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ORIGINAL RESEARCH

Clinical Trial Simulation in Geographic Atrophy: Patient, Caregiver, and Trial Site Staff Perspectives

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ABSTRACT

***Introduction*:** The perspectives of patients with geographic atrophy (GA) should be considered when planning new clinical trials to ensure that real-world patient needs are addressed. The purpose of this study was to explore the perspectives of patients, caregivers, and trial site staff on designing and planning a phase 2 clinical trial in GA.

***Methods*:** This cross-sectional study included patients with GA and their caregivers, trial site staff, and investigators from Germany, the UK, and the USA. Participants were asked to spend 30 min reviewing a simulated trial design communicated as a simple video animation with a voiceover. Subsequently, a 90-min web-assisted telephone interview and survey was conducted to identify problems with the design of the simulated trial and explore potential solutions and improvements.

***Results*:** Patients ($n = 11$), caregivers ($n = 11$), and site staff ($n = 16$) completed the survey after reviewing the simulated trial design. Survey responses suggested that study recruitment could be facilitated via widespread advertisement and by including a short washout period, i.e., the time period during which patients receive no medication prior to commencing the study drug to ensure that other treatments do not impact the study results. Survey suggestions for reducing the burden of trial participation included minimizing the number and frequency of trial visits, enabling assessments to be completed at home, and making the schedule of trial visits flexible. Appropriate investment in study center facilities was recommended. In addition, survey respondents proposed that providing transport could be highly beneficial, potentially enabling patients and caregivers to attend trial visits more easily.

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Conclusions: This study provides valuable information on the viewpoints of patients, caregivers, and trial site staff regarding trial design. Accounting for these perspectives when designing future clinical trials may help ensure successful trial completion and promote positive perceptions of clinical research.

PLAIN LANGUAGE SUMMARY

Geographic atrophy (GA) is an advanced form of age-related macular degeneration and is a major cause of vision loss. GA affects many aspects of everyday life, including carrying out daily tasks, recognizing faces, and driving. Given the limitations experienced by people with GA, when planning clinical trials, patients' points of view should be considered. This trial simulation study explored the views of patients, caregivers, and trial site staff from Germany, the UK, and the USA on designing and planning a phase 2 clinical trial in GA. Participants provided potential improvements to the clinical trial design and solutions to recruitment challenges, including widespread advertisement and reducing patients' time off their existing treatment before starting the study drug. Reducing the number of times and how often patients would need to go to the clinic, allowing patients to schedule these visits at convenient times, or enabling assessments to be completed at home would also make it easier for patients to participate in the study. Providing transport to the clinic for trial visits could help some patients to attend without their caregivers. Considering these factors when designing future clinical trials may enable more patients to participate in and complete trials and may promote a positive view of clinical research.

Keywords: Clinical trial design; Geographic atrophy; Patient perspective; Telephone interview

Key Summary Points

Geographic atrophy (GA), an advanced form of age-related macular degeneration, is a major cause of vision loss that is associated with a significant burden and impact on quality of life for patients.

This quantitative cross-sectional study interviewed and surveyed patients with GA, their caregivers, and trial site staff on their perspectives of a simulated GA phase 2 clinical trial to gather insights that can potentially be utilized in future clinical trial designs.

The study identified several ways the simulated phase 2 trial could be improved to better align with patients' needs, including amending drug washout periods, choosing different endpoints, and reducing burdens associated with treatment center visits.

Implementing these insights into future GA trial designs may improve the patient clinical trial participation experience, encouraging greater participation and enhancing the real-world applicability of trial results.

INTRODUCTION

Geographic atrophy (GA) is an advanced form of age-related macular degeneration (AMD) [1, 2]. GA is characterized by progressive atrophy and thinning of the retinal pigment epithelium and choriocapillaris, leading to irreversible photoreceptor death and vision loss [1, 3, 4]. GA affects approximately 5 million people globally [5], accounting for approximately 25% of cases of legally recognized blindness in the USA and UK [6]. GA is associated with considerable disease progression and burden. A longitudinal study of UK National Health Service data showed that two thirds of patients with GA would have been classified as ineligible to drive after a median 1.6 years post-diagnosis [6]. Ineligibility to drive was defined by a visual acuity score of ≤ 70 letters or a Snellen chart score 6/12 in the better-seeing eye, which is the commonly

used driving standard threshold [6]. Further, 16% of patients progressed to legally recognized blindness after a median 6.2 years [6]. This was defined as a visual acuity score of < 20 letters or a Snellen chart score of 3/60 in the better seeing eye [6]. Decreased visual acuity and function hinder patients' ability to carry out daily tasks, recognize faces, and drive, limiting their independence and mobility and reducing their quality of life in practical, psychological, social, and emotional dimensions [7–11].

Current treatments for GA have limited efficacy, achieving only a reduction in the speed of lesion progression [5, 12, 13]. Therefore, novel candidate therapies to reduce the burden of GA should be explored in clinical trials. Clinical trial design and conduct rarely consider patient perspectives despite recommendations from the European Medicines Agency and US Food and Drug Administration to incorporate patients' points of view into clinical trial design [14–19]. The value of patient consultation is increasingly recognized within the field of ophthalmology [20]. Clinical trials designed without accounting for patient perspectives and experiences may not address real-world clinical needs, and patient recruitment and retention difficulties may be exacerbated [21–23].

Here, we explore the perspectives of patients, caregivers, and trial site staff regarding the design and planning of a phase 2 clinical trial in GA. A trial simulation was used to gather opinions on inclusion/exclusion criteria, administration of intravitreal treatment (IVT), trial outcomes, and scheduling of trial visits and assessments.

METHODS

A phase 2 clinical trial design was used for this simulation to gather perspectives from patients with GA, their caregivers, and trial site staff (nurse coordinators and investigators from GA trial sites). Individuals from Germany, the UK, and the USA were enrolled.

Inclusion/Exclusion Criteria

Trial site staff meeting the following criteria were enrolled in this study: investigators or nurse coordinators specializing in ophthalmology or retinal health, with at least 2 years of experience and previous involvement in at least 4 ophthalmology clinical trials. Eligible patients had been diagnosed with GA due to AMD by an ophthalmologist and had a current visual range of 20/20 or worse. Patients with and without previous clinical trial experience were included. Eligible caregivers supported a person with GA and helped to transport them to and from healthcare appointments.

Study Procedures

Each participant was asked to spend 30 min reviewing a simulated trial design as a preparatory step. The trial design was communicated as a simple video animation with a voiceover, including a fictional narrative told from a patient perspective describing their involvement in the trial [24]; a separate video animation communicated trial information to the site staff. This information was also provided in a written document. Key characteristics of the simulated trial, including the objective, treatment procedure, patient population, endpoints, and visit frequency, are shown in Fig. 1. A sample size of 180 participants was proposed for this simulated phase 2, 56-week trial, to be randomized to 1 of 2 regimens of a novel treatment or standard of care. Patients were informed that one of the treatment groups involved receiving a placebo sham injection intermittently to mask changes in the treatment dosage.

Following preparation, a 90-min web-assisted telephone interview was conducted to identify potential problems with the design of the simulated trial and explore potential improvements or solutions to optimize trial participation. At the end of the interview, patients were asked to indicate their interest in participating in the trial, using a scale from 1 ("not interested at all") to 7 ("extremely interested"). Trial site staff were also asked to indicate how challenging

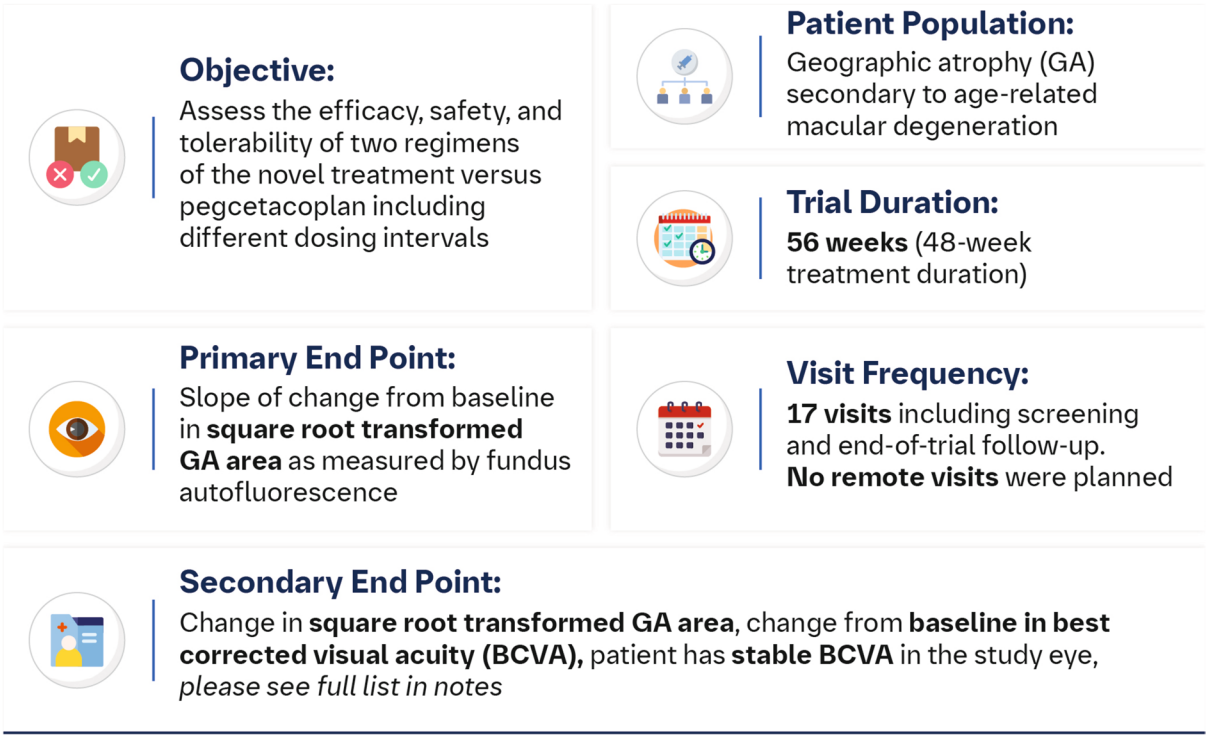

Fig. 1 Key characteristics of the simulated trial. Additional secondary endpoints included change from baseline in low luminance deficit in the study eye as measured by Early Treatment Diabetic Retinopathy Study chart under low luminance conditions at week 52; change from baseline in patient-reported visual function as assessed by the composite score of the National Eye Institute Visual Functioning Questionnaire 25-item version at week 52; mean change from baseline in the Minnesota Low Vision Reading chart maximum reading speed, critical print size, and reading acuity at week 52; change from baseline in contrast sensitivity assessed by the Pelli–Robson test at week 52; development of exudative neovascular age-related macular degeneration in the study eye from drug administration until week 56; and incidence of drug-related adverse events from drug administration until week 56

the trial would be to perform, using a scale from 1 ("not challenging at all") to 7 ("extremely challenging").

All interviews took place between 28 March and 23 June 2023. Four interim debriefs took place between 17 April and 12 July 2023, attended by a small group of patients and clinical trial experts (1 patient and 2 trial site experts) who had watched the interviews or recordings of these prior to debriefing. Attendees were provided with a summary of the main concerns discussed in the interviews, including trial design, eligibility criteria, study length, study assessments, and treatment administration. Experts rated the severity of these concerns, provided their opinions and recommendations on the basis of the interviews, and presented findings.

Data Collection and Analysis

Following the interviews, a thematic analysis of responses was applied to analyze results. The sample size of interview and survey participants had been calculated to ensure that thematic patterns could be identified. Sample size was also influenced by cost and recruitment limitations. Data from patients and caregivers were grouped to show a joint "lived experience" viewpoint, for ease of comprehension, and were only analyzed individually when there were clear differences between the views of patients and caregivers.

Ethics Statement

Market Research does not require institutional review board (IRB) approval because it falls outside the remit of the governance arrangements for research ethics committees. The market research conducted was carried out to understand behavior and opportunities and inform business decision-making. The project was conducted in line with local data protection laws and Market Research Society's Code of Conduct, including British Healthcare Business Intelligence Association, European Society for Opinion and Market Research, European Pharmaceutical Market Research Association, and other relevant national codes of practice. No clinical assessments were undertaken as part of the project that would then necessitate IRB approval. The participants were selected independently of the sponsor and consented to participating in the market research project in line with standard market research guidelines. Consent to publish was not required as no personally identifiable information was included in any part of the manuscript.

RESULTS

A total of 11 patients and 11 caregivers participated in the interviews and survey, from the USA (patients, $n=4$; caregivers, $n=4$), UK (patients, $n=3$, caregivers: $n=3$), and Germany (patients, $n=4$; caregivers, $n=4$). All patients were at least 50 years old. Mean age of patients was 67 years in the USA, 78 years in the UK, and 58 years in Germany. The mean duration since GA diagnosis for patients was 5.6 years in the USA, 5.0 years in the UK, and 3.3 years in Germany. For caregivers, the mean duration since GA diagnosis for the patients in their care was 5.6 years. Prior trial participation was low, with none of the patients and only one caregiver having been involved in a clinical trial previously. Seven (64%) of the patients and 7 (64%) of the caregivers had an educational level of degree or higher.

Of the 16 site staff who participated in the interviews and survey, 6 were from the USA, 4 from the UK, and 6 from Germany. Their job titles included ophthalmologist, nurse or nurse coordinator, clinical research coordinator, or trial coordinator. Most site staff ($n=13$) were based in university teaching hospitals or the regional equivalent, and they had a mean of 13 years of experience at the time of the survey. Site staff had previously been involved in an average (mean) of 25.4 ophthalmology trials and 3.6 GA-specific trials. Over the proceeding 12–24 months, they had been involved in a mean of 9.9 clinical trials. Baseline and demographic data are summarized in Table 1.

The perspectives on different aspects of the simulated trial design gathered from the interviews and survey are described in the following sections.

Inclusion/Exclusion Criteria

The proposed criteria discussed in the interviews were viewed as positive by 10 patients and caregivers (45.5%), and negative by 2 patients (9.1%; Fig. 2A). No caregivers viewed the proposed criteria as negative. The remaining 10 patients and caregivers were neutral (36.4%) or did not respond (9.1%) to this question. Criteria seen as positive and inclusive were the minimum age of 50 years (other trials have had a minimum age of 60 years) and the inclusion of patients with central and non-central vision.

Potential recruitment challenges were identified, including the advanced age of patients with GA, the exclusion of patients on the basis of GA lesion size, and the need for a washout period—the time period during which patients receive no medication prior to commencing the study drug to ensure that other treatments do not impact the study results (Table 2). Furthermore, finding trial participants in the UK was recognized as a potential barrier to recruitment due to transfers away from trial centers owing to treatment access and hospital capacity factors.

Trial site staff made several suggestions for overcoming recruitment challenges (Table 2). One suggestion was to reduce the washout duration from 90 days to either 1 month or 5 half-lives of their prior treatment, whichever is longer. This minimizes the washout period

Table 1 Patient, caregiver, and site staff characteristics

Participant characteristic	Country			Overall
	USA	UK	Germany	
Patients	*n* = 4	*n* = 3	*n* = 4	*N* = 11
Age bracket, years, *n* (%)				
76 and above	0 (0)	2 (67)	0 (0)	2 (18)
66–75	3 (75)	1 (33)	0 (0)	4 (36)
56–65	0 (0)	0 (0)	2 (50)	2 (18)
50–55	1 (25)	0 (0)	2 (50)	3 (27)
Mean age, years	67	78	58	67
Mean duration since diagnosis, years	5.65	5.00	3.25	4.60
Education level of degree or higher, *n* (%)	4 (100)	2 (67)	1 (25)	7 (64)
Prior clinical trial participation, *n* (%)				
Yes	0	0	0	0
No	4 (100)	3 (100)	4 (100)	11 (100)
Best corrected visual acuity (BCVA) 20/20–20/60, *n* (%)	3 (75)	2 (67)	2 (50)	7 (64)
BCVA > 20/60, *n* (%)	1 (25)	1 (33)	2 (50)	4 (36)
Caregivers	***n* = 4**	***n* = 3***	***n* = 4**	***N* = 11**
Age bracket, years, *n* (%)				
76 and above	0 (0)	1 (33)	0 (0)	1 (9)
66–75	1 (25)	0 (0)	0 (0)	1 (9)
56–65	0 (0)	0 (0)	2 (50)	2 (18)
46–55	1 (25)	0 (0)	0 (0)	1 (9)
36–45	2 (50)	0 (0)	0(0)	2 (18)
26–35	0 (0)	1 (33)	2 (50)	3 (27)
Mean duration since diagnosis (for patient you care for), years	2.56	11.67	4.00	5.57
Education level of degree or higher, *n* (%)	4 (100)	2 (67)	1 (25)	7 (64)
Prior clinical trial participation, *n* (%)				
Yes	0	0	1 (25)	1 (9)
No	4 (100)	3 (100)	3 (75)	10 (91)
Site staff	***n* = 6**	***n* = 4**	***n* = 6**	***N* = 16**
Ophthalmology trials participated in previously (mean)	33.3	35.0	11.2	25.4

Table 1 continued

Participant characteristic	Country			Overall
	USA	UK	Germany	
Geographic atrophy trials participated in previously (mean)	2.5	7.5	2.0	3.6
Mean number of trials participated in over in the previous 12–24 months (mean)	7.4	16.5	7.7	9.9

*One caregiver from the UK did not report their age

BCVA Best corrected visual acuity

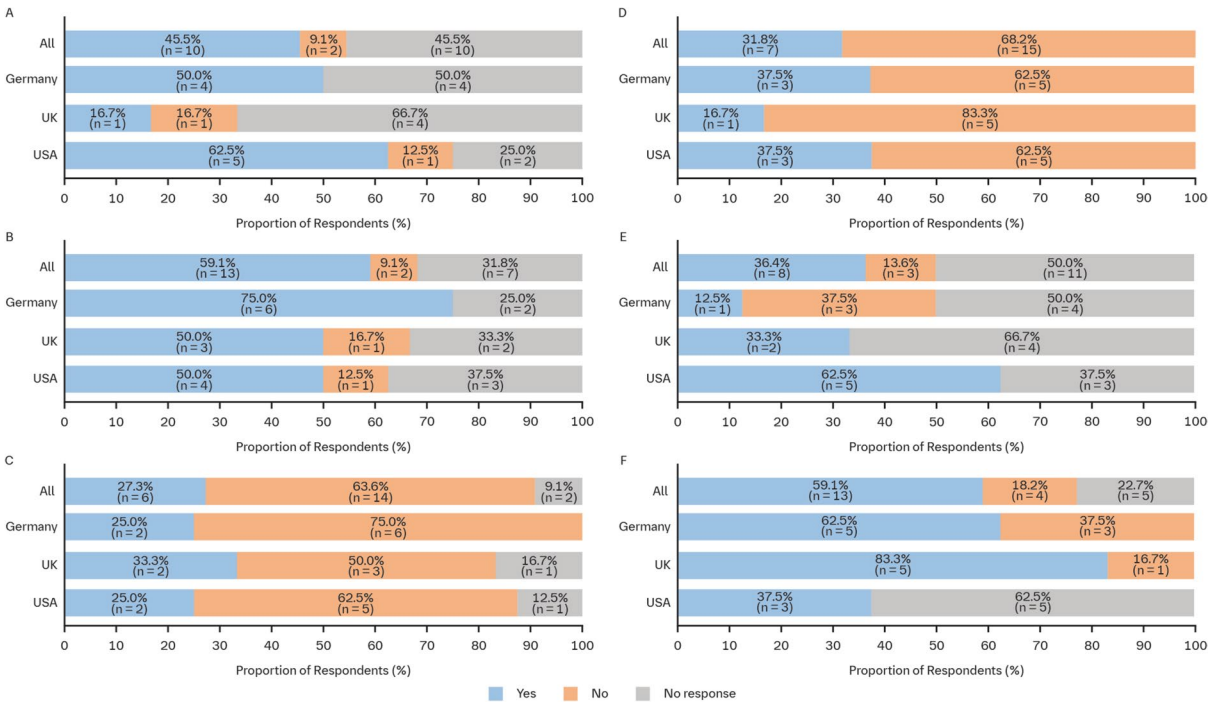

Fig. 2 Patient and caregiver responses regarding: **A** agreement with inclusion and exclusion criteria, **B** approval of simulated trial endpoints, **C** response to "Is the simulated trial too long?" **D** response to "Is a 4–5-h appointment too long?" **E** agreement with proposed placebo versus treatment ratio, and **F** response to "Would a 50% chance of randomization to sham injection be acceptable?"

while ensuring there is sufficient time for the prior treatment to be cleared before administering study treatment. It was also suggested that patients who have previously participated in clinical trials are more likely to be committed to research and be familiar with the process, which may increase the likelihood that they complete all study visits. Clear and accessible information on all trial processes, including treatments and assessments, should be provided to patients and caregivers to set expectations (e.g., regarding trial logistics and treatment effects), reduce treatment-related anxiety, and enable planning around all scheduled trial visits. A schematic was recommended to provide a clear explanation of the trial design (e.g., flowchart design with distinct colors/shapes for treatment groups to show all relevant study steps, including the administration of real and sham treatments). The availability of a range of informative materials,

Table 2 Challenges and solutions relating to different aspects of trial design, as identified by the study participants

Aspect	Challenges	Possible solutions/improvements
Recruitment	• Requirement for a washout period (particularly for patients from previous trials) • High population age, which increases disease comorbidity and affects the ability to understand the trial protocol and sign a consent form • Geographic atrophy (GA) lesion size range (some patients may be excluded) • (UK-specific) Finding patients, as many are transferred from trial centers to satellite units for monitoring	• Shorten the duration of washout from the typical 90 days to 1 month if possible • Use brochures and other materials for clear communication of trial information • Recruit patients who have previously participated in trials as they have familiarity with the process and may be more likely to complete all study visits • Widen patient network by including patients from ophthalmology clinics and sight-loss charities and by using local newspaper/radio advertisements • Use innovative technologies (e.g., online screener tools, artificial intelligence to scan patient notes, video-format informed consent form for patients) • Increase the range of GA lesion size
Assessments	• The National Eye Institute Visual Functioning Questionnaire 25-item version (NEI VFQ-25) and Minnesota Low Vision Reading (MNREAD) chart are time-consuming to complete • Patients require support and may feel self-conscious when assessing the MNREAD chart • Low luminance BCVA can make patients agitated	• Provide an option to complete the NEI VFQ-25 by phone • Reduce the frequency of low luminance best corrected visual acuity (BCVA) assessment to every 3 months • Provide an option for time-intensive assessments to be split across multiple trial visits
Trial visits	• Travel to and from the clinic can be burdensome • Visit duration, number of visits, and trial duration require commitment	• Provide transport and/or fair reimbursement for travel • Provide facilities, such as Wi-Fi and work areas, at trial centers • Ensure that the duration and number of visits are kept to a minimum • Allow flexibility regarding the date and time of day of trial visits
Treatment administration	• Intravitreal treatment can be uncomfortable • Patients may feel nervous about receiving treatment	• Follow optimized injection procedures • Provide information on the injection method ahead of administration • Provide the option to have an "injection buddy"

BCVA Best corrected visual acuity

including digital documents, printed brochures, flip charts/diagrams, audiobooks, and videos, would be helpful for tailoring communication, including for recruitment purposes, according to the needs of each patient and caregiver. For example, some older patients may prefer printed materials to digital information. The layout within these materials should be optimized by using large font sizes and double spacing with clear and consistent font styles. Consistency of terminology and clear explanations of technical terms and abbreviations are also important

in ensuring accessibility. Additional sources of information should be provided for patients and caregivers wishing to learn more, and open discussions with trial site staff should be encouraged. Continued provision of information may be helpful throughout the trial, not just at the recruitment stage.

The breadth of patient recruitment could be increased by including ophthalmology clinics, sight-loss charity members (e.g., Macular Society, Royal National Institute of Blind People), and multiple forms of advertising, including local newspaper/radio advertisements. Innovative technologies, such as screener tools, artificial intelligence to scan patient notes, and video-format informed consent forms, were also suggested.

Endpoints

The trial endpoints were perceived positively by 13 interviewed patients and caregivers (59.1%) and negatively by 1 from each group (9.1%; Fig. 2B). According to the patients, successful treatment would stabilize their condition or slow deterioration, with some specifically framing this in terms of giving them more time with functional vision and to live independently. Patients' comments included:

"Even slowing the decay is a gain."
"I would expect stabilization."

Stabilization and slowing of deterioration were mentioned equally frequently overall, but there were some differences between countries, with stabilization being mentioned more often by patients from the USA and slowing of deterioration being mentioned more often by patients from Germany.

In comparison with the patients, caregivers generally had higher expectations of treatment. They expressed expectations of improvement in patients' condition, often phrased in terms of visual acuity (e.g., increased ability to recognize people, reduction in blurred vision, improved ability to read).

Trial site staff felt that the endpoints discussed in the interviews were consistent with previous GA trials, with an appropriate combination of anatomical and functional endpoints that balanced objective measures and aspects important to patients with GA. A minority of trial site staff said improvements in best corrected visual acuity (BCVA), contrast sensitivity, and visual functioning questionnaires would be more valuable than improvements in lesion size, as the former are more relevant to patients.

Some assessments were considered by trial site staff to be burdensome for patients. For example, the National Eye Institute Visual Functioning Questionnaire 25-item version was described as time-consuming to complete, and low luminance BCVA can make patients feel agitated if they think that they are not performing well. The Minnesota Low Vision Reading chart was described as "time-consuming" and "arduous" to complete, as this requires trial site staff to observe patients reading, which can in turn make patients self-conscious. Trial site staff suggested improving the assessments by offering patients more flexibility in how they are completed (e.g., by phone or by reducing the frequency of assessments; Table 2).

Trial Design

Across all 3 countries, 14 interviewed patients and caregivers (63.6%) thought that the duration of the simulated trial was acceptable, whereas 6 (27.3%) felt that it was too long, and 2 did not respond (9.1%; Fig. 2C). Similarly, as shown in Fig. 2D, 15 patients and caregivers (68.2%) felt that an appointment lasting 4–5 h was acceptable, whereas 7 (31.8%) felt that it was too long. A higher proportion of patients and caregivers from the UK (83.3%) reported that the appointment duration was acceptable compared with those from the USA and Germany (62.5% each).

Travel to and from trial visits can be a substantial burden for patients and caregivers, with the number of visits (17) and trial duration (56 weeks) seen as a large commitment by some individuals. Specific comments included:

"It is the travel time to and from the visits that might be difficult or a problem."
"…it's the amount of times that I have to travel… Even if I was going one time and

I'm in traffic, that's annoying, but it's not as annoying as doing it 17 times."

Fair financial reimbursement should be provided for trial participation, including a caregiver stipend to compensate the cost of their time spent accompanying patients to trial visits. Trial sites could also invest in direct provision of transport for patients, to provide them with a convenient, safe, and streamlined method of traveling to and from appointments. This may reduce or eliminate the need for caregiver attendance at trial visits. Evening appointments could be made available for those who have difficulty taking time off work, and flexibility in booking/amending appointments would help allow for patient illness and other unplanned events.

Investment in trial site facilities was also suggested to maximize the comfort of patients and caregivers during trial visits. Aspects to consider could include TV, access to food and drink, and providing Wi-Fi and charging points.

Regarding the treatment:placebo ratio, 11 patients and caregivers (50.0%) gave a neutral response, 8 (36.4%) gave a positive response, and 3 (13.6%) gave a negative response (Fig. 2E). Patients and caregivers reacted positively to the fact that placebo would not be given in the simulated trial, with comments including:

"You wouldn't be going through all these visits and not getting treatment."

A minority of patients and caregivers expressed confusion about the sham injection, believing it to be a placebo rather than to mask the dosing interval. A suggestion from site staff was that this could be explained in a figure incorporated into consent forms.

A revised trial design, with 50% chance of randomization to placebo, was deemed acceptable by 13 patients and caregivers (59.1%) and unacceptable by 4 (18.2%; Fig. 2F). This trial design had the highest rate of unacceptability among patients and caregivers from Germany (n=3/8, 37.5%), followed by those from the UK (n=1/6, 16.7%). None of the patients or caregivers from the USA considered it to be unacceptable, although 5 out of 8 (62.5%) did not respond to the question.

Treatment Administration

Feelings of nervousness about receiving treatment were reported by interviewed patients, for both those who had and had not previously received IVT. Patients' comments included:

"If you get somebody who doesn't inject very well or doesn't clean your eye up very well, then it can be very, very uncomfortable for 24 hours afterwards."
"I think I might be afraid if it was me."

Patients and caregivers with previous experience of IVT (n=13) indicated that the experience was improved by following optimized procedures, administering anesthetic as appropriate, and offering aftercare as required. Patients said that they would like to be provided with information regarding IVT before receiving treatment and that this should include details of the drug, IVT safety, treatment procedures, and aftercare. Support provided by the Macular Society, known as "injection buddies," was an additional recommendation for patients worried about receiving IVT. Such support would usually be required only for the first injection, after which most patients become more comfortable with receiving treatment.

Interest in Participation and Assessment of Difficulty

Overall, surveyed patients and caregivers reported a mean interest score for trial participation of 4.8/7. Interest was higher among those from the USA (5.3/7) and Germany (5.1/7) than among those from the UK (3.8/7). All trial site staff expressed interest in conducting the trial. The mean score for how challenging the trial would be to perform was 3.2/7. US- and UK-based trial site staff considered the trial to be more challenging to perform (mean scores of 4.2/7 and 4.3/7, respectively) than those from Germany (1.5/7).

DISCUSSION

In this study, key challenges and potential solutions and improvements were identified relating to recruitment and the experience

of participating in a clinical trial. To facilitate recruitment, a short washout period and widespread advertisement were suggested. Pre-screening using patients' latest chart reviews and an online screening tool that allows patients to self-screen at home was suggested for streamlining recruitment. The burden of trial participation could be reduced by minimizing the number and frequency of trial visits and assessments while permitting flexible scheduling. The option to complete study assessments at home rather than during trial visits should be offered where possible. The provision of transport to and from trial visits would also be crucial for many patients to be able to attend.

Differences in characteristics were observed between participants from the 3 countries included in this study. Among the patients interviewed, those from the USA and UK had the longest time since diagnosis, and among the caregivers responses, the average time to diagnosis for the patients in their care was much greater for the UK participants, followed by Germany and then the USA. Of the 22 patients and caregivers, just 1 had prior clinical trial experience (a caregiver from Germany). Recent trial participation and the number of GA trials participated in was highest among UK site staff.

Owing to the real-world nature of our study, we consider the findings broadly applicable to future clinical trials. Differences in the demographic or clinical characteristics of participants in this study could affect this view, but mean ages of 74–81 years across a selection of previous publications for clinical trials in GA suggest broad similarity with our study in which 54% of patients were ≥ 66 years of age [25–31].

Previous studies of patient perspectives in GA have focused on the disease burden. Difficulties with driving, reading, watching television, and enjoying the theater were highlighted, along with broad impairment of quality of life, including in practical, psychological, emotional, and social domains [7–9, 11, 32–34]. One study reported poor patient access to disease-related information and support [34]. There is also evidence that patients may be prepared to accept the burden of IVT, provided that treatment is sufficiently effective and well tolerated and the frequency of injections can be kept low (e.g., once every 2 months) [35]. Although such studies provide helpful information on the burden of GA, they do not address how best to design a clinical trial. We are not aware of any previous studies of patient perspectives specifically on the design of clinical trials in GA.

Our study was strengthened by including 3 groups of participants across 3 countries, providing a range of viewpoints on clinical trial design. Limitations included the small number of participants, lack of statistical robustness, and limited data on the characteristics of the participants (including the absence of insight into the severity of the patients' disease).

CONCLUSIONS

This study provides valuable insights into the viewpoints of patients, caregivers, and site staff regarding trial design. We recommend that teams responsible for designing and running clinical trials take these views into account as much as possible, as this may help ensure successful trial completion and promote positive perceptions of clinical research among patients and their caregivers. Further research is needed to increase our understanding of how to optimize the design of clinical trials in GA; engaging with patient representatives earlier in the trial design process may provide greater insights.

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Data Availability. For publications reporting clinical study results, to ensure independent interpretation and enable authors to fulfill their role and obligations under the ICMJE criteria, Boehringer Ingelheim grants all external authors access to clinical study data pertinent to the development of the publication. In adherence with the Boehringer Ingelheim Policy on Transparency and Publication of Clinical Study Data, scientific and medical researchers can request access to clinical study data when it becomes available on Vivli—Center for Global Clinical Research Data, and earliest after publication of the primary manuscript in a peer-reviewed journal, regulatory activities are complete, and other criteria are met. Please visit Medical & Clinical Trials | Clinical Research | MyStudyWindow for further information. This publication is not reporting results from a clinical trial. Please contact the corresponding author to request the datasets generated and/or analyzed during this study.

Declarations

Conflicts of Interest. Ivana Gunderson and Asma Burale declare receiving consulting fees from Boehringer Ingelheim for an advisory role as part of the trial simulation. Jochen Huber and Lisa Marsh declare that they are employees of Boehringer Ingelheim. Cynthia I. Tung was an employee of Boehringer Ingelheim during the development of this manuscript. Cynthia I. Tung currently works at New York Eye and Ear Infirmary of Mount Sinai. Bill J. Best declares an agreement for consulting fees with Boehringer Ingelheim for an advisory role as part of the trial simulation. These fees were paid to the Macular Society, with Bill J. Best receiving no financial benefit.

Ethical Approval. Market Research does not require institutional review board (IRB) approval because it falls outside the remit of the governance arrangements for research ethics committees. The market research conducted was carried out to understand behavior and opportunities and inform business decision-making. The project was conducted in line with local data protection laws and Market Research Society's Code of Conduct, including British Healthcare Business Intelligence Association, European Society for Opinion and Market Research, European Pharmaceutical Market Research Association, and other relevant national codes of practice. No clinical assessments were undertaken as part of the project that would then necessitate IRB approval. The participants were selected independently of the sponsor and consented to participating in the market research project in line with standard market research guidelines. Consent to publish was not required as no personally identifiable information was included in any part of the manuscript.

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