,[2] Daniel B. Roth, MD,[3] Lauren Hill, MS,[4] Anne E. Fung, MD,[4] Zdenka Haskova, MD, PhD[4]

Study Design



*Patients were stratified by baseline DRSS level; **After 3 initial monthly doses and 1 q8 interval; ***After 5 initial monthly doses, flexible treatment schedule after week 52.
2q8, 2 mg every 8 weeks; 2q16, 2 mg every 16 weeks; q8, every 8 weeks; ASNV, anterior segment neovascularization; CI-DME, center-involved diabetic macular edema; DRSS, Diabetic Retinopathy Severity Score; IAI, intravitreal aflibercept injection; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

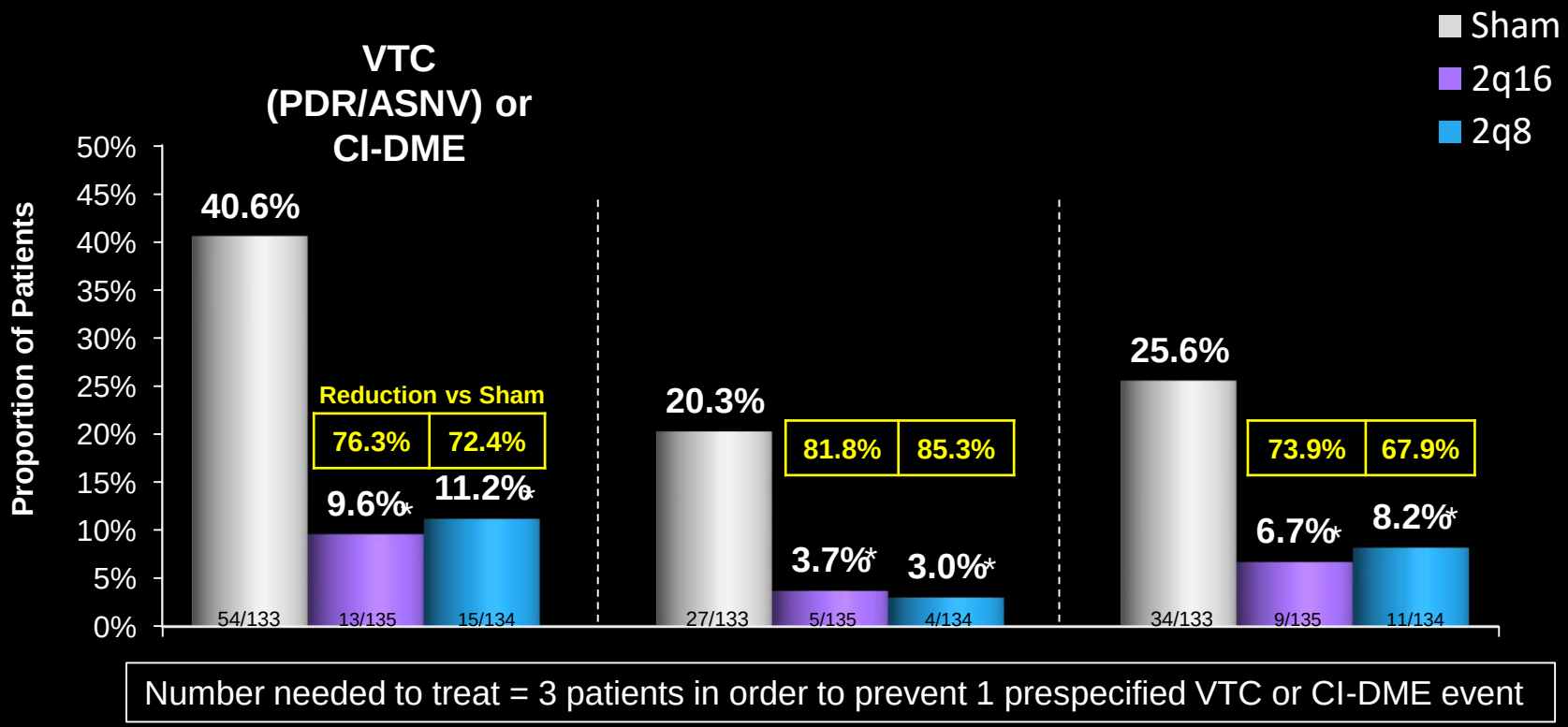
Proportion of Patients with ≥2-Step Improvement from Baseline in DRSS



LOCF; Sham n=133, 2q16 n=135, 2q8 n=134

Intravitreal Aflibercept for Moderately Severe to Severe Non-Proliferative Diabetic Retinopathy: The Phase 3 PANORAMA Study. Wykoff *et al*. Angiogenesis 2019.

Proportion of Patients Developing a Vision Threatening Complication (VTC) or Center Involved (CI)-DME through Week 52



Number needed to treat = 3 patients in order to prevent 1 prespecified VTC or CI-DME event

VTC = Vision threatening complication, PDR/ASNV; FAS; Sham n=133, 2q16 n=135, 2q8 n=134

Intravitreal Aflibercept for Moderately Severe to Severe Non-Proliferative Diabetic Retinopathy: The Phase 3 PANORAMA Study. Wykoff *et al*. Angiogenesis 2019.

p < 0.0003 vs. sham

Frequent Visits
Multiple Injections

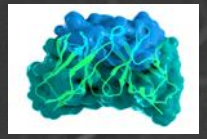
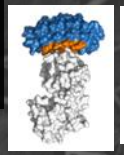
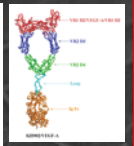
Destructive Laser

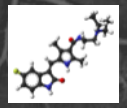
Forward

Creating Our Future

Additional Anti-VEGF Agents

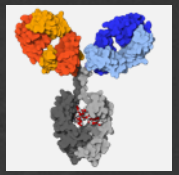
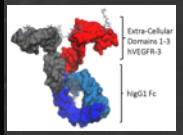
Brolucizumab
Abicipar
Conbercept
KSI-301
GB-102

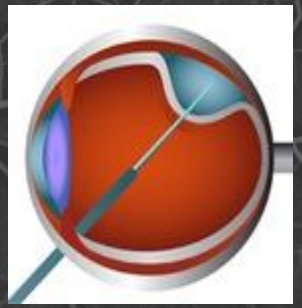
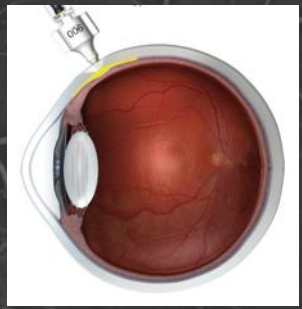


New Targets

Ang-2
IL-6
PIGF
Integrins
VEGF-C & D
Plasma kallikrein
Micochondria

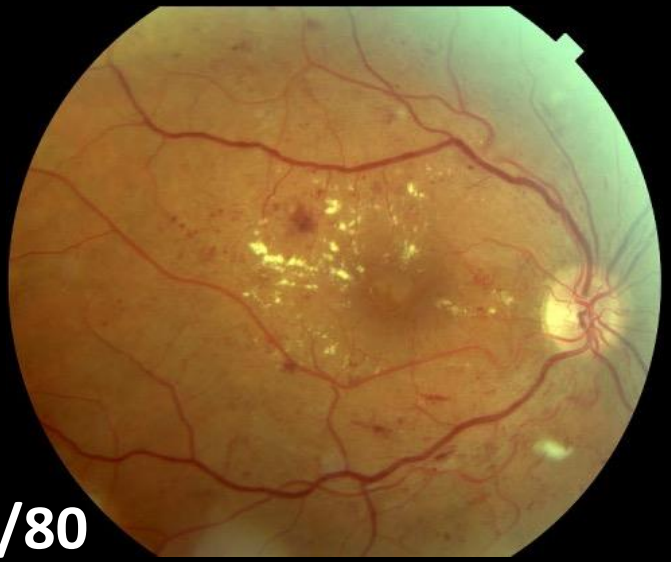



Drug Delivery Approaches

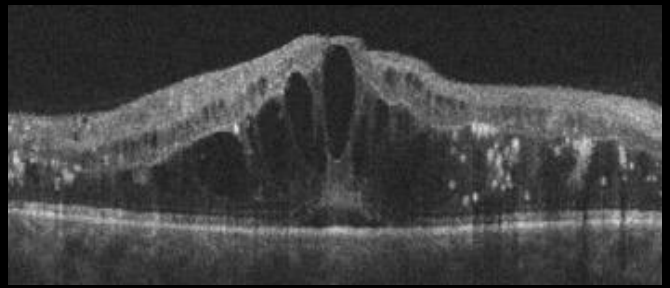



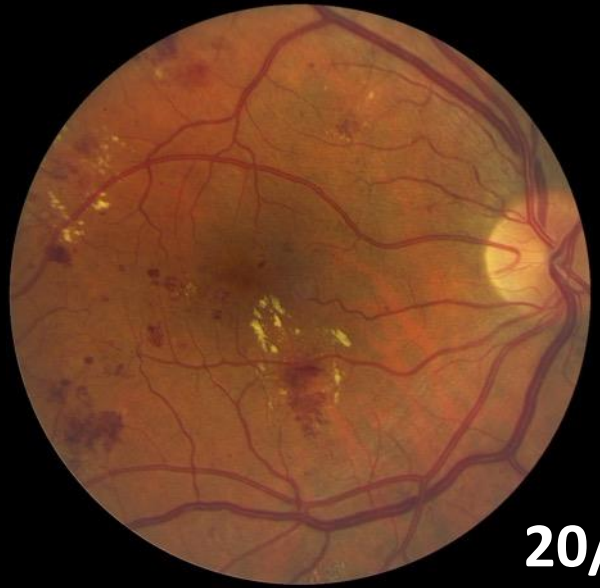

KSI-301: *Improved Durability*

Goals of Treatment

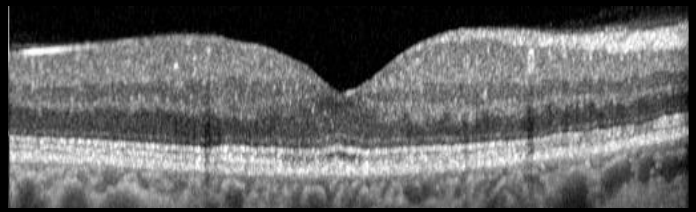


20/80





20/20



DISCUSSION

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Diabetic Eye Disease

KSI-301 Phase 1b

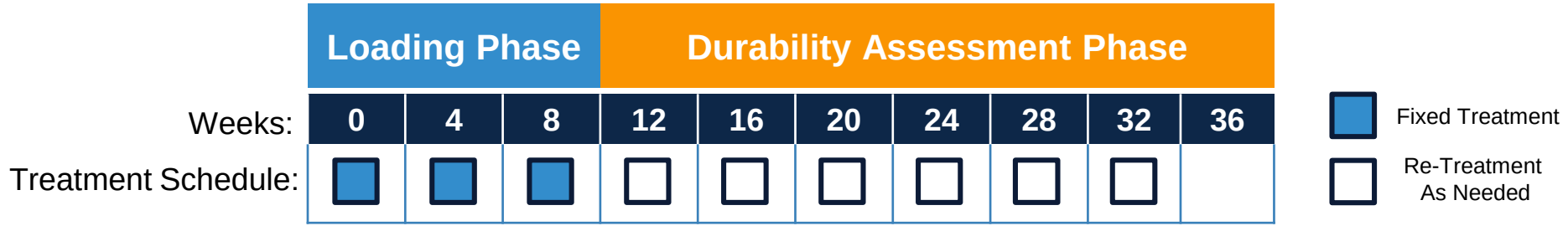
insight into durability among treatment naïve subjects

Randomized, open label study to evaluate multidose safety, efficacy & durability (n=105)

wAMD (n=35) | **DME** (n=35) | **RVO** (n=35)

Randomized 1:3

KSI-301 2.5 mg (50 μL) | KSI-301 5 mg (100 μL)



wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion;
Clinicaltrials.gov ID: NCT03790852

KSI-301 Phase 1b Retreatment Criteria
prespecified by disease state

- **DME and RVO**
  - Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12 or the prior visit, *OR*
  - Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening DME/RVO disease activity

Investigators can retreat at their discretion if significant disease activity is present that does not meet the above criteria

wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion; CST = central subfield retinal thickness; BCVA = best corrected visual acuity.
Clinicaltrials.gov ID: NCT03790852

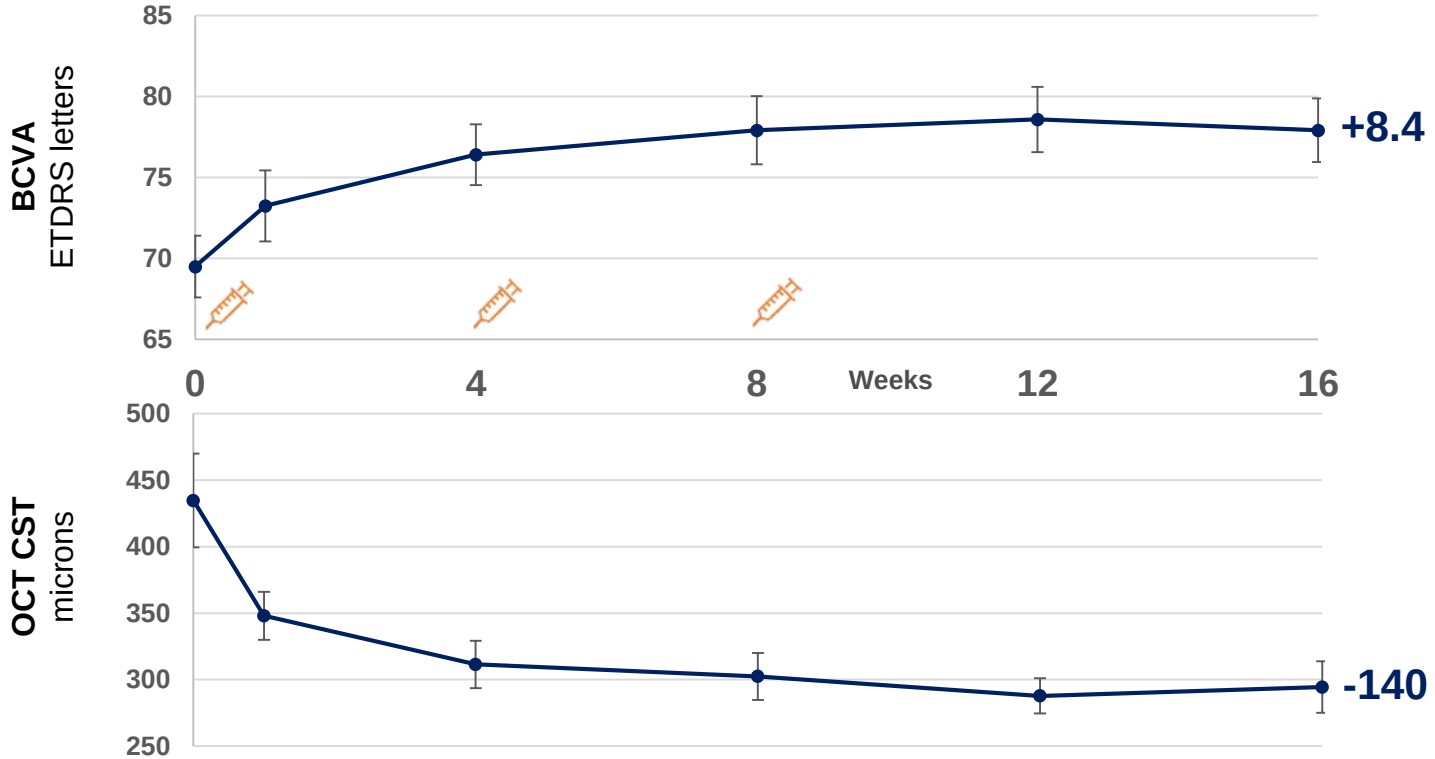
KSI-301 Phase 1b Baseline Characteristics

Variable	DME Cohort (n=34)
Age, mean (SD), years	60.7 (10.4)
Gender, n (%), female	13 (38.2)
Race, n (%), White	28 (82.4)
BCVA, mean (SD), ETDRS letters	66.8 (10.3)
BCVA, Snellen 20/40 or better, n (%)	16 (47.1)
OCT CST, mean (SD), microns	449 (109)
DRSS Score	
35 (Mild NPDR), n (%)	2 (6)
47 (Moderate NPDR), n (%)	23 (70)
53 (Severe NPDR), n (%)	5 (15)
65 (Moderate PDR), n(%)	3 (9)

Includes all patients randomized as of 10 October 2019. SD= standard deviation; BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

Efficacy of KSI-301 in DME

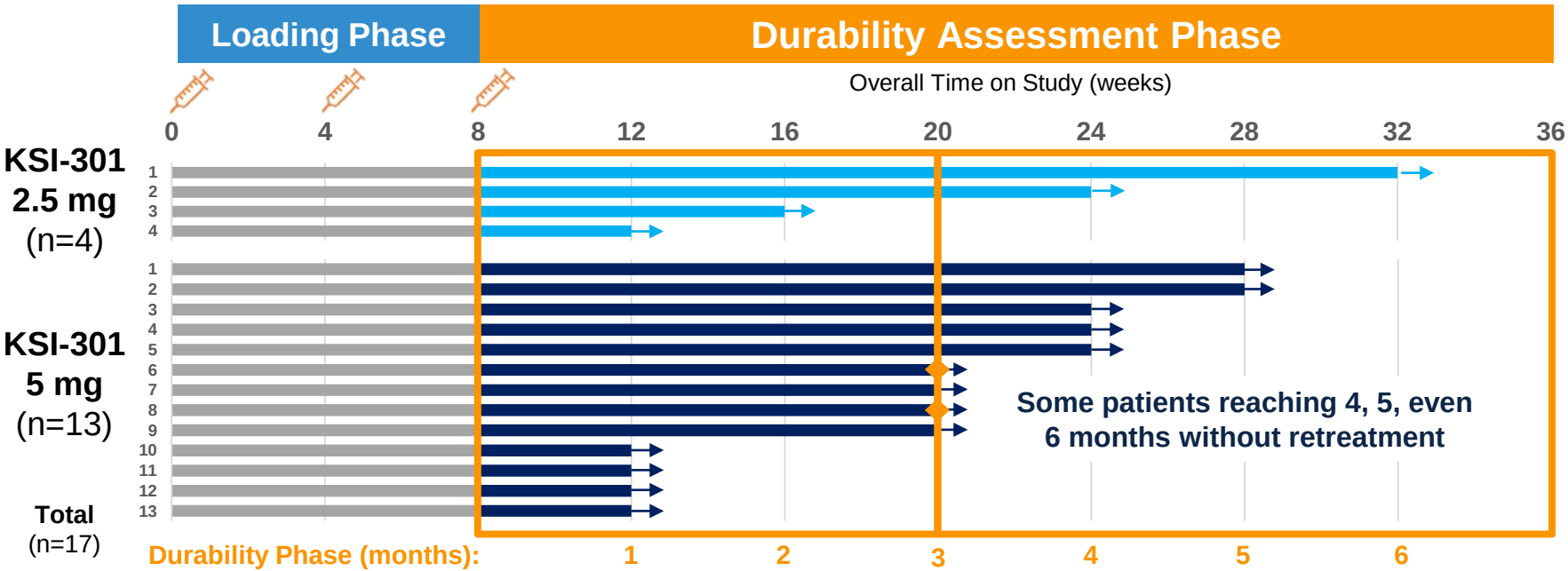
change from baseline to week 16 in mean BCVA & OCT



Interim data. Includes only randomized patients that reached Week 16 visit by the data cutoff date of 10 Oct 2019; 2.5 & 5 mg doses pooled. Error bars represent standard error of the mean. OCT CST values are site reported.
BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

n= 12 **Patients reaching Week 16 visit by data cutoff**

KSI-301 in DME: *3 loading doses can provide sustained disease control of 3 months or longer*



No patient has been retreated yet before 3 months

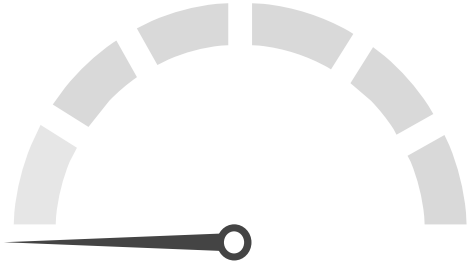
18% (2/11) retreated at 3 months

82% (9/11) have gone longer than 3 months after the last loading dose

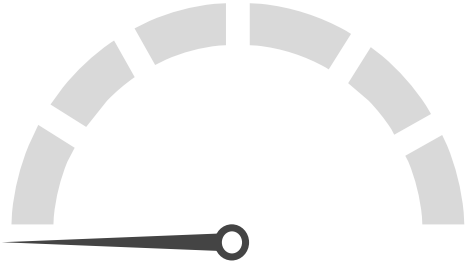
◆ Retreatment with KSI-301
→ Continuing follow-up

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

Healthcare burden to diabetic patients is increased significantly because of DME treatment



Aflibercept*
5 Loading doses

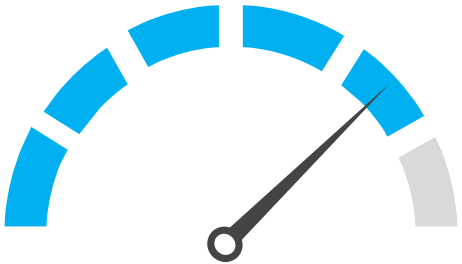


Brolucizumab*
5 Loading doses

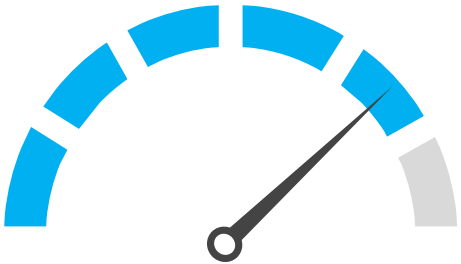
	Maintenance Phase				
	8 Weeks	**12 Weeks**	**16 Weeks**	**20 Weeks**	**24 Weeks**
Aflibercept					
Brolucizumab					

*According to dosing used in the Phase 3 DME trials for aflibercept and brolucizumab.

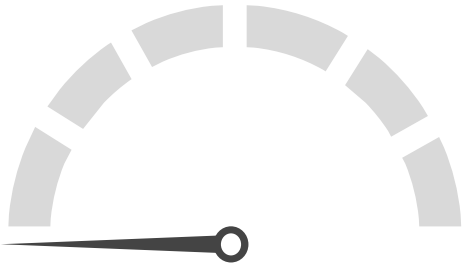
Reducing treatment burden should start with fewer injections during the loading phase



Aflibercept*
5 Loading doses



Brolucizumab*
5 Loading doses

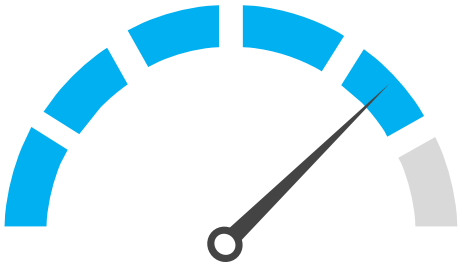


Next Gen
Only 3 Loading doses

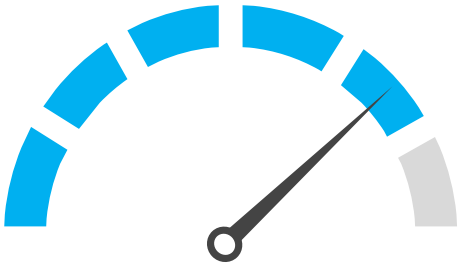
	Maintenance Phase				
	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks
Aflibercept					
Brolucizumab					
Next Gen					

*According to dosing used in the Phase 3 DME trials for aflibercept and brolucizumab.

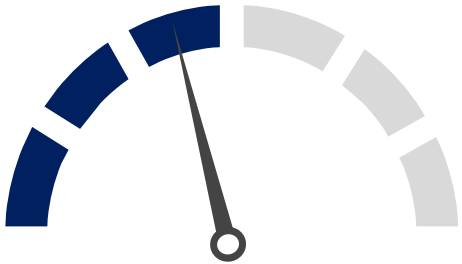
A next-generation DME medicine should also provide disease control for a longer time during the maintenance phase



Aflibercept*
5 Loading doses



Brolucizumab*
5 Loading doses



Next Gen
Only 3 Loading doses

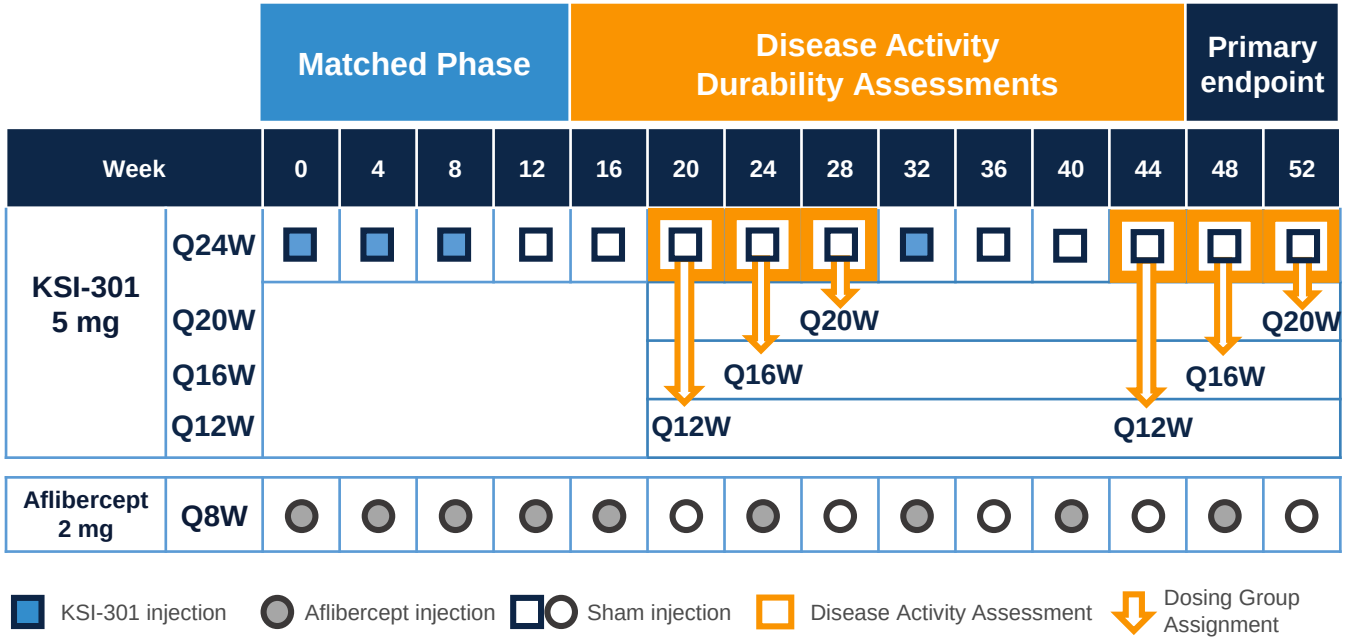
	Maintenance Phase				
	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks
Aflibercept					
Brolucizumab					
Next Gen					

*According to dosing used on the Phase 3 DME trials for aflibercept and brolucizumab.

KSI-301 Potential Study Design in DME

Dosing with KSI-301 as infrequently as every 6 months

- Randomized study vs aflibercept
- Only 3 loading doses
- KSI-301 dosing: every 12, 16, 20 or 24 weeks depending on pre-specified disease activity assessments*

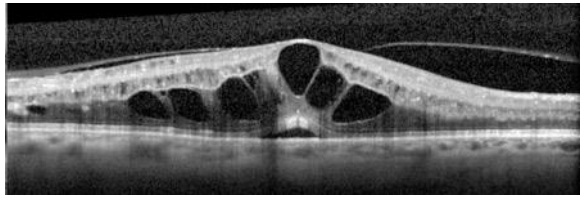


*After the loading phase

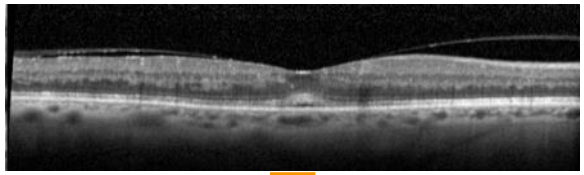
Is a treatment interval of 5 months possible in DME (after only 3 loading injections?)

Case Example of KSI-301 5 mg in the Phase 1b Study

DAY 1

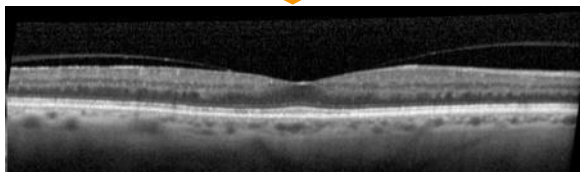


WEEK 1



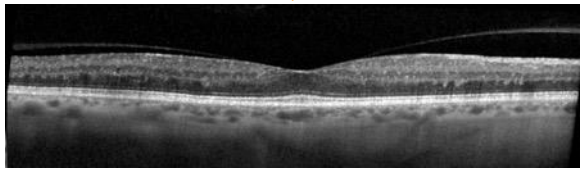
After 1 dose

MONTH 3



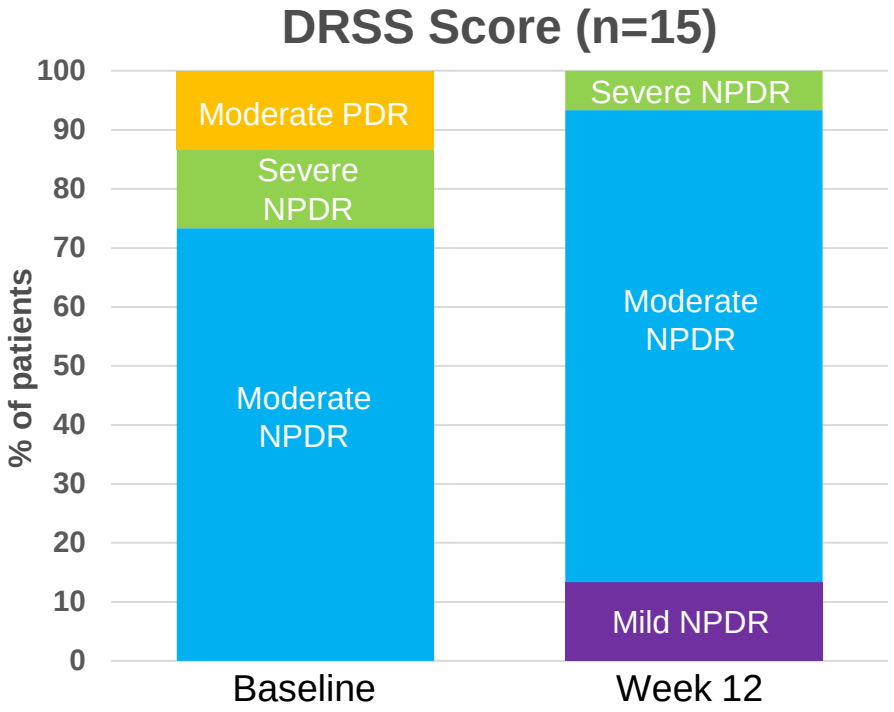
1 month after 3 loading doses

MONTH 7



No retreatment required for 5 months

KSI-301 in DR: *signs of disease modification are seen within 12 weeks*



All patients improved or maintained their DRSS Score

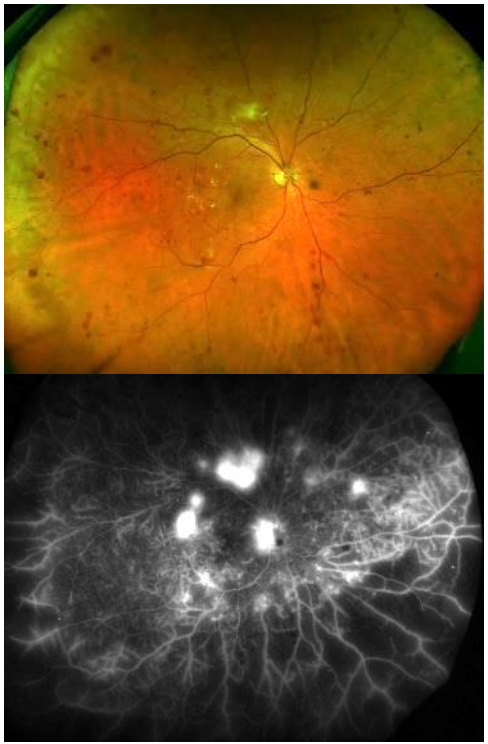
Change from Baseline in DRSS at Week 12 (n=15)	N (%)
Maintained	9 (60)
1-step improvement	2 (13)
≥2-step improvement	4 (27)

Additionally, no patient has developed a PDR event

Includes only randomized patients that reached Week 12 and have gradable color fundus photos by the data cutoff date of 10 Oct 2019 DR= Diabetic Retinopathy; PDR= Proliferative DR; NPDR= Non-Proliferative DR; DRSS = DR Severity Scale. Vision-threatening PDR defined as PDR, need for panretinal photocoagulation or vitrectomy

The sustained disease control of only 3 loading doses of KSI-301 is also seen in proliferative diabetic retinopathy

DAY 1
Proliferative DR (DRSS 65)

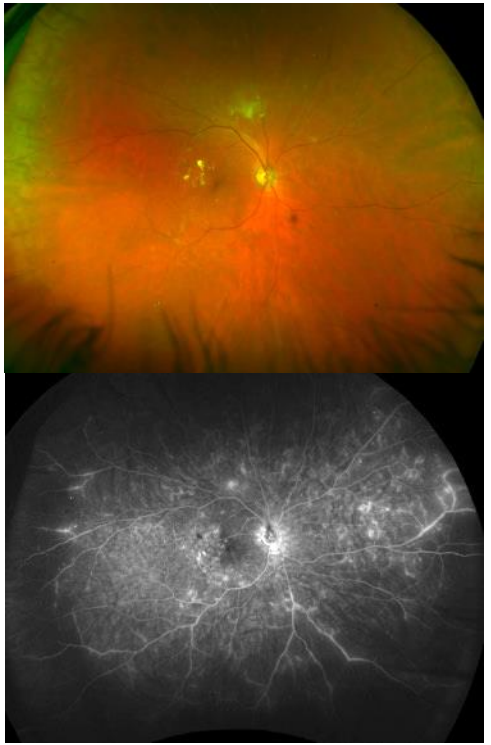


KSI-301 5 mg
3 loading doses

WEEK 12
Non-Proliferative DR (DRSS 53)

No additional doses

WEEK 22
Non-Proliferative DR (DRSS 53)

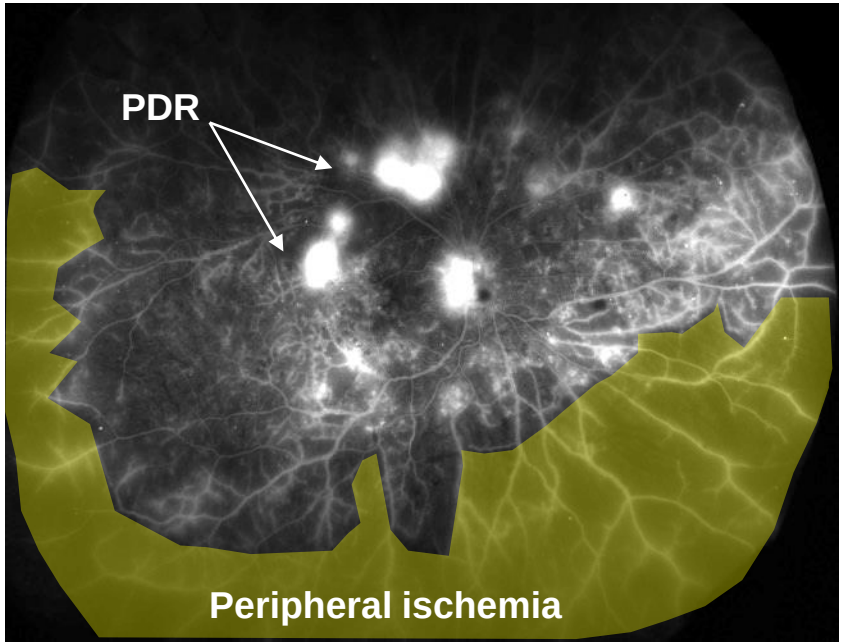


Conversion from PDR to NPDR
Fast and substantial (2-step) improvement, sustained 14 weeks after only 3 loading doses with KSI-301 5 mg

DR= Diabetic Retinopathy; PDR= Proliferative DR; NPDR= Non-Proliferative DR; DRSS = DR Severity Scale; DRSS 53 = Severe NPDR; DRSS 65 = Moderate PDR

In addition to the conversion from PDR to NPDR, this patient exhibits signs of peripheral vascular reperfusion

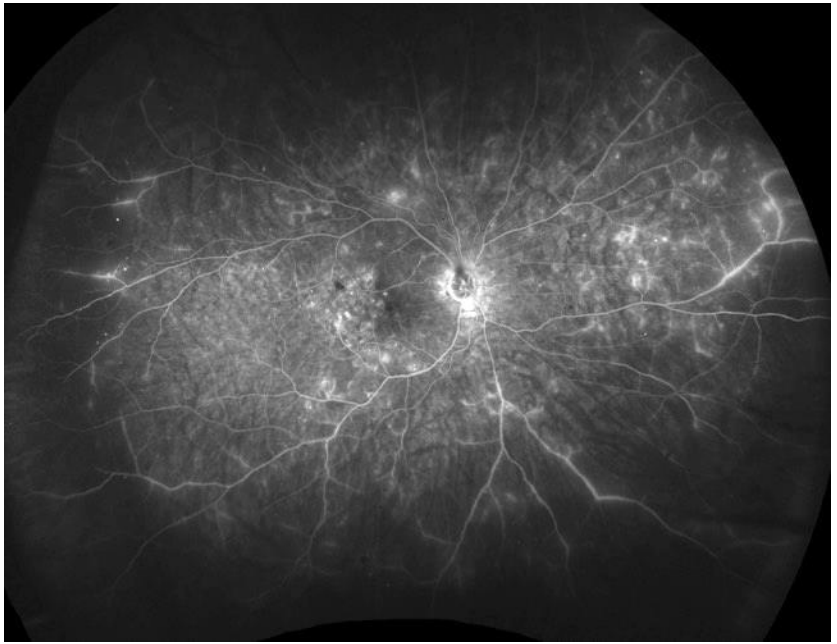
DAY 1
Proliferative DR (DRSS 65)



KSI-301 5 mg

14 weeks after the last loading dose

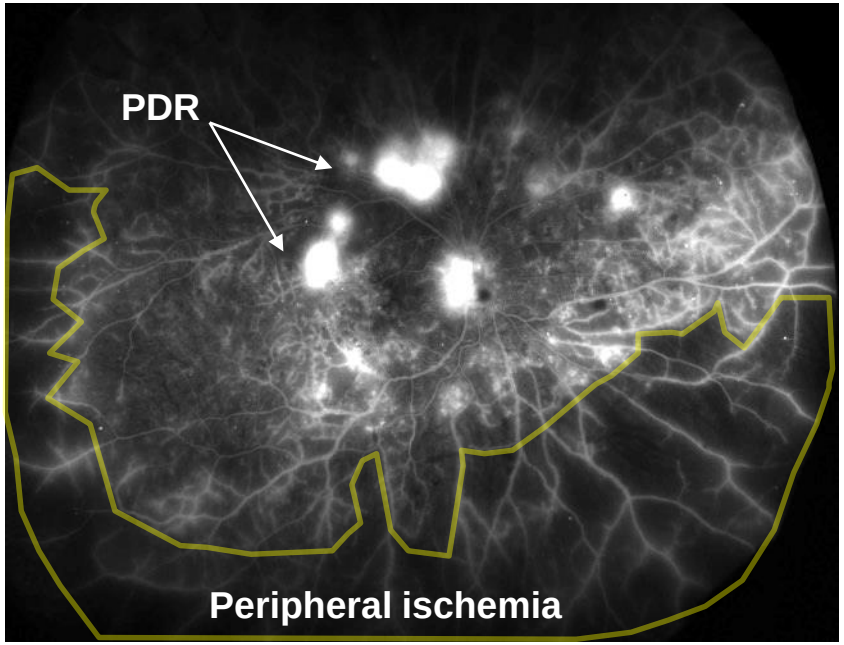
WEEK 22
Non-Proliferative DR (DRSS 53)



DR= Diabetic Retinopathy; PDR= Proliferative DR; NPDR= Non-Proliferative DR; DRSS = DR Severity Scale; DRSS 53 = Severe NPDR; DRSS 65 = Moderate PDR

In addition to the conversion from PDR to NPDR, this patient exhibits signs of peripheral vascular reperfusion

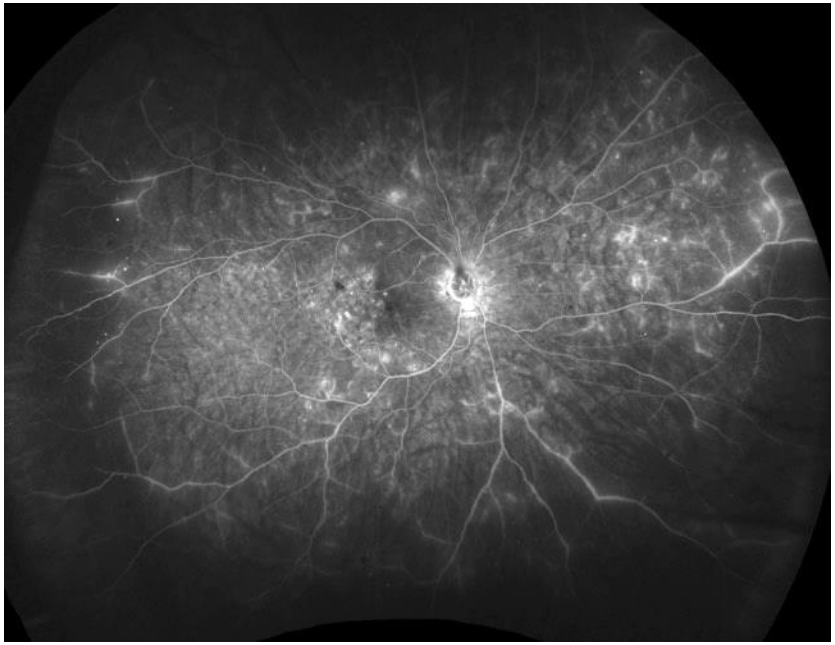
DAY 1
Proliferative DR (DRSS 65)



KSI-301 5 mg

14 weeks after the last loading dose

WEEK 22
Non-Proliferative DR (DRSS 53)



PDR= Proliferative DR; NPDR= Non-Proliferative DR; DRSS = DR Severity Scale; DRSS 53 = Severe NPDR; DRSS 65 = Moderate PDR

KSI-301 Potential Study Design in NPDR

No loading doses and dosing as infrequently as every 6 months

- Current standard of care is close observation
- No loading doses
- Dosing every 4 or 6 months with KSI-301

		Fixed Dosing												PE
Week		**0**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**	**52**
KSI-301 5 mg	**Q16W**	■				■				■				■	
	Q24W	■						■						■	
Sham		□				□		□		□				□	

■ KSI-301 injection □ Sham

ARSHAD KHANANI, M.D.

—

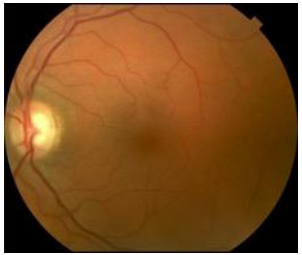
Director of Clinical Research
Sierra Eye Associates

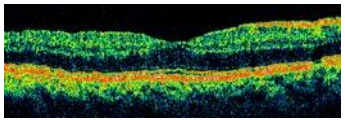
Practice Details

- Multispecialty practice with 6 physicians
- 2 retina specialists and one retina fellow
- 80-90 patients per day
- 1-3 hours of wait time in clinic
- 31 active clinical trials
- 5 research coordinators
- 65 active staff members

Edema Formation in RVO:
Macular edema accounts for the majority of vision loss in RVO

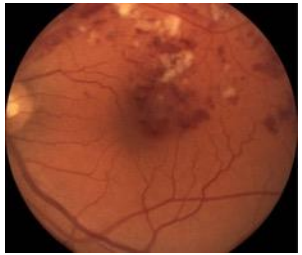
Normal

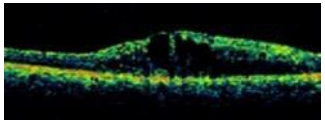


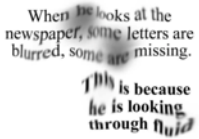


Normal VA (20/20)

BRVO







Loss of VA (variable)

Retinal vein compression and narrowing

↓

Turbulent blood flow

↓

Thrombus formation

↓

Ischemia and hypoxia

↓

Increased VEGF production

↓

Increased capillary permeability

↓

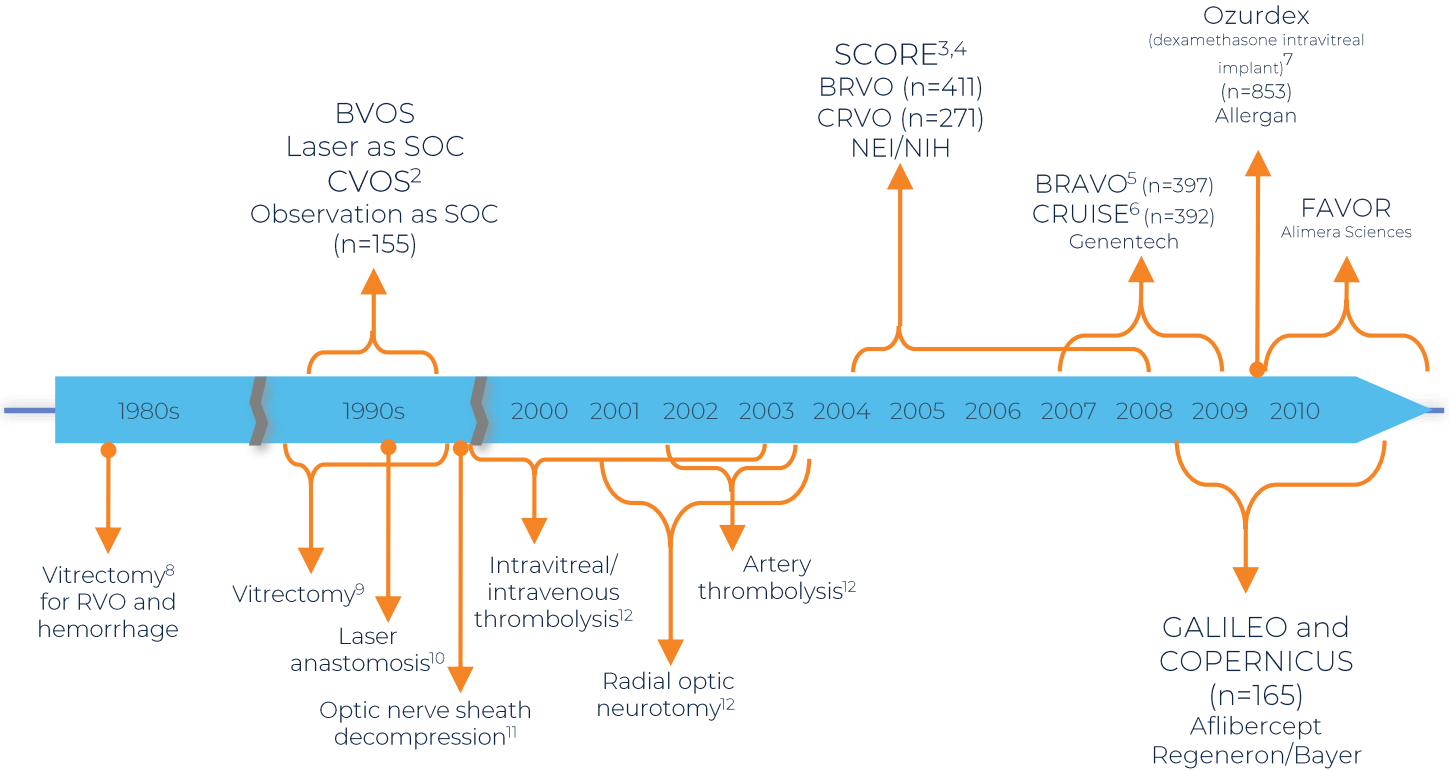
Leakage and edema

↓

Vision loss

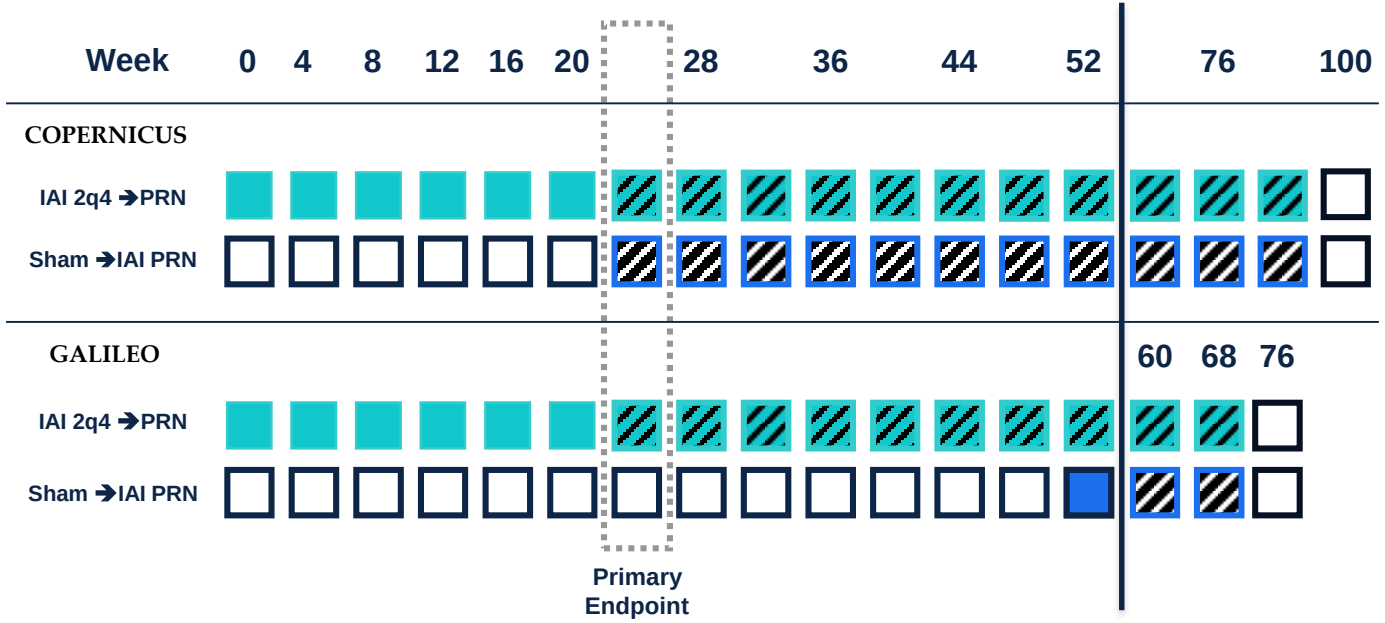
Christoffersen and Larsen. Ophthalmology. 1999;106:2054; Hayreh. Indian J Ophthalmol. 1994;42:109; Noma et al. Graefes Arch Clin Exp Ophthalmol. 2006;244:309; Noma et al. Ophthalmology. 2009;116:87.

Interventions in Retinal Vein Occlusion



SOC = standard of care. 1. BVOS Group. Am J Ophthalmol. 1984;98:271; 2. CVOS Group M. Ophthalmology. 1995;102:1425; 3. Ip et al. Arch Ophthalmol. 2009;127:1101; 4. Scott et al. Arch Ophthalmol. 2009;127:1115; 5. Campochiaro et al. Ophthalmology. 2010;117:1102; 6. Brown et al. Ophthalmology. 2010;117:1124; 7. Haller et al. Ophthalmology. 2010;117:1134; 8. Yeshaya and Treister. Ann Ophthalmol. 1983;15:615; 9. Amirikia et al. Ophthalmology. 2001;108:372; 10. McAllister et al. Arch Ophthalmol. 1995;113:456; 11. Dev and Buckley. Ophthalmic Surg Lasers. 1999;30:181; 12. Shahid et al. Br J Opthalmol. 2006;90:627.

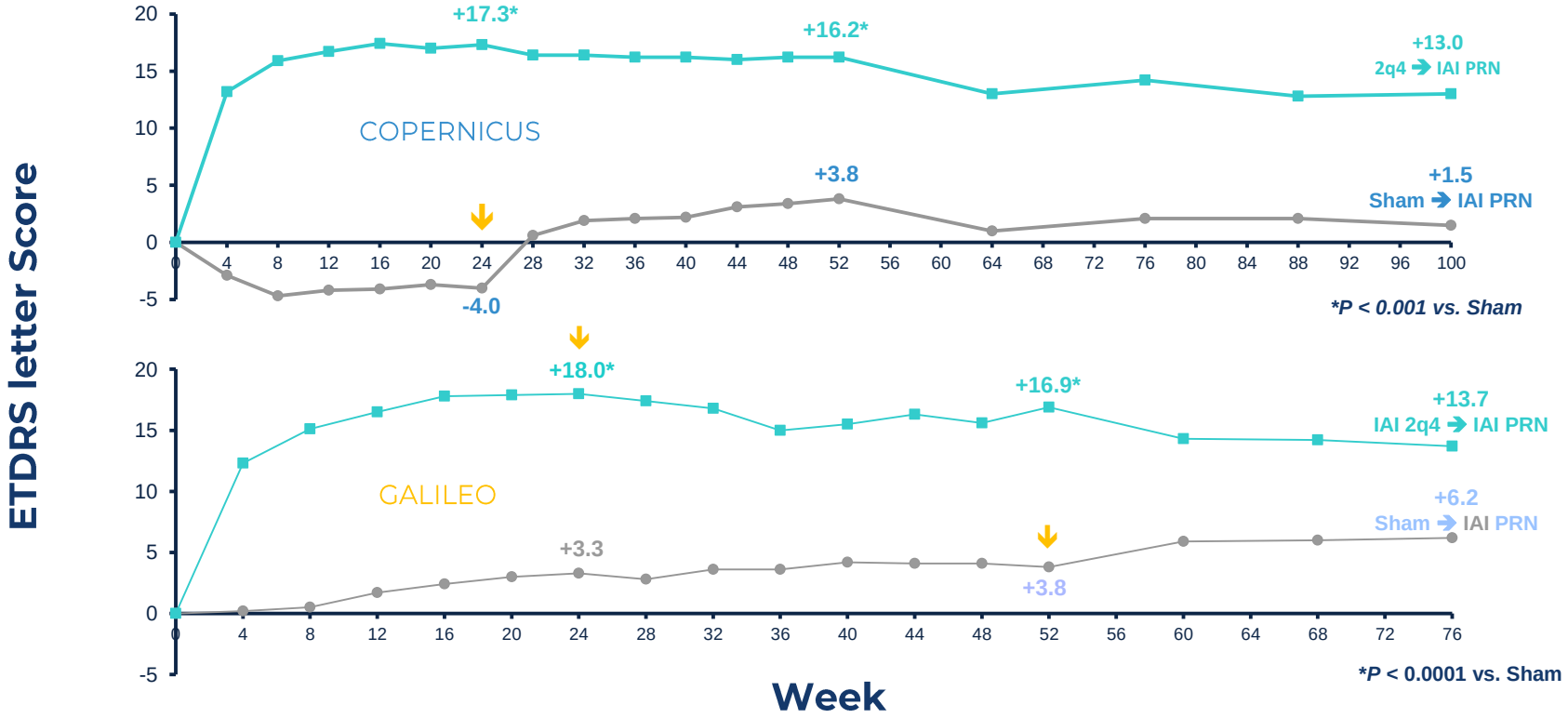
Aflibercept Phase 3 CRVO Program
Study Schedule



IAI 2q4
Sham
IAI PRN
IAI Required
Visit w/o injection

Re-treatment Criteria
- Increase of > 50µm from lowest previous measurement
- New/persistent cystic retinal changes or sub-retinal fluid or persistent diffuse edema ≥ 250 µm in central subfield
- Loss of ≥5 letters from best previous measurement with any increase in CRT
- Increase of ≥ 5 letters between current and most recent visit

Mean Change in Best-Corrected Visual Acuity Over 100 Weeks#

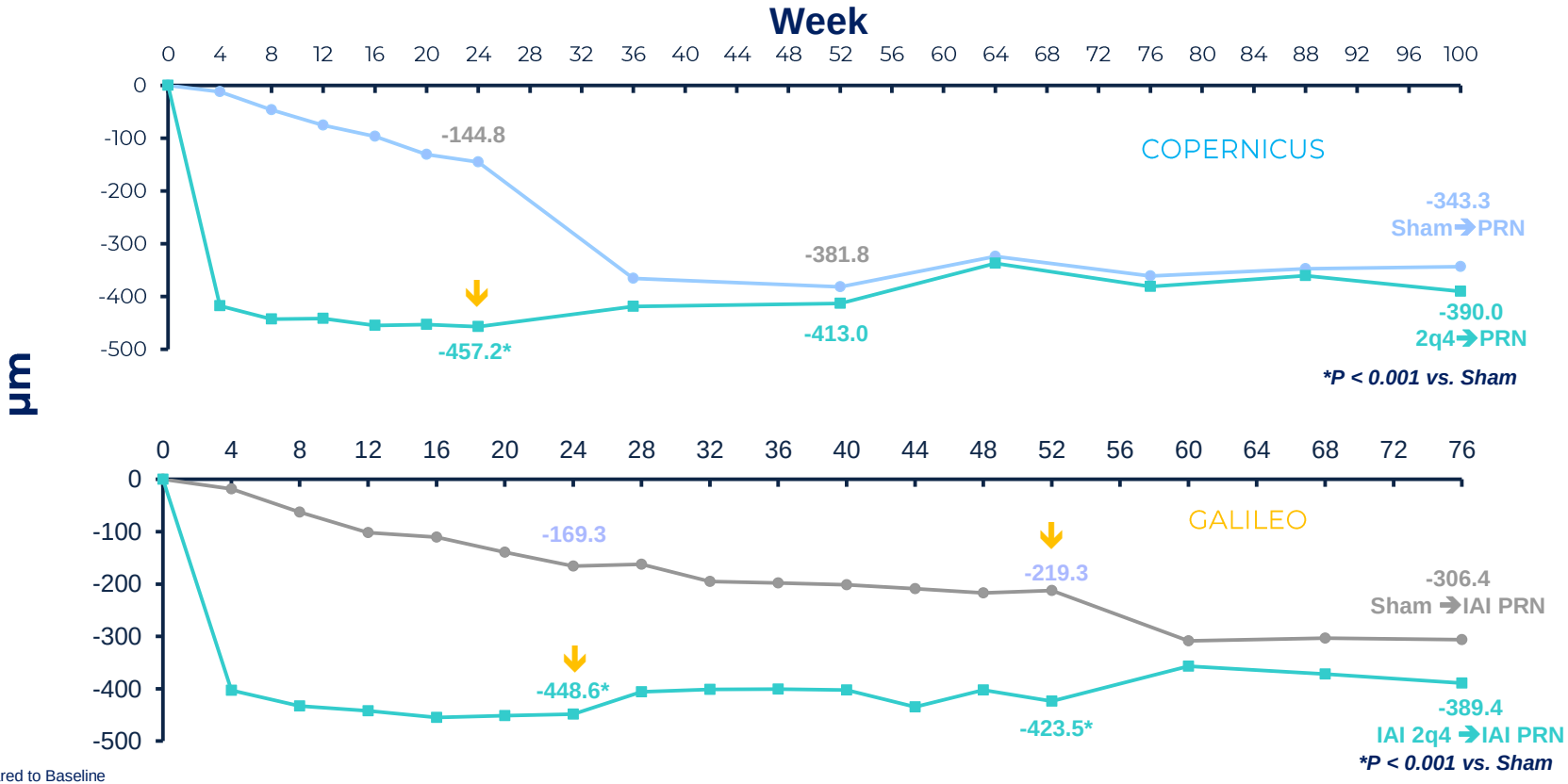


#Compared to Baseline

↓ Patients crossed over from Fixed IAI to IAI PRN or from Sham to IAI PRN

LOCF; full analysis set

Mean Change in Central Retinal Thickness Over 100 Weeks#



#Compared to Baseline

↓ Patients crossed over from Fixed IAI to IAI PRN or from Sham to IAI PRN

LOCF; full analysis set

LEAVO Study of CRVO

Intravitreal Ranibizumab vs Aflibercept vs Bevacizumab for Macular Edema From Retinal Vein Occlusion (LEAVO STUDY)

- Objective:

  To determine whether intravitreal aflibercept or bevacizumab compared with ranibizumab results in a noninferior mean change in vision at 100 weeks for eyes with CRVO-related macular edema.

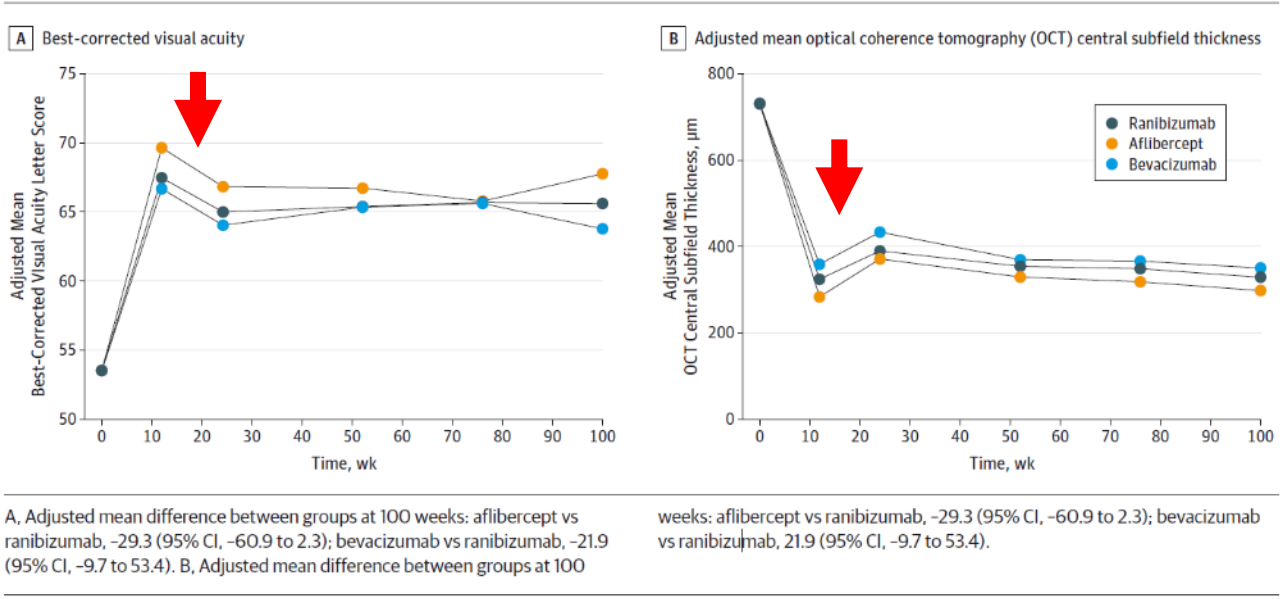
Hykin P, Prevost AT, Vasconcelos JC, et al; LEAVO Study Group. JAMA Ophthalmol. Published online August 29, 2019. doi:10.1001/jamaophthalmol.2019.3305

LEAVO Study of CRVO

Study Design

- Randomized 1:1:1 to aflibercept, bevacizumab, or ranibizumab.
- Participants in all study groups had mandated injection at baseline and 4, 8, and 12 weeks.
- From week 16 through 96, treatment was given if 1 or more of the retreatment criteria were met.

Results: Adjusted Mean BCVA Letter Score and Adjusted Mean OCT CST Across Groups to 100 Weeks



A, Adjusted mean difference between groups at 100 weeks: aflibercept vs ranibizumab, −29.3 (95% CI, −60.9 to 2.3); bevacizumab vs ranibizumab, −21.9 (95% CI, −9.7 to 53.4). B, Adjusted mean difference between groups at 100 weeks: aflibercept vs ranibizumab, −29.3 (95% CI, −60.9 to 2.3); bevacizumab vs ranibizumab, 21.9 (95% CI, −9.7 to 53.4).

Reduction from peak vision and OCT occurs when monthly dosing shifts to less often

LEAVO - Conclusions

- Aflibercept was non-inferior to ranibizumab.
- Bevacizumab was not non-inferior to ranibizumab.
- Visual acuity gains increased from week 24 and were maintained to 100 weeks supporting every 4- to 8-weekly visits during the second year of follow-up regimen.

- The visual gains by 24 weeks (eg, mean [SD] in the aflibercept group, 13.4 [16.4]) were less than those reported in other trials, in which 6, not 4, mandated injections were given.

Summary: RVO trials

	CRUISE	BRAVO	GALILEO/ COPERNICUS	VIBRANT	SCORE2	LEAVO	RAVEN/ RAPTOR
Indication	CRVO	BRVO	CRVO	BRVO	CRVO	CRVO	CRVO/BRVO
Drug	Ranibizumab	Ranibizumab	Aflibercept	Aflibercept	Bevacizumab	Bevacizumab	Brolucizumab
Loading doses	6	6	6	7	6	4	6
Schedule	Monthly PRN	Monthly PRN	Monthly PRN	Q8W	Monthly/T&E or switch	4 to 8 weeks PRN	“Individualized” (monthly PRN)
Comparator	Sham	Sham	Sham	Grid laser	Aflibercept	Aflibercept/ ranibizumab	Aflibercept
Loading doses	-	-	-	-	6	4	6
Schedule	0.5 PRN after month 6	Rescue laser after month 3	-	Baseline +/-	Monthly/T&E or Ozurdex	4 to 8 weeks	“Individualized” (monthly PRN)
Primary Endpoint	BCVA change	BCVA change	% 3-line gainers	% 3-line gainers	BCVA change	BCVA change	BCVA change
Time	Month 6	Month 6	Week 24	Week 24	Month 6	Week 100	Week 24
End of Study	Month 12	Month 12	Week 76/100	Week 52	Month 12	Week 100	72 Weeks

Summary: RVO trials

	CRUISE	BRAVO	GALILEO/ COPERNICUS	VIBRANT	SCORE2	LEAVO	RAVEN/ RAPTOR
Indication	CRVO	BRVO	CRVO	BRVO	CRVO	CRVO	CRVO/BRVO
Sample Size	392 (1:1:1)	397 (1:1:1)	177 (3:2)/ 189 (3:2)	18 (1:1)	362 (1:1)	459 (1:1:1)	750/500
VA Score	70-25 letters	70-20 letters	73-24 letters	73-24 letters	73-19 letters	73-19 letters	78-23 letters
Previously Treated	No	No	No	No	Yes (60d washout)	Yes (90d washout)	No
Diagnosis	< 12 months	< 12 months		< 12 months	No limit	< 12 months	< 6 months
Study Design	Superiority	Superiority	Superiority	Superiority	Non-inferiority (5 letter margin)	Non-inferiority (5 letter margin)	?

Conclusions

- Anti-VEGF agents are first line treatment for RVO
- Aflibercept, ranibizumab, bevacizumab result in significant vision improvements
- Frequent injections are need to maintain vision and OCT improvements
- Clear unmet need for an anti-VEGF agent that is more durable

DISCUSSION

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RVO

KSI-301 Phase 1b

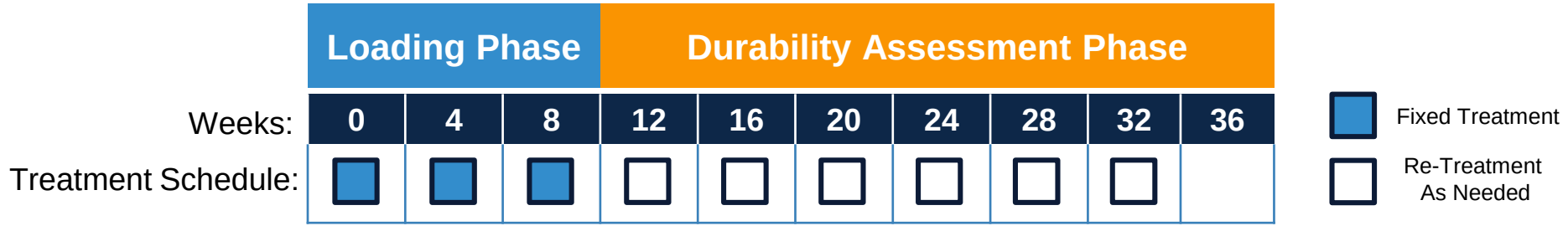
insight into durability among treatment naïve subjects

Randomized, open label study to evaluate multidose safety, efficacy & durability (n=105)

wAMD (n=35) | **DME** (n=35) | **RVO** (n=35)

Randomized 1:3

KSI-301 2.5 mg (50 μL) | KSI-301 5 mg (100 μL)



wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion;
Clinicaltrials.gov ID: NCT03790852

KSI-301 Phase 1b Retreatment Criteria
prespecified by disease state

- **DME and RVO**
  - Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12 or the prior visit, *OR*
  - Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening DME/RVO disease activity

Investigators can retreat at their discretion if significant disease activity is present that does not meet the above criteria

wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion; CST = central subfield retinal thickness; BCVA = best corrected visual acuity.
Clinicaltrials.gov ID: NCT03790852

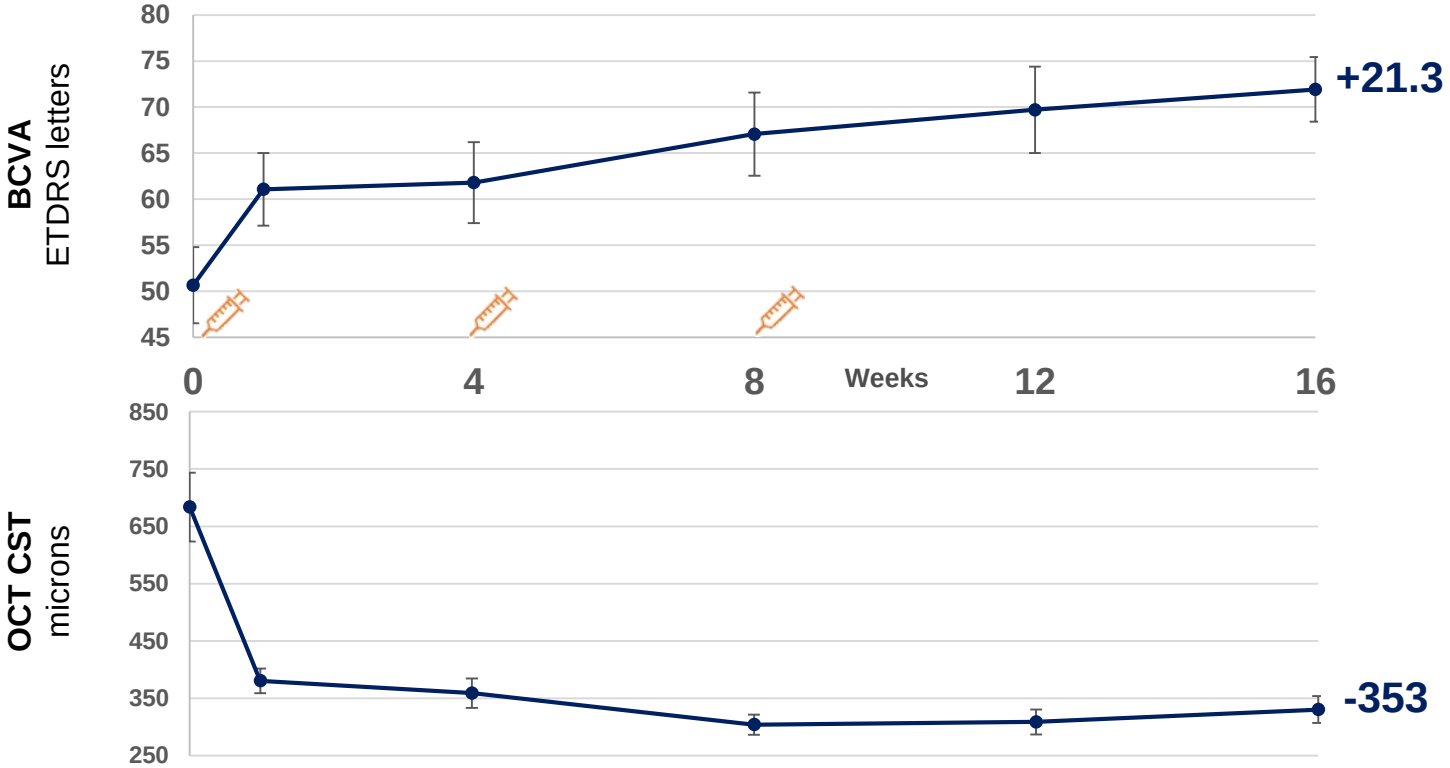
KSI-301 Phase 1b Baseline Characteristics

Variable	RVO Cohort (n=35)
Age, mean (SD), years	63.6 (12.6)
Gender, n (%), female	13 (37.1)
Race, n (%), White	31 (88.6)
BCVA, mean (SD), ETDRS letters	54.9 (15.4)
BCVA, Snellen 20/40 or better, n (%)	6 (17.1)
OCT CST, mean (SD), microns	675 (237)
RVO subtype, n (%)	
Branch RVO	19 (54)
Central RVO	15 (43)
Hemi RVO	1 (3)

Includes all patients randomized as of 10 October 2019. SD= standard deviation; BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

Efficacy of KSI-301 in RVO

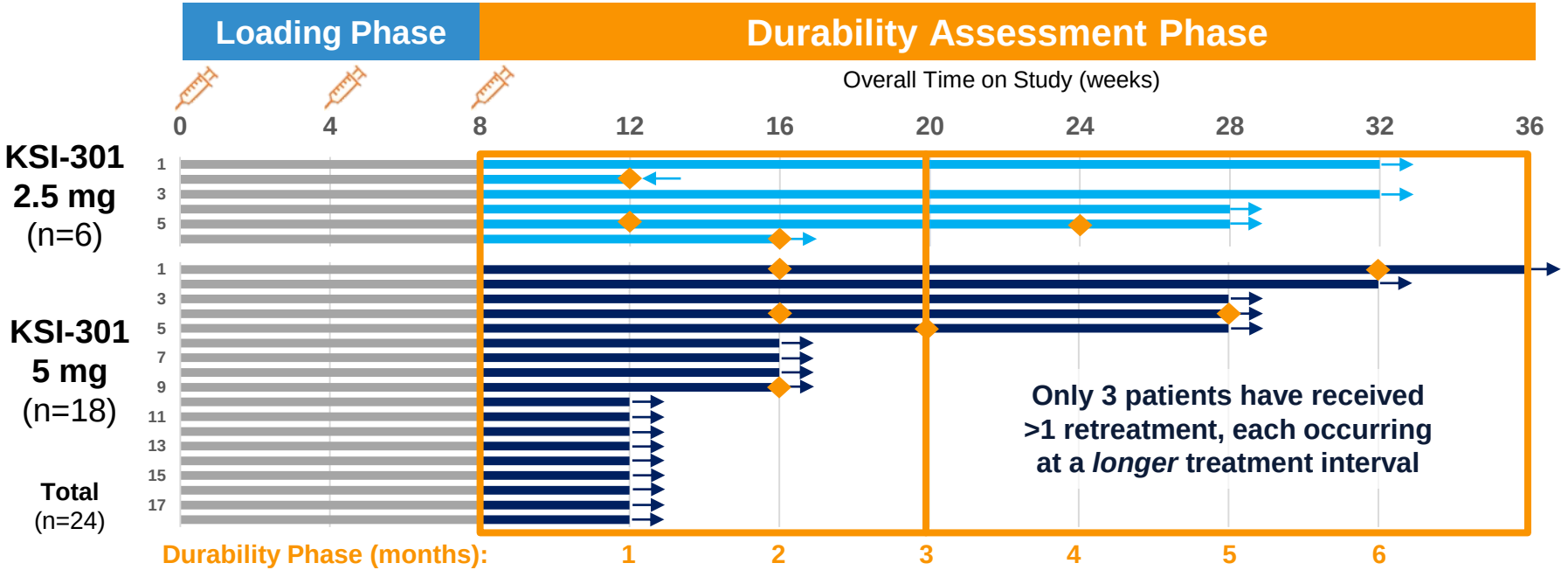
change from baseline to week 16 in mean BCVA & OCT



Interim data. Includes only randomized patients that reached Week 16 visit by the data cutoff date of 10 Oct 2019; 2.5 & 5 mg doses pooled. Datapoints include one subject that discontinued after Week 12. Error bars represent standard error of the mean. OCT CST values are site reported. BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

n= 15 **Patients reaching Week 16 visit by data cutoff**

KSI-301 in RVO: *emerging durability data show potential for 2 to 3 month or longer dosing*



8% (2/24), 28% (4/14) & 11% (1/9) received first retreatment at 1, 2 & 3 months respectively

56% (5/9) have gone longer than 3 months after the last loading dose

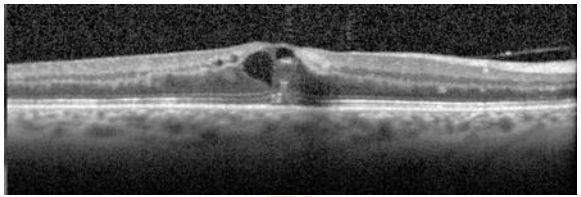
◆ Retreatment
→ Continuing follow-up
← Discontinuation

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 10 Oct 2019. Each bar represents an individual patient.

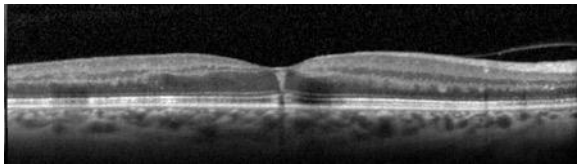
Is it possible to get a fast *AND* lasting effect of up to 5 months without retreatment after only 3 loading injections in RVO?

Case Example of KSI-301 5 mg in the Phase 1b Study

DAY 1

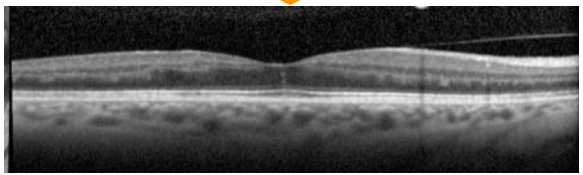


WEEK 1



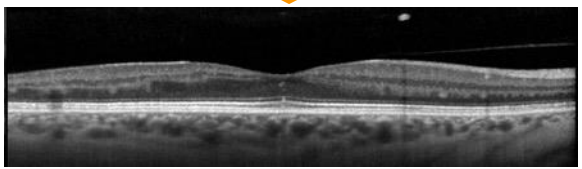
After 1 dose

MONTH 3



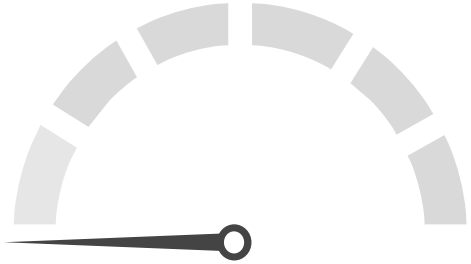
1 month after 3 loading doses

MONTH 7

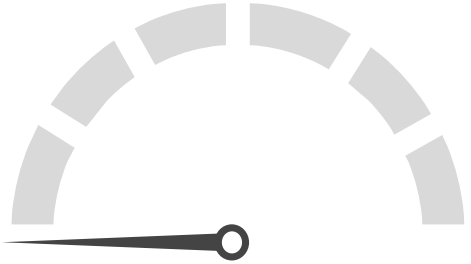


No retreatment required for 5 months

RVO requires early monthly treatment with current anti-VEGF therapies



Aflibercept
6 Monthly Injections
during fixed dosing*

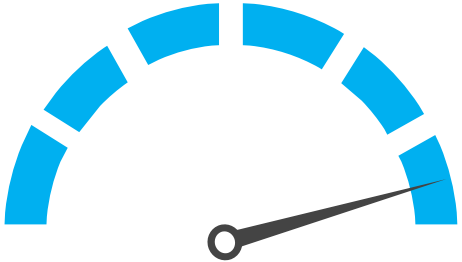


Brolucizumab
6 Monthly Injections
during fixed dosing*

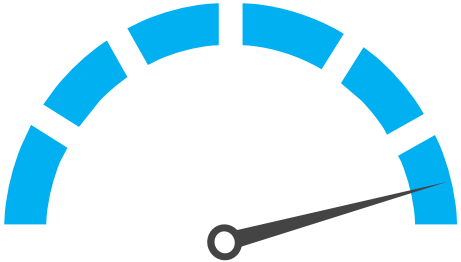
Fixed Dosing Phase	
Aflibercept	Monthly
Brolucizumab	Monthly

*According to dosing used on the Phase 3 RVO trials for aflibercept and brolucizumab.

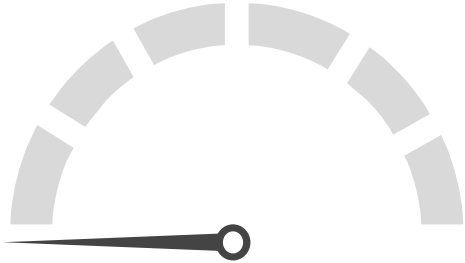
A next generation therapy for RVO should halve the number of monthly loading injections



Aflibercept
6 Monthly Injections
during fixed dosing



Brolucizumab
6 Monthly Injections
during fixed dosing

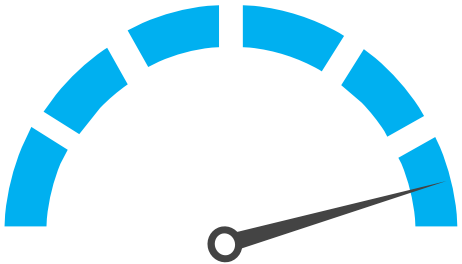


Next Gen.
3 or fewer monthly
injections

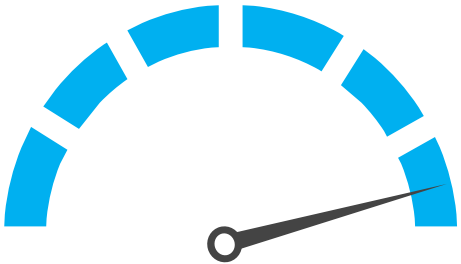
Fixed Dosing Phase	
Aflibercept	Monthly
Brolucizumab	Monthly

*According to dosing used on the Phase 3 RVO trials for aflibercept and brolucizumab.

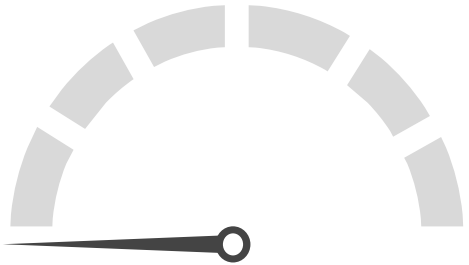
A next generation therapy for RVO should double the treatment interval from 1 to 2 months



Aflibercept
6 Monthly Injections during fixed dosing



Brolucizumab
6 Monthly Injections during fixed dosing



Next Gen.
Every other month dosing (after loading)

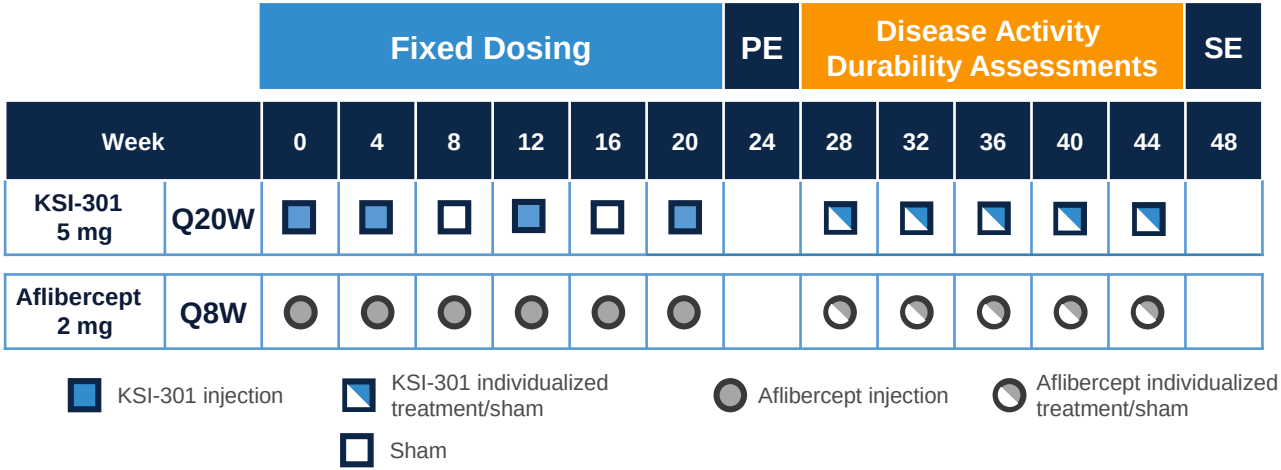
Fixed Dosing Phase	
Aflibercept	Monthly
Brolucizumab	Monthly
Next Gen.	Every 2 Months

*According to dosing used on the Phase 3 RVO trials for aflibercept and brolucizumab.

KSI-301 Proposed Phase 3 Design in RVO

Reduced loading doses with fixed Q8W dosing in the first 6 months

- Current standard of care (per label) is aflibercept ***monthly***
- Overall RVO data from existing anti-VEGFs show that less than monthly dosing in first 6 months is associated with worse outcomes
- Brolucizumab Phase 3 is studying 6 monthly doses, then disease activity-based retreatments



The second half of Year 1 patients would receive personalized treatment

MAX CAMBRAS, M.A.

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L.E.K. CONSULTING

KODIAK

KSI-301 R&D day
Select Market Dynamics

Discussion document

October 14, 2019

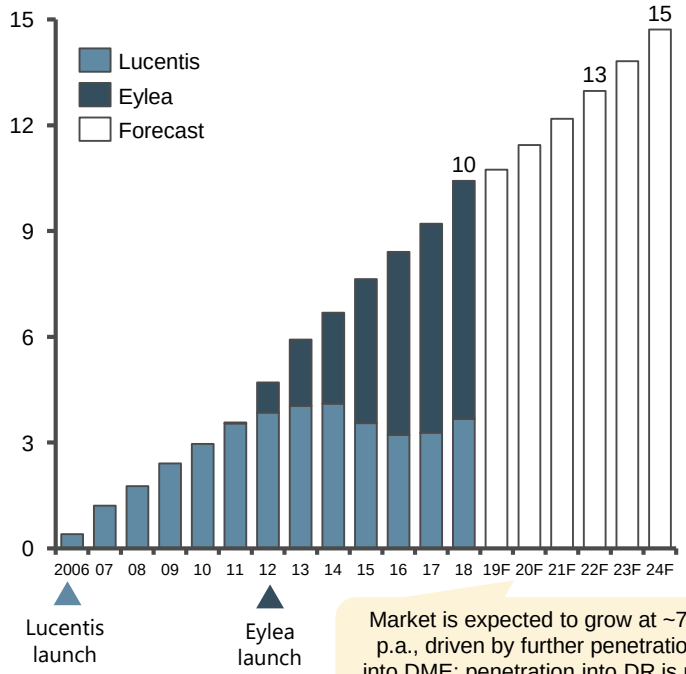
L.E.K.

Agenda

- **Project background**
- KSI-301 opportunity summary presentation
- Supporting materials

The global branded anti-VEGF market exceeded $10B in 2018; analysts expect the market to grow ~7% p.a. driven by further penetration into DME

Worldwide branded anti-VEGF market
Billlions of USD



Market is expected to grow at ~7% p.a., driven by further penetration into DME; penetration into DR is not currently included in forecast

- Anti-VEGFs are widely used to treat numerous "back-of-the-eye" indications, including:
  - Wet age-related macular degeneration
  - Retinal vein occlusion
  - Diabetic retinopathy with or without diabetic macular edema
- Retina specialists (RS) in the U.S. frequently use Avastin off-label over branded anti-VEGFs given significant cost savings (~$55 per dose compared to ~$2K per dose) :
  - Lucentis and Avastin are perceived to have equivalent clinical performance (similar efficacy, safety, and durability)
  - Eylea is perceived to have slightly improved binding affinity and extended dosing intervals
  - Beovu (brolucizumab) was just approved for wAMD and will likely take share from the above
- Novartis is developing a novel anti-VEGF that is likely to launch in 2019 and may incrementally improve upon Eylea's anatomic performance (e.g., retinal drying), but does not demonstrate BCVA gain over Eylea

Source: L.E.K. interviews and analysis of company filings and analyst reports

Retina specialists administer anti-VEGF therapies and are the primary stakeholders influencing which anti-VEGF therapy may be prescribed

Anti-VEGF therapy stakeholders and level of influence

Stakeholder	Institutional	Individual	Description	Level of influence
Retina specialist (RS)	✓ *Dependent on practice setting*	✓	• Retina specialists aim to improve or maintain their patients' vision • RS also seek to reduce the number of IVT injections administered and may be influenced by practice economics	High
Patients		✓	• Patients seek to improve or maintain their vision and reduce the number of intravitreal (IVT) injections received • Patients aim to reduce out-of-pocket expenses	Moderate / High
Diabetologist		✓	• Endocrinologists and PCPs seek to prevent vision loss in diabetic patients due to concomitant DME / NPDR	Low
Practice administrators	✓		• Practice administrators seek to optimize practice economics through optimized reimbursement and favorable drug purchase arrangements	Moderate
Ophth. Practice networks	✓		• Opthalmology systems seek to optimize practice economics through optimized reimbursement and volume of patients managed	Moderate
Payers	✓		• Payers are incentivized to reduce the total cost of care and improve patient outcomes	Moderate

Source: L.E.K. interviews and analysis

Clinical performance factors are the most influential incentives for physicians when selecting anti-VEGF therapies for wAMD

Anti-VEGF selection incentives

	Incentive	Definition	*Influential incentives*
Clinical performance	Improved efficacy	● Improved visual acuity and / or morphologic outcomes as demonstrated in clinical trials	
	Improved safety	● Improved safety / tolerability profile as demonstrated in clinical trials	
	Improved dosing intervals	● Less frequent injections as demonstrated in clinical trials	
	Superior outcomes through durability	● Improved patient visual acuity and / or morphologic outcomes as demonstrated in clinical trials or real-world experience	
	Improved convenience	● Reduction in the burden associated with receiving anti-VEGF injections	
Practice economics	Maximized reimbursement	● Maximization of the reimbursement recognized per injection (injection and buy-and-bill drug reimbursement)	
	Optimal drug inventory benefits	● Optimization of the rebates and programs supporting RS practices purchasing drug inventory	
Practice workflow	Reimbursement burden on practice	● Burden of fulfilling payer access controls in order to administer banded anti-VEGF therapies	
	Practice productivity	● Improvement in patient throughput and / or optimization of RS administered procedure mix	
Health economics	Lower total cost of care	● Reduction in the annual cost to maintain patient's vision and overall health	
Patient economics	Lower patient OOP	● Reduction in patient out-of-pocket costs	

Source: L.E.K. interviews and analysis

Current anti-VEGF therapies are minimally differentiated and do not adequately address key unmet needs

Current anti-VEGF therapies

	Off-label use		Approved	
	AVASTIN bevacizumab	LUCENTIS RANIBIZUMAB INJECTION	EYLEA (aflibercept) Injection For Intravitreal Injection	Beovu (brolucizumab-dbll) Injection
Approved indications	**Off-label use** in wAMD, RVO, and DME	wAMD RVO PDR & NPDR DME	wAMD RVO NPDR DME	wAMD (10/19) RVO (2021E) DME (2022E)
Efficacy	Perceived to be broadly equivalent		Perceived to have improved durability vs Lucentis and Avastin, and improved efficacy particularly in DME	Trial results show superior retinal fluid reduction compared to Eylea (changes in BCVA is equivalent)
Safety	Broadly equivalent safety profiles			Early safety data indicates increased inflammatory events
Labeled dosing intervals*	Q4W across indications		**wAMD:** 3 monthly loading, followed by Q8W or Q4W **RVO:** Q4W **DME:** 5 monthly loading, followed by Q8W **DR:** 5 monthly loading, followed by Q8W	**wAMD:** 3 monthly loading, followed by Q8W^ or Q12W **RVO:** 6 monthly loading, followed by PRN **DME:** 5 monthly loading, followed by PRN

Physician perception of performance: Favorable | Less favorable

Note: * Based on U.S. label ; EU labels may indicate a dose and extend approach ; Dosages delivered in 0.05 mL
^ Patients in Brolucizumab's Hawk and Harrrier study were interval adjusted to Q8W if disease was present at Q12W

Source: Company websites, National Eye Institute, Package inserts, Cowen Therapeutic Categories Outlook 2019, Klufas et. al (2018), Dugel et. al (2019), Clinicaltrials.gov

RS consistently cite unmet needs for extended durability, improved outcomes, and reduced patient treatment burden

Key unmet needs in anti-VEGF therapy

Improved real world outcomes	• Physicians seek therapies that offer better vision and outcomes in the real world, for instance in the setting of the extended treatment dosing intervals most patients experience
Extended "on mechanism" durability	• Physicians desire **improved durability** to maintain therapeutic benefit **through extended dosing intervals** seen in real word "treat and extend" and PRN anti-VEGF dosing
Reduced patient burden	• Physicians and patients want therapies that **require less frequent injections** during **anti-VEGF loading and maintenance** to **promote compliance** and **prevent discontinuation**
Improved clinical trial outcomes	• Physicians seek more sustained **outcomes**; some physicians indicate a **need for faster response time**
Patient selection *NPDR w/out DME only*	• Physicians need the ability to **identify NPDR patients w/out DME that will benefit most from anti-VEGF therapy** and outweigh the burden of anti-VEGF treatments

Source: L.E.K. interviews and analysis

Market overview and unmet needs discussion in RVO, wAMD and DME

Select retinal diseases of interest

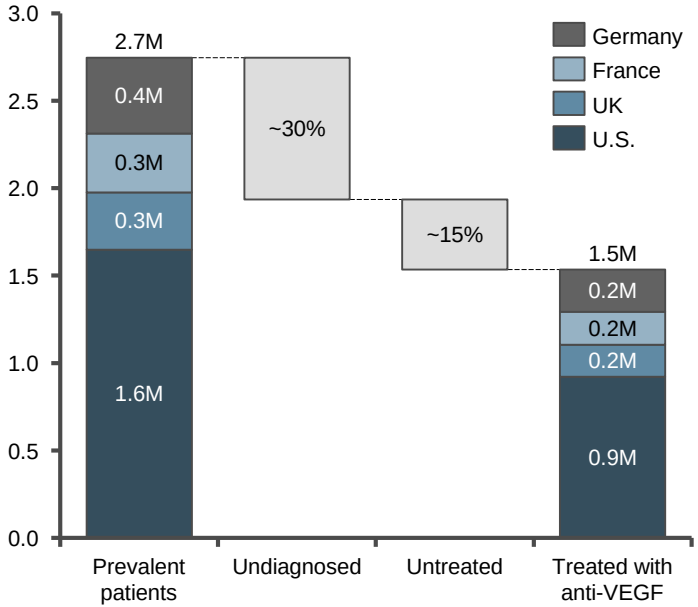
	Indication	Description
1	**Wet age-related macular degeneration (wAMD)**	wAMD is characterized by abrupt central vision loss caused by abnormal blood vessels that bleed or leak fluid which may swell and damage the macula
2	**Retinal vein occlusion (RVO)**	RVO is a blockage of the small veins that carry blood away from the retina and may cause sudden blurring or vision loss, and / or temporary loss or disturbance of central / peripheral vision
3	**Diabetic macular edema (DME)**	Diabetic macular edema (DME) occurs as a result of diabetic retinopathy and is defined by significant swelling of the retinal tissue caused by retinal vessels leaking blood and fluid into the macula

Source: L.E.K. interviews and analysis of National Eye Institute, Mayo Clinic

An estimated ~1.5M of the ~2.7M prevalent wAMD patients are treated with anti-VEGFs in 2019

1

wAMD addressable patients (2019E)
Millions of patients



- The leakage points reducing the anti-VEGF treated patient population include:
  - **Diagnosis rate:** ~30% of wAMD patients are undiagnosed due to mild, unapparent symptomatology
  - **Treatment rate:** ~15% of wAMD patients are not treated as their disease has progressed too far to benefit from treatment or have declined treatment
- Patients that decline treatment due to the burden associated with frequent injections may become addressable as anti-VEGF dosing intervals are increased
  - Persistence on therapy may increase as dosing intervals are increased

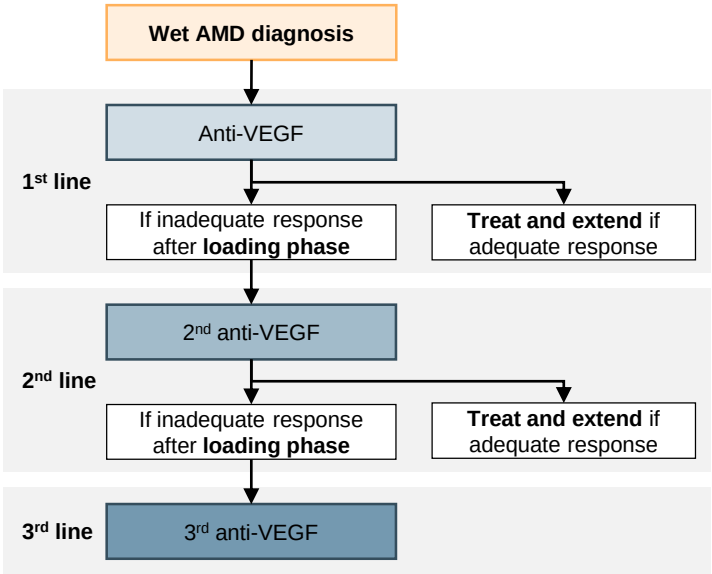
An estimated ~60% of patients are treated with branded anti-VEGFs (Eylea, Lucentis)

Source: L.E.K. interviews and analysis of BMJ, Cowen, and Journal of Ophthalmology

RS currently treat wAMD patients with suboptimal dosing which leads to poorer outcomes in the real world

1

wAMD treatment paradigm

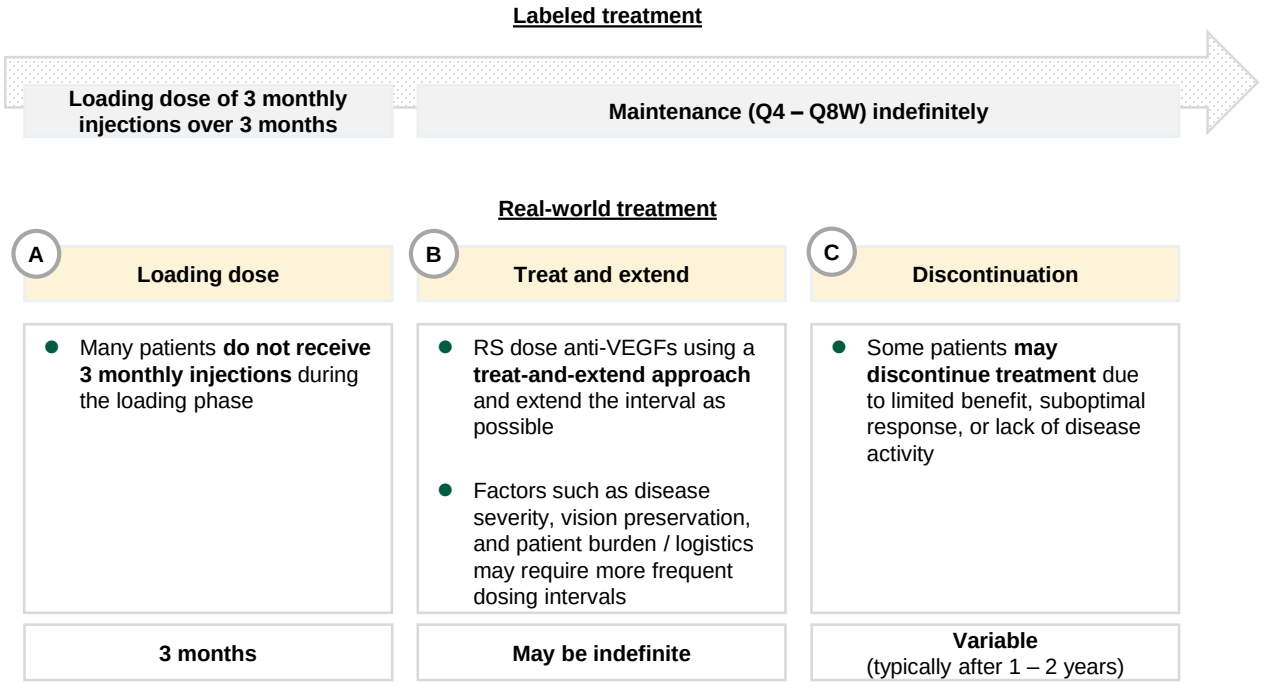


- RS do not typically follow labeled dosing intervals
  - Nearly all retina specialists report using treat and extend dosing as opposed to labeled dosing
- In real world practice, RS aim to inject anti-VEGFs on a "treat and extend" basis; however, **dosing frequency is often suboptimal** due to patient logistical challenges*
  - "Treat and extend" dosing necessitates 3 monthly loading doses before extending the interval 2 weeks at a time to a maximum of 12 weeks based on patient response
  - If the disease is "re-activated," dosing interval is shortened by 2 weeks
  - **Many patients do not receive 3 monthly loading doses** and do not strictly adhere to "treat and extend" intervals
- Suboptimal dosing with current anti-VEGFs leads to no long-term vision gains and often results in vision dropping below baseline BCVA

Note: * There is currently no data that switching therapies improves patient vision outcomes
Source: L.E.K. interviews and analysis of American Association of Ophthalmologists, MD Magazine, FDA, company websites, American Society of Retina Specialists (PAT) survey

Most RS do not follow the labeled dosing interval and treat wAMD patients on a treat-and-extend basis to balance outcomes with patient convenience

1

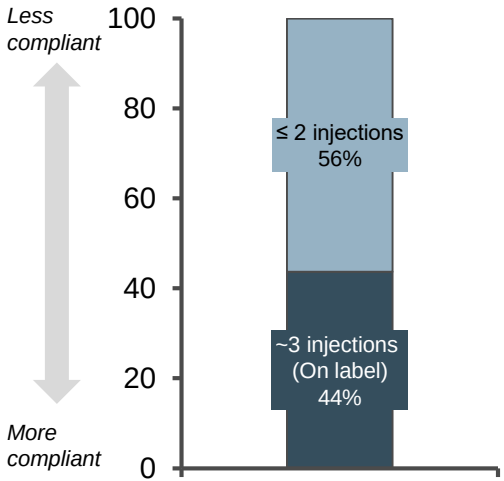


Source: L.E.K. interviews, research, and analysis

<50% of new wAMD patients receive 3 loading doses due to a variety of patient barriers and varying physician perceptions on value

1

Real-world (EHR) loading phase injections
Percent of patients



Average number of loading doses (EHR)	
Avastin	2.1
Lucentis	2.3
Eylea	2.3

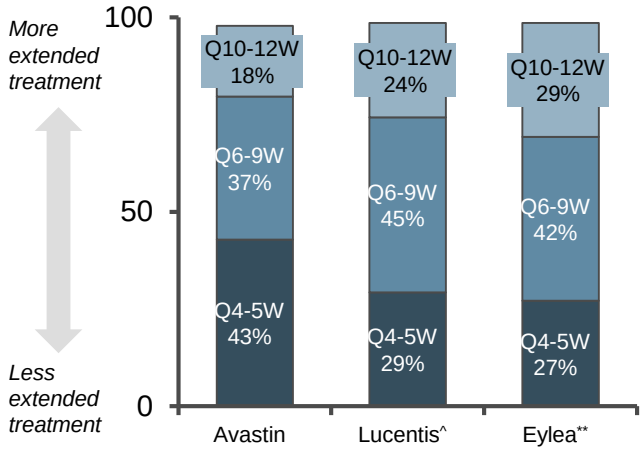
- EHR data suggests >50% of patients receive 2 or fewer injections within the first 3 months of therapy, likely due to patient travel burden and out-of-pocket concerns
- Physicians also have mixed opinions on the perceived value of adhering to 3 monthly loading injections
- Patients who receive 2 or fewer loading doses in the first 3 months may receive a delayed 3rd loading injection or begin the treat and extend phase early

Source: L.E.K. interviews and analysis of Am J Ophthalmol – Clinical utilization of anti-VEGF agents and disease monitoring in nAMD

As part of the treat-and-extend behavior, RS are injecting anti-VEGFs less frequently (Q6W – Q8W dosing schedule) than indicated …

1

Physician reported dosing intervals* (N = 7)
% of patients



Average dosing schedule			
Interviewee feedback (weighted avg)	Q6W	Q7W	Q7-8W
Labeled dosing	Q4W	Q4W	Q8W

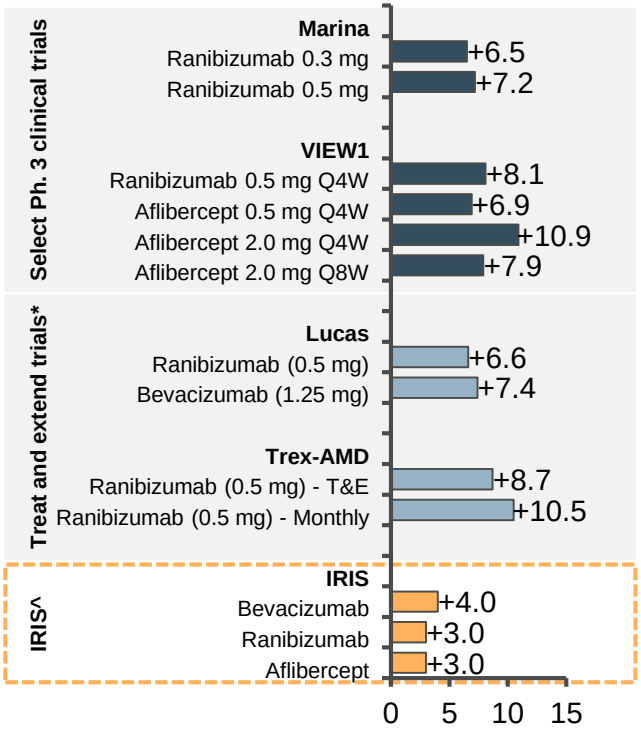
- Physicians understand that more frequent injections typically lead to better outcomes, but note that they balance injection frequency with maintaining / improving the patient's quality of life
- Some physicians concede that if treat and extend is not managed properly, patient outcomes may be suboptimal

Notes: * Dosing performed by retina specialists; does not include loading period doses (typically administered monthly for first 4 injections)
^ Lucentis label indicates up to Q12W with reduced efficacy
** Eylea label indicates that some patients may need Q4W dosing
Source: L.E.K. interviews and analysis of UBS RS survey and IRIS EHR study data

… this translates into inferior patient outcomes in the real-world when compared to clinical trials

1

Anti-VEGF clinical trial BCVA changes
Average change in letters (1 year)

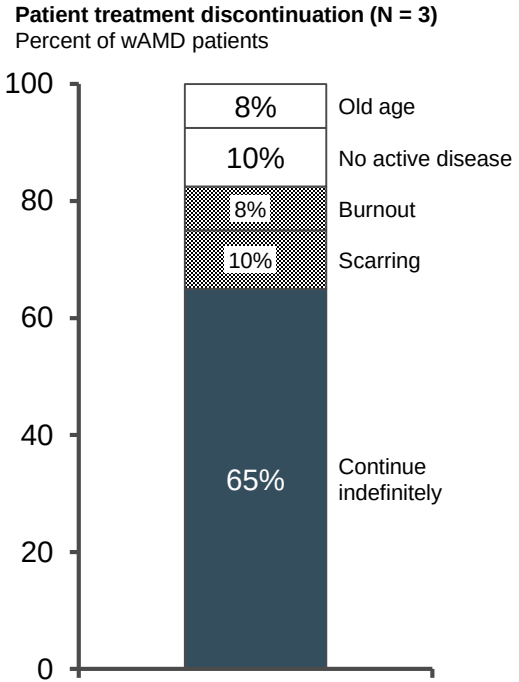


- A comparison of improvement in BCVA across clinical trials indicate that optimal treat and extend approaches may yield similar outcomes as clinical trials
- However, an IRIS study evaluating real-world anti-VEGF outcomes suggests real-world visual acuity gains are inferior to trials; limiting factors may include:
  - Differences in clinical trial patients and real-world patients
  - Delays in diagnosis and / or treatment approval and initiation
  - Individual patient responses to anti-VEGF therapies
  - Lapses in RS regimentation of anti-VEGF injections and monitoring
  - Inadequate patient adherence to treatment and monitoring
- A minority of physicians are aware of this

Note: * Average change in letters at 2 years
^ Converted logMARS to ETDRS
Source: L.E.K. interviews and analysis of JMCP and clinical trial outcomes data

RS indicate a portion of patients discontinue treatment; burnout and scarring patients may be addressable with more durable treatments

1



- Wet AMD patients are indicated to be treated indefinitely and typically exhibit improved outcomes with continuous treatment
- However, some patients discontinue and may not be further addressed with anti-VEGFs due to:
  - **No active disease:** Patients may respond exceptionally well to therapy and no longer need therapy
- Other patients who discontinue treatment may continue to be addressed with anti-VEGF therapies
  - **Burnout:** Patients may find the frequency of injections too burdensome, which may be compounded by a possible fear of injections, high out-of-pocket costs, and difficulty traveling to injecting clinic

Source: L.E.K. interviews and analysis M.D. Magazine and Am J Ophthalmol

RS cite a number of unmet needs to improve durability, outcomes and patient convenience

1

Key unmet needs in wAMD

Improved durability	• Physicians desire improved durability and ability to consistently maintain patients at extended dosing intervals
Improved outcomes	• Physicians want more substantial improvements to BCVA and drying of retina in a broader portion of patients
Reduced patient burden	• Physicians also seek products that reduce treatment burden including fibrotic scarring that may lead to burnout and drop off

Need for improved safety / tolerability is negligible given safety profile of current anti-VEGF therapies

Source: L.E.K. interviews and analysis

Anti-VEGFs with greater durability may not only improve outcomes, but also improve convenience and reduce drop off rates

1

Improving the durability of an anti-VEGF may enable…

Improved real world efficacy	Improved patient quality of life	Reduced patient drop off
• RS aim to **maximize the real world efficacy** that they're able achieve with anti-VEGF injections • Improving durability will enable patients to **stay on mechanism for longer** and potentially improve real world efficacy	• RS attempt to **minimize the treatment burden** placed on a patient by extending dosing intervals • Improved durability **enables extended dosing intervals** and gives RS **more flexibility when** managing patient's treat and extend dosing	• RS are concerned with **patients discontinuing therapy** • Improved durability / extended dosing also address patients that find **injections too burdensome** and patients that experience **scarring**

Source: L.E.K. interviews and analysis

Market overview and unmet needs discussion in RVO, wAMD and DME

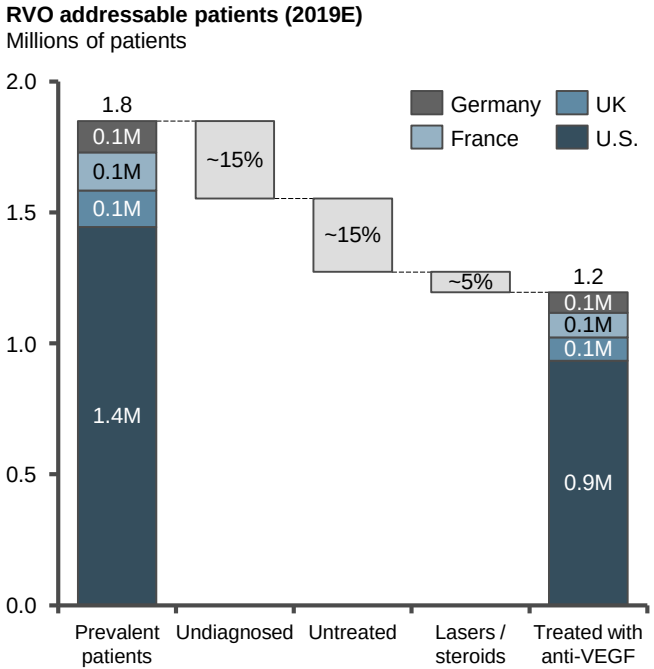
Select retinal diseases of interest

	Indication	Description
1	**Wet age-related macular degeneration (wAMD)**	wAMD is characterized by abrupt central vision loss caused by abnormal blood vessels that bleed or leak fluid which may swell and damage the macula
2	**Retinal vein occlusion (RVO)**	RVO is a blockage of the small veins that carry blood away from the retina and may cause sudden blurring or vision loss, and / or temporary loss or disturbance of central / peripheral vision
3	**Diabetic macular edema (DME)**	Diabetic macular edema (DME) occurs as a result of diabetic retinopathy and is defined by significant swelling of the retinal tissue caused by retinal vessels leaking blood and fluid into the macula

Source: L.E.K. interviews and analysis of National Eye Institute, Mayo Clinic

An estimated ~1.2M of the ~1.8M prevalent RVO patients are treated with anti-VEGF therapies in 2019

2



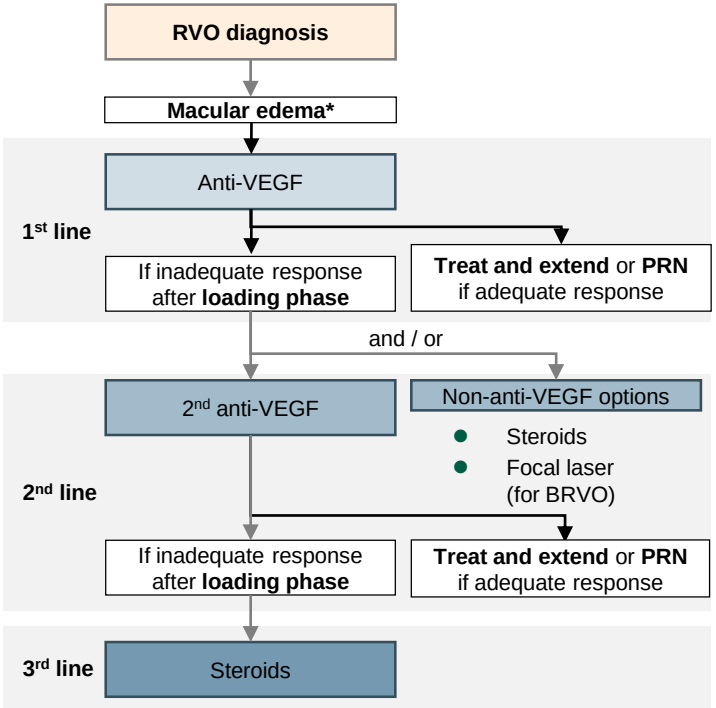
- The leakage points reducing currently anti-VEGF treated patients include:
  - **Diagnosis rate:** ~15% of RVO patients are estimated to be undiagnosed due to mild symptoms not detected by optometrists or noticed by patients
  - **Treatment rate:** ~15% of diagnosed do not initiate treatment because providers do not perceive the symptoms to be severe enough to justify the treatment burden
  - **Laser / steroids[2]:** ~5% of patients will begin with steroid or laser treatment without anti-VEGF treatment, potentially due to severity or inflammatory nature of their condition
- **Addressable population of ~1.2M** includes new patients, patients on treat and extend, PRN patients, and those that have received anti-VEGFs but have become inactive

Source: L.E.K. interviews and analysis of BMJ, Cowen, and Journal of Ophthalmology

RVO patients typically do not receive the recommended monthly injections of current anti-VEGFs needed to maintain improvement in BCVA, leading to suboptimal outcomes

2

RVO treatment paradigm



- RS do not typically follow labeled dosing intervals
  - German and French physicians typically do not use Avastin as it is off label
  - UK physicians decide on treatment based on presence or absence of ischemia^
- In real world practice, RS aim to dose anti-VEGFs on a "treat and extend" or PRN basis; however, dosing frequency is often suboptimal due to patient logistical challenges
  - Many patients receive only 2-3 monthly loading injections instead of the 6 recommended by branded anti-VEGF labels
  - Given RS perception that RVO patients respond well to anti-VEGFs, patients may discontinue therapy at a higher rate than other indications
- Recent studies (LEAVO, May 2019) indicate that **failure to adhere to labeled loading dose recommendations leads to poorer outcomes**

Note: * Patients with neovascularization are treated with a combination of laser and anti-VEGF injections
^ Treatment paradigm for ischemic patients corresponds with that for neovascularization patients
Source: L.E.K. interviews and analysis of American Association of Ophthalmologists, MD Magazine, FDA, and company websites

Most RS treat RVO with ME patients on a treat-and-extend or PRN basis to optimize the balance of patient outcomes with quality of life

2

Labeled treatment strategy

Loading dose of 3 monthly injections over 3 months	Maintenance (Q4) indefinitely

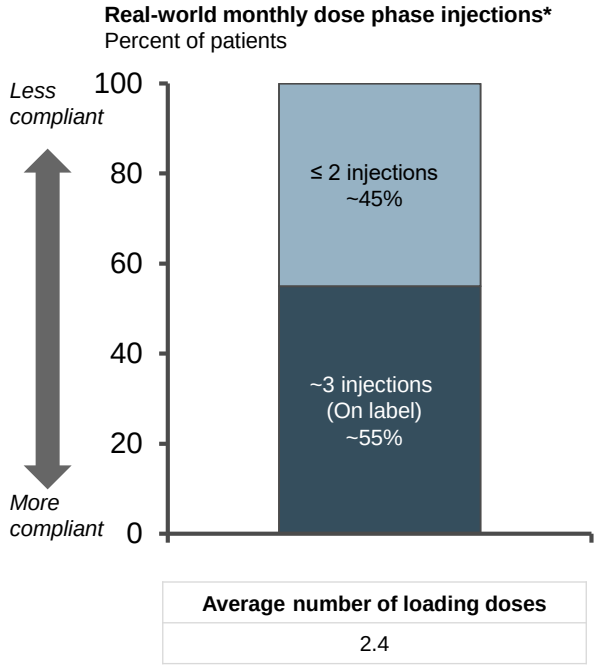
Real-world treatment

Monthly doses	Treat and extend	Discontinuation
• Many patients **do not receive 6 monthly injections** during the loading phase	• RS dose anti-VEGFs using a **treat-and-extend approach** and extend the interval as possible • Patients respond well to initial anti-VEGF injections and receive dosing as needed (PRN)	• Some patients **may discontinue treatment** due to success or limited benefit, suboptimal response, or lack of disease activity
6 months	**May be indefinite**	**Variable** (typically after 1 – 2 years)

Source: L.E.K. interviews, research, and analysis

The majority of new RVO patients receive < 3 injections during the first 3 months of treatment

2



Average number of loading doses
2.4

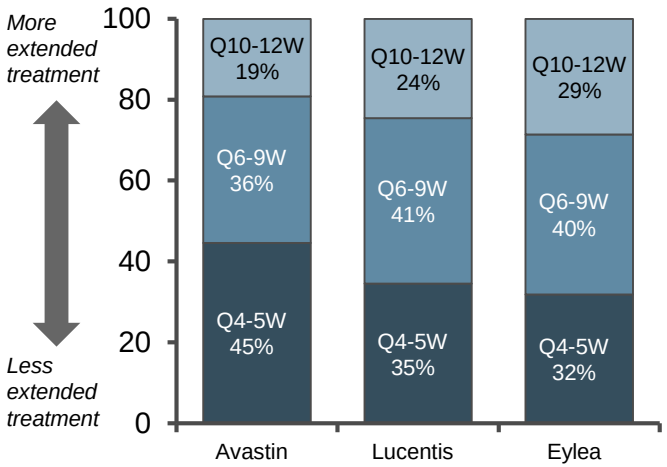
- Physician opinions vary on the optimal dosing interval for RVO patients
- Rationale for not receiving on-label dosing varies; some reasons include:
  - A subset of patients show immediate response and RS extend dosing intervals early
  - Other retina specialists indicate other non-clinical factors (e.g., patient convenience) may impede RS ability to administer monthly anti-VEGF injections

Note: * Based on real-world ex-U.S. studies with limited N
Source: L.E.K. interviews and analysis of Clinical Ophthalmology and Saudi Journal of Ophthalmology

RS extend anti-VEGF dosing to Q6-9W (nearly 2x as labeled) in RVO patients

2

Physician reported dosing intervals*
(N = 7)
% of patients



Annual dosing schedule			
Interviewee feedback (weighted avg)	Q6W	Q6-7W	Q7W
Label dosing	Q4W		

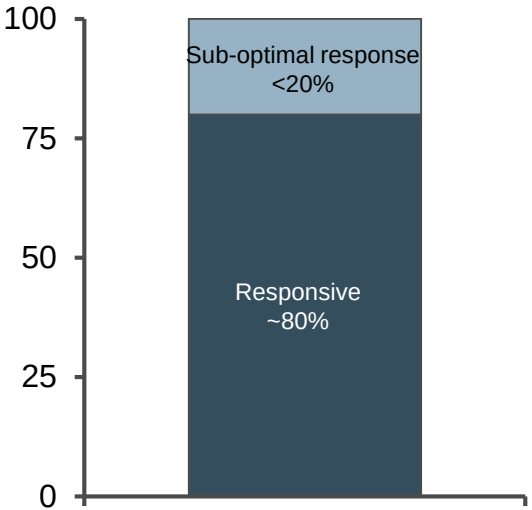
- RS seek to balance patient outcomes with maintenance and / or improvement of the patient's convenience
- RS preferentially treat at Q6-9W as opposed to extending beyond, given the likelihood of shifting patients to a treat as needed dosing regimen
- Some RS indicate that RVO patients typically respond very well to anti-VEGFs and may place the patient on PRN during or soon after the loading phase

Note: * Dosing performed by retina specialists; does not include loading period doses (typically administered monthly for first 4 injections)
Source: L.E.K. interviews and analysis, UBS

<20% of patients have sub-optimal responses to 1st line anti-VEGFs and may receive a combination of laser, steroid, or 2nd line anti-VEGF

2

Patient responsiveness to 1st line anti-VEGF
Percentage



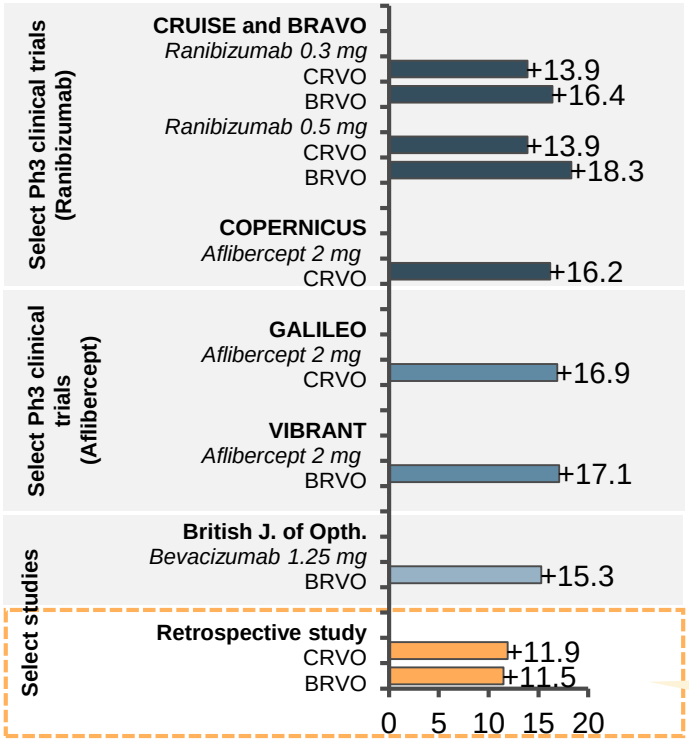
- 10-20% of RVO patients may show sub-optimal response to 1st line anti-VEGFs and are treated with a 2nd line therapy
  - Patients with glaucoma or cataracts are typically switched to another anti-VEGF if their response after 3 – 4 injections of the 1st line anti-VEGF is suboptimal
  - Other patients may receive steroids and / or focal laser with / without anti-VEGF

Source: UBS; L.E.K. interviews and analysis

Real-world outcomes of anti-VEGF therapies in RVO may be slightly inferior compared to outcomes demonstrated in clinical trials

2

Anti-VEGF clinical trial BCVA changes
Average change in letters (1 year)



- A retrospective real-world outcomes study from University of Sydney demonstrated inferior outcomes compared to clinical trials; limiting factors may include:
  - Differences in clinical trials patients and real-world patients
  - Study subjects are not representative of international RVO patients
  - Differences in dosing regimen in the real world; studies employed monthly dosing before extending whereas real world providers may switch to PRN
  - Real world delays in diagnosis and / or treatment approval and initiation
  - Differences in standards for data collection by real-world providers and clinical trial physicians / scientists

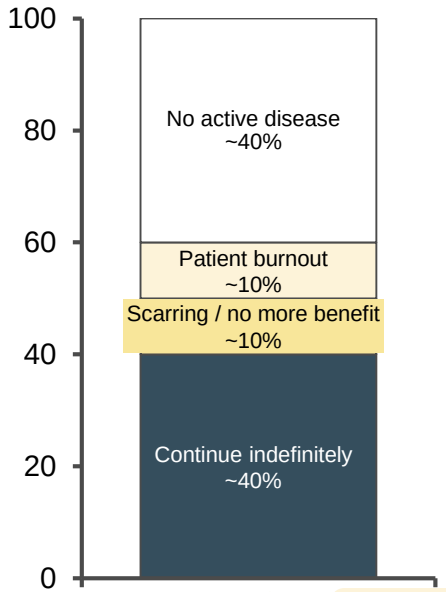
Retrospective study did not distinguish between anti-VEGF therapies

Source: L.E.K. interviews and analysis of Ophthalmology, American Journal of Ophthalmology, British Journal of Ophthalmology, BMJ Open Ophthalmology

~40% of patients maintain anti-VEGF therapy indefinitely, ~40% discontinue due to good response, and ~20% discontinue due to burnout or scarring

2

Patient treatment discontinuation
Percent of discontinued RVO patients



A portion of patients who are treated indefinitely may be treated with a PRN approach

- RVO patients are indicated to be treated indefinitely and likely exhibit better outcomes with continuous treatment
- However, many patients will discontinue therapy and may be difficult to address with anti-VEGFs due to:
  - **No active disease:** Patients typically respond well to anti-VEGF therapy and may no longer need injections
- Other patients who discontinue treatment may continue to be addressed with anti-VEGF therapies
  - **Burnout:** Patients may find the frequency of injections too burdensome, which may be compounded by a possible fear of injections, high out-of-pocket costs, and difficulty traveling to injecting clinic

Source: L.E.K. interviews and analysis

Novel MoAs for reducing breakdown of blood-retinal barrier are in development, but RS are most interested in extended anti-VEGF dosing to reduce under treatment

2

Pipeline drugs for DME

Drug class	Overview	Key examples
Novel anti-VEGFs	Novel, longer-acting anti-VEGFs may improve compliance among DME patients	**Novartis's Beovu (RTH258)** is an antibody fragment that effectively penetrates tissues due to small molecular weight and is highly efficacious in drying the retina
Biologics	Non-VEGF biologics provide novel options for patients not responsive to anti-VEGFs	**Daiichi Sankyo's DS-7080a** is a monoclonal antibody that inhibits angiogenesis
VEGF biosimilars	Physicians indicate that VEGF biosimilars may displace biologics due to lower price	**Momenta's M-710** is an Eylea biosimilar being developed for DME
Bispecific antibodies	Inhibit multiple targets to theoretically increase efficacy	**Roche's Faricimab** targets VEGF and ANG2 and demonstrated significant visual acuity gains in Phase II trials
Implantable devices	Implanted devices that deliver anti-angiogenic drugs in a sustained fashion	**Aerie's ENV-1105** is a bioerodible implant that delivers extended release version of dexamethasone
Small molecules	Small molecules that target non-VEGF factors that stabilize or prevent DME symptoms	**Allegro's Luminate** is an integrin inhibitor that reduces oxidative stress upstream of increased vascular permeability, angiogenesis, inflammation, and cell death
Steroids	Option for refractory patients due to broad anti-inflammatory and anti-angiogenic functions	**EyeGate Pharma's EGP-437** utilizes an iontophoresis to deliver a high ocular concentration of dexamethasone

Source: L.E.K. interviews and analysis of Kodiak management presentation, company websites, PharmaProjects

Market overview and unmet needs discussion in RVO, wAMD and DME

Select retinal diseases of interest

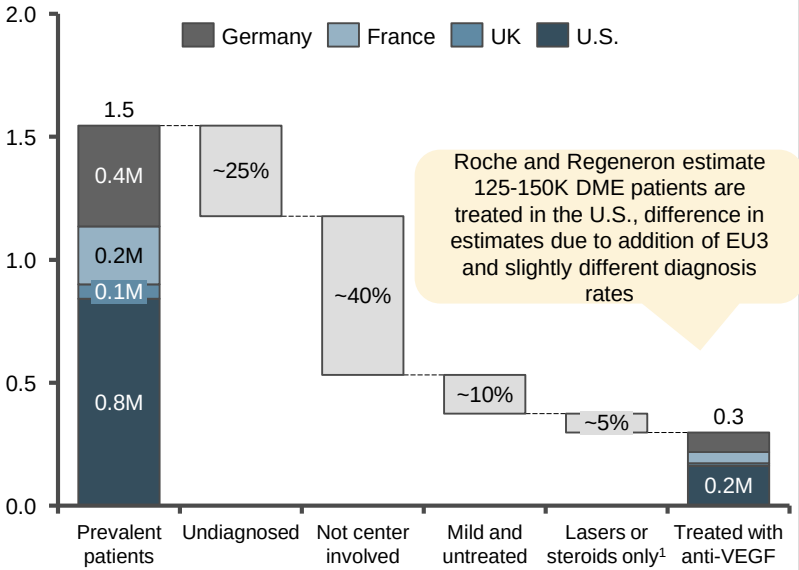
	Indication	Description
1	**Wet age-related macular degeneration (wAMD)**	wAMD is characterized by abrupt central vision loss caused by abnormal blood vessels that bleed or leak fluid which may swell and damage the macula
2	**Retinal vein occlusion (RVO)**	RVO is a blockage of the small veins that carry blood away from the retina and may cause sudden blurring or vision loss, and / or temporary loss or disturbance of central / peripheral vision
3	**Diabetic macular edema (DME)**	Diabetic macular edema (DME) occurs as a result of diabetic retinopathy and is defined by significant swelling of the retinal tissue caused by retinal vessels leaking blood and fluid into the macula

Source: L.E.K. interviews and analysis of National Eye Institute, Mayo Clinic

~0.3M / ~1.5M prevalent DME patients are treated with anti-VEGFs as most patients with not center involved or mild disease are not currently treated

3

DME addressable patients (2019E)
Millions of patients



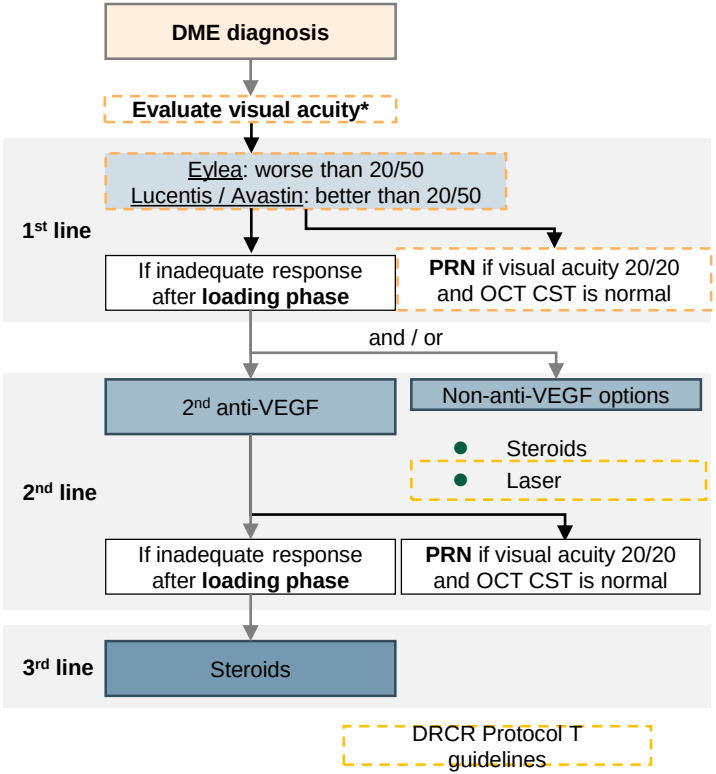
- Patient leakage points include:
  - **Diagnosis rate**: ~25% of patients remain undiagnosed due to mild symptomology
  - **Laser / steroids***: ~5% of patients begin with steroid or laser treatment (e.g. mild symptoms in the periphery) and are never treated with an anti-VEGF
- **Not center involved (~40%) and mild (~10%) DME** patients are typically not treated due to current anti-VEGF treatment burden and limited visual symptoms
- Addressable population of **~0.3M** includes patients who will receive at least 1 dose of anti-VEGF

Notes: * These patients may have disease localized to periphery or exhibit intraocular inflammation and / or epiretinal membranes
Source: L.E.K. interviews and analysis of Cowen, Regeneron investor presentation, Roche investor presentation, Journal of Diabetes Research, JAMA Ophthalmology

DME patients currently receive suboptimal anti-VEGF dosing, leading to poorer real world outcomes

3

DME treatment paradigm



- RS do not typically follow labeled dosing intervals
- In real world practice, RS attempt to adhere to a "treat and extend" or PRN regimen
  - Adherence to Eylea's label recommended loading injections (5 monthly injections) is low due to patient treatment burden and noncompliance
- Real world outcomes are inferior to those demonstrated in clinical trials due to less frequent injections

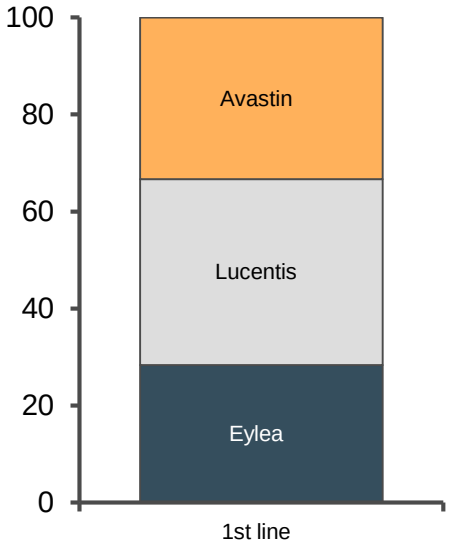
Note: * DRCR's Protocol T recommends stratifying anti-VEGF selection based on visual acuity, but providers may treat with Avastin if patient insurance is prohibitive

Source: L.E.K. interviews and analysis of American Association of Ophthalmologists, MD Magazine, FDA, and company websites

RS administer anti-VEGF therapies 1st line and often use focal lasers 2nd line based on Protocol T; however, some physicians may use steroids or another anti-VEGF

3

First line anti-VEGF treatment used
Percent of physician respondents



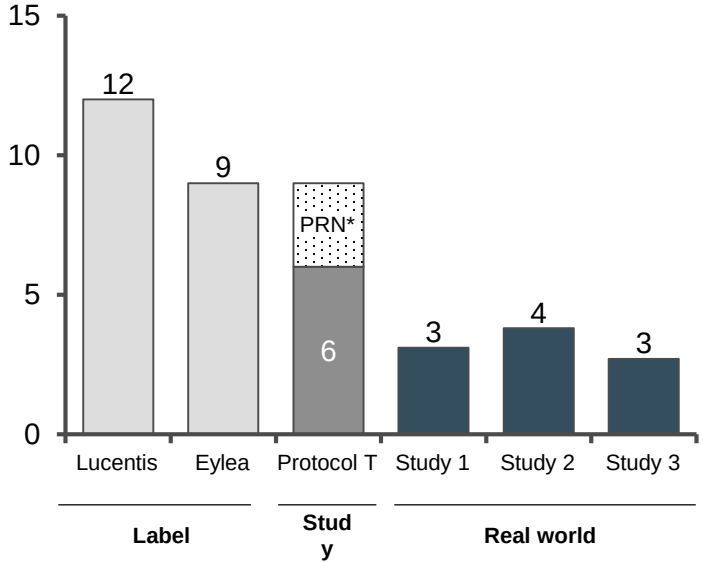
- Retina specialists will prescribe **Eylea** or **Lucentis** first line in accordance with DRCR.net Protocol T guidelines, but may still prescribe Avastin first line
- DRCR guidelines recommend laser as second-line treatment, but providers may use steroids or another anti-VEGF due to **potential vision loss caused by lasers**

Source: L.E.K. interviews and analysis of UBS analyst report

DME patients are dosed less frequently than drug labels and Protocol T guideline recommendations…

3

Anti-VEGF injections in first 12 months of treatment
Number of injections



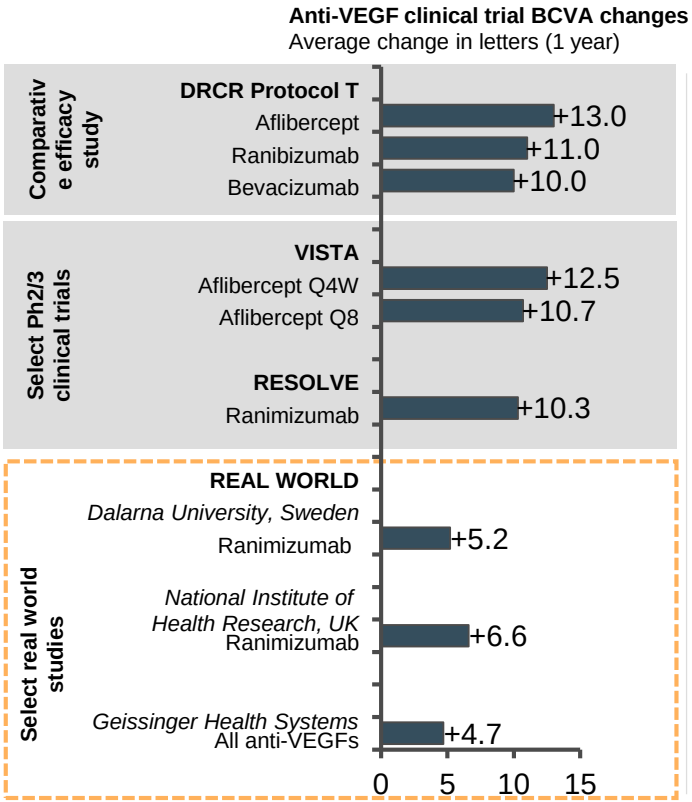
- Lucentis and Eylea labels recommend 9-12 injections in the first year of treatment
- DRCR Protocol T recommends 6 monthly injections before transitioning responsive patients to PRN
- Some RS may use treat and extend dosing as it facilitates practice workflow

  Analyses of EHR data demonstrate that DME patients receive 3-4 injections on average in the first year of treatment

Note: * Protocol T recommends PRN treatment after 5 monthly injections
Source: L.E.K. interviews and analysis of Am. Jo. Opthal., Clinical Opthalmology, and PLOS ONE

... which has resulted in real world outcomes that are inferior to those demonstrated in clinical trials

3



- Retrospective studies on real-world outcomes in the U.S., UK, and Sweden demonstrate inferior real world outcomes compared to clinical trials primarily due to less frequent dosing
- Additional limiting factors may include:
  - Differences in clinical trials patients and real-world patients
  - Real world delays in diagnosis and / or treatment approval and initiation
  - Differences in standards for data collection by real-world providers and clinical trial physicians / scientists

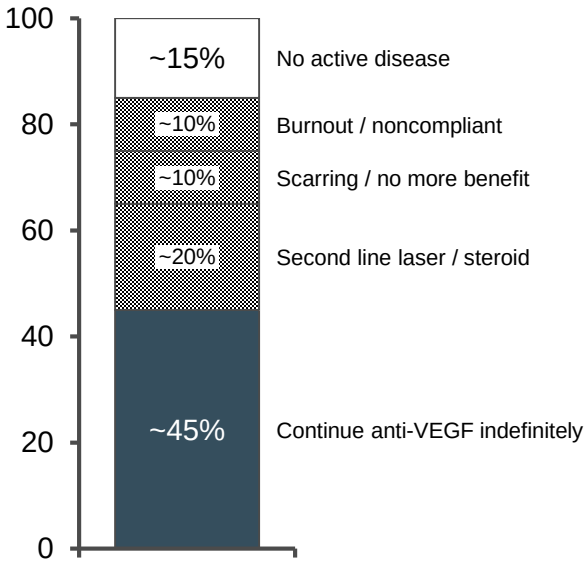
Source: L.E.K. interviews and analysis of Ophthalmology, American Journal of Ophthalmology, British Journal of Ophthalmology, BMJ Open Ophthalmology

Patients who discontinue anti-VEGFs by switching to 2nd line therapy or due to scarring or burnout may be addressable with improved dosing intervals

3

Directional – Low N

Patient treatment discontinuation
Percent of DME patients



- DME patients are indicated to be treated indefinitely and likely exhibit better outcomes with continuous treatment
- Patients with no active disease will discontinue therapy and may be difficult to address with anti-VEGFs
- Some patients who discontinue treatment may continue to be addressed with use of KSI-301:
  - **Burnout:** Patients may find the frequency of injections too burdensome, which may be compounded by a possible fear of injections, high out-of-pocket costs, and difficulty traveling to injecting clinic
  - **Second line laser / steroid:** Patients showing sub-optimal response to anti-VEGFs may transition to laser or steroid treatments second line

Source: L.E.K. interviews and analysis

Retina specialists identify a number of unmet needs affecting anti-VEGF use in DME patients

3

Key unmet needs in DME

Improved durability	• Physicians desire improved durability and ability to consistently maintain patients at extended dosing intervals
Improved outcomes	• Physicians want more substantial improvements to BCVA and drying of retina in a broader portion of patients
Reduced patient burden	• Physicians also seek products that reduce the burden associated with frequent intravitreal injections to encourage compliance in diabetic patients and reduce treatment discontinuation
Reduced loading doses	• Physicians seek fewer loading doses without sacrificing efficacy because in real-world practice, patients are unlikely to comply to 5 injections due to low compliance

Source: L.E.K. interviews and analysis

NANCY HOLEKAMP, M.D.

—

Director of Retina Services
Pepose Vision Institute

Dosing Approaches in Clinical Trials

Treat-and-Extend
- LUCAS
- TREX
- TREND
- RIVAL
- CANTREAT
- ATLAS
- ALTAIR

Monthly
- ANCHOR
- CATT
- HARBOR
- MARINA
- RISE/RIDE
- TREX
- VIEW 1/2
- VISTA/VIVID

Bimonthly
- VIEW 1/2
- VISTA/VIVID
- HAWK
- HARRIER
- CEDAR
- SEQUOIA

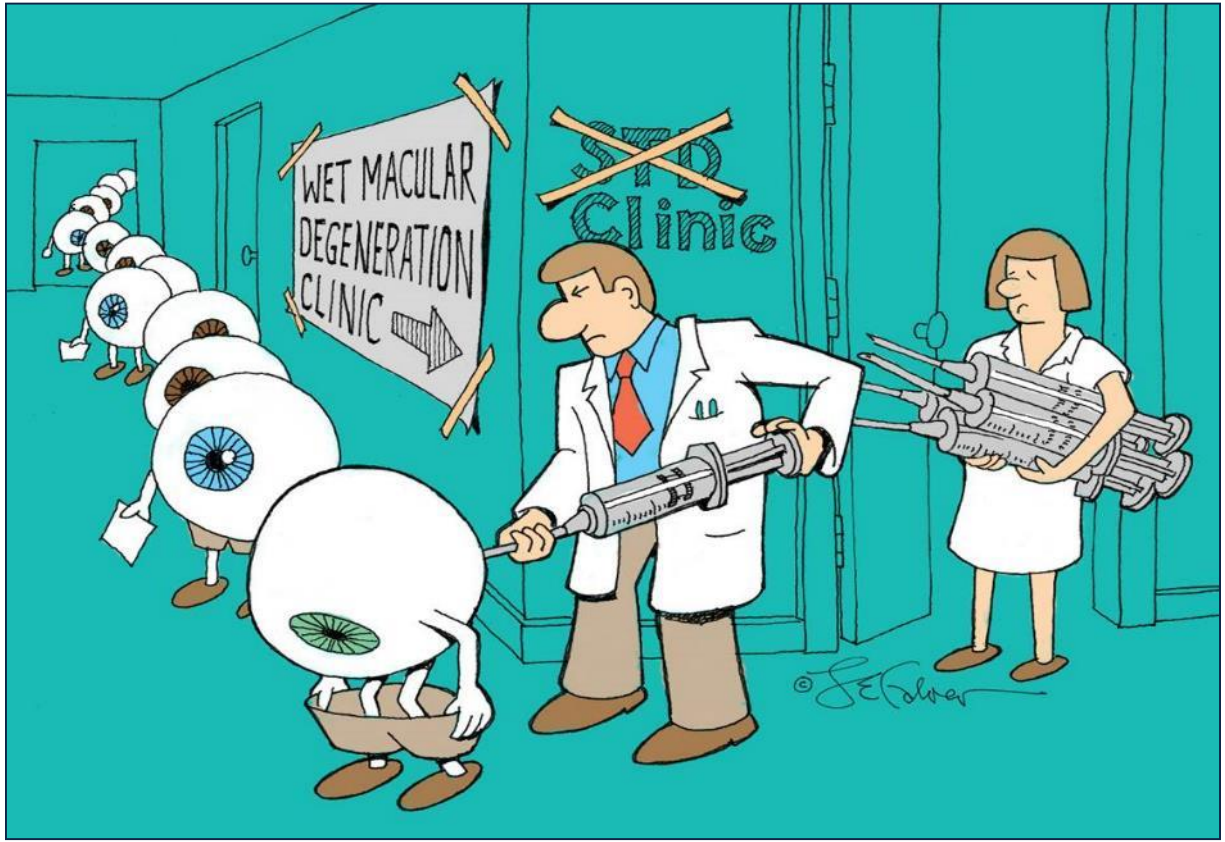
Strategic manipulation of dosing “Me Too” drugs

PRN
- CATT
- HARBOR
- PROTOCOL I
- PROTOCOL T
- RESOLVE
- RESTORE
- SAILOR

Quarterly
- EXCITE
- PIER
- HAWK
- HARRIER
- CEDAR
- SEQUOIA

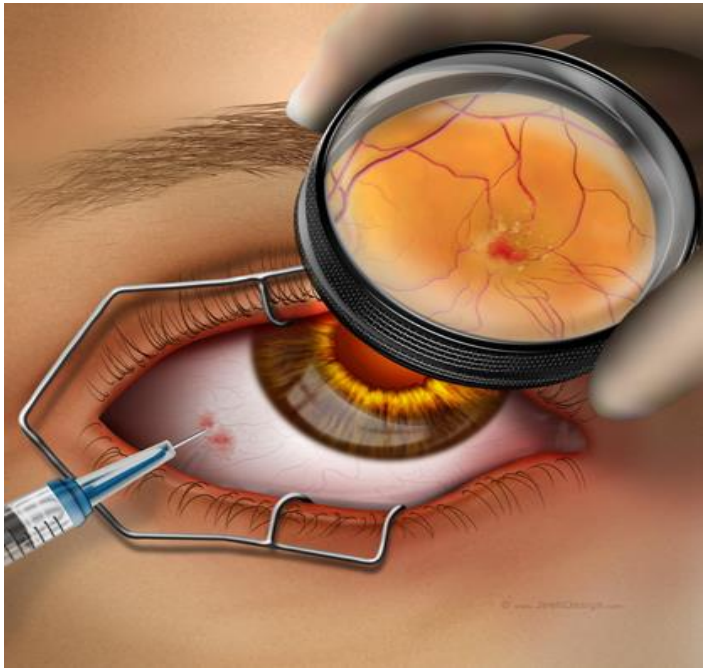
Baby steps in advancing therapy for nAMD

In nAMD, We are Injection Clinics!



Real-World Data: Most Patients With Wet AMD Received 5 Injections/Year

	Study Population	Injection Duration, Y	Mean Injection Rate
Medicare analysis[1]	459,237	1	4.3
LUMINOUS[2]	4,437	1	4.3-5.5
Retrospective claims analysis[3]	11,688	1	4.5-6.8
Retrospective claims analysis[4]	53,621	1	4.6-6.9



1. Lad EM et al. *Am J Ophthalmol*. 2014;158(3):537-543.e2, 2. Holz FG et al. *Br J Ophthalmol*. 2013;97(9):1161-1167, 3. Kiss S et al. *Ophthalmic Surg Lasers Imaging Retina*. 2014;45(4):285-291, 4. Holekamp NM, et al. *Am J Ophthalmol*. 2014;157(4):825-833.e1.

Major unmet need = More durable anti-VEGF

Anti-VEGF therapy for nAMD in 2019

- Available agents: Ranibizumab, aflibercept, bevacizumab
  - ”Me Too Drugs”: Similar efficacy, safety and durability
  - Biosimilars, Avastin, anti-VEGF C and D will not change the landscape
  - Even brolucizumab and abicipar are not disruptive
- Dosing:
  - Individualized, SD OCT-guided Treat and Extend most common, but requires frequent injections
  - Competitor strategies to extend dosing are surgically implanted devices or gene therapy
- Real world
  - The limits of “Healthcare” delivery of anti-VEGF therapy is 5 injections/year
  - This under treatment is prevalent and problematic: poor long-term VA outcomes

Kodiak ABC Platform and KSI-301

- The tolerance of the current health care system is 5 injections – Make it a durable, effective drug
- Better durability promises better long-term visual outcomes with a reasonable number of doses
- Ideal platform for retina drug development across all disease states

The Promise of KSI-301 for Stakeholders

A. The Physician:
   1. Flexible dosing with extended intervals of 12, 16, and 20 weeks after 3 loading doses
   2. Currently, RW average of 5 injections/patient. Reimbursement will not change.
   3. Will give a more durable drug, better patient care, better visual acuity in the real world

B. The Patient:
   1. Patients absolutely love extended dosing
   2. Patients absolutely love maintaining initial VA gains long term

C. The Payor
   1. A realistically finite number of injections per year will be given per patient
   2. A more predictable number of injections per year
   3. Potentially less monitoring visits, OCT's and related expenses
   4. Better vision = Better health for each patient

Q & A

KODIAK SCIENCES

R&D DAY WRAP UP

- Science-driven approach led to design of ABC Platform and KSI-301
- Phase 1b data has generated durability proof of concept, and the emerging results lend high confidence in demonstrating meaningful differentiation in pivotal studies across the four major retinal vascular diseases
- Kodiak is planning to initiate four pivotal studies, beginning with DAZZLE, to execute on its accelerated 2022 Vision
- Important commercial opportunity exists for a medicine with the durability potential of KSI-301
- Kodiak continues to invest in a pipeline of retinal disease medicines built on the ABC Platform

THANK YOU

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