Industry Perspective

on behalf of EFPIA
& BRIDGE Study Group

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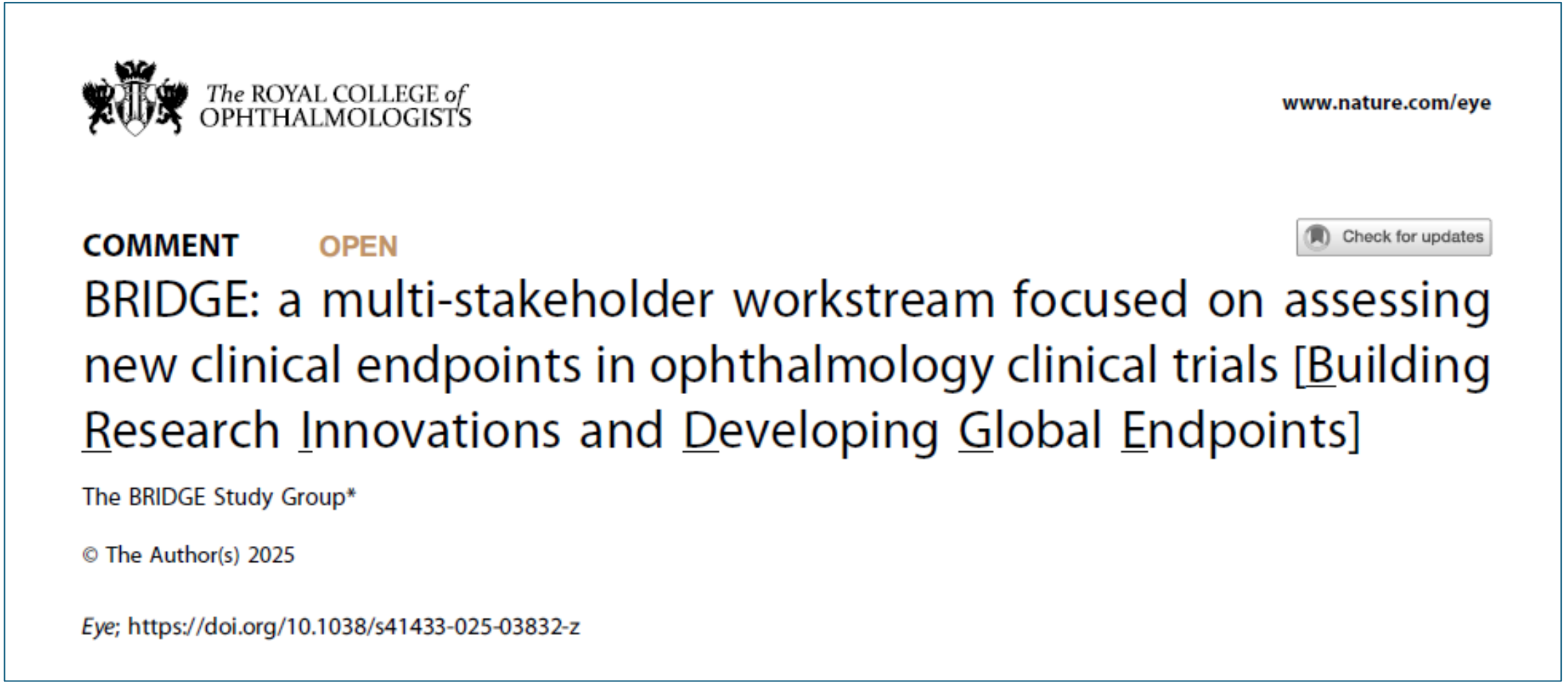
BRIDGE* study Group: Led by Clinicians, co-chaired by Prof. Loewenstein and Prof. Sivaprasad, Non-profit partnerships and Industry

*Building Research Innovations and Developing Global Endpoints

- **Retina International** [Avril Daly, Nabin Paudel]
- **Mary Tyler Moore Vision Initiative** [Robert Levine, Jennifer Sun, Thomas Gardner, Patrice Fort, Dorene Markel, Latrice Faulkner, Shelby Unsworth].
- The **Macular Society** [Peter Bloomfield].

Industry contribution:



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Developing treatments for Geographic Atrophy – an Industry Perspective

- Geographic atrophy [GA], an advanced form of non-exudative age-related macular degeneration [AMD], causes significant vision loss and patient burden that increases with age[1-5] .
- Atrophic lesions in GA are characterised by the progressive loss of the essential architecture required for vision including photoreceptors, RPE cells and choriocapillaris[2].
- Although treatments are available for the neovascular form of AMD, options for non-exudative AMD are limited[6]. Best Corrected Visual Acuity (BCVA) is considered an approvable endpoint for nAMD but it does not fit the progressive stages of non-exudative AMD[7] .

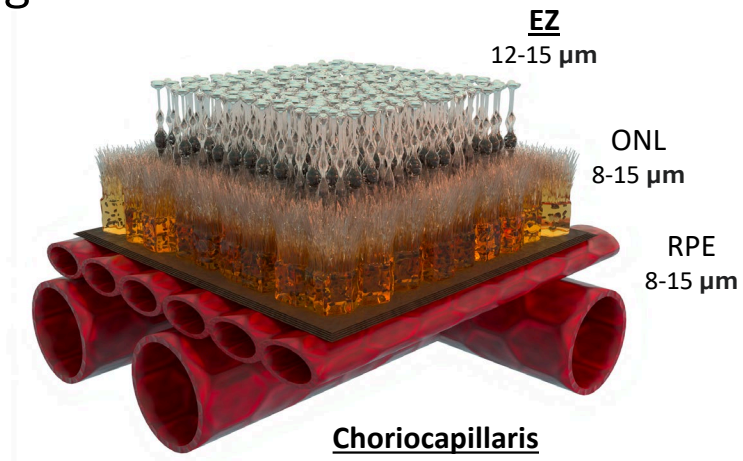


Image: courtesy of Carl G Glittenberg

[[1]Broadbent et al., 2025; [2]Fleckenstein et al., 2018; [3]Sadda et al., 2018; [4]Colijin et al. 2021; [5]Chakravarthy et al. 2018; [6]Liberski et al., 2022; [7]Anegondi et al., 2025]

Vision is more than BCVA

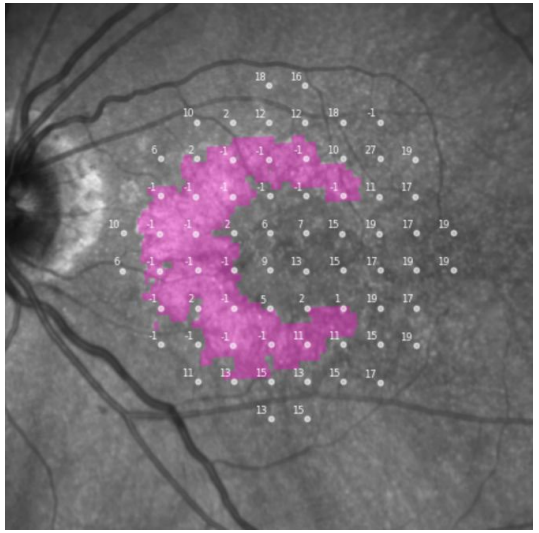
- Because GA typically begins perifoveally, spares the fovea, and shows variable residual function, BCVA is insensitive to early treatment effects and poorly captures early disease progression[2] .
- GA lesion size is known to increase over time and is associated with visual function loss measured by microperimetry, while BCVA declines only after the central fovea is involved[8].
- Beyond BCVA, key functional vision parameters for subjects with glaucoma range from integrated visual field (IVF), Reading Speed to contrast sensitivity (CS)[9], while in subjects with Retinitis Pigmentosa it can span from Electroretinography (ERG) to Dark Adaptation and Humphrey Visual Field[10].
- Therefore, novel surrogate endpoints are needed to accelerate treatment development, addressing patient's functional vision beyond high contrast visual acuity.

[[2]Fleckenstein et al., 2018; [8]Csaky et al., 2019; [9]Shakarchi et al., 2019; [10]Burstedt et al., 2023]

Structure has been shown to correlate with vision function

- GA area shows consistent spatial correspondence with reduced retinal function on perimetric testing, with larger lesions associated with reduction in retinal function[11].
- Microperimetry tailored to the patient is the preferred method, where testing points are positioned relative to the lesion edge observed on FAF[12] .

- The establishment of a surrogate endpoint linked to preserving visual function, hence a relevant clinical benefit as outcome, follows a validation procedure satisfying several steps: *Plausibility, Construct validity, Reliability, Content validity, Predictability and Change to intervention*[13].
- Novel methodologies may provide quantifiable biomarkers that could constitute the link between GA disease progression and end-stage loss of visual function (e.g. microperimetry).



[[11]Csaky et al., 2019; [12] Schmitz-Vackenberg et al., 2004; [13]Wickström & Mosley 2017]

Image: courtesy of Prof. Sivaprasad

BRIDGE Proposal

- In the absence of validated GA-specific MCIDs, a statistically significant reduction in structural progression - such as GA lesion enlargement, cRORA expansion, or EZ attenuation - measured over a minimum 12-month period provides evidence of disease-modifying activity.
- When accompanied by a prespecified, directionally consistent trend in functional endpoints, this constitutes coherent structure-function evidence in a slowly progressive neurodegenerative disease.

Thank you

Back-up

References:

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