



Simultaneous GA and CNV / MNV: incidence, characteristics, and treatments

The Vision Academy is a group of over 80 international experts who, through their collective expertise, provide consensus guidance for managing clinically challenging situations, especially in areas of controversy or with insufficient conclusive evidence.

The Vision Academy is funded and facilitated by Bayer.

This presentation is based on the Vision Academy publication:

Kataoka K *et al. Graefes Arch Clin Exp Ophthalmol* 2025; 263 (5):1197–212 and is intended for healthcare professionals.

The opinions expressed, and guidance laid out, by the Vision Academy are developed independently by the members and do not necessarily reflect the opinions of Bayer.

Contents

Objectives

Background

Clinical challenges

**Insights from
published literature**

**Vision Academy
recommendations**

Summary



Click on a section

Objectives

To characterize the incidence, risk factors, and clinical characteristics associated with simultaneous GA and CNV / MNV

To provide guidance on the diagnosis and management of simultaneous GA and CNV / MNV in clinical trials and clinical practice



QUESTION

How can we refine current practice for the diagnosis and management of simultaneous GA and CNV / MNV?



Background





GA and CNV / MNV in AMD

GA and **MNV** typically occur in the late stages of **AMD**, a leading cause of blindness in the elderly worldwide¹



CNV or MNV refers to the pathological formation of abnormal new blood vessels from the choroid or retinal circulation into²⁻⁴:

- Sub-RPE (type 1 MNV)
- Subretinal space (type 2 MNV)
- Retinal deep capillary plexus (type 3 MNV)

GA, or macular atrophy, is marked by⁵:

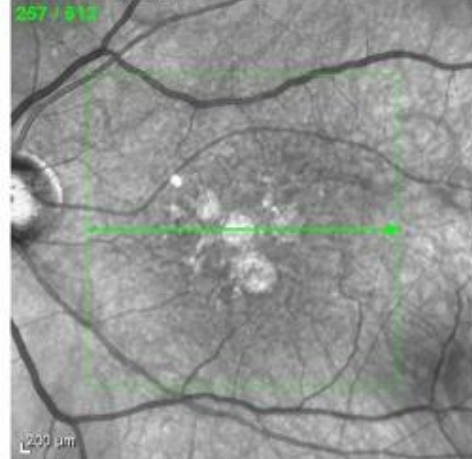
- Well-defined round or oval areas of RPE loss
- Thinning or loss of the outer retina, revealing choroidal vessels

AMD, age-related macular degeneration; CNV, choroidal neovascularization; GA, geographic atrophy; MNV, macular neovascularization; RPE, retinal pigment epithelium / epithelial.

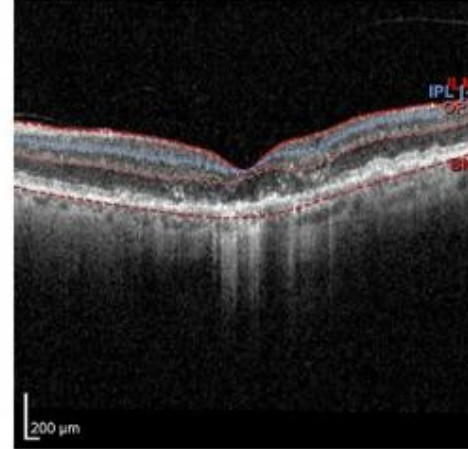
1. Ferris FL *et al. Ophthalmology* 2013; 120 (4): 844–851; 2. Sacconi R *et al. Prog Retin Eye Res* 2023; 92: 101113; 3. Mathis T *et al. Eye* 2023; 37 (9): 1758–1765; 4. Spaide RF *et al. Ophthalmology* 2020; 127 (5): 616–636; 5. Sadda SR *et al. Ophthalmology* 2018; 125 (4): 537–548.

Case study

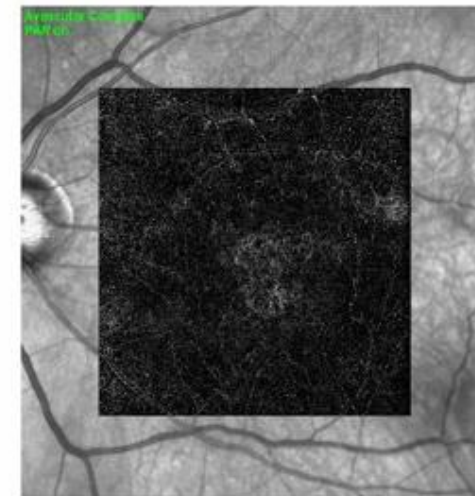
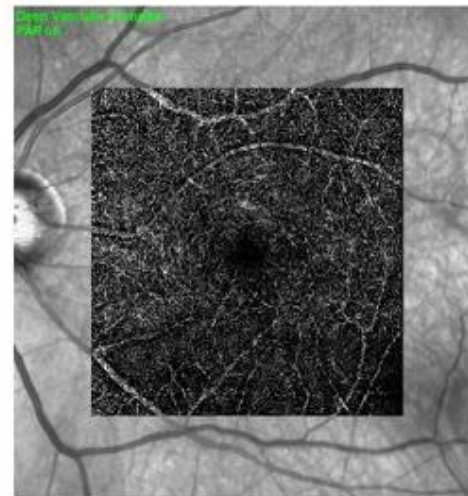
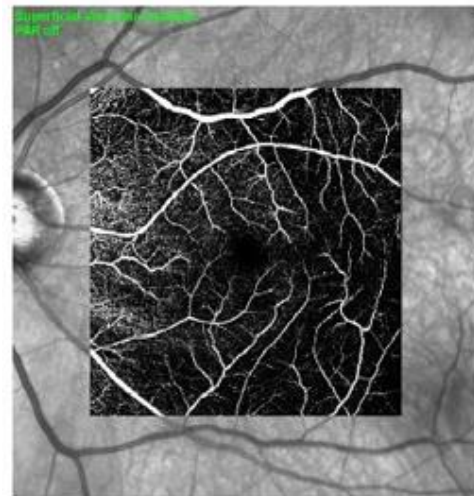
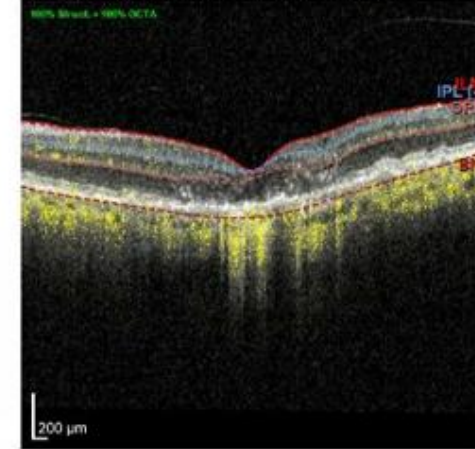
IR 30° ART [HS]



OCT 20° (5.9 mm) ART (4) Q: 32 [HS]



OCT 20° (5.9 mm) ART (4) Q: 32 [HS]





Recognition of simultaneous GA and CNV / MNV



GA and **MNV** have historically been regarded as two distinct entities; as a result, studies typically focused on **only GA** or **only MNV**¹

There have been several reports of coexistent GA and CNV / MNV, leading to the recognition of simultaneous GA and CNV / MNV¹⁻³

Understanding of treatment options for simultaneous GA and CNV / MNV is **currently lacking**¹



CHALLENGE REQUIRING VISION ACADEMY GUIDANCE

Guidance is needed for the diagnosis and management of simultaneous GA and CNV / MNV in clinical practice



CNV, choroidal neovascularization; GA, geographic atrophy; MNV, macular neovascularization.

1. Chakravarthy U *et al. Ophthalmology* 2018; 125 (6): 842–849; 2. Hwang CK *et al. Ophthalmol Retina* 2021; 5 (2): 108–117; 3. Capuano V *et al. Am J Ophthalmol* 2017; 182: 45–55.



Clinical challenges



Clinical challenges requiring guidance



Clinical characteristics

What new insights into simultaneous GA and CNV / MNV could aid recognition of coexistence?



Practical recommendations

How can we use this current evidence to produce recommendations for management of simultaneous GA and CNV / MNV?



Click on a section



Insights from published literature



Incidence



The incidence of CNV / MNV in eyes with GA has been reported as 7.4% per patient-year (mean follow-up period: 1.4 years)¹ or 13.8% (mean follow-up period: 4.1 years)²



The incidence of GA subsequent to CNV / MNV in eyes treated with anti-VEGF therapies has been reported as 24.4%,³ 29.4%,^{4,5} or 37%⁶ at 24 months

CNV, choroidal neovascularization; GA, geographic atrophy; MNV, macular neovascularization; VEGF, vascular endothelial growth factor.

1. Chakravarthy U *et al. Ophthalmology* 2018; 125 (6): 842–849; 2. Hwang CK *et al. Ophthalmol Retina* 2021; 5 (2): 108–117; 3. Bailey C *et al. Ophthalmology* 2019; 126 (1): 75–86; 4. Sadda SR *et al. Ophthalmology* 2018; 125 (6): 878–886; 5. Gune S *et al. Ophthalmology* 2020; 127 (4): 523–532; 6. Gillies MC *et al. Ophthalmology* 2020; 127 (2): 198–210.

Shared clinical characteristics and risk factors

GA and CNV / MNV share genetic risk factors and early disease clinical characteristics



Genetic factors

HTRA1, complement factor H, complement factors 3 and 2, and *ARMS2*^{1,2}



Clinical characteristics

- Large drusen, drusenoid PED, cuticular drusen, subretinal drusenoid deposits, intraretinal hyperreflective foci, hyporefective foci within drusenoid lesions, and drusen volume of 0.03 mm³ or more³⁻⁷
- Patients with simultaneous GA and CNV / MNV are typically older and have a higher prevalence of late AMD in fellow eyes compared with patients with GA or CNV alone²



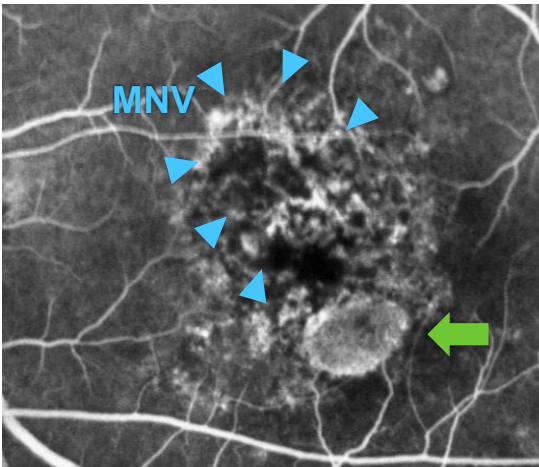
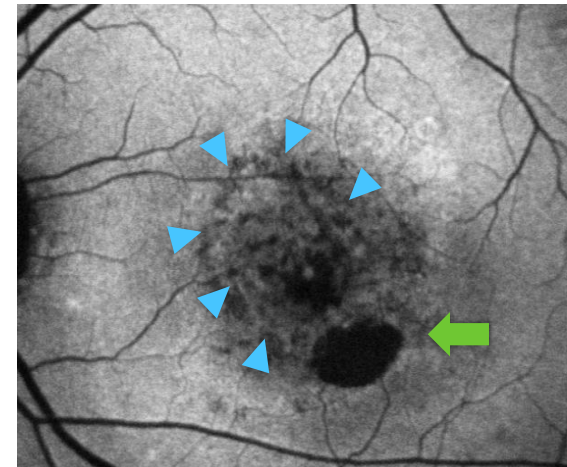
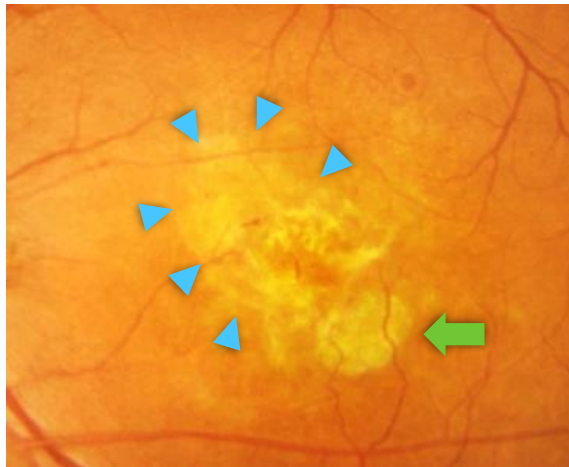
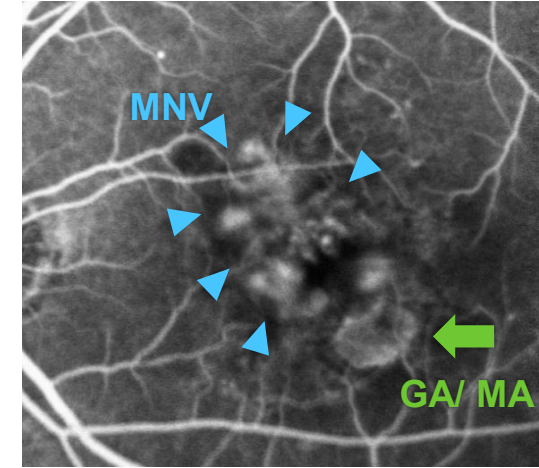
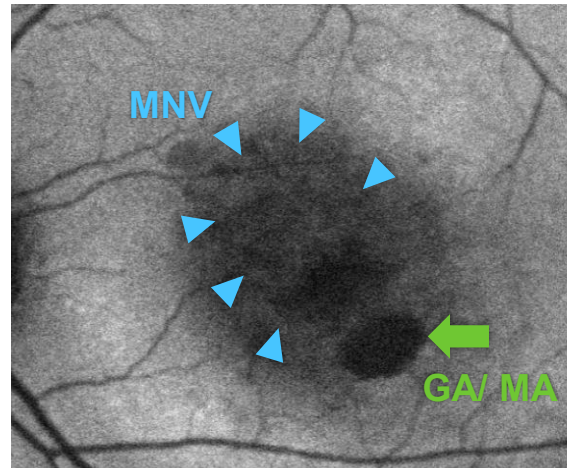
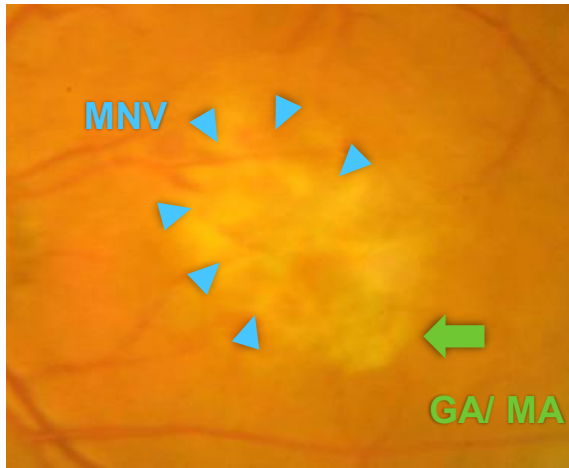
These commonalities suggest that simultaneous GA and CNV / MNV represent a continuum of late-stage AMD

AMD, age-related macular degeneration; *ARMS2*, age-related maculopathy susceptibility 2; CNV, choroidal neovascularization; GA, geographic atrophy; *HTRA1*, high-temperature requirement factor A1; MNV, macular neovascularization; PED, pigment epithelial detachment.

1. Grob S *et al. Eye* 2012; 26 (8): 1106–1113; 2. Saade C *et al. Br J Ophthalmol* 2014; 98 (12): 1729–1732; 3. Alexandre de Amorim Garcia Filho C *et al. Retina* 2013; 33 (8): 1558–1566; 4. Abdelfattah NS *et al. Invest Ophthalmol Vis Sci* 2016; 57 (4): 1839–1846; 5. Balaratnasingam C *et al. Ophthalmology* 2018; 125 (1): 100–118; 6. Finger RP *et al. Ophthalmology* 2016; 123 (3): 599–608; 7. Nassisi M *et al. Ophthalmology* 2019; 126 (12): 1667–1674.

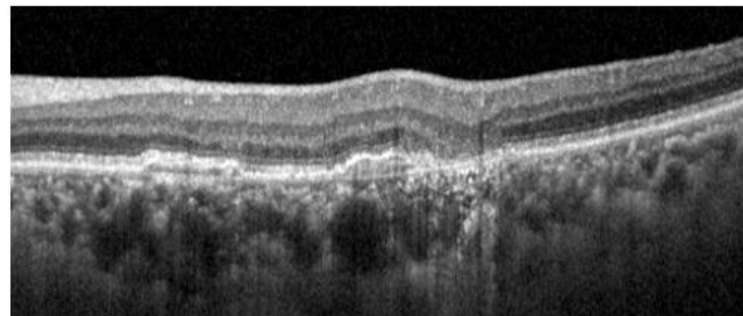
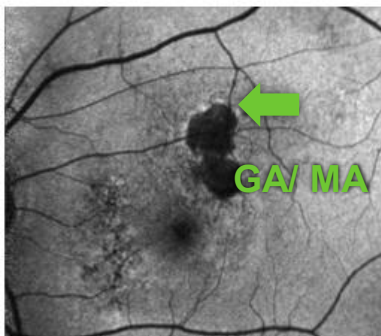
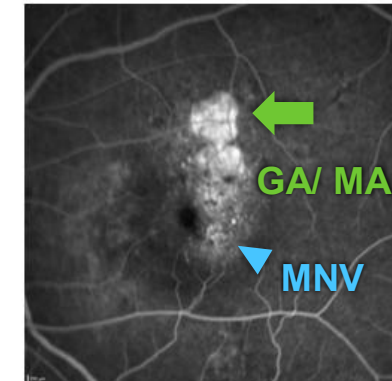
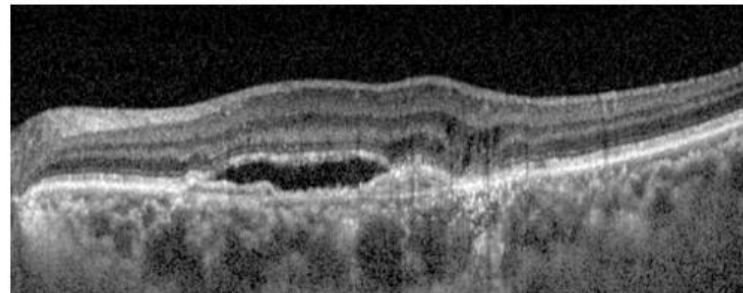
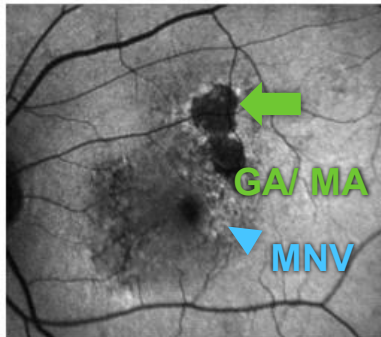
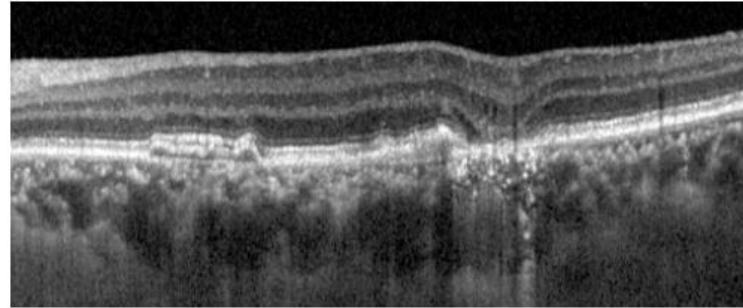
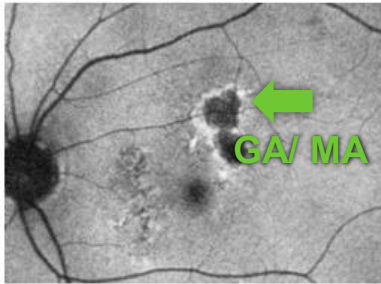


Case study





Case study of initial GA developing neovascularization



Diagnosis of CNV / MNV in GA



Multimodal imaging, including **FAF**, **OCT**, and **NIR**, is recommended for the detection of both macular atrophy and CNV / MNV, although CNV / MNV and associated exudation may mask macular atrophy, making GA diagnosis difficult



For studies in nAMD, SD- or SS-OCT volume scans should be performed at every visit, and fluorescein angiography, FAF color fundus photo, and NIR are recommended at baseline and selected follow-up visits¹



OCT-A has demonstrated high specificity (95.2%) and sensitivity (95.2%) in detecting MNV in eyes with simultaneous GA and CNV / MNV²

- A recent study using OCT-A reported the detection of subclinical CNV / MNV in **11–16%** of eyes with GA^{3,4}



Treatment and prognosis

No clinical trial to date has focused on the treatment of simultaneous GA and CNV / MNV

Development of GA during anti-VEGF treatment

- Patients with CNV / MNV, with or without macular atrophy, are treated with anti-VEGF therapy¹
- Macular atrophy, whether pre-existing or treatment-emergent, is linked to poor visual outcomes²⁻⁴
- Several studies report no direct link between anti-VEGF treatment and macular atrophy enlargement⁵⁻⁷
- Delaying anti-VEGF treatment has shown poorer vision outcomes and accelerated progression of macular atrophy⁸
- Early diagnosis of nAMD does not influence the prevalence of macular atrophy⁹

Development of new CNV / MNV during clinical trials for GA

- Complement inhibitors slow GA progression but are associated with a dose-dependent increased incidence of CNV / MNV and exudative AMD,^{10,11} raising questions about long-term safety and the optimal approach to managing emergent CNV / MNV

AMD, age-related macular degeneration; CNV, choroidal neovascularization; GA, geographic atrophy; MNV, macular neovascularization; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

1. Amaro MH, Roller AB. *Arq Bras Oftalmol* 2012; 75 (4): 273–276; 2. Rofagha S *et al. Ophthalmology* 2013; 120 (11): 2292–2299; 3. Cohen SY *et al. Retina* 2012; 32 (8): 1480–1485; 4. Ying GS *et al. Ophthalmology* 2015; 122 (12): 2523–2531.e1; 5. Casalino G *et al. Curr Eye Res* 2021; 46 (7): 988–994; 6. Siedlecki J *et al. BMC Ophthalmol* 2021; 21 (4): 4; 7. Hwang CK *et al. Ophthalmol Retina* 2021; 5 (2): 108–117; 8. Bhisitkul RB *et al. Ophthalmology* 2016; 123 (6): 1269–1277; 9. Gale RP *et al. Ophthalmol Retina* 2024; 8 (6): 545–552; 10. Liao DS *et al. Ophthalmology* 2020; 127 (2): 186–195; 11. Wykoff CC *et al. Ophthalmology* 2021; 128 (9): 1325–1336.

Risk factors and protective factors for development and progression of macular atrophy during anti-VEGF therapy



Risk factors

- Development of fibrotic scars¹
- Presence of type 3 neovascularization,²
- Presence of intraretinal cysts at baseline^{3,4}
- Atrophy in fellow eye^{3,4}
- Older age^{3,4}
- Higher central drusen volume⁴
- Lower choroidal thickness⁴
- Nascent atrophy (loss of outer retinal layers with no loss or thinning of RPE)⁴
- Subretinal drusenoid deposits⁴
- Increased central foveal thickness⁴



Protective factors

- SRF at baseline^{3,4}
- predominantly classic CNV at baseline, SRF or PED at final visit⁵
- subsequent appearance of exudative nAMD in eyes with recent macular atrophy⁶
- type 1 CNV / MNV⁷

CNV, choroidal neovascularization; GA, geographic atrophy; MNV, macular neovascularization; nAMD, neovascular age-related macular degeneration; PED, pigment epithelial detachment; RPE, retinal pigment epithelium; SRF, subretinal fluid; VEGF, vascular endothelial growth factor.

1. Daniel E *et al. Ophthalmology* 2018; 125 (7): 1037–1046; 2. Daniel E *et al. Ophthalmology* 2016; 123 (3): 609–616; 3. Sadda SR *et al. Ophthalmology* 2018; 125 (6): 878–886; 4. Sadda SR *et al. Ophthalmology* 2020; 127 (10): 1360–1370; 5. Bailey C *et al. Ophthalmology* 2019; 126 (1): 75–86; 6. Hwang CK *et al. Ophthalmol Retina* 2021; 5 (2): 108–117; 7. Christenbury JG *et al. Retina* 2018; 38 (7): 1276–1288.



Vision Academy recommendations





Clinicians and patients should be aware of the potential coexistence and / or development of GA and CNV / MNV

- Clinicians managing AMD should be **vigilant** and assess for GA in patients being treated for CNV / MNV and for CNV / MNV in patients with GA



In clinical trials, multimodal imaging should be performed during assessment for both GA and CNV / MNV

- Detailed assessment for both GA and CNV / MNV (including quiescent CNV / MNV) should be performed at **each trial visit**
- Assessments should include **multimodal imaging** consisting of:
 - Fundus autofluorescence
 - Near-infrared reflectance
 - Cross-sectional OCT
 - OCT angiography
- Dye-based angiography should be performed at **trial entry** and any time point when there is **development of new CNV / MNV**

In clinical practice, multimodal imaging should be performed at each visit



- Assessment via **multimodal imaging** is recommended at **each visit**
- Assessment should **ideally** include:
 - Fundus autofluorescence
 - Near-infrared reflectance
 - Cross-sectional OCT
 - OCT angiography
- If these assessments are not feasible, **cross-sectional OCT** should be **performed at each visit** as a minimum



Summary





Vision Academy recommendations



Clinicians should assess for GA in patients with CNV / MNV and for CNV / MNV in patients with GA



In clinical trials, assessment for GA and CNV / MNV with multimodal imaging should be performed at each trial visit



In clinical practice, assessment with multimodal imaging at each visit is ideal. Cross-sectional OCT should be performed at each visit as a minimum

Further considerations

Evidence suggests that **GA and CNV / MNV** are part of a continuum of late-stage AMD, sharing common genetic risk factors and clinical characteristics

Simultaneous **GA and CNV / MNV** should be considered **in the long-term management of late AMD** in clinical practice, as well as in research into new treatment options

To better inform clinical decision-making, additional **systemically collected real-world data on the treatment** of simultaneous GA and CNV / MNV are needed