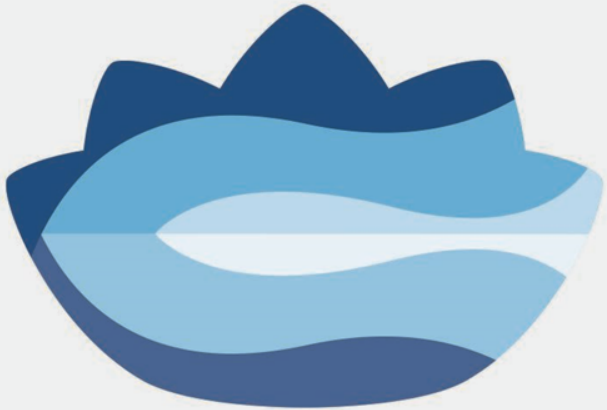
POYANG

A PHASE III, MULTICENTER, RANDOMIZED, DOUBLE-MASKED, ACTIVE COMPARATOR-CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF FARICIMAB IN PATIENTS WITH CHOROIDAL NEOVASCULARIZATION SECONDARY TO PATHOLOGIC MYOPIA



Version 1.0 22-Dec-23

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Myopia Epidemic

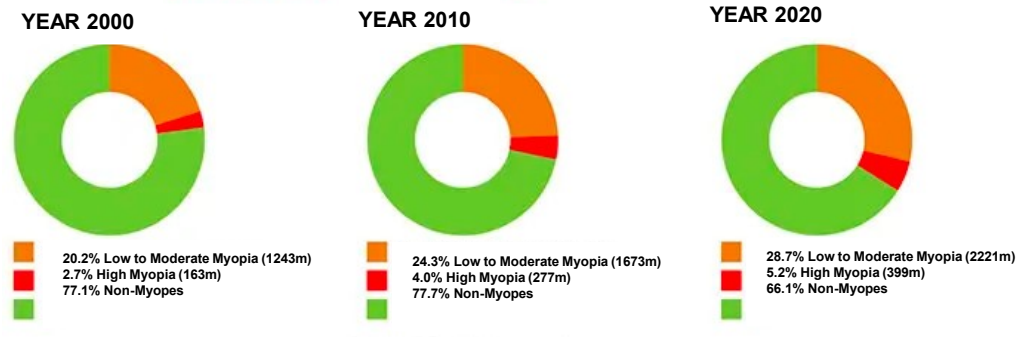
The myopia epidemic has become a very important global health issue.

In 2010, 28% of the world's population was affected.

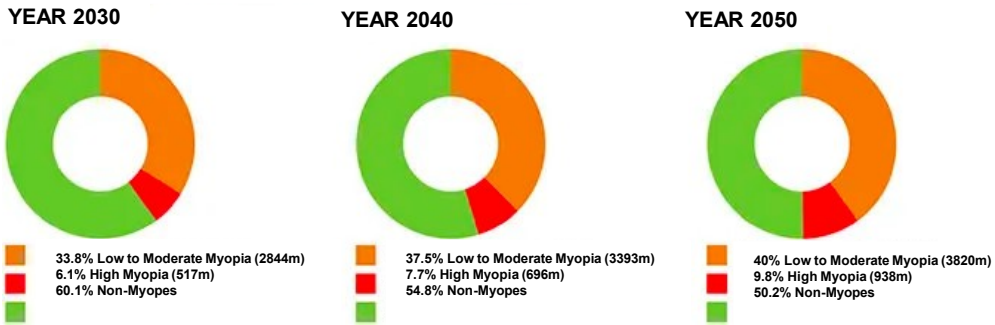
By 2050, the proportion could reach 50%.

The burden has been felt most strongly in APAC, where rates can be as high as 90%

Severity Levels 2000-2020

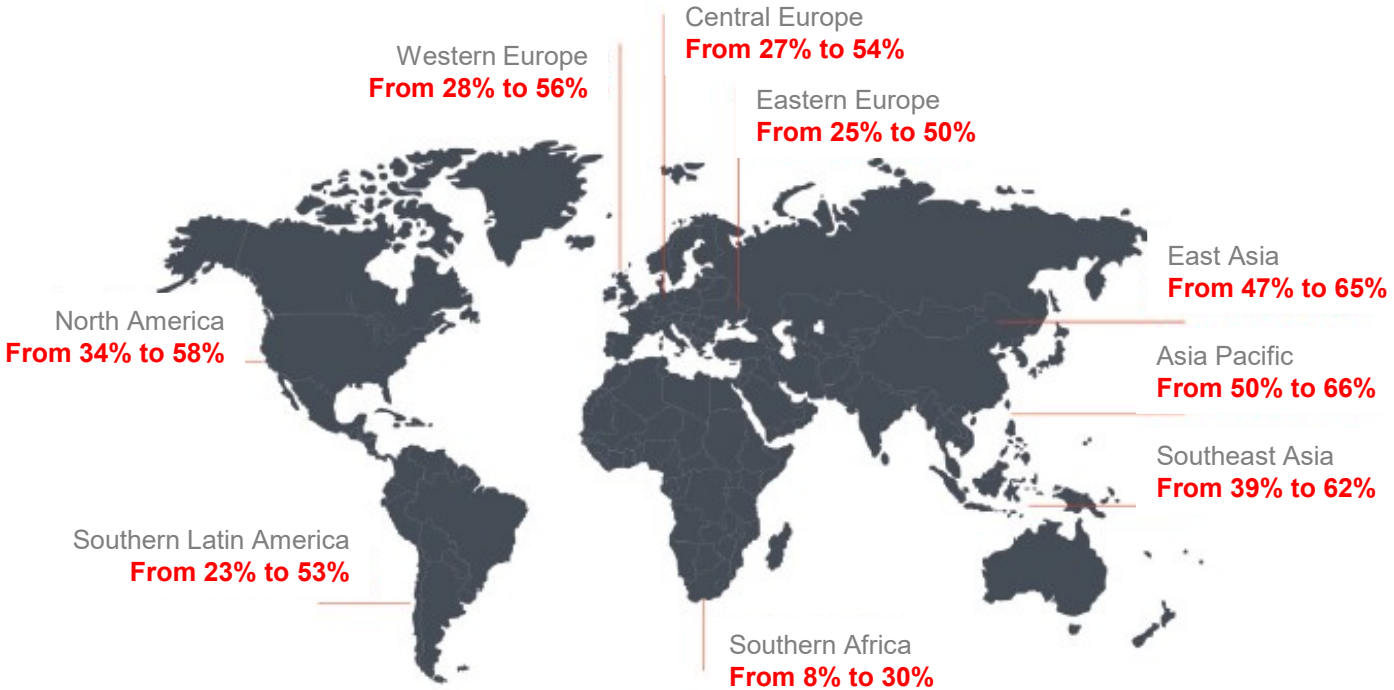


Severity Levels 2030-2050



https://www.aao.org/eyenet/article/facing-the-myopia-epidemic#:~:text=The%20myopia%20epidemic%20has%20become,that%20number%20could%20reach%2050%25.

Current and Projected by 2050 Myopia Prevalence



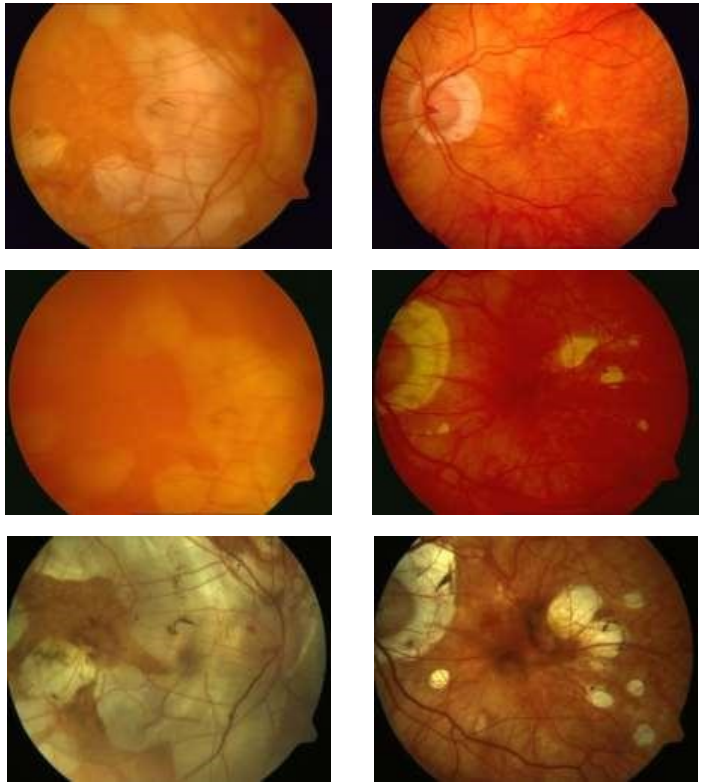
Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-1042.

Pathological Myopia

- High myopia is defined as refractive error of at least -6.0D spherical equivalence or an axial length of 26.0mm or more

- Pathologic myopia (high myopia with degenerative changes of the sclera, choroid and retina) represents a subgroup of myopia and affects up to 3% of the world population

- Vision loss related to pathologic myopia is of great clinical significance as it can be progressive, irreversible and affects individuals during their most productive years.



Classic Features

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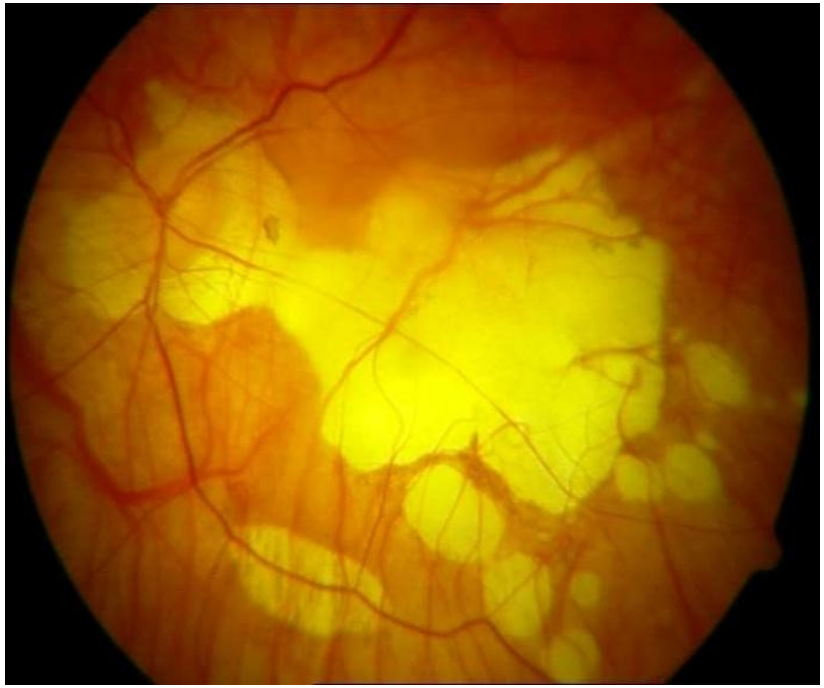
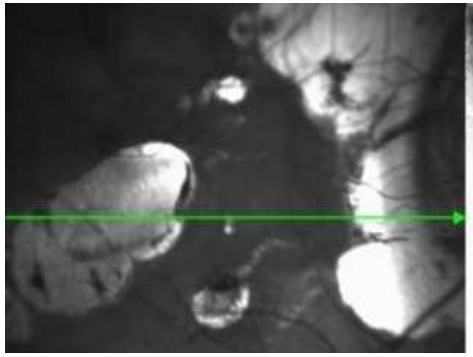
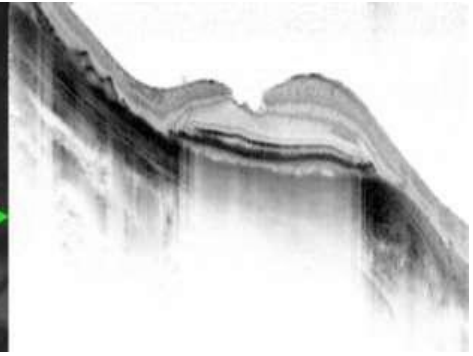
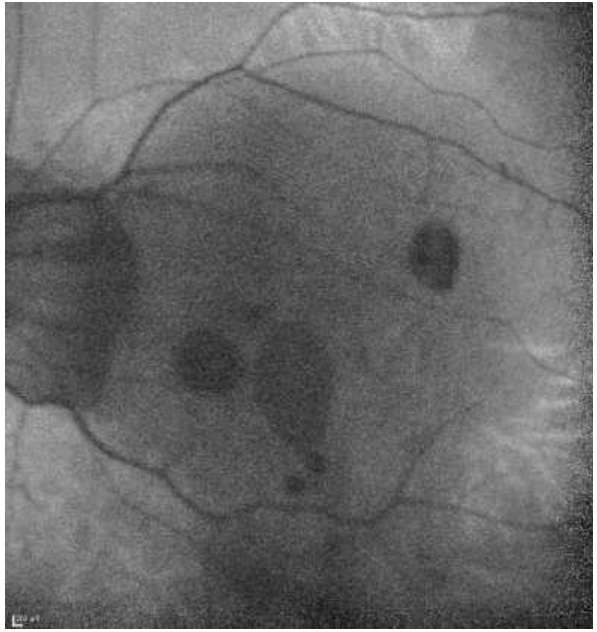
Patchy atrophy

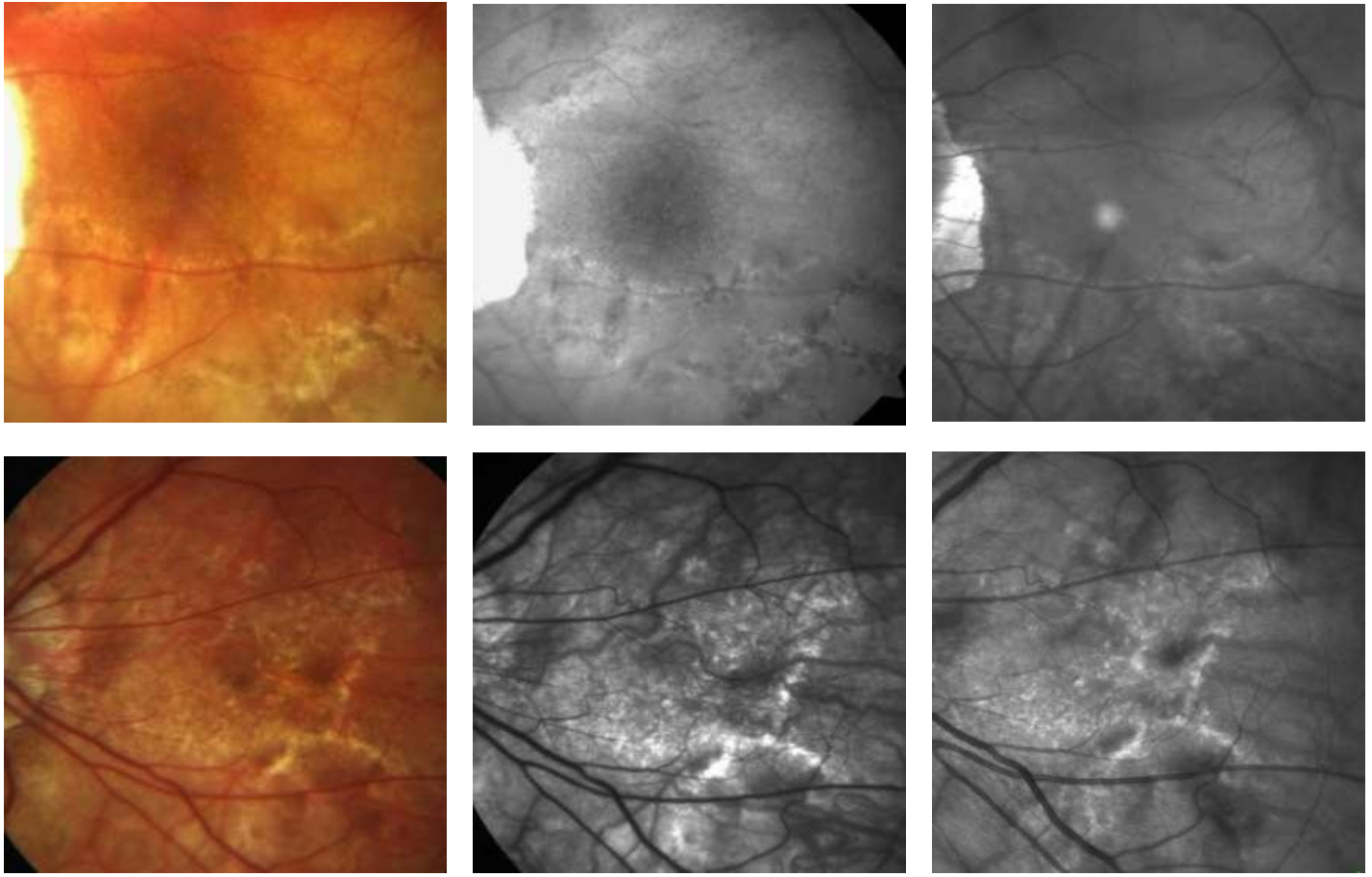




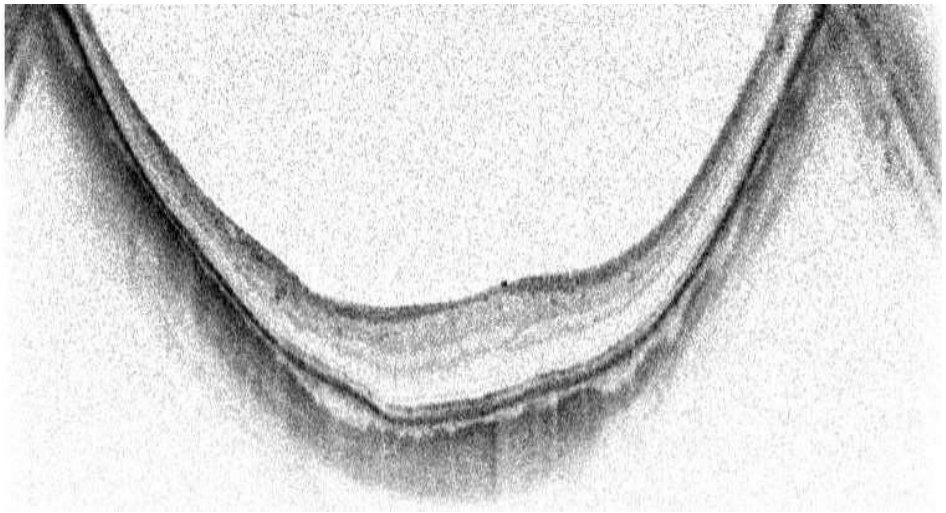




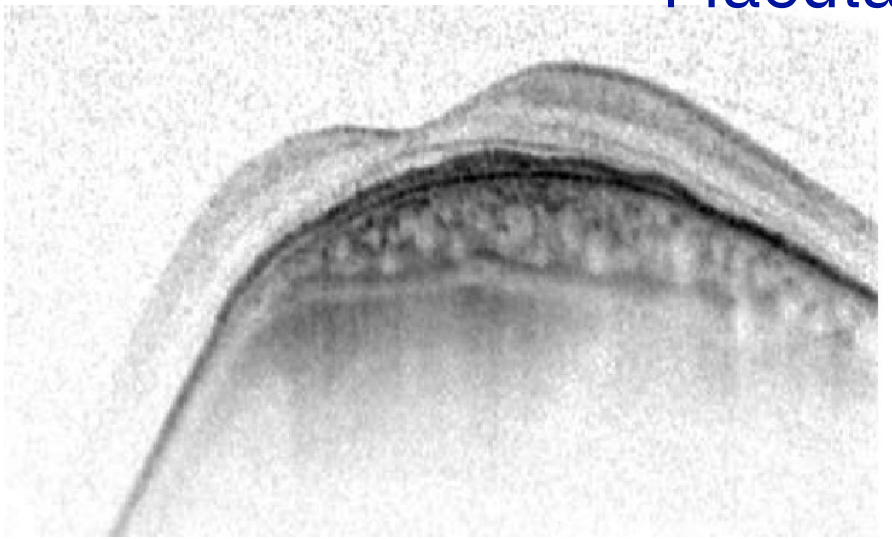
Lacquer cracks

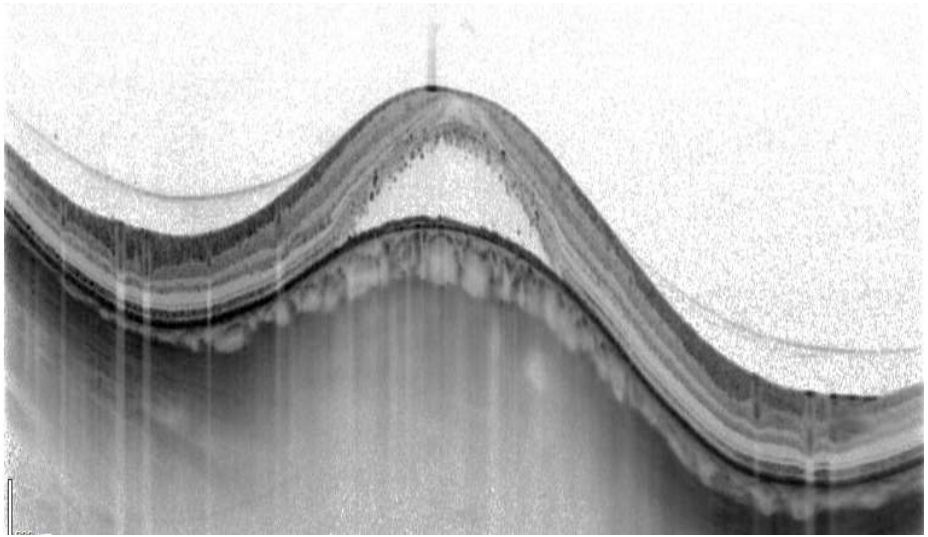


Choroidal thinning

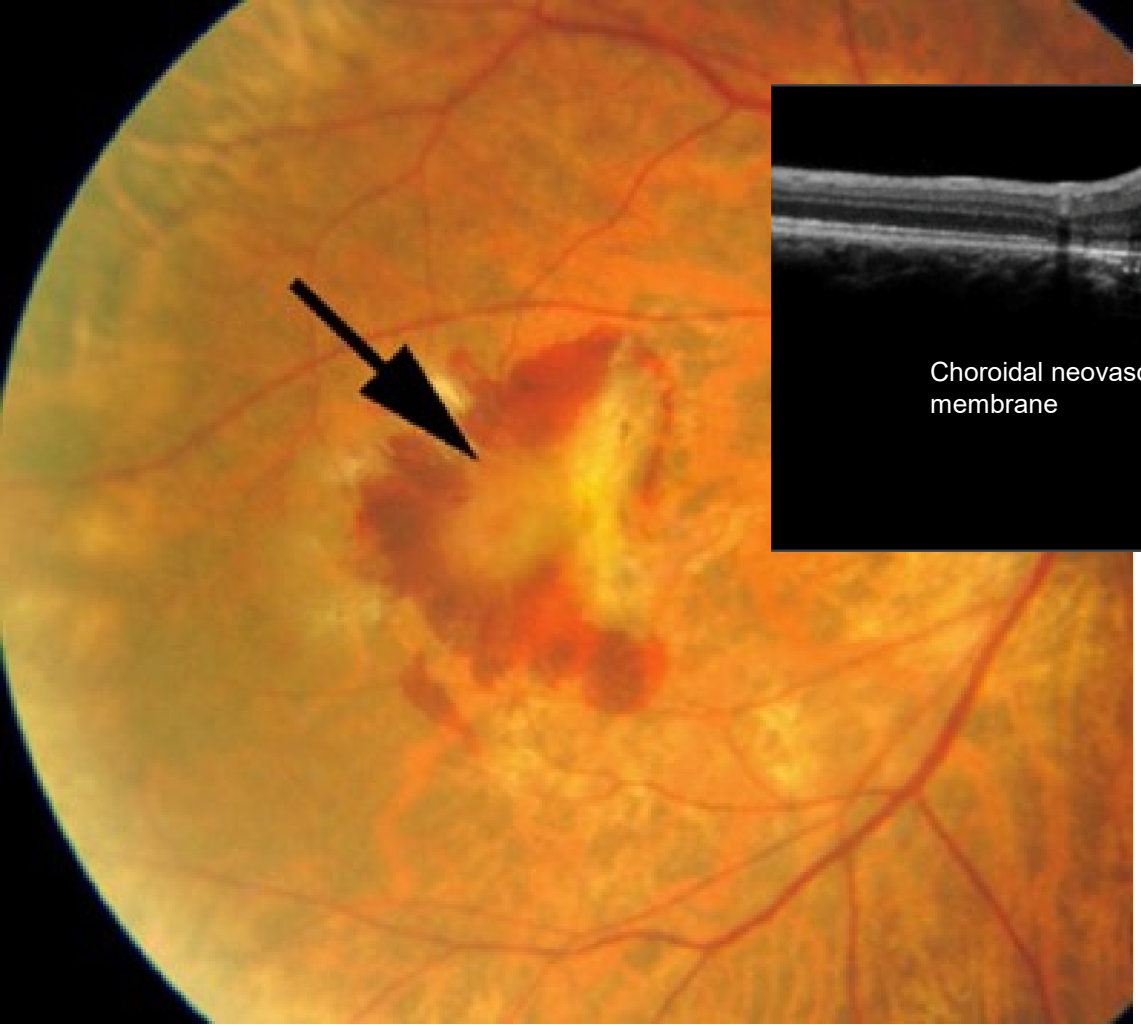


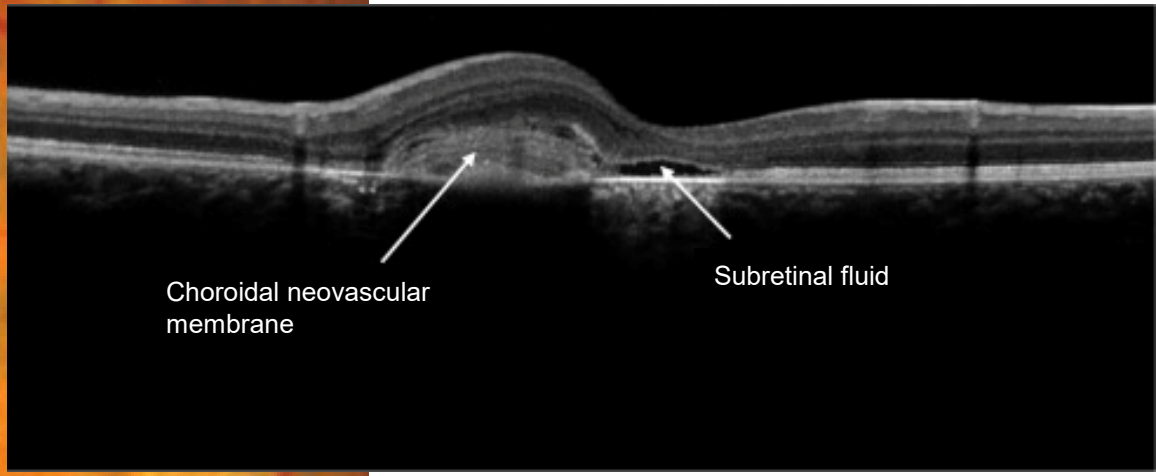
Dome-shaped Macula





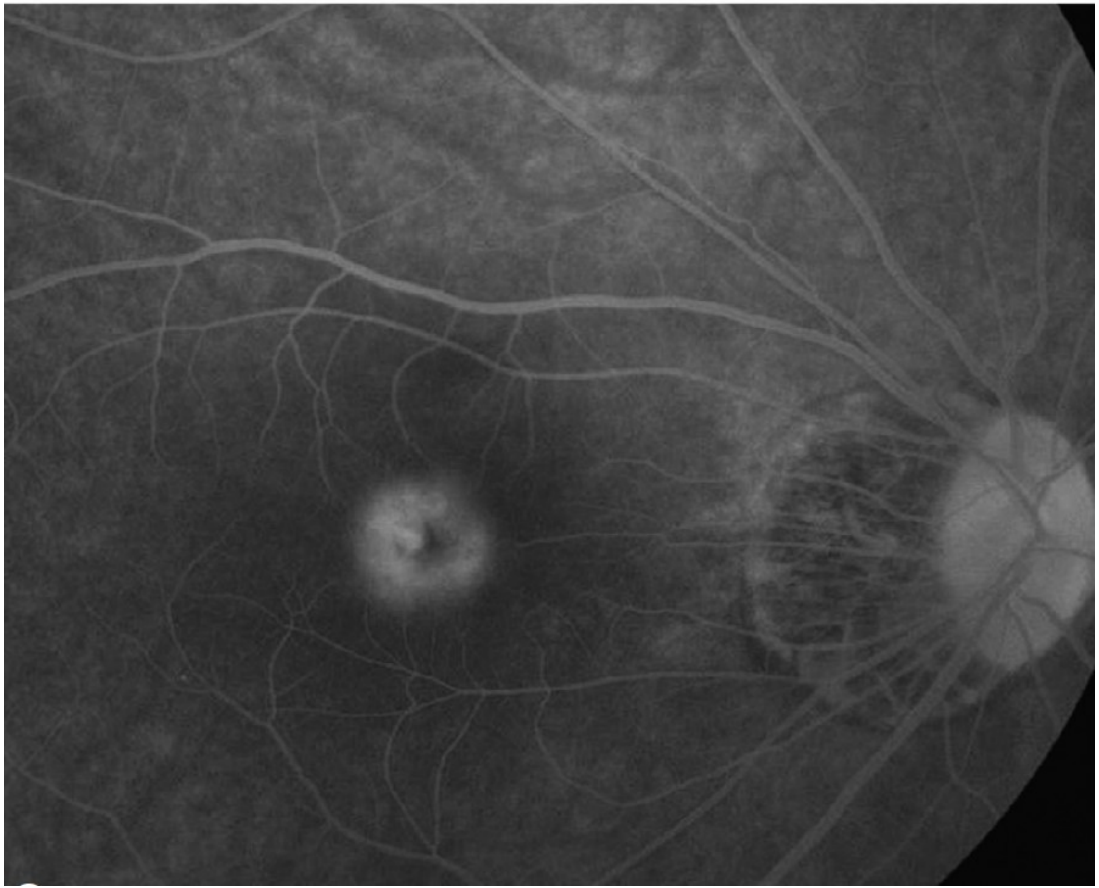
(Prevalence 10-18%)





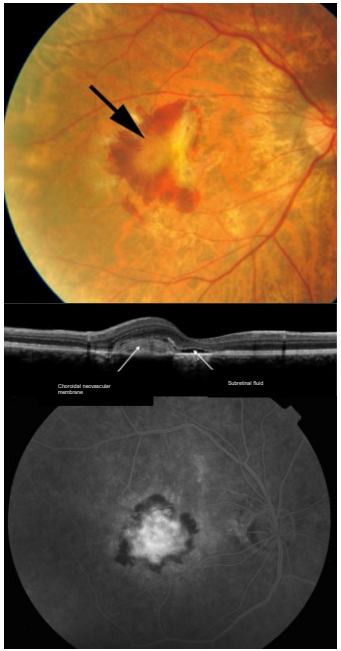
Choroidal Neovascularization

Choroidal Neovascularization



Myopic CNV

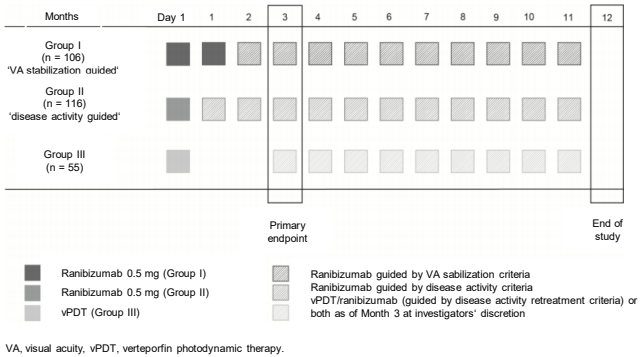
- Serious complication of high and pathological myopia is myopic choroidal neovascularization (mCNV)
  - 5% - 11% of individuals with PM will develop mCNV
- mCNV reported as the most common cause of CNV in the under 50 year age group



1: https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/nearsightedness-myopia-data-and-statistics (accessed July 2021), 2.. Holden et al., Ophthalmology 2016 May;123(5):1036-42 3. Cheung et al. Ophthalmology 2017;124:1690-17113

Previous RCT studies for myopic CNV

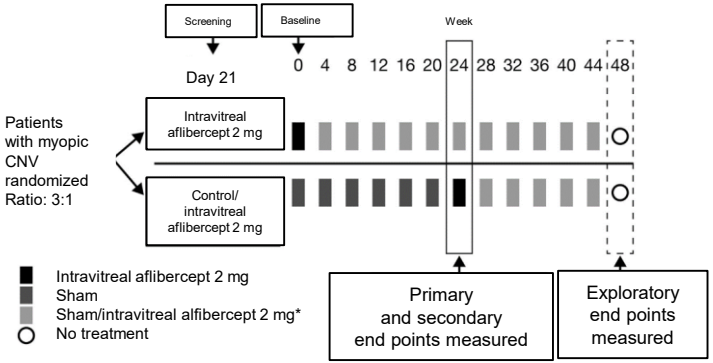
RADIANCE (ranibizumab in mCNV)*



Comparator	Verteporfin PDT (superiority study)
Study Length	12 months (PEP @ 3 months)
PEP	BCVA change from baseline to average of month 1 to 3
Retreatment criteria	VA stabilisation guided arm: defined as no change in VA based on PI judgment Disease activity arm: visual impairment attributable to SRF, IRF, or active leakage secondary to mCNV in PI judgement

**Identical study BRILLIANCE conducted to get mCNV indication in China (China, Hong Kong, India, South Korea, Philippines, Thailand)*

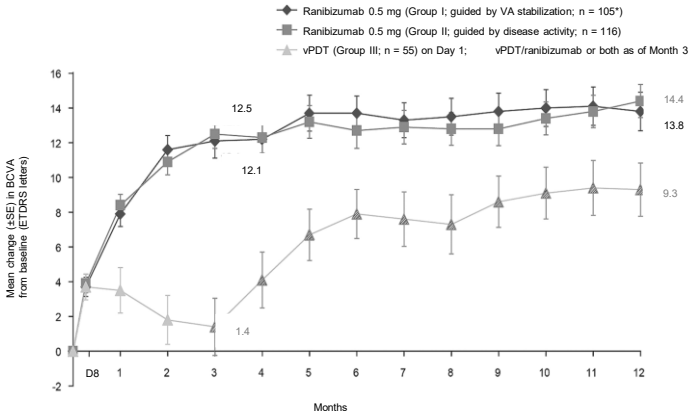
MYRROR (aflibercept in mCNV)



Comparator	Sham (superiority study)
Study Length	12 months (PEP @ 6 months)
PEP	BCVA change from baseline to month 6
Retreatment criteria	(1) > 5 letter BCVA reduction from the previous exam; (2) > 50 micron increase in CST, new or persistent cystic retinal changes, SRF or PED and new or persistent CNV or bleeding; or (3) deemed necessary by the investigator

Previous RCT outcomes for myopic CNV

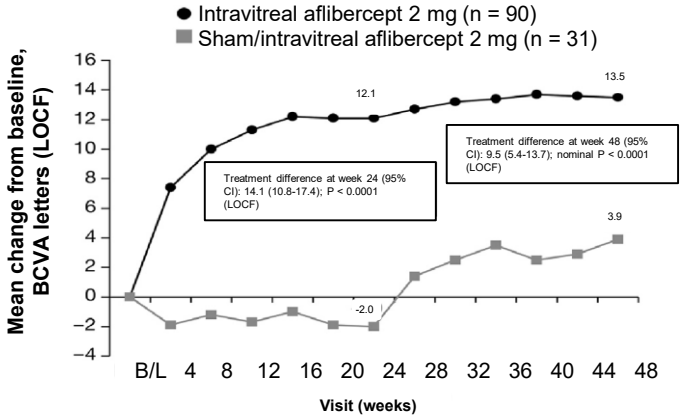
RADIANCE (ranibizumab in mCNV)*



Arm	3m VA gain	12m VA gain	No. of injections 12m
RBZ (VA-guided tx)	12.1	13.8	4.6
RBZ (anatomical-guided tx)	12.5	14.4	3.5
PDT	1.4	9.3	2.4

*Identical study BRILLIANCE conducted to get mCNV indication in China (China, Hong Kong, India, South Korea, Philippines, Thailand)

MYRROR (aflibercept in mCNV)



Arm	6m VA gain	12m VA gain	No. of injections 12m
AFL	12.1	13.5	4.2
Sham	-2.0	3.9	3.0

Current Options

Ranibizumab licensed indications (RADIANCE/BRILLIANCE Study - ranibizumab vs. PDT)

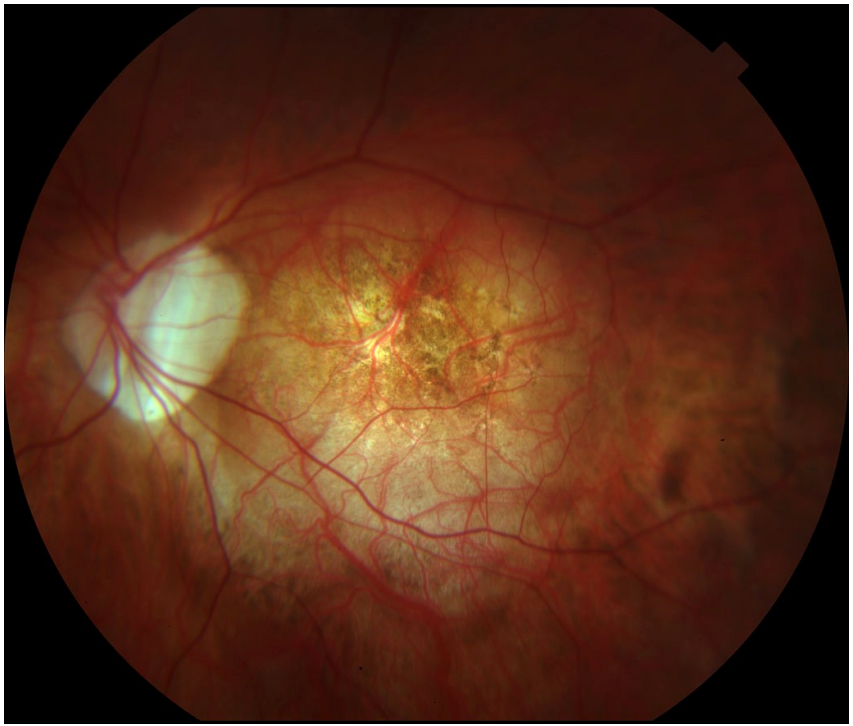
- US = mCNV
- EU/ROW = visual impairment due to CNV

Aflibercept licensed indications (MYRROR Study - aflibercept vs. sham)

- US = not approved
- China = not approved
- EU/ROW = mCNV

Studies show a clear benefit of anti-VEGF therapy in treating myopic CNV, with 3-4 injections in the first year to improve and maintain BCVA

Unmet need with current mCNV treatment options…



Approximately 10 to 20% CNV recurrence rate necessitating treatment

Up to 12.5% of patients with significant (10+ letter) vision loss over time

Initial visual acuity benefits may not persist with longer (5+ year) followup

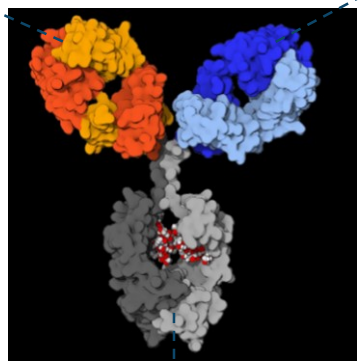
Myopic macular neovascularization eyes lose vision mainly because of **multiple recurrences (median time to recurrence ~ 14 months)**

Cicinelli, Maria Vittoria MD*,†; L T De Felice, Elisabetta MD*; La Franca, Lamberto MD*,†; Rabiolo, Alessandro MD†; Marchese, Alessandro MD*,†; Battaglia Parodi, Maurizio MD*,†; Introini, Ugo MD†; Bandello, Francesco MD*,†. RISK FACTORS OF VISION LOSS AND MULTIPLE RECURRENCES IN MYOPIC MACULAR NEOVASCULARIZATION. Retina 43(2):p 275-285, February 2023. | DOI: 10.1097/IAE.0000000000003673

Faricimab:
1 Molecule Targeting 2 Signaling Pathways via Ang-2 and VEGF-A to Improve Vascular Stability for Durable Efficacy

Anti–Ang-2 Fab
Stabilizes vessels
Reduces vascular leakage
Reduces inflammation

Anti–VEGF-A Fab
Reduces vascular leakage
Inhibits neovascularization



Modified Fc
Reduces systemic exposure
Reduces inflammatory potential

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

Clinical Biomarker Targets for Dual Pathway Inhibition

Evidence from biology

Dual pathway inhibition with faricimab: Anti-Ang-2 + Anti-VEGF-A[1]

Elevated VEGF[2]

Elevated Ang-2[1,3–4]

- **Neovascularization[5,6]**
- **Vascular leakage[7]**
- **Inflammation[5,6,8]**
- **Fibrosis[9–13]**

Clinical biomarkers

Greater* **reduction** of **fluid on OCT** (DME, nAMD)[14,15]
Greater* **reduction of IRF** (DME)[14]

Greater* **reduction** of **macular leakage** (DME, RVO)[18,19]

Greater* **reduction** of **HRF** (DME)[16]

Greater* **reduction** of **ERM** development (DME)[17]

Disease control with faricimab vs anti-VEGF monotherapy[14–19]

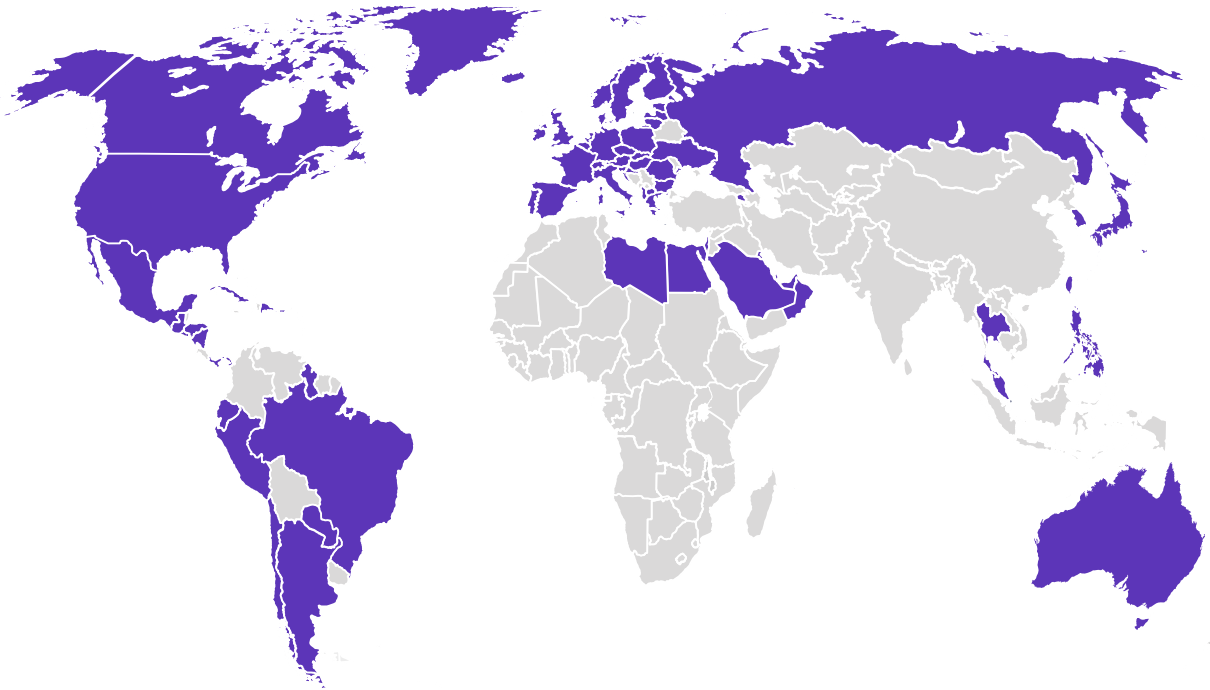
Extended durability beyond Q12W[17,20–24]

VEGF | VEGF & Ang-2 | Ang-2

***Based on secondary endpoints and post-hoc exploratory analyses of IRF/SRF, macular leakage, HRF and ERM in the Phase 3 clinical trial program, with nominal p value statistical testing (not adjusted for multiple testing). No formal statistical conclusions can be drawn.** Ang-2, angiopoietin-2; DME, diabetic macular edema; ERM, epiretinal membrane; HRF, hyperreflective foci; IRF, intraretinal fluid; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; Q12W, every 12 weeks; RVO, retinal vein occlusion; SRF, subretinal fluid; VEGF, vascular endothelial growth factor; VEGF-A, vascular endothelial growth factor A.

1. Regula JT, et al. *EMBO Mol Med*. 2016;8:1265–88; 2. Aiello LP, et al. *N Engl J Med*. 1994;331:1480–7; 3. Tsai T, et al. *PLoS One*. 2023;18:e0280488; 4. Ng D, et al. *Sci Rep*. 2017;7:45081; 5. Kim S-Y, et al. *Ann Eye Sci*. 2021;6:24; 6. Collazos-Aleman JD, et al. *Diabetes Ther*. 2022;13:1811; 7. Rangasamy S, et al. *Invest Ophth Vis Sci*. 2011;52–9; 8. Hirasawa M, et al. *J Biol Chem*. 2016;291:7373–85; 9. Larsen OH, et al. *Ophth Ther*. 2023;12:2253–64; 10. Canonica J, et al. *Front Cell Neurosci*. 2023;17:1192464; 11. Klaassen I, et al. *PLoS One*. 2017;12:e0187304; 12. Takagi H, et al. *Invest Ophth Vis Sci*. 2003;44:393–402; 13. Umeda N, et al. *Ophth Res*. 2003;35:217–23; 14. Pollreiz A, et al. *Invest Ophthalmol Vis Sci*. 2023;64:2817; 15. Querques G, et al. *Invest Ophthalmol Vis Sci*. 2023;64:2185; 16. Maunz A, et al. ARVO 2023; 17. Jaffe G, et al. Presented at ASRS 2023, presentation available at medically.roche.com; 18. Goldberg RA, et al.

As of October 2023, > 2 million vials have been distributed



Faricimab is approved in
> 80 countries

~ 2 years
in the market in the US

> 2 million vials
distributed worldwide

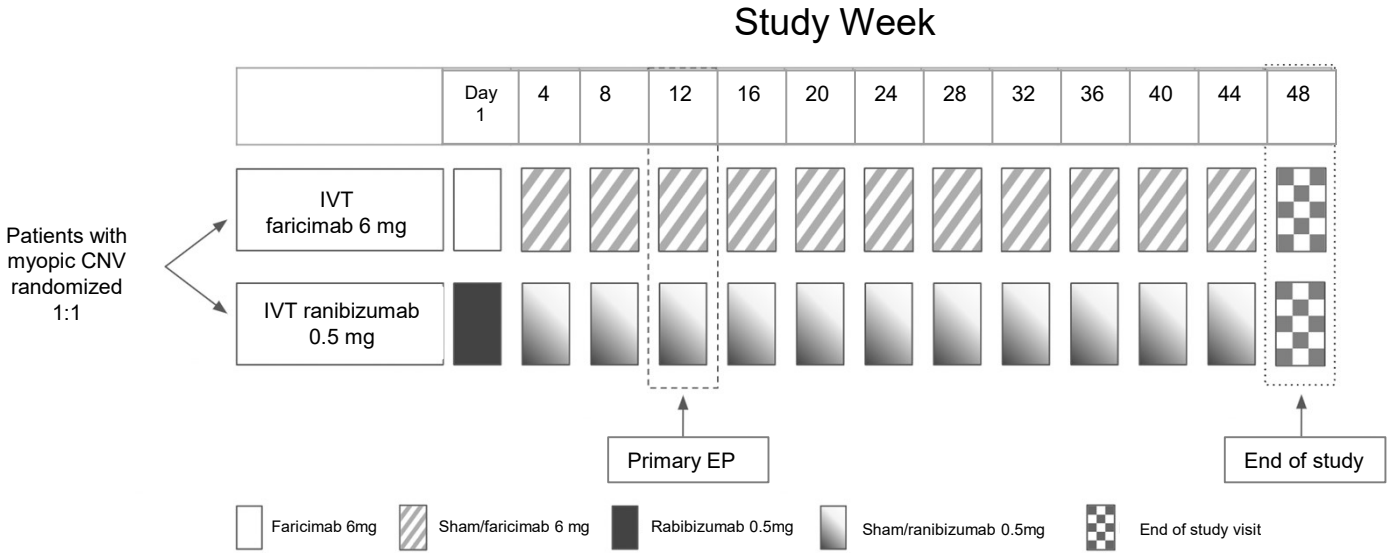
POYANG Study Objectives

To investigate …

- **Efficacy of faricimab on visual acuity in patients with CNV secondary to pathologic myopia**
- **Benefits of faricimab on anatomical endpoints**
- **Safety of faricimab**

Study Design

- Non-inferiority study of 280 treatment-naive myopic CNV patients
- Faricimab 6.0mg vs. ranibizumab 0.5mg
- Active dosing at Day 1 followed by PRN based on Retreatment Criteria
- Non-dosing End of Study visit at Week 48
- Total Duration: Screening Period + 48 weeks
- Monthly assessments with BCVA and OCT at every visit



Study Population (Key Study Eye Ocular Criteria)

Inclusion	Exclusion
• Diagnosis of active CNV secondary to pathologic myopia (reading center confirmed) • BCVA ≥24 and ≤78 letters (20/320-20/32 Snellen equivalent) • anti-VEGF treatment-naive adults • Sufficiently clear ocular media and adequate pupillary dilatation to allow acquisition of good quality retinal images to confirm diagnosis	• History of previous pan-retinal or focal/grid laser photocoagulation with involvement of the macular area in the study eye at any time • History of intraocular treatment with corticosteroids, or treatment with anti-VEGF or vPDT at any time in the study eye • Presence of CNV secondary to any cause other than pathologic myopia • Myopic tractional maculopathy/schisis • Epiretinal membrane • History of uveitis

Study Population (General Criteria)

Inclusion

- **Adult patients** (≥18 years)
  - ≥19 in Korea
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use acceptable contraceptive measures, as defined in protocol

Exclusion

- Any **major illness** or **major surgical procedure** within 1 month before screening
- Recent history of **stroke** or **myocardial infarction** (within 6 months)
- Systemic treatment for suspected or active **systemic infection**
- **Uncontrolled Blood Pressure** (>180/100)
- Pregnancy or breastfeeding
- **Active cancer in past 12 months** (except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, and prostate cancer)

Summary

- The prevalence of high myopia and pathologic myopia are increasing rapidly globally over time
- Anti-VEGF agents are the standard of care treatment for mCNV, though there are opportunities to improve outcomes in these younger patients
- Faricimab, a dual-pathway inhibitor of VEGF-A and Ang-2, may serve as an exciting new option to help these patients

If you have patients who would be good candidates for this study, please contact:

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