

Next-Generation Retinal Care: Emerging Therapies and Best Practices for Modern Co-Management

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Speaker Disclosures

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- **Speaker/ Advisory Board Member for**
 - Allergan Pharmaceuticals
 - Astellas Pharmaceuticals
 - Heidelberg Engineering
 - B & L
 - Tarsus Pharmaceuticals
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Retina Care Begins in the Optometry Chair

2/3


Primary Eye Care

Optometrists deliver the majority of primary eye care in the U.S.

1st

Point of Detection

Most retinal disease first identified during routine optometric exams



Collaborative Care

Comprehensive Exams

- Baseline evaluations
- Functional testing
- Fundus examination
- Disease detection

Ancillary Testing

- Imaging

Patient Education

- Continuous pre & post treatment


Referral

Ongoing Monitoring / Post Treatment

- Functional testing/evaluations
- Structural & fundus examination
- Patient reported outcomes & assessments




Common Retinal Conditions




Age-Related Macular Degeneration (AMD)

- Affects 11 million Americans
- Leading cause of vision loss in adults >60 years old
- Projected to reach 22 million by 2050
- Treatment/Management: Varies




Diabetic Retinopathy (DR)

- Affects 7.7 million Americans
- Leading cause of blindness in working-age adults
- 90% of cases potentially **preventable** with early detection and treatment
- Treatment/Management: Varies



Retinal Vein Occlusion (RVO)


- Affects approximately 1%-2% of people >40 years old
- Risk increases significantly with age
- Strong association with systemic conditions
- Treatment/Management: Varies



Inherited Retinal Disorders (IRDs)

- Affect 1 in 3,000 people globally
- Over 260 genes identified
- Most common: Retinitis pigmentosa (1 in 4,000)
- Treatment/Management: Limited

Diabetes and the Eye



Retinopathy Prevalence

Diabetic Ophthalmic Complications

- Refractive changes
- Ocular Surface Disease
 - Dry Eye Syndrome
 - Diabetic keratopathy
- Extraocular movement disorders
- Cataracts
- Neovascular glaucoma
- Papillopathy/Papillitis
- Retinopathy
- Macular Edema

Critical Impact

- **Leading cause of blindness in working-age adults**
- Systemic control directly affects ocular outcomes

Systemic Connection

- DR is a marker of systemic vascular health
- Reflects overall disease management quality

My Vision Got Worse After Going to Retina

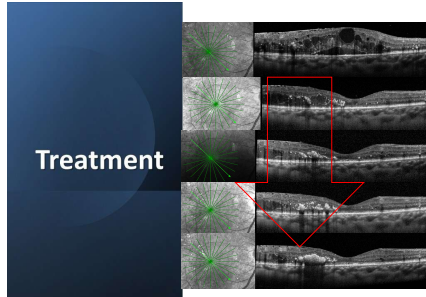
54 yo BF returns with complaint of worsening vision after treatment for diabetic retinopathy

- States sees worse, "like watching an old TV"
- **Visual Acuity**
 - At time of referral 20/60
 - Current Acuity 20/30-



Patient states does not want to go back to see retina specialist and is tired of getting multiple injections


Treatment



Requires **multiple** injections

Patient Education and Counseling


Educate	Discuss
Educate patients about their retinal conditions, treatment options, and the importance of adherence to prescribed therapies.	Discuss lifestyle changes and preventive measures that can help manage or mitigate the progression of retinal diseases.



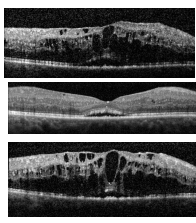
EDUCATE → EMPOWER

My Vision Got Better, but I Can't See Again

- 68 yo HM referred to retina for diabetic retinopathy with macular edema
- RTC for follow-up for with complaint of worsening vision after initially improving following treatment



Anti-VEGF: Effective but not durable



- Baseline
- One week after anti-VEGF
- One month after

PRP for Proliferative Diabetic Retinopathy

- Is effective
- Can be overdone!

Laser Complications

- Immediate Complications**
 - Macular Edema
 - Choroidal Effusion
- Delayed Complications**
 - Epiretinal Membrane
 - Subretinal Fibrosis
- Vision-Threatening Complications**
 - Foveal Burns
 - CNV Formation

Laser in the Modern Era

Advanced Laser Technologies

Micropulse laser—tissue-sparing thermal therapy

- Delivers laser energy in repetitive short pulses rather than continuous exposure
- Creates subthreshold tissue effect without visible burns
- Reduces collateral thermal damage to surrounding retina
- Particularly useful for DME near fixation

Navigated laser systems—precision targeting with eye tracking

- Eye-tracking technology ensures precise spot placement
- Digital planning of treatment patterns on fundus images
- Automated spot delivery improves accuracy and reduces treatment time
- Pattern scanning enables rapid panretinal photocoagulation

Combination Therapy Approaches

Anti-VEGF + Laser

Indications:

- Proliferative diabetic retinopathy
- Branch retinal vein occlusion

Benefits:

- Reduced treatment burden
- Better anatomic outcomes

Anti-VEGF + Steroids

Indications:

- Resistant diabetic macular edema
- Chronic vein occlusion

Benefits:

- Multiple mechanism approach
- Longer treatment intervals

Current Retinal Clinical Trials Exploring Novel Treatment Approaches

New Pharmacologic Treatments

- Oculis: Eye drop (OCS-01) for treatment of DME – phase 3 enrollment complete
- Opus: APX3330, an oral tablet treatment of diabetic retinopathy (Received FDA Agreement Under Special Protocol Assessment for Phase 3 Trial of APX3330 in Diabetic Retinopathy – Dec 2024)

One time, in-office injection of gene therapy could potentially provide long-lasting improvement in DR severity and reduce risk of vision-threatening complications

Legend:
 DME = Diabetic Macular Edema
 DR = Diabetic Retinopathy
 PDR = Proliferative Diabetic Retinopathy

Images courtesy of Regeneron, used with permission

Investigational In-office ABBV-RGX-314 for the Treatment of Diabetic Retinopathy (DR)

ABBV-RGX-314 PRODUCT CANDIDATE

Vector: AAV8 | Gene: anti-VEGF fab

Route of administration: Suprachoroidal

Mechanism of action: Reducing leaky blood vessel formation by giving ocular cells the ability to produce an anti-VEGF fab

Improved AAV vector technology (AAV8, AAV2) + Leveraging current standard of care in transgene = **ABBV-RGX-314: AAV8 encoding anti-VEGF fab**

More efficient gene delivery to the RPE*

- FDA approved mAbs and mAb fragments that inhibit VEGF are used for the prevention of DR complications
- ABBV-RGX-314 gene encodes an anti-VEGF mAb fragment (fab)

Potential for long-term therapeutic anti-VEGF expression

* Intraday et al. 2012. Current Translational Medicine. AAV: Adeno-Associated Virus.

Images courtesy of Regeneron, used with permission

77 WF with AMD– urgent appt for sudden decrease in vision

Seen 2 weeks prior with ophthalmology and has diagnosis of early AMD

Age-Related Macular Degeneration

AMD

- Affects 11 million Americans
- Leading cause of vision loss in adults >60 years old
- Projected to reach 22 million by 2050
- Treatment/Management: Varies

©2019 Blomquist and Vision Treatment Collaborators. Vision Loss Expert Group of the Global Burden of Disease Study. Lancet Glob Health. 2019;9(2):e144-e160.
Deng Y, Qiao L, Du M, et al. Age-related macular degeneration: epidemiology, genetics, pathophysiology, diagnosis, and targeted therapy. Genes Dis. 2021;9(1):62-79

AMD Often Misdiagnosed

39 Y/O F

- Several conditions resemble or mimic AMD
- These masquerading conditions lead to misdiagnosis and mismanagement
- Presenting history and assessment of risk factors play a role in making the correct diagnosis
- Assessment of visual function, dark adaptation and genetic testing may play a role in differential diagnosis, but each have limitations
- AMD a specific entity with certain clinical and diagnostic findings
- These findings change at different stages of AMD

***Spectrum of conditions with similar genotypic and phenotypic findings.**
***Similarities of structural damage due to pathology**
***Morphological changes due to chronicity adds to the confusion**

AMD-Management

- Atrophic or Dry AMD has no Effective Approved Treatment
 - Smoking Cessation
 - Nutrition and Supplements
 - Management of Comorbidities
 - Sleep Apnea
 - Low Vision Rehabilitation
 - Patient Education and Proper Follow-up Care
- GA an Advanced form of dry AMD – new treatments available
- Wet or nAMD
 - Intravitreal Anti-VEGF
 - Various Agents
 - On the Horizon
 - Gene therapy
 - Regeneron: ABBV-RGX-314 is being developed as a potential one-time treatment for wet AMD, diabetic retinopathy, and other additional chronic retinal conditions treated with anti-VEGF

NO SMOKING NO VAPING

PreserVision AREDS2

Supplement Facts		Serving Size: 1 Soft-Gel Capsule	
	Amount Per Serving	% Daily Value*	By Age
Vitamin C (Ascorbic Acid)	500 mg	500%	18+
Vitamin E (d-Alpha-Tocopherol)	400 IU	800%	18+
Zinc (Zinc Oxide)	80 mg	160%	18+
Copper (Copper Gluconate)	2 mg	40%	18+
Lutein	10 mg	200%	18+
Zeaxanthin	2 mg	40%	18+
Total Polyphenols	100 mg	100%	18+

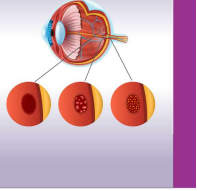
REDUCE OXIDATIVE STRESS

AMD and Genetic Testing

- AMD is associated with multiple environmental and genetic risk factors
 - **AMD is not a monogenic disorder**
- Multiple commercial companies offer genetic testing
- (±) Diagnostic Value
- (+) Availability
- The AAO and the American Society of Retina Specialists currently recommends against routine genetic testing for AMD

AAO: American Academy of Ophthalmology

AMD: Incorporating Genetic Testing into the Practice



Visible GENOMICS

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AMDiGuard Genetic Tests

- For Patients with early or intermediate AMD, or For Patients 55 years and older

Provides a score of your risk for progressing to advanced AMD
- For patients with a Family History of AMD, or For patients younger than 55 years without AMD

Provides a risk of your lifetime risk of developing advanced AMD

- Arctic Medical Laboratories offers Macula Risk PGx®, an algorithm to identify Caucasians at high risk for progression of early or intermediate AMD to advanced forms of AMD.
- Nicox offers Sequenom's RetnaGene™ AMD in North America, which evaluates the risk of a patient with early or intermediate AMD progressing to advanced choroidal neovascular disease (wet AMD) within 2, 5, and 10 years.

Visible GENOMICS

Images courtesy of Visible Genomics, used with permission.

Early and Intermediate AMD: Beyond Traditional

- Electrical impulse therapy, also known as microcurrent stimulation, is a treatment that uses electrical currents to treat AMD under clinical investigation

Source: <https://www.aao.org/education/complementary-therapy-assessment/microcurrent-stimulation-macular-degeneration-06>
Challen L, Kashwa K, Bennett M, Papaioannou G, Gregory W. Microcurrent stimulation in the treatment of dry and wet macular degeneration. Clin Optom. 2015 Dec; 17(3):245-53. doi: 10.31137/17102025.1940.20119677.PMID: 26445927

FDA Authorizes Breakthrough Valeda Therapeutic for Dry AMD to Improve Vision (November 04, 2024)



Valeda Light Delivery System

- Five successful clinical studies
- US LIGHTSITE III pivotal trial data met BCVA primary endpoint
- Data from two-year LIGHTSITE III trial used to support Valeda FDA submission
- First FDA authorized therapy for Dry AMD Patients to improve vision
- CE marked: Available in Europe and other countries
- Non-invasive, safe therapy for patients

VALEDA

Images courtesy of Valeda Therapeutics, used with permission.

First FDA treatment for Dry AMD Patients to Improve Vision

Indications for Use:

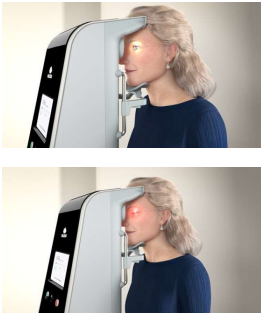
The Valeda Light Delivery System is intended to provide improved visual acuity in patients with best corrected visual acuity (BCVA) of 20/32 through 20/70 and who have dry age-related macular degeneration (AMD) characterized by:

- The presence of at least 3 medium drusen (> 63 µm and 125 µm in diameter), or large drusen (> 125 µm in diameter), or non-central geographic atrophy, AND
- The absence of neovascular maculopathy or center-involving geographic atrophy

After about two years, the Valeda Light Delivery System treatment provides improved mean visual acuity of approximately one line of visual acuity (ETDRS) compared to those not receiving the treatment.

Valeda® Light Delivery System

Parameter	Specification
Size	530 mm height x 300 mm width x 330 mm depth (20.8" x 11.8" x 13")
Weight	10.8 Kg (23.8 lbs.)
Light sources	Light Emitting Diodes (LEDs)
Light emission	590 nm output: 5 mW/cm ²
	660 nm output: 65 mW/cm ²
	850 nm output: 8 mW/cm ²
Beam diameter	30 mm (nominal) at treatment plane
	A total of 250 seconds (4 minutes 10 seconds). There are 4 phases:
Treatment exposure time	• Phase 1: 590 and 850 nm pulsed: 35 seconds
	• Phase 2: 660 nm continuous waveform: 90 seconds
	• Phase 3: 590 and 850 nm pulsed: 35 seconds
	• Phase 4: 660 and 850 nm continuous waveform: 90 seconds




Images courtesy of Valeda Therapeutics used with permission.

Valeda® Light Delivery System

Valeda Overview

- Valeda treatment delivery very similar to many eye care office diagnostic and treatment devices
- Implementation support available from LumiThera Customer Success Team
- Treatment is simple to learn and easy to train for operators
- No pupil dilation required
- Nine (9) flexible treatment sessions delivered over 3-4 weeks
- 2-3 treatment cycles per annum

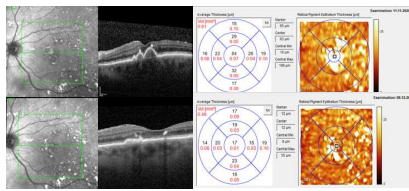


Images courtesy of Valeda Therapeutics, used with permission.

Macular Drusen Reduction Following PBM Treatment

Reduction of drusen volume at 13 months without progressive outer retinal degeneration following PBM treatment

Age: 77 years
Sex: Female
Baseline BCVA: 75 letters
13-Mo BCVA: 79 letters
24-Mo BCVA: 80 letters

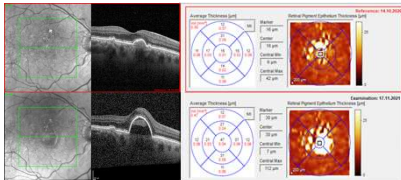


Images courtesy of Valeda Therapeutics, used with permission.

Macular Drusen Increase Following Sham Treatment

Increase of macular drusen volume observed in a Sham-treated subject after 13-months

Age: 73 years
Sex: Male
Eye: OD
Baseline BCVA: 72 letters
13-Month BCVA: 69 letters
16-Month turned wet

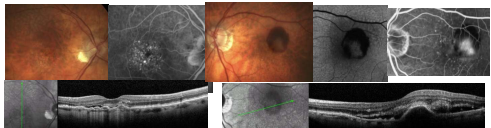


➤ A significant increase in macular drusen volume was observed following four series of Sham with confluent drusen that further developed into large retinal pigment epithelial detachments. A 3-letter decrease in BCVA was observed from 72 letters to 69 letters.

Images courtesy of Valeda Therapeutics, used with permission.

AMD Progression

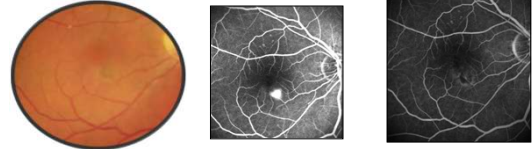
The incidence of GA, which constitutes an advance stage of AMD, is almost equal to that of neovascular AMD. Neovascular or wet AMD is associated with development of choroidal neovascular membrane and rapid vision loss if not treated in a timely manner.



Neovascular AMD presentation may differ from patient to patient, including the patient's symptomatology and visual acuity. As seen above, the case to the right has nearly no clinical sign of a neovascular membrane with minimal speckled fluorescein leakage, whereas the other case presents with a subretinal hemorrhage and typical fluorescein leakage. SD-OCT is very helpful in both cases to make or confirm the diagnosis.

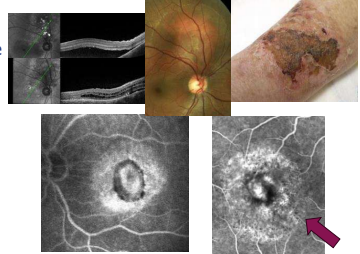
Neovascular (Wet) AMD- nAMD

- Past
 - Macular Photocoagulation Study 1980
 - Focal laser for extrafoveal choroidal neovascular membrane (CNV or CNVM)
 - CNV involving the macular lesion such as in patients with AMD is now referred to as Macular Neovascularization (MNV)



The Treatment of Age-Related Macular Degeneration With Photodynamic Therapy (TAP) Investigation 2001

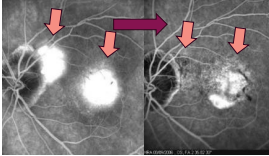
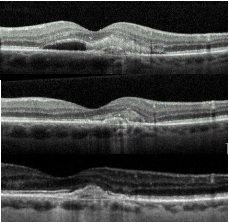
- Photodynamic Therapy
 - A reasonable option at the time
 - Was supposed to be low-risk while effective
 - Requires repeated sessions in most AMD cases
- Current trends
 - Access (few devices remain)
 - Use in CSCR and Choroidal Tumors (Hemangioma)



CSCR: Central Serous Chorioretinopathy

Current Trend: Intravitreal Injections

- Multiple Approved Agents
- Different Efficacy and Durability
 - Related to the etiology
 - Related to the agent
- Repeated Applications

The Evolution of Anti-VEGF Therapy for Retinal Diseases

- 2004: Macugen® (pegaptanib)**
 - First FDA-approved anti-VEGF for ophthalmic use
 - Selective VEGF165 inhibitor
 - Limited clinical success
- 2006: Avastin® (bevacizumab)**
 - Originally FDA-approved for cancer (2004)
 - First reported intravitreal use
 - Off-label use revolutionized retinal care
- 2006-2007: Lucentis® (ranibizumab)**
 - FDA approval for wet AMD
 - First anti-VEGF specifically developed for eye
 - Demonstrated vision improvement possibility
- 2011: Eylea® (afibercept)**
 - FDA approval
 - VEGF Trap-Eye technology
 - Extended duration of action
- 2019-2023: Next Generation**
 - Beovu® (brocizumab)
 - Vabysmo® (faricimab)
 - Eylea HD® (afibercept)
 - Development of sustained delivery systems

Anti-VEGF Therapy Overview

The Anti-VEGF "OGs"

Bevacizumab (Avastin®) All-label use \$50-\$100 per dose	Ranibizumab (Lucentis®) \$1,800-\$2,000 per dose FDA-approved for: • nAMD • All forms of DR • Macular edema secondary to RVO • Myopic CNV	Aflibercept (Eylea®) \$1,800-2,000 per dose FDA-approved for: • nAMD • All forms of DR • Macular edema secondary to RVO
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New Generation Compounds

Brocizumab (Beovu®) \$1,850 per dose FDA approved for: • nAMD • DME	Faricimab (Vabysmo®) \$2,200 per dose FDA approved for: • nAMD • DME	Eylea HD® \$2,625 per dose FDA approved for: • nAMD • DME
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Plus Biosimilars

Anti-VEGF Therapy—What's New

Recent Trials

PULSAR, PHOTON, YOSEMITE, RHINE

New Agents

Faricimab: targets VEGF-A & Ang-2
Aflibercept 8mg

Individualized Care

Treat-and-extend protocols

- Personalized Intervals: Treatment frequency adjusted based on individual response
- Reduced Burden: Fewer clinic visits and injections improve patient compliance
- Maintained Efficacy: Outcomes comparable to fixed dosing in clinical trials
- Real-World Feasibility: More sustainable for patients and healthcare systems

Anti-VEGF Biosimilars

- Per the FDA:
 - "A biosimilar is a biological product that is approved based on data showing that it is highly similar to a biological product already approved by the FDA (reference product) and has no clinically meaningful differences in terms of safety, purity and potency (i.e., safety and effectiveness) from the reference product, in addition to meeting other criteria specified by law."
- Currently, 2 FDA approved Ranibizumab Biosimilars
 - Byovavis (Samsung) approved Sept 2021
 - Cimerli (Coherus) approved Oct 2022
- Many in development
 - Ranibizumab ≥ 5
 - Aflibercept ≥ 8
 - Bevacizumab ≥ 1 Outlook Pharmaceuticals (Iytenova) <https://www.outlookpharma.com/>

Biosimilars

2 FDA approved Lucentis (Ranibizumab) Biosimilars

- Byovavis (Samsung) approved Sept 2021
- Cimerli (Coherus) approved Oct 2022

6 FDA approved two Eylea (Aflibercept) Biosimilars

- Yezali (aflibercept-lyz) Biogen Biologics: May 2024
- Opavivi (aflibercept-lyz) Samsung Biologics (Biogen/May) 2024
- Alapavivi (aflibercept-miba) Formymco: June 2024
- Praxivu (aflibercept-eyyl) Amgen: August 2024
- Hyrevevu (aflibercept-obav) Sanofi: Dec 2024
- Hytervevu (aflibercept-bocav) Cellgene: Oct 2025

(MANY others in the works...)

Approved for:

- Neovascular AMD
- Macula edema following RVO
- Diabetic macular edema
- Diabetic retinopathy


Safety and Adverse Events to Monitor For

Ocular Adverse Events	Systemic Considerations
<ul style="list-style-type: none"> • Common (>1%): <ul style="list-style-type: none"> • Conjunctival hemorrhage • Eye pain • Vitreous floaters • Serious (<1%): <ul style="list-style-type: none"> • Endophthalmitis • Retinal detachment • Traumatic cataract 	<ul style="list-style-type: none"> • Adverse events: <ul style="list-style-type: none"> • Stroke risk: 0.3%-0.5% • MI risk: 0.3%-0.6% • Monitoring: <ul style="list-style-type: none"> • Blood pressure • Cardiovascular status • Thromboembolic history

88. Myocardial Infarction

Nguyen, C. D., et al. (2022). Safety profile of intravitreal anti-VEGF therapy: A comprehensive review. *JBMR Open*, 1(12), 155-165.

Anti-VEGF Treatment Protocols

Traditional Protocols	<ul style="list-style-type: none"> • Fixed Monthly/Bimonthly <ul style="list-style-type: none"> • Loading: Monthly x 3-6 months • Maintenance: Every 4-8 weeks 	
Flexible Protocols	<ul style="list-style-type: none"> • Treat-and-Extend <ul style="list-style-type: none"> • Extension by 2-week intervals • Maximum interval: 12-16 weeks • Reduction if disease activity noted 	
PRN (As-Needed) Protocol	<ul style="list-style-type: none"> • Monthly monitoring <ul style="list-style-type: none"> • Treatment based on: <ul style="list-style-type: none"> • Visual acuity changes • OCT findings • Clinical examination 	

Shah, N., et al. (2022). Anti-VEGF treatment protocols in retinal disease: A systematic review. *Ophthalmology*, 130, 191-205.

Specific Indications and Response Rates

<div style="display: flex; align-items: center;"> <div> <p>Neovascular AMD</p> <p>First-line: Any anti-VEGF</p> <p>Response rates:</p> <ul style="list-style-type: none"> • Vision maintenance: 90% • Vision improvement: 30%-40% </div> </div>	<div style="display: flex; align-items: center;"> <div> <p>Diabetic Macular Edema</p> <p>First-line: Aflibercept or Faricimab</p> <p>Response rates:</p> <ul style="list-style-type: none"> • Vision improvement: 40%-60% • Complete resolution: 30%-40% </div> </div>	<div style="display: flex; align-items: center;"> <div> <p>Retinal Vein Occlusion</p> <p>First-line: Any anti-VEGF</p> <p>Response rates:</p> <ul style="list-style-type: none"> • Vision improvement: 50%-70% • Edema resolution: 60%-80% </div> </div>
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Benefits of injections typically include improvement in vision or prevention of worsening vision

Goal = Stabilization


Schmidt-Ehrhart, U., et al. (2022). Guidelines for the management of retinal vascular diseases. *Retina*, 42(1), 1-28.

Anti-VEGF Therapy Impact

- **Before Anti-VEGF:**
 - 43% of wet AMD patients legally blind within 3 years
- **After Anti-VEGF:**
 - 90% maintain vision
 - 30%-40% gain significant vision
 - Leading cause of blindness among older adults became treatable

Shah, N., et al. (2022). Twenty years of anti-VEGF therapy for neovascular age-related macular degeneration: Impact and future directions. *Ophthalmology*, 130(2), 11-21.

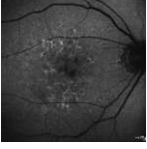
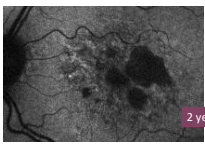
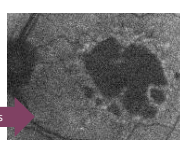
New Port Delivery System for Retinal Diseases

Overview	The Port Delivery System (PDS) is an innovative, long-acting drug-delivery system designed to reduce the treatment burden for patients with retinal diseases.	
Purpose	To provide continuous, controlled release of medication, specifically ranibizumab, over extended periods.	
Implantation	The PDS is surgically implanted in the superotemporal quadrant of the eye.	
Drug Delivery	The implant continuously releases ranibizumab through passive diffusion. The PDS can be refilled in-office every 24 weeks using a proprietary refill needle.	
Reduced Treatment Burden	Patients require fewer injections compared with traditional intravitreal injections.	
Sustained Drug Delivery	Maintains therapeutic drug levels over 6 months, ensuring consistent treatment.	
Improved Patient Compliance	Easier for patients to manage their treatment regimen.	
Status	The PDS with ranibizumab (Susivmo) has been approved by the FDA for the treatment of wet age-related macular degeneration (AMD).	

© 2024 Novartis. All rights reserved. The Port Delivery System with ranibizumab (PDS) is a new product.

76-year-old retired teacher

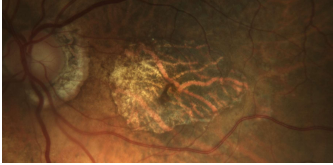
- "I can still see, but reading feels slower and faces look incomplete, worse in OS"

2 years


Geographic Atrophy (GA)

- An Advanced Form of Age-Related Macular Degeneration (AMD)



Geographic Atrophy

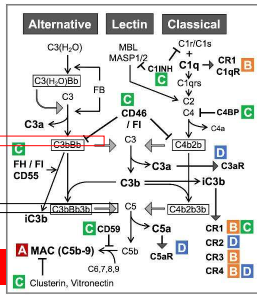
- Common and underdiagnosed
- 1-2 million Americans suffer from GA
- 75% are undiagnosed
- Progressive
 - 2 1/2 years from diagnosis to foveal involvement
- Snellen activity may remain normal or near normal for a long time.
- Irreversible vision loss
 - 50% - Lose two lines in two years
 - 66% - Severely impaired or legally blind



Geographic Atrophy Impact

Symptoms	Functional Effects
<ul style="list-style-type: none"> Blurred Vision Scotomas Metamorphopsia Reduced Contrast Reduced Dark Adaptation 	<ul style="list-style-type: none"> Activities of daily living <ul style="list-style-type: none"> Reading, driving, cooking, personal hygiene, work and hobbies Loss of independence Physical harm (fall risk) Challenges with managing comorbidities Psychologic and social effects Impacts on caregivers

Complement inhibition



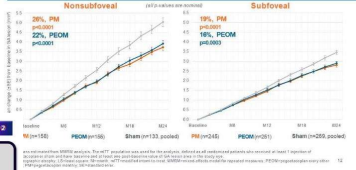
Functions

- A Cell lysis**
 - Killing of pathogens
- B Opsonization / Phagocytosis**
 - Clearance of apoptotic cells and debris (CR1, CR2, CR3, CR4, CR1q, CR3q, CR4q)
 - Synaptic pruning (CR3)
- C Regulation**
 - Inhibition of the complement cascade
- D Other functions**
 - Promotion of cell differentiation and recruitment (C3aR/C3aR1)
 - Modulation of immune cell migration (C3aR)
 - Regulation of B-cell functions (CR2)
 - Leukocyte adhesion (CR4)

Drugs: Pegcetacoplan (SYFOVRE) (Apellis), Avacincaptad pegol (IZERVAY) (Astellas), Membrane attack complex and Inflammasome formation.

Complement Inhibition

OAKS and DERBY combined / pre-specified analysis
 Reductions in GA lesion growth by lesion location



Avacincaptad pegol (Izervay) (Astellas)

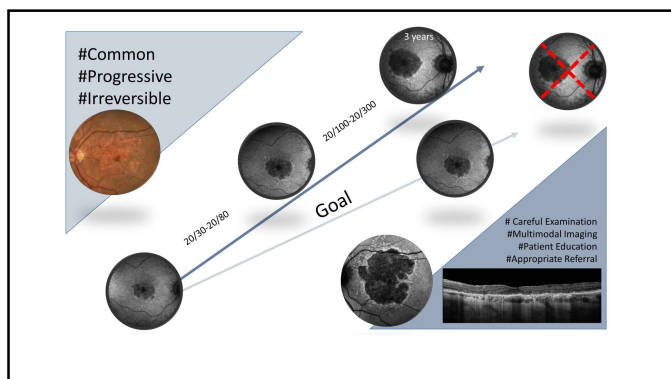
GATHER 01

GATHER 02

Images courtesy of Astellas and Apellis, used with permission

Considerations for GA Therapy

- Importance of *early identification* (familiarity with multimodal imaging, biomarkers, etc)
- Patient education
 - A different conversation than nAMD therapies
 - Slowing down progression, not stopping, and not reversal of the disease
- Frequency of injections (lifetime)
 - Logistical considerations
- Adverse effects and events



GA-Treatment Options (Current and Future)

- Complement Inhibition
- Antioxidants (mitochondrial dysfunction)
- Anti-Inflammatory Agents
- Visual Cycle Modulators
- Gene Therapy
- Cell-Based Therapy

U.S. National Library of Medicine
ClinicalTrials.gov

Search Results

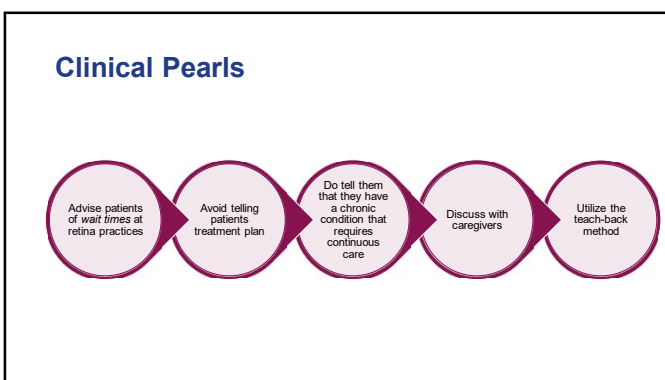
Search Details: Viewing 1-10 out of 199 studies for: Geographic Atrophy

Showing results for: **geographic atrophy**

Referrals and Co-management

Patients getting treatment for retinal diseases often have pre-existing conditions that should still be managed

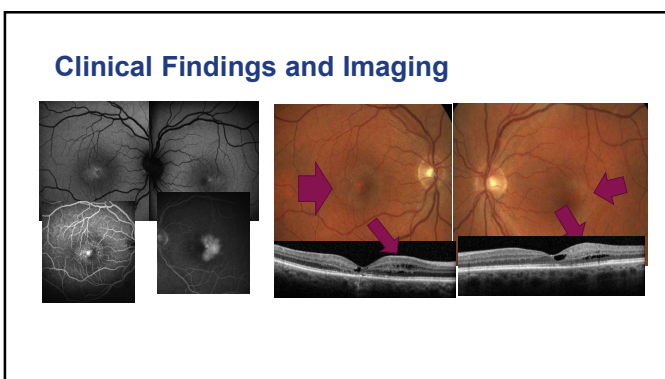
- Dry eyes
- Demodex blepharitis
- Refractive error
- Glaucoma, Cataracts
- And more...



“Why didn’t anyone tell me this before?”

- New patient 63-year-old WM, accountant with complaints of words “dropping out” while reading.
- BCVA = 20/30 OD, OS

BCVA = Best Corrected Visual Acuity

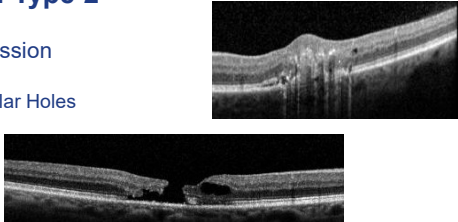


Macular Telangiectasia type 2 (MacTel)

- A rare, progressive, neurodegenerative disease that causes gradual central vision loss
- An AMD masquerader
- Typically diagnosed in middle-aged or older patients
- Diagnosed by clinical findings (challenging), OCT, OCTA, FAF and fluorescein angiography (FA) can confirm the diagnosis

MacTel Type 2

- Progression
 - MNV
 - Macular Holes



MacTel

- **Treatment:** The FDA has approved revakinogene tarovecel-lwey (Encelto), marking the first treatment for macular telangiectasia type 2 (MacTel), which aims to slow vision loss in affected patients.


FDA Approves First Treatment for MacTel

Neuretech's ocular insert Encelto aims to slow vision loss in patients with this degenerative retinal disease.

RETINAL PHYSICIAN | MARCH 6, 2025

Neuroprotection

- Encapsulated Cell Therapy (ECT): Platform releases Ciliary Neurotrophic Factor (CNTF), a protein shown to protect against the progressive loss of photoreceptors.
- Provides a steady-state therapeutic and safe concentration following single intraocular application.
- Potentially mitigates the risk associated with repeated intraocular injections or drugs, sub-retinal injections required of gene therapy and bypasses the restrictions of conventional allogeneic cellular transplantation.

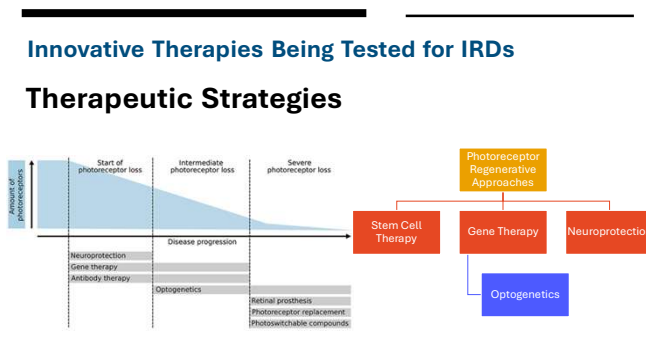


Tao et al., IOVS 2002 43:3292-3298

Source: <https://www.neuretechpharmaceuticals.com/science-technology/>

Innovative Therapies Being Tested for IRDs

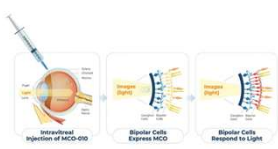
Therapeutic Strategies



IRDs: Inherited Retinal Disorders

Optogenetics

- Does **not** address specific genes or mutations
- Transgenes are introduced into the retina that produce opsins, or light-sensitive proteins.
 - This can preserve and even restore vision, even when many photoreceptors are no longer functioning.
 - May restore **light perception and functional vision signals** in selected patients; depends on inner retinal integrity.



For Details: <https://www.neuretechpharmaceuticals.com/science-technology/>

Optogenetics: Shih, Prabha, et al. Treatment of Inherited Retinal Disease | Retinal Physician

GENETIC TESTING

Available Tests- Foundation for Fighting Blindness

SPONSOR ORGANIZATIONS PROVIDE FREE TESTING

OTHER COMMERCIALLY AVAILABLE

- Direct-to-consumer; not a clinical IRD diagnostic test

CHECK YOUR STATE OPTOMETRY REGULATIONS

- Genetic Testing Registry (NIH)
- Database for Available Tests
- Advance Research Options
- ClinVar (NIH)
- Info on known clinical effect of gene variants

AAO guidelines now recognize and support offering genetic testing and counseling for suspected IRDs when results may affect diagnosis, prognosis, family planning, or trial eligibility.

PREVENTION GENETICS part of ENACT SCIENCES

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IMPROVING LIVING THE TEST

My Retina Tracker Program

The My Retina Tracker genetic testing Program offers individuals with a clinical diagnosis of an inherited Retinal Disease (IRD) access to high-quality diagnostic testing, genetic counseling, and connection to a growing IRD registry at no cost to the patient. Targeted familial variant testing is also available to blood relatives of individuals who receive a positive result through the Program. The Foundation Fighting Blindness, a nonprofit organization dedicated to finding treatments for IRD, Spark Therapeutics and Johnson & Johnson sponsor the Program.

Our Cookie Policy

Johnson & Johnson

Promising Clinical Trials

CLINICALTRIALS.GOV

RD / disease	Therapeutic approach	Molecule / therapy	Company / sponsor	Phase (NCT ID)
RP (gene-agnostic)	Reduces oxidative stress	N-acetylcysteine	Johns Hopkins / Wilmer	Phase 3 (NCT05537220)
Advanced RP (mutation-agnostic)	Restores photosensitivity (optogenetics)	MCO-010	Nanoscope Therapeutics	Phase 2b/3 (NCT04945772)
XLRP (RPGR)	Replaces RPGR (subretinal AAV)	botaretigene sparaparovect	Janssen / Johnson & Johnson (w/ MeiraGTx)	Phase 3 (NCT04671433)
XLRP (RPGR)	Replaces RPGR (subretinal AAV)	lanu-zova (AGTC-501)	Beacon Therapeutics	Phase 2/3 (NCT04850118)
RP (RHO + other genotypes)	Modifies retinal pathways (AAV modifier gene)	OCU400 (NR2E3 AAV)	Ocugen	Phase 3 (NCT05638200)
Stargardt (STGD1; ABCA4)	Reduces vitamin-A dimerization	glideuretimol acetate (ALK-001)	Alkermes Pharmaceuticals	Phase 2 program (NCT04262696; NCT04239625)
Stargardt (adolescent STGD1)	Slows retinal delivery (RBP4 pathway)	tinlarebant (LBS-008)	Belite Bio	Phase 3 (NCT05244304)
LCA10 (CEP290)	Corrects splicing (intravitreal ASO)	sopofarsen	Sepul Bio (Thera)	Phase 3 (NCT05891443)

Challenges in Clinical Trials

BY THE NUMBERS: CLINICAL TRIALS AWARENESS

- 11% OF SITES FAIL TO ENROLL EVEN A SINGLE PATIENT
- 37% OF SITES DO NOT MEET THEIR ENROLLMENT GOALS
- 40% OF SURVEYED ADULTS DON'T UNDERSTAND CLINICAL TRIALS
- 32% OF SURVEYED ADULTS SAY THEY'D CONSIDER PARTICIPATING—IF THEY UNDERSTOOD WHAT A CLINICAL TRIAL IS

- Recruitment and Retention
- Ensuring sufficient patient enrollment

Patient Recruitment

Methods used to search for clinical trials

- 38% Major Search Engines
- 14% Disease-Specific Health Association Sites
- 11% Referrals From Family/Friends
- 10% Referrals From Physician/Nurse
- 10% Newspapers
- 9% Other
- 8% Social Media

PARTICIPATION

In a survey by National Institutes of Health about clinical trial awareness:

- 85% didn't know a clinical trial was an option at diagnosis
- 75% would have been willing to enroll, if available

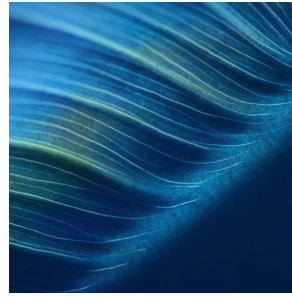
MORE INFORMATION CAN BE FOUND AT: CLINICALTRIALS.GOV

Benefits of Participation

- Access to New Treatments** - Early access to cutting-edge therapies
- Contribution to Scientific Knowledge** - Helping to advance medical understanding and treatment options
- Close Medical Supervision** - Regular check-ups and monitoring

Referrals Should Not Mean Goodbye

- Schedule follow-up for referred patients
 - Ensure adherence with treatment
 - **Address patient concerns and anxieties**
- Continue treating other ocular conditions
 - Pre-existing conditions
 - Resulting conditions
- **Adapting treatment plans based on outcomes**
 - Refractive correction
 - Low vision services



*Thank
you*