1

Co-Chair

Arshad M. Khanani, MD, MA
Managing Partner
Director of Clinical Research
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2

Disclosures

Commercial Interest	Type of Financial Relationship
Adverum; Allergan; Bausch & Lomb Incorporated; Chengdu Kanghong Pharmaceutical Group Co Ltd; D.O.R.C. Dutch Ophthalmic Research Center (International) B.V.; EyePoint Pharmaceuticals; Gemini Therapeutics; Genentech, Inc; Gyroscope; Kodiak Sciences Inc; Novartis Pharmaceuticals Corporation; Opthea; Oxurion NV; Recens Medical, Inc; and Regenxbio Inc	Consulting Fee
Allergan; Genentech, Inc; and Novartis Pharmaceuticals Corporation	Speakers Bureau
Adverum; Allergan; Chengdu Kanghong Pharmaceutical Group Co Ltd; F. Hoffman-La Roche Ltd; Gemini Therapeutics; Genentech, Inc; Gyroscope; IVERIC bio; Kodiak Sciences Inc; Novartis Pharmaceuticals Corporation; Opthea; Oxurion NV; Recens Medical, Inc; and Regenxbio Inc	Contracted Research

3

Co-Chair

Dante J. Pieramici, MD
Partner
California Retina Consultants
Director
California Retina Research Foundation
Santa Barbara, California

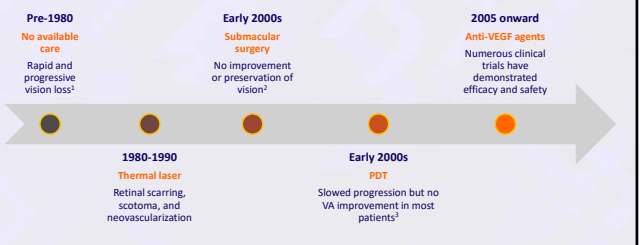
4

Disclosures

Commercial Interest	Type of Financial Relationship
Adverum; Allegro Ophthalmics, LLC; Gemini Therapeutics; Genentech, Inc; Novartis Pharmaceuticals Corporation; Regeneron Pharmaceuticals, Inc; and Regenxbio Inc	Consulting Fee
Adverum; Aerie Pharmaceuticals, Inc; Apellis Pharmaceuticals; Chengdu Kanghong Pharmaceutical Group Co Ltd; Gemini Therapeutics; Genentech, Inc; GrayBug, Inc; Ionis Pharmaceuticals, Inc; Kodiac Sciences Inc; Novartis Pharmaceuticals Corporation; Regeneron Pharmaceuticals, Inc; Regenxbio Inc; Santen Inc; and Stealth BioTherapeutics Inc	Contracted Research

5

Approaches to Improve or Maintain Vision in Patients With nAMD



1. Fine SL. *Am J Ophthalmol*. 2005;139(3):405-420.
2. Hawkins BS, et al. *Ophthalmology*. 2004;111(11):1967-1980.
3. Bressler NM. *Arch Ophthalmol*. 2001;119(2):198-207.

Abbreviation: PDT, photodynamic therapy.

10

Clinical Trials Have Demonstrated Efficacy and Safety of Anti-VEGF Therapy

2006
ANCHOR[1]
MARINA[2]
Ranibizumab superior to sham or laser

2008
PIER[3]
Ranibizumab prn superior to sham

2012
VIEW1/VIEW2[4]
Aflibercept comparable to ranibizumab

2013
HARBOR[5]
Ranibizumab prn inferior to ranibizumab monthly

2020
HAWK/HARRIER[6]
Brolucizumab comparable to aflibercept

1. Brown DM, et al. *N Engl J Med.* 2006;355(14):1432-1444.
2. Rosenfeld PJ, et al. *N Engl J Med.* 2006;355(14):1419-1431.
3. Regillo CD, et al. *Am J Ophthalmol.* 2008;145(2):239-248.
4. Heier JS, et al. *Ophthalmology.* 2012;119(12):2537-2548.
5. Ho AC, et al. *Ophthalmology.* 2014;121(11):2181-2192.
6. Dugel PU, et al. *Ophthalmology.* 2020;127(1):72-84.

11

Current Standard of Care for nAMD Involves Frequent Injections

Drug	Trial	Dose	Mean BCVA Δ at 2 Years, Letters	Safety
Bevacizumab*	CATT[1]	1.25 mg q4w	+7.8	• Higher systemic adverse events with bevacizumab vs ranibizumab
Ranibizumab	ANCHOR/ MARINA[2,3]	0.5 mg q4w	+6.6 to +10.7	• 1.3%-2.1% endophthalmitis • 6.4%-14.6% ocular inflammation ≥ 1+
Aflibercept	VIEW1/ VIEW2[4]	2 mg q4w or q8w	+7.6 to +7.9	• Endophthalmitis in < 1% in each group
Brolucizumab	HAWK/ HARRIER[5]	6 mg q12w or q8w	+5.9 to +6.1	• Endophthalmitis < 1% • Inflammation 4.7% • Rare postmarketing reports of vasculitis[6,7]

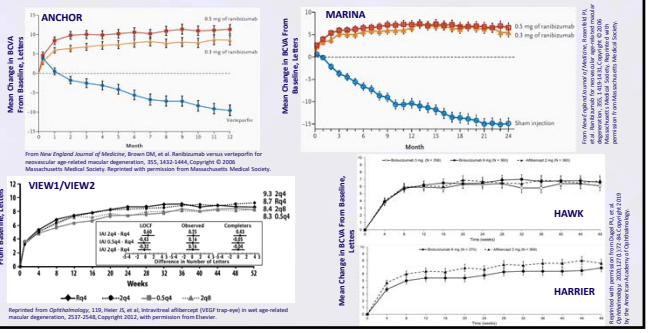
* Used off-label to treat nAMD

1. Martin DF, et al. *Ophthalmology.* 2012;119(7):1388-1398.
2. Brown DM, et al. *N Engl J Med.* 2006;355(14):1432-1444.
3. Rosenfeld PJ, et al. *N Engl J Med.* 2006;355(14):1419-1431.
4. Schmidt-Erfurth U, et al. *Ophthalmology.* 2014;121(1):193-201.
5. Dugel PU, et al. *Ophthalmology.* 2020;127(1):72-84.
6. Novartis AG. Accessed September 22, 2020. https://www.brolucizumab.info/post-marketing-data
7. Wilkin AJ, et al. *J Vitreoretin Dis.* 2020;4(4):269-279.

Abbreviations: q4w, every 4 weeks; q8w, every 8 weeks; q12w, every 12 weeks.

12

VA in Hallmark Phase 3 Clinical Trials



13

Current Anti-VEGF Agents and Treatment Methods: Clinical Trials Compared With Real-World Outcomes

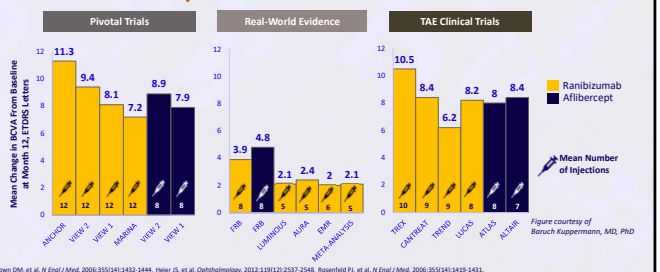


Figure courtesy of Baruch Kuppermann, MD, PhD

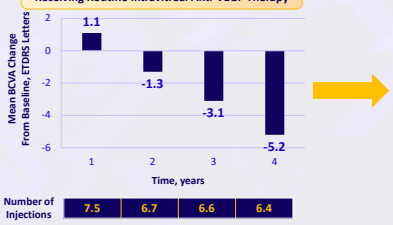
Brown DM, et al. *N Engl J Med.* 2006;355(14):1432-1444. Heier JS, et al. *Ophthalmology.* 2012;119(12):2537-2548. Rosenfeld PJ, et al. *N Engl J Med.* 2006;355(14):1419-1431. Gillies MC, et al. *Ophthalmology.* 2016;123(12):2545-2553. Holz FG, et al. *Br J Ophthalmol.* 2013;97(9):1165-1167. Holz FG, et al. *Br J Ophthalmol.* 2015;99(2):220-226. Writing Committee for the UK Age-Related Macular Degeneration EMR Users Group. *Ophthalmology.* 2014;121(5):1092-1101. Kim LN, et al. *Retina.* 2016;36(8):1418-1431. Wykoff CC, et al. *Ophthalmology.* 2015;122(12):2514-2522. Kertes PJ, et al. *Ophthalmology.* 2019;126(6):841-848. Silva R, et al. *Ophthalmology.* 2018;125(1):57-65. Berg K, et al. *Ophthalmology.* 2015;122(1):146-152. DeCroos FC, et al. *Am J Ophthalmol.* 2017;180:142-150. Ohji M, et al. Paper presented at: 18th Euretina Congress; September 20-23, 2018; Vienna, Austria.

Abbreviation: TAE, treat and extend.

14

Real-World Anti-VEGF Patient Outcomes: Undertreatment Leads to Vision Loss Over Time

98,821 Eyes From 79,885 US Patients Receiving Routine Intravitreal Anti-VEGF Therapy



Need for sustained delivery

Khanani AM, et al. *Ophthalmol Retina.* 2020;4(2):122-133.

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Top Unmet Needs Reported by Retina Specialists: 2018 ASRS PAT Survey (n = 743)

© Can Stock Photo / Shaycobi

Reduce the treatment burden

73% of retina specialists cite the need to reduce treatment burden

Long-acting/ sustained delivery

56% of retina specialists cite the need for a long-acting anti-VEGF therapy

© Can Stock Photo / Asmati

Singh R, Stone T. *2018 Membership Survey: Preferences and Trends.* American Society of Retina Specialists; 2018.

Abbreviation: PAT, Preferences and Trends.

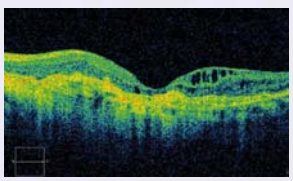
16

Treat-and-Extend Strategies

Study	Proportion of Patients on ≥ 12-Week Dosing
TREX-AMD[1] Ranibizumab (n = 60)	**17%** (2 years)
LUCAS[2] Ranibizumab (n = 218) Bevacizumab (n = 213)	**33% to 57%** (2 years)
TREND[3] Ranibizumab (n = 650)	**22.3%** (1 year)
CANTREAT[4-6] Ranibizumab (n = 580)	**29.9%** (1 year) **43.1%** (2 years)
ATLAS[7] Aflibercept (n = 40)	**35%** (1 year) **38%** (2 years)
ALTAIR[8,9] Aflibercept (n = 225)	**60%** (2 years)

1. Wykoff CC, et al; TREX-AMD Study Group. *Ophthalmol Retina*. 2017;1(4):314-321. 2. Berg K, et al. *Ophthalmology*. 2016;123(1):51-59. 3. Silva R, et al; TREND Study Group. *Ophthalmology*. 2018;125(1):57-65. 4. Kertes PJ, et al. *Ophthalmology*. 2019;126(6):841-848. 5. Kertes PJ, et al. *JAMA Ophthalmol*. 2020;138(3):244-250. 6. Kertes PJ. Paper presented at: 38th Annual Scientific Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual. 7. DeCroos FC, et al. *Am J Ophthalmol*. 2017;180:142-150. 8. Wai KM, Singh RP. *Am J Ophthalmic Clin Trials*. 2019;1:1-6. 9. Ohji M, et al. *Adv Ther*. 2020;37(3):1173-1187.

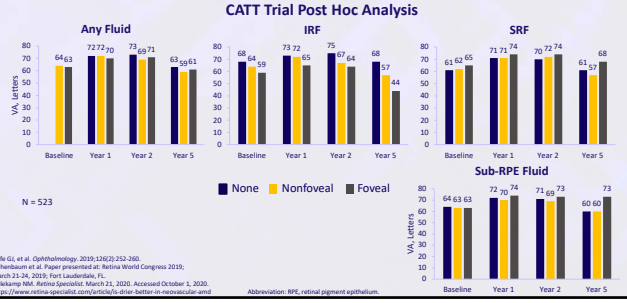
17



Reproduced with permission from Garcia-Layana A, et al. www.amdbook.org. Updated July 2017. Accessed October 1, 2020. https://amdbook.org/content/optical-coherence-tomography-age-related-macular-degeneration

18

IRF Is Inversely Correlated With VA, SRF Is Correlated With Better VA

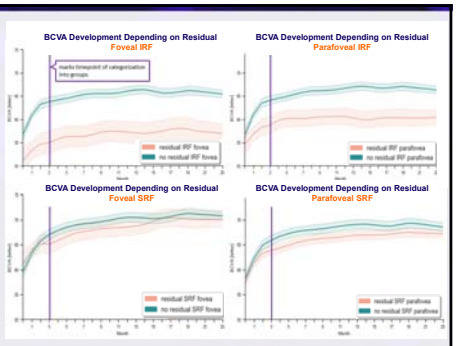


Jaffe GJ, et al. *Ophthalmology*. 2019;126(2):252-260.
Eichenbaum et al. Paper presented at: Retina World Congress 2019; March 21-24, 2019; Fort Lauderdale, FL.
Holekamp NM. *Retina Specialist*. March 21, 2020. Accessed October 1, 2020. https://www.retina-specialist.com/article/is-drier-better-in-neovascular-amd

Abbreviation: RPE, retinal pigment epithelium.

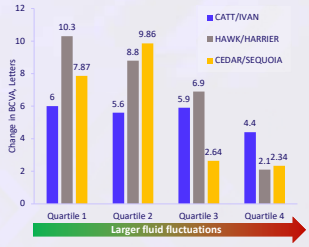
19

IRF Is Inversely Correlated With VA, SRF Is Correlated With Better VA



20

Larger Fluctuations in Fluid Correlate With Poorer Visual Outcomes



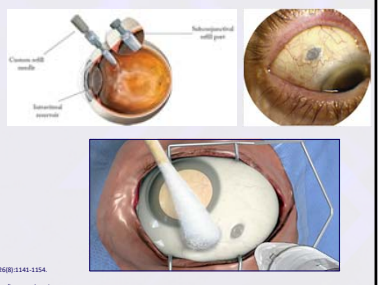
	CATT/ IVAN (2 Years)	HAWK/ HARRIER (2 Years)	CEDAR/ SEQUOIA (1 Year)
Quartile 1, µM	< 34	< 27	< 50
Quartile 2, µM	34-51.4	27-44	50-75
Quartile 3, µM	51.5-80.6	44-68	75-100
Quartile 4, µM	> 80.6	≥ 68	≥ 100

Evans RN, et al. *JAMA Ophthalmol.* 2020;138(10):1043-1051.
Jhaveri CD, et al. Paper presented at: 37th Annual Meeting of the American Society of Retina Specialists; July 26-30, 2019; Chicago, IL.
Wolfe JD, et al. Paper presented at: 38th Annual Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.

21

Port Delivery System (PDS) With Ranibizumab

- Novel drug delivery system/reservoir
  - Permanent, refillable intraocular implant
  - Customized formulation of ranibizumab
  - Implant is surgically placed at the pars plana
  - Refills performed in office
- Enables continuous delivery of ranibizumab into vitreous
- Passive diffusion follows Fick's law



Kaiser P. November 2, 2017. Accessed October 2, 2020. https://theophthalmologist.com/subspecialties/keep-on-keeping-on
Dhoot DS, et al. Paper presented at: 38th Annual Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.

22

Ladder Trial: 80% of Patients Went ≥ 6 Months Without Requiring a Refill in the PDS 100 mg/mL Arm

Primary End Point: Time to the first required PDS refill
Mean time on study = 22.1 months for all PDS patients (range, 10.8-37.6 months)

Data unavailable; please refer to cited reference for more information

Eichenbaum D, et al. Paper presented at: 38th Annual Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.

Censoring date defined as the date of a patient's last visit before the cutoff date or the date he/she discontinued the study, whichever occurred first. Time to first refill censored at the time of IVT injection, at the time refill criteria could not be assessed, and at the time of explant before the first refill.

Abbreviation: IVT, intravitreal.

23

Archway Phase 3 Trial

To evaluate noninferiority and equivalence of PDS 100 mg/mL q24w vs intravitreal ranibizumab 0.5 mg monthly*

Patients with nAMD responsive to any anti-VEGF treatment
N = 360†
Randomized 2:3

- **Intravitreal ranibizumab 0.5 mg monthly** n = 144
- **PDS with ranibizumab 100 mg/mL q24w** n = 216

→ Weeks 36 and 40: Primary end point
→ Week 96: Final visit

Primary End Point

Change in BCVA score from baseline averaged over weeks 36 and 40

Secondary End Points

- Additional VA outcomes, average at weeks 36/40 and 60/64
- Change in CPT from baseline over time and at week 36
- Incidence and severity of ocular and systemic AEs, serious AEs, and AEs of special interest
- Incidence and severity of PDS-associated AEs

* Noninferiority margin of 4.5 letters; equivalence margin of ± 4.5 letters
† Target enrollment; enrollment ongoing

Campochiaro P. Paper presented at: 38th Annual Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.
ClinicalTrials.gov. September 19, 2018. Updated July 15, 2020. Accessed October 2, 2020. https://clinicaltrials.gov/ct2/show/NCT03677934

Abbreviations: AE, adverse event; CPT, center point thickness; q24w, every 24 weeks.

24

Primary End Point: PDS q24w Was Noninferior and Equivalent to Monthly Ranibizumab for BCVA

Change in BCVA From Baseline Averaged Over Weeks 36 and 40, ETDRS Letters

	PDS With Ranibizumab 100 mg/mL q24w (n = 248)	Intravitreal Ranibizumab 0.5 mg q4w (n = 167)	Difference in Adjusted Mean
Adjusted mean (95% CI)	+0.2 (-0.7 to +1.1)	+0.5 (-0.6 to +1.6)	-0.3 (-1.7 to +1.1)

Data unavailable; please refer to cited reference for more information

Patients received a mean of 5.0 anti-VEGF injections before baseline. 95% CI is a rounding of 95.03% CI; the type 1 error was adjusted for interim safety monitoring. Adjusted means estimated using a mixed-effect model for repeated measures, with adjustment for change from baseline in BCVA as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline BCVA (< 74 ETDRS letters vs ≥ 74 ETDRS letters). The protocol-specified noninferiority lower bound margin was 4.5 letters, and the equivalence margin was ± 4.5 letters.

Abbreviations: CI, confidence interval; EQ, equivalence; NI, noninferiority.

Campochiaro P. Paper presented at: 38th Annual Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.

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PDS q24w Maintained Vision and Controlled Retinal Thickness Over 36 to 40 Weeks

Adjusted Mean BCVA Change From Baseline

Mean of 5.0 Previous Anti-VEGF Injections

	Treatment	ETDRS	Snellen
Baseline	PDS with ranibizumab 100 mg/mL q24w (n = 248)	74.4	20/32
	Intravitreal ranibizumab 0.5 mg q4w (n = 167)	75.5	20/32
Weeks 36/40	PDS with ranibizumab 100 mg/mL q24w (n = 248)	74.6	20/32
	Intravitreal ranibizumab 0.5 mg q4w (n = 167)	76.0	20/32

Adjusted Mean CPT Change From Baseline

Mean of 5.0 Previous Anti-VEGF Injections

	Treatment	Retinal Thickness, µm
Baseline	PDS with ranibizumab 100 mg/mL q24w (n = 248)	176.9
	Intravitreal ranibizumab 0.5 mg q4w (n = 167)	177.4
Week 36	PDS with ranibizumab 100 mg/mL q24w (n = 248)	182.3
	Intravitreal ranibizumab 0.5 mg q4w (n = 167)	180.0

Adjusted means estimated using a mixed-effect model for repeated measures, with adjustment for change from baseline in BCVA and CPT score as the response and included terms for treatment group, visit, treatment-by-visit interaction, and baseline BCVA (< 74 ETDRS letters vs ≥ 74 ETDRS letters).

Campochiaro P. Paper presented at: 38th Annual Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.

26

Ocular Adverse Events of Special Interest*

PDS implant insertion and refill-exchange procedures were generally well tolerated

MedDRA Preferred Term, n (%)†	PDS With Ranibizumab 100 mg/mL q24w (n = 248)			Intravitreal Ranibizumab 0.5 mg q4w (n = 167)
	Time From Surgery			
	≤ 1 Month	> 1 Month	Total‡	Total‡
Conjunctival bleb/ Conjunctival filtering bleb leak	11 (4.4%)	6 (2.4%)	16 (6.5%)	0
Vitreous hemorrhage	12 (4.8%)	1 (0.4%)	13 (5.2%)	4 (2.4%)
Cataract§	1 (0.4%)	9 (3.6%)	10 (4.0%)	6 (3.6%)
Conjunctival erosion	1 (0.4%)	5 (2.0%)	6 (2.4%)	0
Conjunctival retraction	1 (0.4%)	4 (1.6%)	5 (2.0%)	0
Endophthalmitis	0	4 (1.6%)	4 (1.6%)	0
Rhegmatogenous retinal detachment	1 (0.4%)	1 (0.4%)	2 (0.8%)	0
Hyphema	1 (0.4%)	0	1 (0.4%)	0

Predominately subconjunctival thickening; all cases classified as nonserious

- All cases of vitreous hemorrhage resolved spontaneously; no cases required vitrectomy
- 1 of 248 PDS-treated patients had irreversible vision loss due to an AE (*Enterococcus faecalis* endophthalmitis)
- 1 PDS patient experienced device dislocation into the eye during a refill-exchange procedure; following removal, the patient's vision returned to baseline

* Protocol-defined ocular AEs of special interest potentially related to the PDS implant or implant procedure.
† Frequency counts by preferred term. Multiple occurrences of the same AE in an individual are counted only once for each column.
‡ All data through week 40
§ Includes the following terms: cataract, cataract nuclear, cataract cortical, cataract subcapsular
Campochiaro P. Paper presented at: 38th Annual Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.
Abbreviation: Medical Dictionary for Regulatory Activities.

27

Ocular Adverse Events of Special Interest*

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Conjunctival bleb/ Conjunctival filtering bleb leak	11 (4.4%)	6 (2.4%)	[illegible]	[illegible]
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Hyphema	1 (0.4%)	0	1 (0.4%)	0

All cases resolved spontaneously; none required vitrectomy

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28

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Conjunctival retraction	1 (0.4%)	4 (1.6%)	5 (2.0%)	0
Endophthalmitis	0	4 (1.6%)	4 (1.6%)	0
Rhegmatogenous retinal detachment	1 (0.4%)	1 (0.4%)	2 (0.8%)	0
Hyphema	1 (0.4%)	0	1 (0.4%)	0

Cataract rates comparable across arms; no cases of traumatic cataracts

- All cases of vitreous hemorrhage resolved spontaneously; no cases required vitrectomy
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29

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Vitreous hemorrhage	12 (4.8%)	1 (0.4%)	[illegible]	[illegible]
Cataract§	1 (0.4%)	9 (3.6%)	10 (4.0%)	[illegible]
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Rhegmatogenous retinal detachment	1 (0.4%)	1 (0.4%)	2 (0.8%)	0
Hyphema	1 (0.4%)	0	1 (0.4%)	0

9 cases were addressed with flap revisions or coverage of implant flange with partial thickness cornea

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	≤ 1 Month	> 1 Month		
Conjunctival bleb/ Conjunctival filtering bleb leak	11 (4.4%)	6 (2.4%)	[illegible]	[illegible]
Vitreous hemorrhage	12 (4.8%)	1 (0.4%)	[illegible]	[illegible]
Cataract§	1 (0.4%)	9 (3.6%)	[illegible]	[illegible]
Conjunctival erosion	1 (0.4%)	5 (2.0%)	[illegible]	[illegible]
Conjunctival retraction	1 (0.4%)	4 (1.6%)	5 (2.0%)	0
Endophthalmitis	0	4 (1.6%)	4 (1.6%)	0
Rhegmatogenous retinal detachment	1 (0.4%)	1 (0.4%)	2 (0.8%)	0
Hyphema	1 (0.4%)	0	1 (0.4%)	0

- 3 of 4 cases were related to conjunctival retraction
- 1 of 4 cases associated with irreversible vision loss
- 3 of 4 cases vision returned to baseline
- 2 of 4 patients remained on PDS treatment

- All cases of vitreous hemorrhage resolved spontaneously; no cases required vitrectomy
- 1 of 248 PDS-treated patients had irreversible vision loss due to an AE (*Enterococcus faecalis* endophthalmitis)
- 1 PDS patient experienced device dislocation into the eye during a refill-exchange procedure; following removal, the patient's vision returned to baseline

* Protocol-defined ocular AEs of special interest potentially related to the PDS implant or implant procedure.
† Frequency counts by preferred term. Multiple occurrences of the same AE in an individual are counted only once for each column.
‡ All data through week 40
§ Includes the following terms: Cataract, cataract nuclear, cataract cortical, cataract subcapsular
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Ocular Adverse Events of Special Interest*

PDS implant insertion and refill-exchange procedures were generally well tolerated

MedDRA Preferred Term, n (%)†	PDS With Ranibizumab 100 mg/mL q24w (n = 248)			Intravitreal Ranibizumab 0.5 mg q4w (n = 167)
	Time From Surgery		Total‡	Total‡
	≤ 1 Month	> 1 Month		
Conjunctival bleb/ Conjunctival filtering bleb leak	11 (4.4%)	6 (2.4%)	16 (6.5%)	0
Vitreous hemorrhage	12 (4.8%)	1 (0.4%)	13 (5.2%)	4 (2.4%)
Cataract§	1 (0.4%)	9 (3.6%)	10 (4.0%)	6 (3.6%)
Conjunctival erosion	1 (0.4%)	5 (2.0%)	[illegible]	[illegible]
Conjunctival retraction	1 (0.4%)	4 (1.6%)	[illegible]	[illegible]
Endophthalmitis	0	4 (1.6%)	[illegible]	[illegible]
Rhegmatogenous retinal detachment	1 (0.4%)	1 (0.4%)	2 (0.8%)	0
Hyphema	1 (0.4%)	0	1 (0.4%)	0

2 of 2 cases repaired with vitrectomy

- All cases of vitreous hemorrhage resolved spontaneously; no cases required vitrectomy
- 1 of 248 PDS-treated patients had irreversible vision loss due to an AE (*Enterococcus faecalis* endophthalmitis)
- 1 PDS patient experienced device dislocation into the eye during a refill-exchange procedure; following removal, the patient's vision returned to baseline

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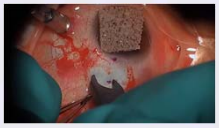
PDS With Ranibizumab

- Proof of concept for efficacy
- Reasonable risk profile
- Optimize surgical procedure
  - *Scleral dissection followed by laser ablation of the pars plana*
  - *Conjunctiva and Tenon dissection at peritomy and anchorage of both layers to limbus during closure*
  - *Extensive surgical training*



Campochiaro P. Paper presented at: 38th Annual Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.
Eichenbaum DA, et al. Paper Presented at: Retina Society 2020; August 25-September 22, 2020; Virtual.
Reprinted with permission from Campochiaro PA, Marcus DM, Awh CC, et al. *Ophthalmology*. 2019;126(8):1141-1154. Copyright 2019 by the American Academy of Ophthalmology.

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Sustained Drug Delivery Options: Gene Therapy

RGX-314	ADVM-022
• Phase 1/2a (nAMD)	• OPTIC phase 1 (nAMD)

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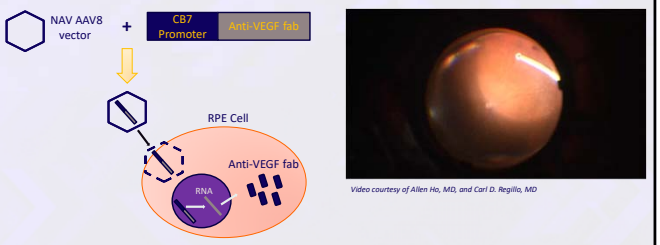
RGX-314 Gene Therapy: Overview



Video courtesy of Allen Ho, MD, and Carl D. Regillo, MD

Khanani AM. Paper presented at: 38th Annual Scientific Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.
Liu Y, et al. Mol Ther. 2018;26(2):542-549.

Abbreviations: AAV, adeno-associated virus; fab, fragment antigen binding.

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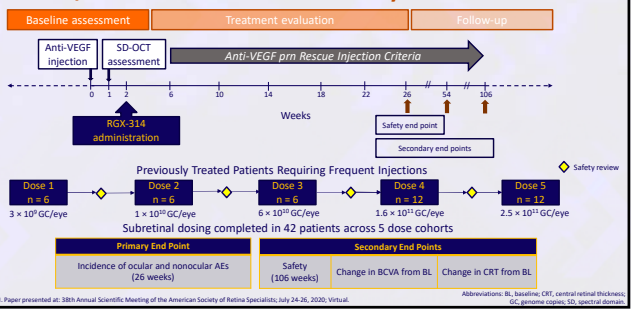
Phase 1/2a Trial of RGX-314 in Previously Treated nAMD



Subretinal dosing completed in 42 patients across 5 dose cohorts

Primary End Point	Secondary End Points		
Incidence of ocular and nonocular AEs (26 weeks)	Safety (106 weeks)	Change in BCVA from BL	Change in CRT from BL

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Abbreviations: BL, baseline; CRT, central retinal thickness; GC, genome copies; SD, spectral domain.

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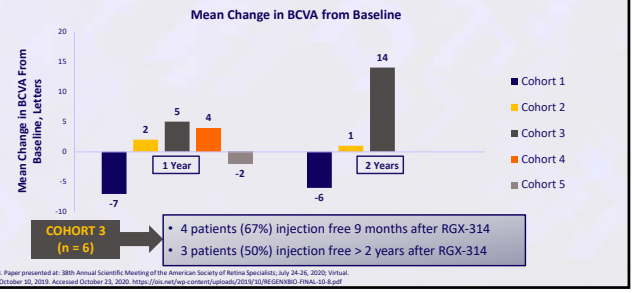
RGX-314 Phase 1/2a: Mean Change in BCVA



COHORT 3 (n = 6)

- 4 patients (67%) injection free 9 months after RGX-314
- 3 patients (50%) injection free > 2 years after RGX-314

Khanani AM. Paper presented at: 38th Annual Scientific Meeting of the American Society of Retina Specialists; July 24-26, 2020; Virtual.
Regenxbio. October 10, 2019. Accessed October 23, 2020. https://ois.net/wp-content/uploads/2019/10/REGENXBIO-FINAL-10-8.pdf

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Treatment Burden Reduction With RGX-314

Mean Change in Annualized Injection Rate Before and After RGX-314

RGX-314 Treatment Arm	Before RGX-314	Year 1 (Change From Before RGX-314)	Year 2 (Change From Before RGX-314)
Cohort 1 3×10^9 GC/eye (n = 6)	9.6	9.8 (+ 1.8%)	10.3 (+9.5%)
Cohort 2 1×10^{10} GC/eye (n = 6)	10.5	8.2 (-11.5%)	9.3 (-2.7%)
Cohort 3 6×10^{10} GC/eye (n = 6)	6.8	2.2 (-68.4%)	2.8 (-62.2%)
Cohort 4 1.6×10^{11} GC/eye (n = 12)	10.2	4.1 (-61.3%)	–
Cohort 5 2.5×10^{11} GC/eye (n = 12)	9.9	1.4 (-84.5%)	–

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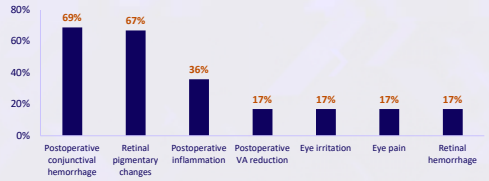
RGX-314 Phase 1/2a: Overall Safety

- RGX-314 well tolerated across all doses (n = 42); no serious treatment-emergent AEs
- No reports of clinically determined immune responses, drug-related ocular inflammation, or postsurgical inflammation beyond what is expected following routine vitrectomy

Common Ocular AEs in Study Eye



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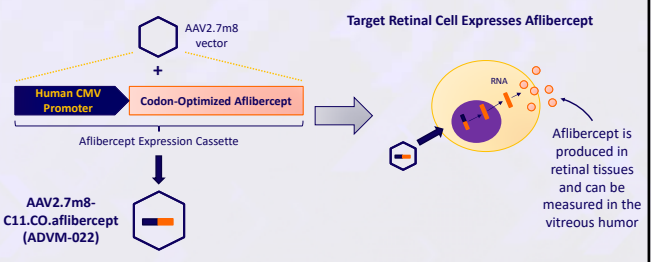
ADVM-022: AAV Gene Therapy Vector

Viral Vector Engineered to Deliver Aflibercept



Grishanin R, et al. *Mol Ther*. 2019;27(1):118-129.

Abbreviation: CMV, cytomegalovirus.

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OPTIC: Phase 1, 2-Year Multicenter Dose-Ranging Study of ADVM-022 in Previously Treated nAMD

Primary Objective
- Assess the safety and tolerability of a single IVT injection of ADVM-022

Secondary Objectives
- Evaluate vision (BCVA)
- Evaluate anatomy (SD-OCT)
- Assess the need for rescue therapy

Oral steroid prophylaxis*: Cohort 1 (6×10^{11} vg/eye, n = 6) and Cohort 2 (2×10^{11} vg/eye, n = 6)
Steroid eye drop prophylaxis†: Cohort 3 (2×10^{11} vg/eye, n = 9) and Cohort 4 (6×10^{11} vg/eye, n = 9)

Patients Received Rescue Aflibercept (2 mg IVT) if *Any* of the Following Criteria Were Met:
1. Loss of ≥ 10 letters in BCVA from baseline that is attributed to IRF or SRF observed by the investigator
2. Increase in CST > 75 µm from baseline
3. Presence of vision-threatening hemorrhage due to AMD

* Subjects received prophylaxis of 60 mg of oral prednisone for 6 days starting at day -3, followed by 7-day taper
† Subjects received prophylaxis of qid difluprednate eye drops for 3 weeks starting at day 1, followed by a 3-week taper

Khanani AM. Paper presented at: European Society of Retina Specialists 2020 Virtual Meeting. October 2-4, 2020; Virtual.
ClinicalTrials.gov. November 21, 2018. Updated May 15, 2020. Accessed October 1, 2020. https://clinicaltrials.gov/ct2/show/NCT03748784

Abbreviations: CST, central subfield thickness; vg, viral genomes.

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Cohorts 1 to 3: BCVA and CST Outcomes

	Cohort 1 (6×10^{11} vg/eye, n = 6)	Cohort 2 (2×10^{11} vg/eye, n = 6)	Cohort 3 (2×10^{11} vg/eye, n = 9)
Number of patients	6 (5 from week 56 to 72)	6 (5 for week 36 and 40 visits)	9 (8 for weeks 4, 16, and 20)
Follow-up, weeks	64-84 (median: 72)	52-56 (median: 52)	20-40 (median: 36)
Rescue-free patients, %	100 (6/6)	50 (3/6)	78 (7/9)
Mean BCVA change from baseline, letters			
All patients	-3.2	-2.0	+4.0
Rescue-free patients		+0	+6.4
Mean CST change from baseline, µm			
All patients	-21.0	-24.8	-118.6
Rescue-free patients		8.3	-152.7

Data as of July 23, 2020

Khanani AM. Paper presented at: European Society of Retina Specialists 2020 Virtual Meeting. October 2-4, 2020; Virtual.

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Safety Summary Across Cohorts

- No ADVM-022–related nonocular AEs
  - No deaths or discontinuations in OPTIC
- When observed, inflammation has been responsive to and manageable with steroid eye drops
  - Minimal early inflammation with steroid eye drop prophylaxis in cohorts 3 and 4
- No clinical or fluorescein angiographic evidence of posterior inflammation
  - No vasculitis, retinitis, choroiditis, vascular occlusions, or endophthalmitis
- All ADVM-022–related ocular AEs were mild (78%) to moderate (22%)
  - One AE of special interest, moderate recurrent uveitis, was deemed to be related to ADVM-022 and was responsive to steroid eye drops (cohort 1)
- One unrelated ocular serious AE of retinal detachment surgically repaired and resolved (cohort 1)
- Two patients had mild AEs of IOP elevation that resolved

Khanani AM. Paper presented at: European Society of Retina Specialists 2020 Virtual Meeting; October 2-4, 2020; Virtual.

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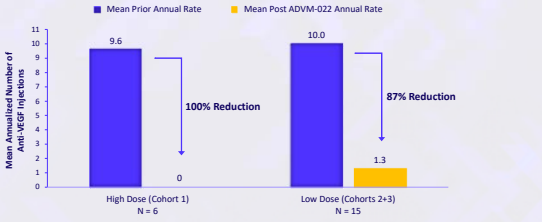
Substantial Reduction in Annualized Anti-VEGF Injection Frequency Following ADVM-022



Annualized rate (prior) = (number of IVT injections in 12 months prior to ADVM-022) / (days from the first IVT injection in the past 12 months to ADVM-022 / 365.25).
Annualized rate (post) = (number of aflibercept IVT injections since ADVM-022) / (days from ADVM-022 to the last study follow-up / 365.25).

Khanani AM. Paper presented at: European Society of Retina Specialists 2020 Virtual Meeting; October 2-4, 2020; Virtual.