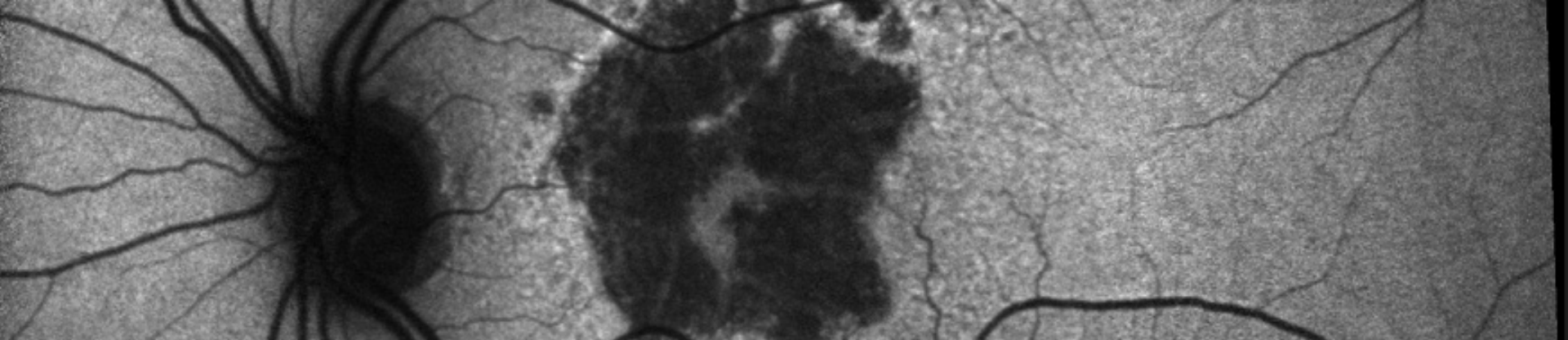




Opening statement

Academic/health care professional Perspective

Frank G. Holz

Department of Ophthalmology, University of Bonn, Germany

EMRN Workshop on Geographic Atrophy Endpoints
April 29, 2026



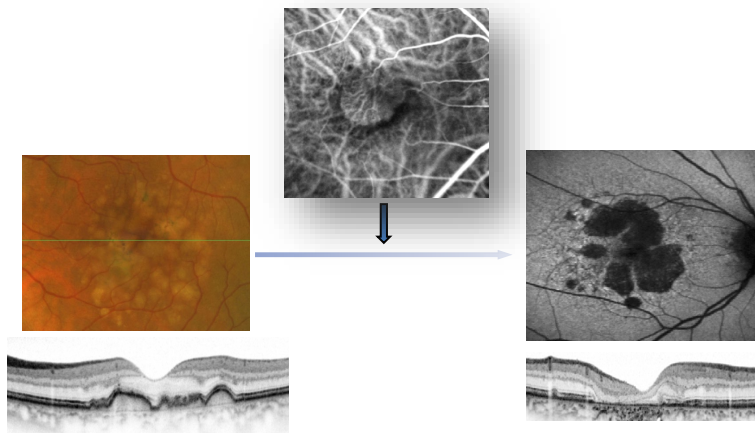
Financial Disclosures

Financial support - Acucela, Abbvie, Allergan, Annexon, Apellis, Astellas, Bayer, Bioeq, Centervue, Geuder, Genentech/Roche, Heidelberg Engineering, NightStar, Novartis, Science, Zeiss, 4D Molecular Therapeutics.

Consultant - Abbvie, Acucela, Alcon, Alexion, Alnylam, Annexon, Apellis, Astellas, Bayer, Biogen, Boehringer-Ingelheim, Cirrus, Eyepoint, Galimedix, Genentech/Roche, Grayburg Vision, Heidelberg Engineering, Lin Bioscience, Jansen, Merck, Novartis, Oculis, Okuvision, Opthea, Oxurion, Sanofi, Science, Stealth Biotherapeutics, RetinAI, TenPoint, Topcon, Zeiss.

Geographic Atrophy due to Age-related Macular Degeneration

- **Chronic progressive multifactorial** disease
- **Most common cause of incurable blindness** in the elderly
- Even with effective treatments for neovascular AMD, **atrophy is still the long-term outcome**
- Knowledge gap: need for mechanistic insights that can inform targeted interventions
- **Heterogeneity** within AMD: distinct endophenotypes
- **No approved therapy** in Europe
- Large **unmet need**
- Suitable **endpoints** to demonstrate benefit for patients from therapeutic approaches



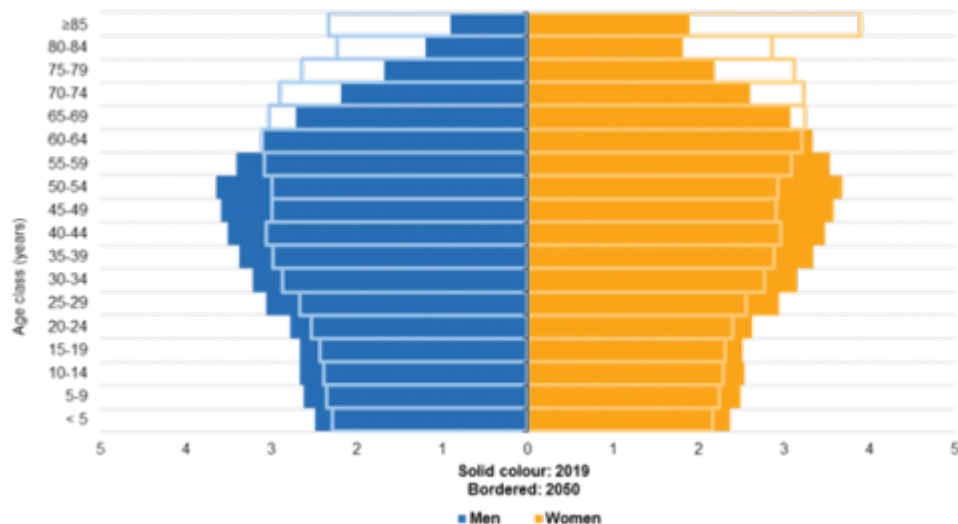
The European population is ageing fast

Geographic atrophy: Rising public health burden in aging populations

101.1 million older people - **aged 65 years or more** - living in the EU-28 at the start of **2018**
(**19.7 %** of the total population)

Peaking at **149.2 million** inhabitants (**28,5 %** of the total population) in **2050**

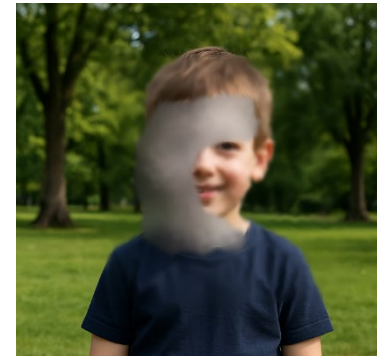
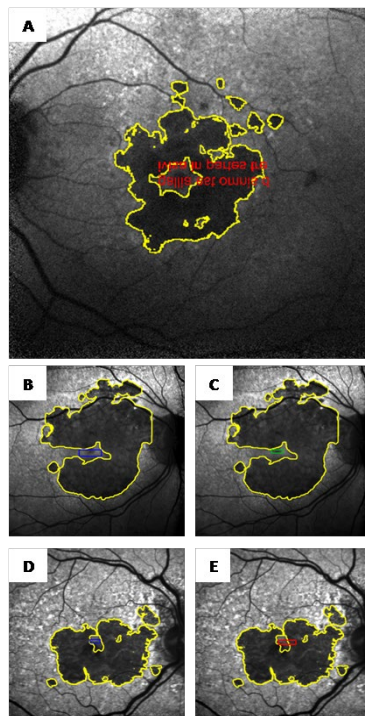
Population pyramids, EU-27, 2019 and 2050 (% share of total population)



Source: EUROSAT

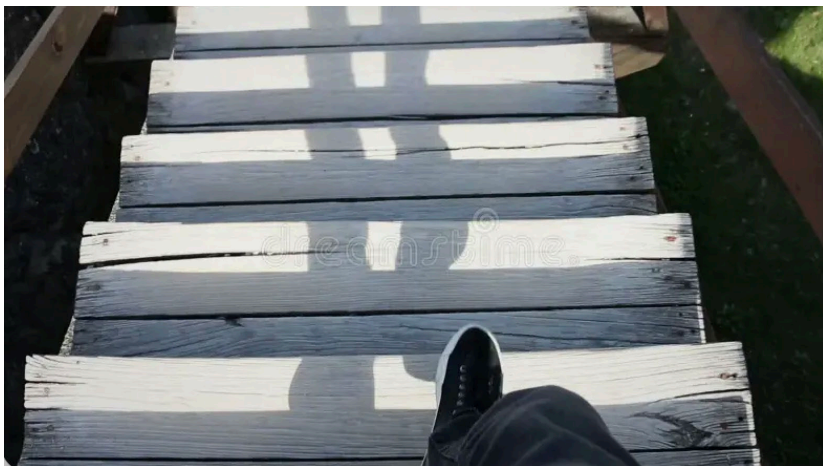
Patient experience: What matters for patients?

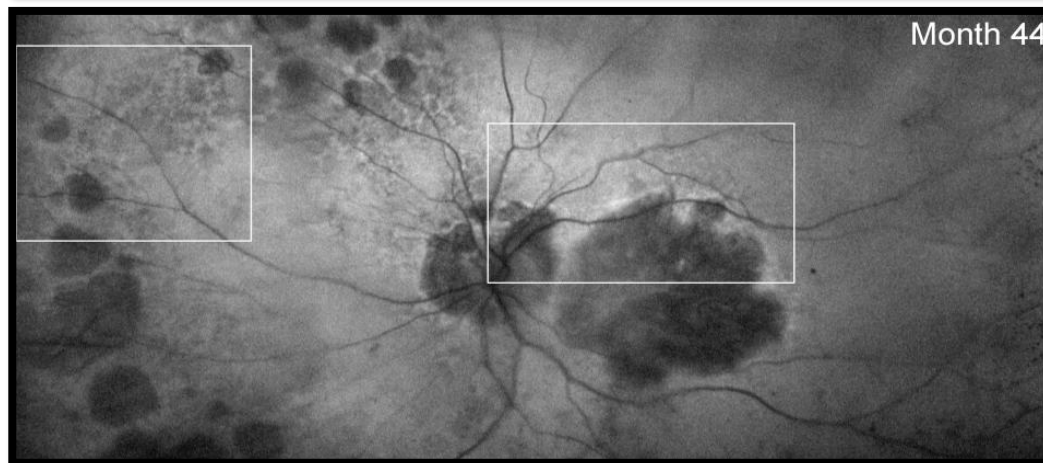
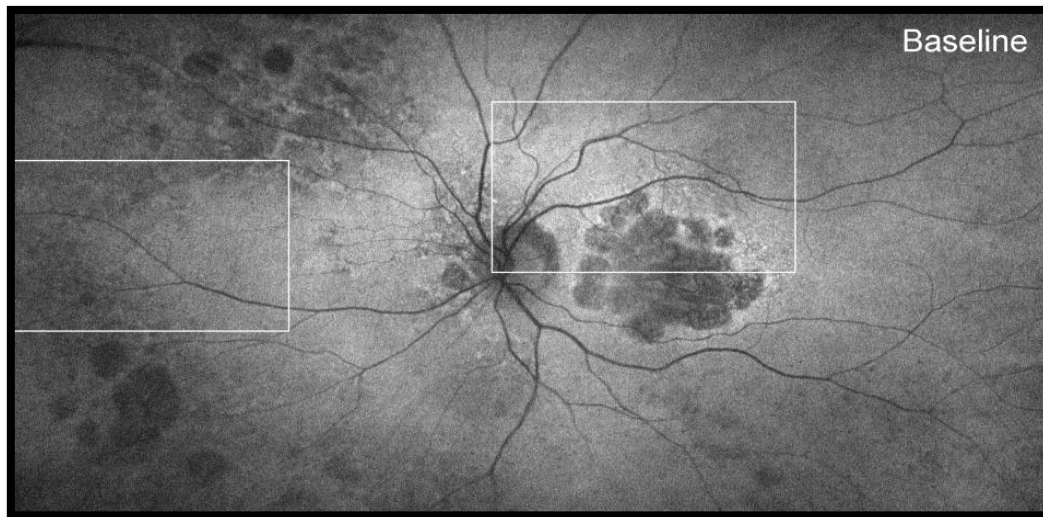
- Reading
- Recognizing faces
- Mobility
- Independency
- Fall risk
- ...



M Lindner, M Pfau, J Czauderna, L Goerd, S Schmitz-Valckenberg, FG Holz, M Fleckenstein. Determinants of Reading Performance in Eyes with Foveal Sparing Geographic Atrophy. Ophthalmol Retina 2019;3:201-210

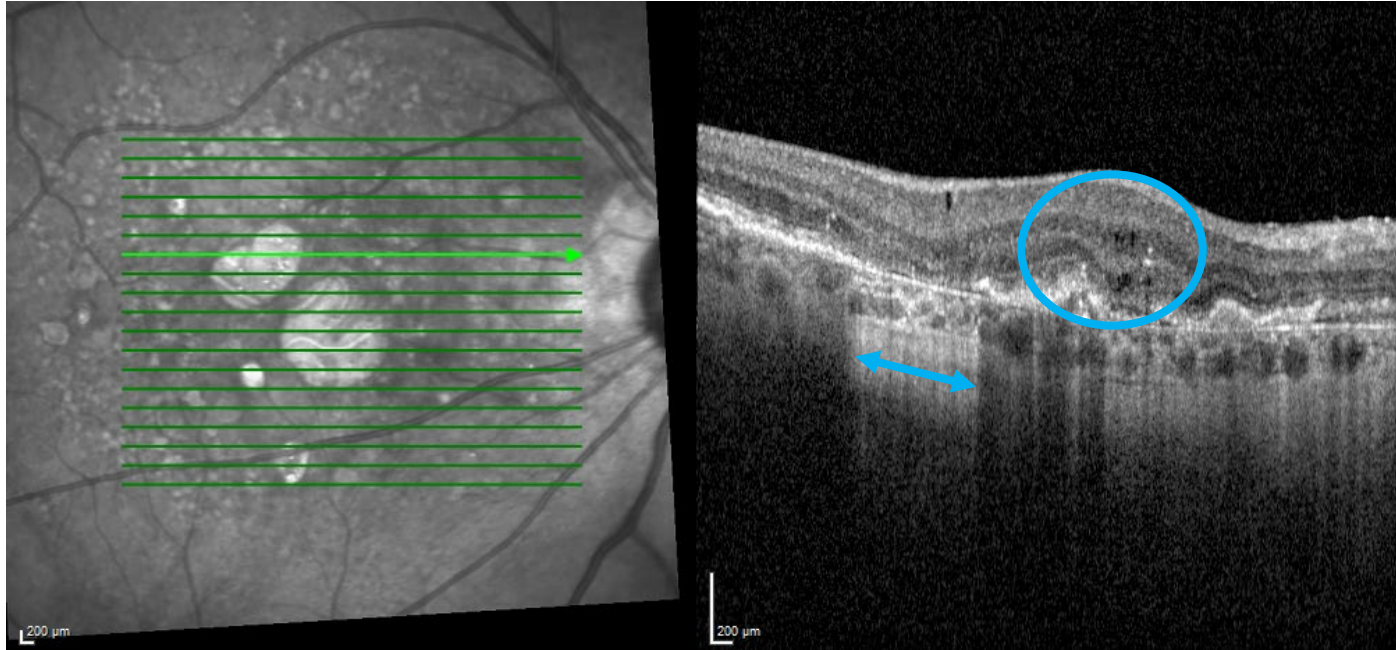
What matters for patients?





No exclusive dichotomy

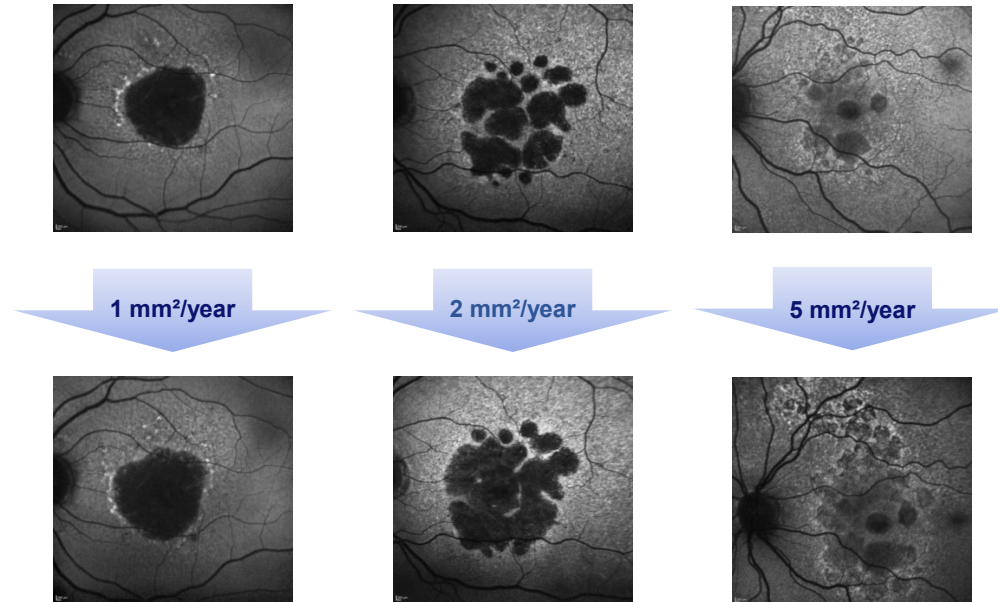
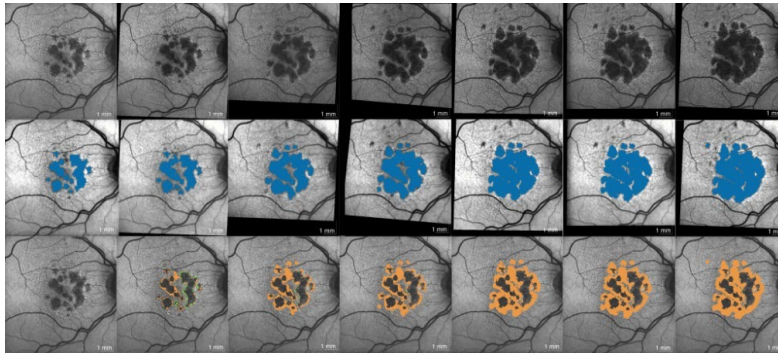
Neovascular AMD – Geographic Atrophy



Interventional clinical trials: study designs and endpoints

Challenges

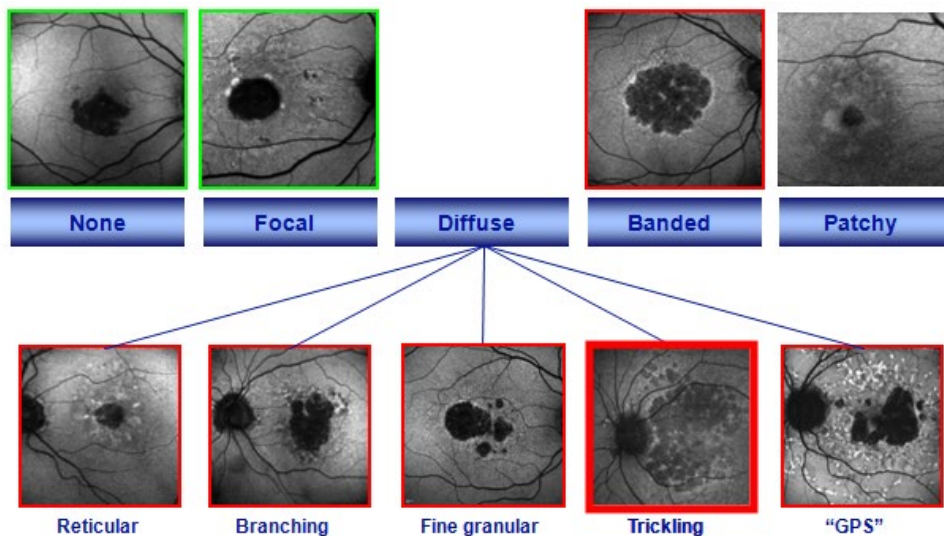
- Slowly progressing disease
- Highly variable progression rates
- Foveal sparing



AREDS Lindblad et al. 2009, **BDES** Klein et al. 2008, **BMES** Joachim et al. 2013, **FAM** Holz et al. 2007, **GAIN** Biarnes et al. 2015, **GAP** Schmitz-Valckenberg et al. 2016, **GAS** Sunness et al. 1999

Predictive markers for GA progression

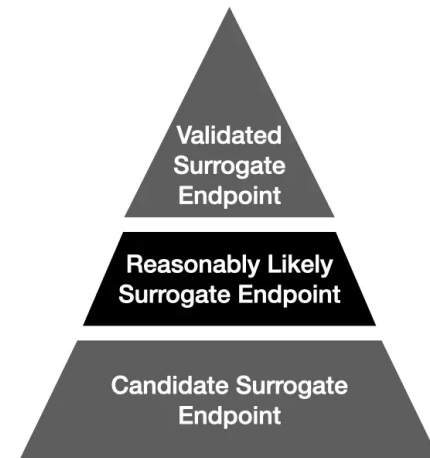
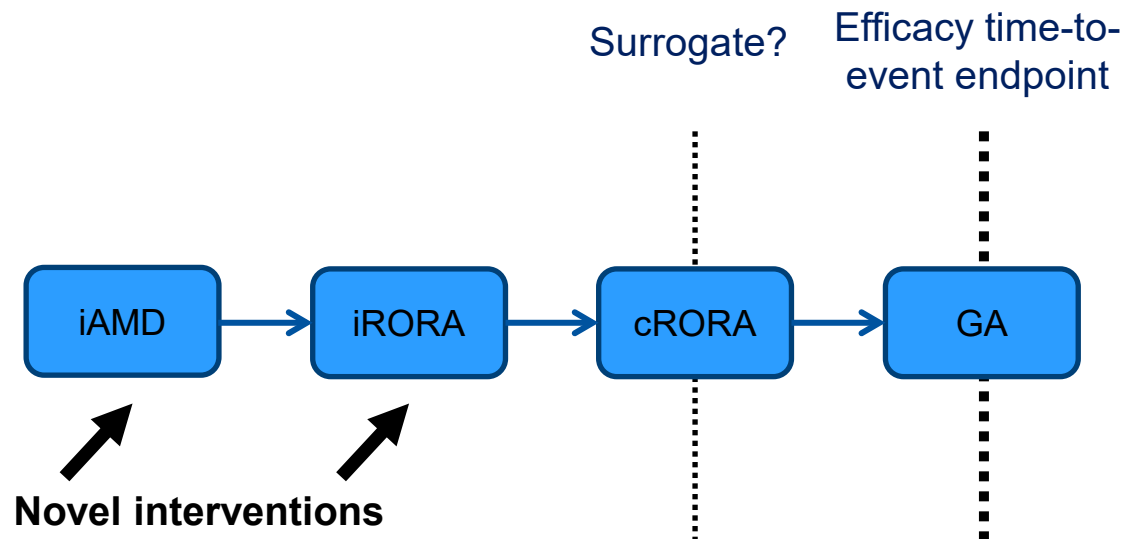
- Good understanding of structural, functional, genetic, environmental, and lifestyle factors associated with rate of GA progression
- Enrichment for fast progressors



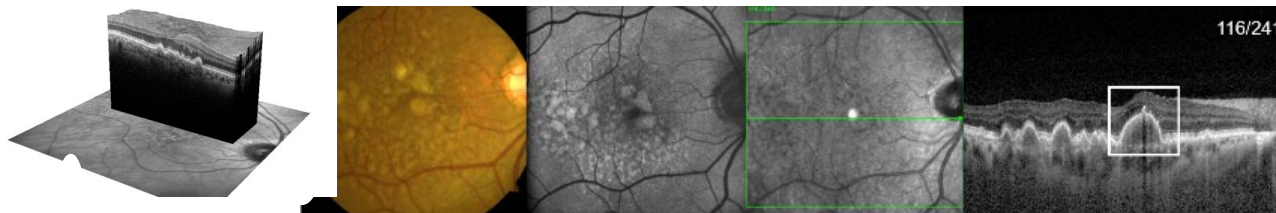
Risk-marker	Unit	Imaging modality
Lesion and eye specific prognostic factors		
Baseline GA size	mm ²	cSLO FAF/NIR
Focality of GA	Number	cSLO FAF
Multilobularity	Yes/no	cSLO FAF
Circularity index	Range 0-1.0	cSLO FAF
Excentricity to the fovea	mm ²	cSLO FAF
FAF pattern	'none' and 'focal' vs. 'banded' and 'diffuse'	cSLO FAF
Extent of abnormal FAF	mm ²	cSLO FAF
Prior GA progression	mm ² /year	cSLO FAF/NIR
Border type	'regular' vs. 'irregular' vs. 'splitting'	SD-OCT B-scan
Outer retinal tubulation	Present/not present	SD-OCT B-scan
Irregular elevations of RPE/BM	Present/not present	SD-OCT B-scan
OCT minimal intensity (MI)	MI value	SD-OCT en face
Vitreoretinal traction	Present/not present	SD-OCT B scan
Subfoveal choroidal thickness	µm	SD-OCT
Fellow-eye specific		
Diagnosis of fellow-eye	Early/intermediate AMD, CNV, and GA	Multimodal imaging
GA progression in fellow-eye	mm ² /year	cSLO FAF/NIR
Genetic variants		
ARMS2_rs10490924	Present/not present	DNA
C3_rs2230199		

Identification of high-risk conversion factors: may serve as earlier endpoints

cRORA as a potential surrogate response biomarker



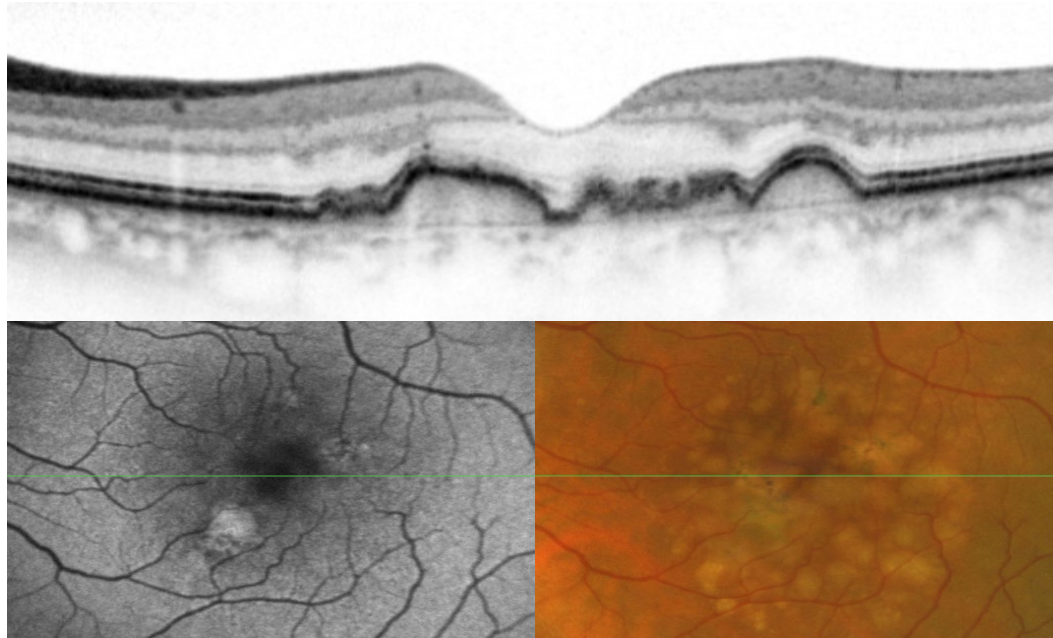
O'Leary, 2025



When to start?

→ **Intervene during early/intermediate AMD**

Key unmet need: prevent intermediate AMD to progress into GA



MACUSTAR multi-center European clinical study

- Evaluation and validation of candidate endpoints for intermediate AMD
- Define clinical enrichment strategies for fast-progressing patients



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Moorfields Eye Hospital **NHS**
NHS Foundation Trust

The University Of Sheffield.

F O N D A T I O N
V O I R & E N T E N D R E



United Kingdom:

- Moorfields Eye Hospital, London
- City University London
- University College London
- University of Sheffield
- The Queen's University, Belfast
- Gloucestershire Hospitals, Cheltenham

France:

- Institut de la Vision, Paris
- European Clinical Research Infrastructure Network (ECRIN), Paris
- Centre Hospitalier, Creteil

Portugal:

- Association for Innovation and Biomedical Research on Light and Image (AIBILI), Coimbra
- Porto Medical School, Porto

association for innovation and biomedical research on light and image

Radboudumc
university medical center

The Netherlands:

- Radboud University Medical Center, Nijmegen
- Leiden University, Leiden

Denmark:

- Rigshospitalet, Copenhagen

Germany:

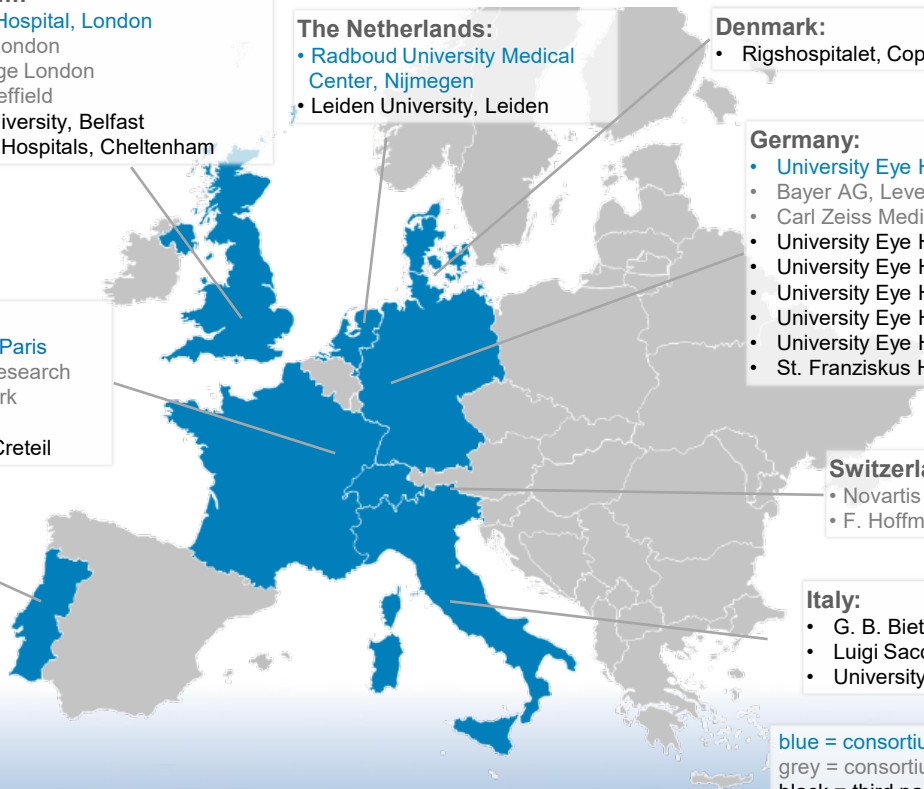
- University Eye Hospital Bonn
- Bayer AG, Leverkusen
- Carl Zeiss Meditec AG, Jena
- University Eye Hospital Tübingen
- University Eye Hospital Munich
- University Eye Hospital Freiburg
- University Eye Hospital Cologne
- University Eye Hospital Ulm
- St. Franziskus Hospital Münster

Switzerland:

- Novartis Pharma AG, Basel
- F. Hoffmann-La Roche Ltd., Basel

Italy:

- G. B. Bietti Eye Foundation, Rome
- Luigi Sacco Hospital, Milan
- University Vita Salute, Milan



blue = consortium members and clinical site (beneficiaries)
grey = consortium members (beneficiaries)
black = third parties providing in-kind against payment

Expectations and goals for the workshop

- Discuss functional, structural and PRO clinical endpoints to meet regulatory expectations
- Which endpoints or combination of endpoints will be most promising to show benefit of new treatments for GA?
- NEI/FDA Workshop 9 November, 2016
Wiley Chambers: “The preference is for functional endpoints – there is always that preference - if you can measure it“

