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CORRESPONDENCE

Intravitreal treatment for geographic atrophy: coming soon to a patient near you?

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To the Editor:

Geographic atrophy (GA) is estimated to account for one-quarter of legal blindness in the UK [1], with an estimated prevalence of 276,000 cases in the UK in 2012 compared to 263,000 cases of neovascular AMD (nAMD), and an estimated annual incidence of 39,000 cases [2]. Globally, ~5 million people have GA in at least one eye [3], and the incidence is expected to rise with ageing populations. GA involves progressive loss of areas of the retinal pigment epithelium, photoreceptors and underlying choriocapillaris, and leads to irreversible vision loss. About one-half of patients develop GA in both eyes within 7 years of initial diagnosis [4]. People with GA have worse vision-related quality-of-life even when their visual acuity is preserved; for example, we have previously shown that they have increased anxiety about mobility, problems with searching for objects and difficulty recognising faces [5–9]. With no current treatment for GA, patients diagnosed in hospital eye service are typically discharged to the community for monitoring [10, 11].

New therapies may soon be available for GA based on recent advances in our understanding of the pathogenesis of the disease. While the mechanisms of action for these therapies fall into several categories, including cell-based therapy, complement inhibition, neuroprotection and visual cycle modulation [12], regular intravitreal injections are a common mode of delivery in the current pipeline of treatments for GA in clinical trials. Inhibitors of components of the complement cascade are an area of intense research with two such agents, pegcetacoplan and avacincaptad pegol, demonstrating ability to slow the mean rate of GA growth in phase 2 trials by 29.0% and 27.4% respectively, when delivered monthly [13, 14]. Global phase 3 trials of two agents are due to report primary outcomes later in 2021, with cautious optimism that these may herald the arrival of effective treatment for GA in the clinics for the first time. However, it is unknown whether regular intravitreal therapy will be acceptable to GA patients for the proposed benefit of slowing down, but not halting or reversing, visual loss. It is also unknown whether resource constraints would limit implementation of these therapies, given the sheer volume of patients affected.

Acceptability is critical for adherence to and persistence with therapy [15, 16]. In nAMD, patients report a high treatment burden [17–19]; however, concerns about further sight loss may outweigh negative experiences and motivate patients to continue the treatment [18]. In contrast to nAMD, where loss of vision is typically sudden and treatment can lead to improvements in vision, vision loss in GA is a gradual process. Moreover, current intravitreal treatments proposed for GA slow down, rather than halt or reverse, vision loss. So, will patients with GA be similarly motivated to adhere to frequent intravitreal treatments, and what factors would make such treatments acceptable?

An understanding of GA treatment acceptability and its determinants (Table 1) could influence design of future interventions; identify patients who may require targeted counselling; and support a shared-care service delivery model for patients with GA.

GA severity, progression and outcomes demonstrate considerable between-person variability [20, 21]. Should treatments become available, it will be necessary to identify patients at high risk of progression, and thus more likely to benefit from intervention. With increasing evidence that shared-care models can work in the management of nAMD [22, 23], we foresee that a similar pathway could be established for GA and that a GA referral tool—incorporating indices of GA severity, progression and acceptability of intervention—would facilitate this.

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Table 1 The seven component constructs in Sekhon et al.'s theoretical framework of acceptability (TFA) [16], and examples of how they are explored in the pilot study.

Component construct in TFA	Definition within the TFA	Example with potential relevance to GA treatment
Affective attitude	How an individual feels about the intervention	Anxiety about the injection, despair and fear of losing vision, or hope of slowing vision loss.
Burden	The perceived amount of effort that is required to participate in the intervention	The challenges of monthly visits to clinic for injections, and associated pain and discomfort, transport issues or potential impact on accompanying relatives.
Ethicality	The extent to which the intervention has a good fit with an individual's value system	Some individuals with GA may be more proactive and feel they can take control by having injections. Meanwhile, other individuals could be more fatalistic (or accepting) about the inevitability of vision loss, especially if the treatment outcomes are unclear or uncertain. Our patient advisors also highlighted that some people with GA may have concerns around the high expense and resource implications for the NHS.
Intervention coherence	The extent to which the participant understands the intervention and how it works; the face validity of the intervention for the recipient	Clear understanding of the impact the intravitreal injections would have, in terms of slowing down the rate of vision loss from GA (rather than halting or reversing it).
Opportunity costs	The extent to which benefits, profits or values must be given up to engage in the intervention	If a person with GA (and/or an accompanying relative/caregiver) has to take time off work or cancel commitments to attend injections.
Perceived effectiveness	The extent to which the intervention is perceived as likely to achieve its purpose	An appreciable sense that the intravitreal injections are slowing the patient's rate of vision loss.
Self-efficacy	The participant's confidence that they can perform the behaviour required to participate in the intervention	Confidence in ability to attend regular injections and to persist with treatment over the long-term.

Our ongoing pilot study investigates acceptability of intravitreal injections among GA patients, using a questionnaire and semi-structured interview guide co-designed with eight GA patients. Our detailed methodology is reported elsewhere [24]; in summary, we are conducting interviews with 30 participants with a GA diagnosis, to explore in-depth their beliefs, hopes and concerns, regarding GA and intravitreal treatment. We are recruiting an ethnically diverse and clinically varied sample of participants with GA, using a maximum variation purposive sampling strategy. The sample will include 15 participants with a history of intravitreal injections in their fellow eye, and 15 who are naive to intravitreal injections. We will also use a task inspired by discrete choice experiments, to facilitate participant discussion of the benefits versus drawbacks of intravitreal treatment for GA. Interviews will be audio-recorded and transcribed, and qualitative data analysis will be conducted using the Framework Method of analysis [25] to identify key themes from participants' accounts. The results will contribute to our understanding of patients' knowledge of GA and quality-of-life in GA, and will be used to design a large quantitative study to validate an acceptability tool generalisable to patients with GA.

We hope that better understanding of acceptability will guide GA treatment design and delivery, and maximise patient benefit when treatment becomes available.

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Compliance with ethical standards

Conflict of interest CD has served on advisory boards for Novartis, Allergan and Apellis. JE, AG and DJT have no interests to declare. DPC reports grants from Roche, grants and personal fees from Santen, grants and personal fees from Apellis, grants from Allergan, personal fees from Thea, personal fees from Bayer and personal fees from Centervue, outside the submitted work. DPC receives funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant 116076 (Macustar). This joint undertaking receives support from the European Union's Horizon 2020 research and innovation programme and European Federation of Pharmaceutical Industries and Associations (EFPIA). The communication reflects the author's view and that neither IMI nor the European Union, EFPIA or any associated partners are responsible for any use that may be made of the information contained therein.

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