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1 Exploring patient acceptability of emerging intravitreal therapies for
2 Geographic Atrophy: a mixed-methods study

3 Jamie Enoch¹, Arevik Ghulakhszian², Mandeep Sekhon³, David P. Crabb¹, Deanna J. Taylor¹,
4 Christiana Dinah^{2,4*}

¹Department of Optometry and Visual Sciences, City, University of London, London, UK.

²Ophthalmology Department, London North West University Healthcare NHS Trust, Central Middlesex Hospital, London, UK.

³Population Health Research Institute, St George's, University of London, London, UK.

⁴Department of Brain Sciences, Imperial College, London, UK.

*Denotes corresponding author

Corresponding author postal address: Ophthalmology Department, London North West University Healthcare NHS Trust, Central Middlesex Hospital, London, United Kingdom.

ORCID ID: 0000-0002-0815-4771

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Running head: Exploring acceptability of therapies for Geographic Atrophy

Abbreviations and Acronyms: **AMD** = Age-related Macular Degeneration; **GA** = Geographic Atrophy; **NHS** = National Health Service; **TFA** = Theoretical Framework of Acceptability; **VEGF** = Vascular Endothelial Growth Factor

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5 **Abstract (247 words)**

6 **Background/Objectives:** The acceptability of emerging intravitreal therapies for patients
7 with Geographic Atrophy (GA) is currently unknown. This study therefore aimed to
8 investigate the extent to which regular intravitreal injections may be acceptable to GA
9 patients.

10 **Subjects/Methods:** 30 UK-based individuals with GA secondary to age-related macular
11 degeneration (AMD), recruited from two London-based hospitals, were interviewed in April-
12 October 2021 regarding acceptability of new GA treatments. Participants responded to a
13 structured questionnaire, as well as open-ended questions in a semi-structured interview.
14 The Theoretical Framework of Acceptability (TFA) informed framework analysis of the
15 qualitative data.

16 **Results:** Twenty participants (67%) were female, and median (interquartile range (IQR)) age
17 was 83 (78, 87) years. 37% of participants had foveal centre-involving GA, and better eye
18 median (IQR) logMAR visual acuity was 0.30 (0.17, 0.58). Data suggested that 18
19 participants (60% (95% CI: 41-79%)) would accept the treatment, despite awareness of
20 potential drawbacks. Eight participants (27% (95% CI: 10-43%)) were ambivalent or
21 undecided about treatment, and four (13%) (95% CI: 0-26%) would be unlikely to accept
22 treatment. Reducing the frequency of injections from monthly to every other month increased
23 the proportion of participants who considered the treatments acceptable. Conversely, factors
24 limiting acceptability clustered around: the limited magnitude of treatment efficacy; concerns
25 about side effects or the increased risk of neovascular AMD; and the logistical burden of
26 regular clinic visits for intravitreal injections. Misunderstandings of potential benefits indicate
27 the need for appropriately-designed patient education tools to support decision-making.

28 **Conclusions:** Our study suggests a majority of participants would be positive about
29 intravitreal treatment for GA, in spite of potential burdens.

30

31 **Introduction**

32 Geographic Atrophy (GA) is the advanced form of the non-neovascular ('dry') type of
33 age-related macular degeneration (AMD), affecting 276,000 people in the UK (1). While
34 there are now approved treatments for wet AMD, until recently there has been no therapy for
35 GA, a significant unmet need (2). Even before the foveal centre is involved, GA can have
36 significant impact on functional activities and vision-related quality-of-life (3)(4).

37 Dysregulation of the complement cascade has been implicated in the pathogenesis
38 of GA, and there are now two intravitreal complement inhibitors in late-stage development
39 for the treatment of GA (2). Regular intravitreal injections are the standard of care for wet
40 AMD, and a common mode of delivery in the current pipeline of treatments for GA in clinical
41 trials. Recent positive results from phase 3 clinical trials of two intravitreal complement
42 inhibitors provide hope for a treatment for GA (5–7). Indeed, in February 2023, the first-ever
43 treatment for GA, pegcetacoplan, was approved for use by the Food and Drug
44 Administration (FDA) in the US under the brand name Syfovre, based on reduced rates of
45 lesion growth in the DERBY and OAKS trials (8). However, it is not yet known whether such
46 treatments will be acceptable to patients outside clinical trial settings.

47 Current evidence from wet AMD suggests people will persevere with regular
48 intravitreal treatment, even when associated with a high burden, when motivated by outcome
49 expectations (9)(10). Despite efficacious outcomes of anti-VEGF therapy (11), some wet
50 AMD patients report significant treatment burden associated with regular intravitreal
51 injections, not only in terms of anxiety, discomfort, pain and/or side effects associated with
52 these injections, but also the logistics of regularly travelling to the eye clinic, waiting times,
53 and impacts on accompanying relatives or caregivers (12–14).

54 However, GA is different to wet AMD, being slower to progress, with well-
55 documented variation in rates of progression across individuals, and asymptomatic in some
56 patients until involving the fovea (15,16). Therefore, it is vital to understand whether patients

57 with GA would find it acceptable to commence and adhere to frequent intravitreal treatments,
58 in order to slow GA progression.

59 Acceptability, as defined by Sekhon and colleagues in their Theoretical Framework of
60 Acceptability (TFA), is a “multi-faceted construct that reflects the extent to which people
61 delivering or receiving a healthcare intervention consider it to be appropriate, based on
62 anticipated or experienced cognitive and emotional responses to the intervention” (17).
63 Acceptability is a crucial yet complex factor which can have implications for patients deciding
64 to undergo a treatment, as well as adhering and persisting with it. As such, assessment of
65 acceptability to patients should be a critical first step in the design, evaluation and delivery of
66 healthcare interventions (18).

67 Our study’s central objective was to explore the overall acceptability of current
68 intravitreal treatments in late-stage development for a sample of GA patients. We aimed to
69 identify which aspects of the treatment are considered less acceptable; and to understand
70 whether specific patient-related factors, contexts and circumstances influence GA treatment
71 acceptability. A secondary aim was to explore what people with GA understand about their
72 disease, its progression, current service provision, and their hopes for GA treatment and/or
73 cure.

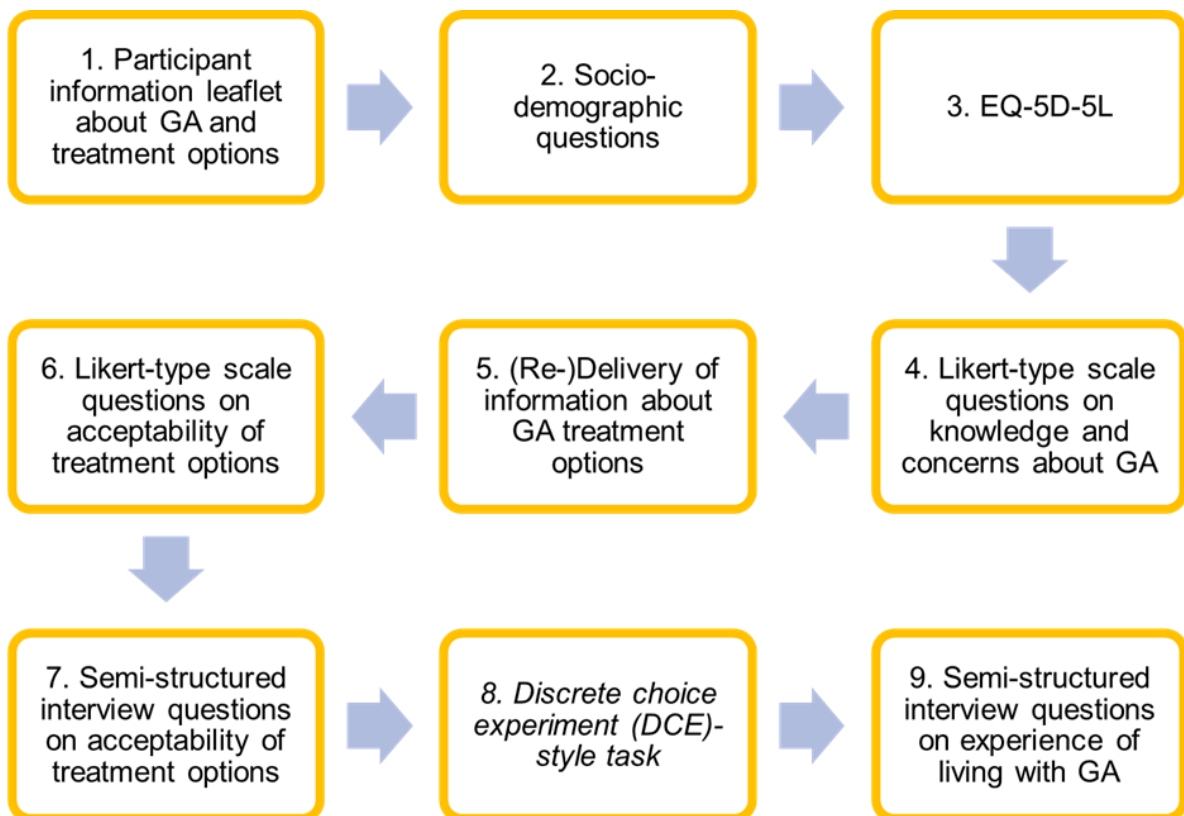
74

75 **Methods**

76 **Study design and procedure**

77 This study employed a cross-sectional, mixed-methods design (19), and full detail on
78 methodological aspects is presented in the published study protocol (20). In summary, a
79 structured questionnaire was used to quantify participants' attitudes to acceptability, as well
80 as open-ended questions to explore participants' beliefs, hopes and concerns regarding GA
81 treatment within their unique contexts and circumstances. Information communicated to
82 participants about the treatments' efficacy was based on Phase 2 clinical trial results (21–
83 23).

84 **Figure 1. Summary of study procedure**



85
86 The study procedure is summarised in Figure 1. The interview schedule, including
87 Likert-type scale questions and semi-structured open-ended questions, is shown in
88 Appendix 1. This interview schedule was developed in consultation with a group of eight

89 patient advisors, individuals living with GA who did not participate in this study but
90 generously volunteered their time and insights.

91

92 **Participant recruitment**

93 Individuals with a diagnosis of GA were recruited from two Medical Retina clinics in
94 London including Brent, one of the most ethnically diverse boroughs in London, UK (24).
95 Included participants were required to be aged ≥ 50 years, and have a diagnosis of GA
96 (bilateral or unilateral) secondary to age-related macular degeneration. Patients with other
97 causes of GA - such as Stargardt's - or with concurrent retinal conditions were excluded.
98 The aim was to recruit a cohort representative of the population in the community; therefore,
99 some participants required an accompanying relative/caregiver to interpret parts of the
100 interview.

101 In order to explore the views of participants with varied demographic and clinical
102 characteristics, a purposive sampling strategy was employed, aiming to achieve maximum
103 variation (25) in terms of: age; gender; ethnicity; education level; overall health status; prior
104 experience of intravitreal injections (for wet AMD); best-corrected visual acuity (BCVA);
105 laterality; and foveal involvement, with extrafoveal defined as greater than 0 microns from
106 the fovea (26).

107 Consenting participants undertook an audio-recorded interview face-to-face or via
108 telephone with authors AG, CD or JE between April and October 2021. This decision to
109 undertake certain interviews by telephone was a pragmatic response to COVID-19
110 restrictions in place in the UK at the time (27).

111

112 **Ethical considerations**

113 Ethics Committee approval was obtained from the NHS Health Research Authority
114 on 23 March 2021 (IRAS Project ID: 287824), and the study adhered to the tenets of the
115 Declaration of Helsinki.

116

117 **Data analysis**

118 Quantitative responses

119 Descriptive analysis of demographic information and responses to the Likert-type
120 scale questions was undertaken. Where appropriate, Spearman's rank (r_s) correlation
121 coefficients were calculated to explore potential associations between responses to the
122 Likert-type scale questions on acceptability (dependent variables) and demographic and
123 clinical characteristics (independent variables). A p -value of $<.05$ was considered statistically
124 significant. Statistical tests were conducted using SPSS, version 27.0 (SPSS Inc., Chicago,
125 IL, USA).

126

127 Qualitative responses

128 Data from the semi-structured interview were transcribed verbatim, and analysed
129 using the Framework Method of analysis (28,29). This systematic qualitative data analysis
130 method allowed for both inductive analysis (whereby open coding of the data leads to
131 generation of themes) and deductive analysis (whereby pre-existing theory – in this case,
132 the TFA - shapes the development of themes). Initial coding was conducted by author JE,
133 followed by a second round of coding involving authors JE, AG, DJT and CD working
134 collaboratively. Discrepancies regarding the best fit of text segments within the TFA matrix
135 were resolved by author MS, an expert in acceptability who developed the TFA. This was an
136 iterative, recursive process, and over time the team collaboratively developed a codebook
137 (Appendix 2), establishing decision rules for coding the data into the seven TFA constructs.
138 The software package NVIVO V.10.2 (QSR International, Cambridge, Massachusetts, USA)
139 was used to manage the qualitative data.

140 In tandem, data which did not fit within a TFA construct were coded inductively by
141 authors JE, AG and CD, to develop a second framework matrix encapsulating important
142 patterns in the data falling outside the TFA.

143 Analysis of qualitative data within the framework matrix illustrated that participants'
144 responses fell within three distinct and recognisable positive, ambivalent, and negative
145 categories.(30) The categorisation was based on participants' expressed intentions
146 regarding the potential treatments. For example, a participant concluding that "*I think I would*
147 *have the treatment at almost any cost*" (P26) would be placed in the positive category, while
148 a participant concluding that the treatment "*is not for me*" (P24) would be placed in the
149 negative category. Two authors (CD and JE) independently assigned the participants into
150 the three categories, and then compared and collaboratively refined the categorisation.
151 Certain disagreements in categorisation were discussed with reference to the individual case
152 in the framework matrix, and all authors subsequently met to consider these disputed cases
153 and reach consensus. After whole team discussion, the three categories were termed
154 "Treatment at any cost" (positive), "Ambivalent", and "Unlikely to Proceed" (negative).

155

156 **Results**

157 **Participants**

158 Thirty participants (67% female) were interviewed, and demographic and clinical
159 characteristics for each participant are displayed in Appendix 3. Median (interquartile range
160 (IQR)) age was 83 (78, 87) years. Nineteen (63%) of participants identified as white, eight
161 (27%) as South Asian, one (3%) as Black, and two (7%) as another ethnicity. The range of
162 participants' primary languages is displayed in Appendix 4. In the case of three participants
163 (P16, P20, and P25), interviews were interpreted by or mediated through an accompanying
164 relative, due to English language or communication difficulties.

165 Better eye median (IQR) logMAR visual acuity (VA) was 0.30 (0.17, 0.58). Nineteen
166 (63%) of the 30 participants had prior experience of intravitreal injections for neovascular
167 (wet) AMD, while 11 (37%) were injection-naïve. Eleven (37%) of participants had centre-
168 involving GA.

169 When asked to self-report their GA severity (Appendix 1, Q16), 13 participants self-
170 rated their GA as mild, 13 as moderate, and 4 as severe. A more severe self-report was
171 associated with worse VA in the better eye ($r_s(28) = 0.40, p = 0.029$). This is consistent with
172 previous reports demonstrating that vision-related quality of life is primarily dependent on the
173 better eye (31). However, there was no statistically significant correlation between self-
174 reported GA severity and: worse eye VA; VA in the GA eye; VA in the fellow eye; GA
175 laterality; or centre-involvement.

176 Median (IQR) time to travel to the eye clinic was 30 (15, 45) minutes. Ten (33%)
177 participants lived alone while the other 20 (67%) lived with spouses or partners, children or
178 carers. Fourteen (47%) participants reported attending eye clinic appointments alone, while
179 the other 16 (53%) were accompanied by relatives, friends or caregivers. Twenty-three
180 (77%) of participants reported living with other chronic health conditions apart from AMD/GA,
181 with 8 (27%) living with diabetes. In the EQ-5D, the domains in which participants reported
182 most problems were mobility (mean score = 2.3) and usual activities (mean score = 2.1).

183 Interview times with participants ranged from 27 minutes to 120 minutes. Twenty-four
184 of the interviews (80%) were conducted in person, and six (20%) by telephone.

185

186 **Quantitative findings on acceptability of intravitreal injections for GA**

187 Findings from the Likert-type scale questions about acceptability of GA treatment are
188 shown below in Table 1, while Figure 2 displays responses to questions about participants'
189 willingness to undergo intravitreal injections at different intervals. Figure 2 demonstrates the
190 increase in acceptability when injections were proposed every other month rather than

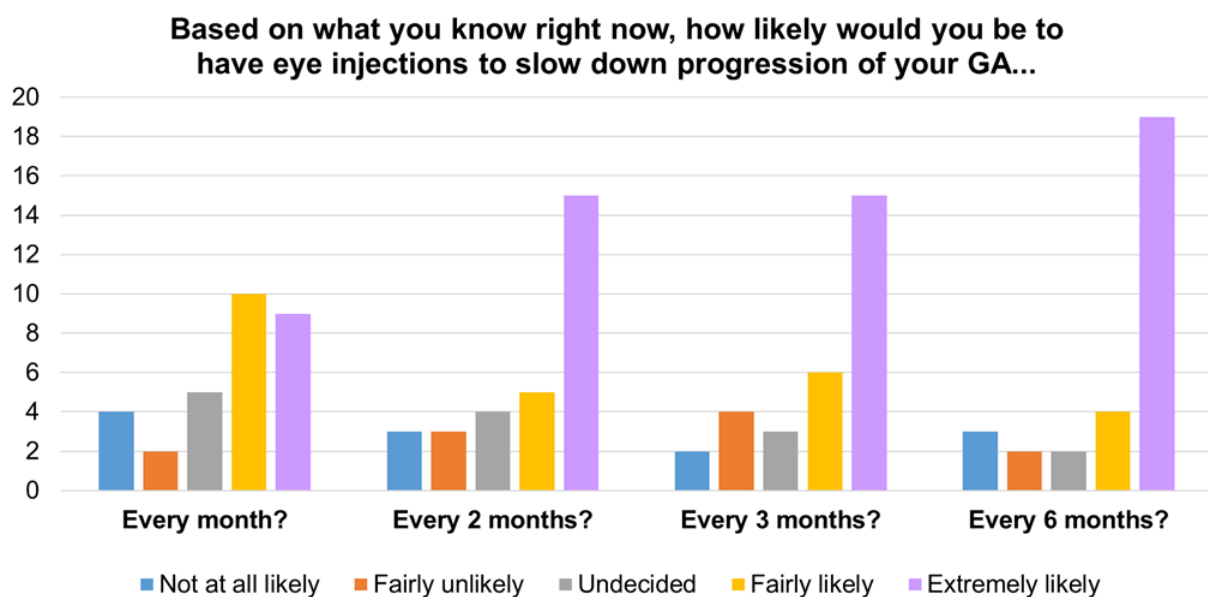
191 monthly, with 15 of 30 (50%) participants extremely likely to accept GA injections every other
 192 month, compared with 9 of 30 (30%) extremely likely to accept monthly GA injections.

193 Table 1. Responses to Likert-type scale questions on acceptability of GA treatments

Likert-type scale question and responses	N	%
In your view, are the risks of the injection procedure, as explained, worth the potential benefit of slowing down the progression of geographic atrophy?		
Yes	17	57
Not sure	11	37
No	2	7
Are you afraid of having an injection in your eye?		
Yes	10	33
Not sure	4	13
No	16	53
Are you concerned about the side effects of injections into your eye?		
Yes	10	33
Not sure	3	10
No	17	57

194

195 Figure 2. Responses to questions on acceptability of GA treatment at different intervals



196

197 Qualitative responses analysed within the TFA (see below) were additionally

198 categorised into three groups, following analysis of the qualitative framework and reaching

199 consensus among all authors. Eighteen (60% (95% CI: 41-79%)) participants were deemed
200 to be positively accepting of the treatment despite their awareness of the burdens and
201 drawbacks, and this group was termed "Treatment at any cost". Eight (27% (95% CI: 10-
202 43%)) participants were deemed to be "Ambivalent", hesitant about treatment and unsure
203 about the balance of benefits versus risks and drawbacks. Four (13% (95% CI: 0-26%))
204 participants were deemed "Unlikely to proceed" with treatment. These figures correlate
205 strongly with participants' responses on the Likert-type scale question asking whether the
206 risks of treatment are worth the benefits (Table 1), $r_s(28) = 0.69$, $p < 0.001$. Table 2 shows
207 these acceptability levels, overall and as stratified by select ocular and demographic
208 characteristics.

209

210 Table 2. Select ocular and demographic characteristics of participants, with overall
 211 acceptability levels

	N (%)	Positive (%)	Ambivalent (%)	Negative (%)	P-value (from Fisher Exact Test)
All participants	30 (100)	18 (60)	8 (27)	4 (13)	N/A
Age					1.00
<80	10 (33)	6 (20)	3 (10)	1 (3)	
≥80	20 (67)	12 (40)	5 (17)	3 (10)	
Gender					0.74
Female	20 (67)	12 (40)	6 (20)	2 (7)	
Male	10 (33)	6 (20)	2 (7)	2 (7)	
Ethnicity					0.59
Black	1 (3)	0	1 (3)	0	
South Asian	8 (27)	4 (13)	2 (7)	2 (7)	
White	19 (63)	12 (40)	5 (17)	2 (7)	
Other ethnicity	2 (7)	2 (7)	0	0	
Highest education level					0.31
Primary	3 (10)	1 (3)	2 (7)	0	
Secondary	18 (60)	11 (37)	5 (17)	2 (7)	
University	6 (20)	5 (17)	0	1 (3)	
Postgraduate	3 (10)	1 (3)	1 (3)	1 (3)	
EQ5D mean score					0.045*
<2 (better self-reported health)	17 (57)	7 (23)	6 (20)	4 (13)	
≥2 (worse self-reported health)	13 (43)	11 (37)	2 (7)	0 (0)	
Previous experience of intravitreal injections?					0.76
Yes	19 (63)	11 (37)	6 (20)	2 (7)	
No	11 (37)	7 (23)	2 (7)	2 (7)	
Foveal involving?					0.66
Yes	11 (37)	6 (20)	4 (13)	1 (3)	
No	19 (63)	12 (40)	4 (13)	3 (10)	
Better eye VA (logMAR)					0.81
≤0.3	16 (53)	9 (30)	4 (13)	3 (10)	
0.31-0.8	10 (33)	7 (23)	2 (7)	1 (3)	
>0.8	4 (13)	2 (7)	2 (7)	0 (0)	
GA eye VA (logMAR)					0.55
≤0.3	11 (37)	7 (23)	2 (7)	2 (7)	
0.31-0.8	11 (37)	7 (23)	2 (7)	2 (7)	
>0.8	8 (27)	4 (13)	4 (13)	0 (0)	

212 * $P < 0.05$

213

214 Inferential analysis demonstrated a statistically significant, moderate correlation

215 between overall acceptability level (i.e. membership in the three groups discussed in the

216 paragraph above) and EQ-5D score, $r_s(28) = 0.42$, $p = 0.021$. Participants with worse self-

217 reported health (higher EQ-5D score) were more likely to be in the “Treatment at any cost”
218 group. Otherwise, there were no statistically significant associations between treatment
219 acceptability and demographic/clinical factors, such as intravitreal injection history.

220 When considering correlations between other Likert-type scale question responses
221 and demographic/clinical factors, statistically significant moderate correlations were only
222 found for the question around concern about side effects of injections (Table 2). Concern
223 about side effects correlated positively with: increased age, $r_s(28) = 0.44, p = 0.014$;
224 presence of other chronic health conditions, $r_s(28) = 0.47, p = 0.009$; and naivety to
225 intravitreal injections, $r_s(28) = 0.43, p = 0.018$.

226

227 **Qualitative findings on acceptability of intravitreal injections for GA, based around the** 228 **Theoretical Framework of Acceptability (TFA)**

229 Participants’ responses to the semi-structured, open-ended interview questions were
230 coded into the seven constructs of the TFA (17). Table 3 displays the seven constructs as
231 defined in the TFA, and different reflections of the construct as generated from participants’
232 responses, illustrated with example verbatim quotations. Appendix 5 provides an extended
233 version of these qualitative findings, with additional participant quotations.

234

235 Table 3. Participant reflections on prospective acceptability of GA treatment, categorised within the seven component constructs of the TFA

TFA construct, with definition	Positive (+), negative (-), or neutral (?) reflection of TFA construct	Example quotation (q)
Affective attitude: "How an individual feels about the intervention"	(+) Wish to delay further vision loss	1. "I think I would have the treatment at almost any cost" (P26) 2. "That's the main advantage, if it slows down what is going on with my eye." (P14)
	(+) Good relationship with eye clinic staff	3. "The girl who does it is very good, I always have the same one who does my injections... She puts you at ease because I was terrible when I first came in. I am still dying a thousand deaths but I am braver." (P10)
	(-) Anxiety around intravitreal injections	4. "I just don't like having the needle in the eye, the feeling of the injections, but it will not put me off if it will save my eyesight. The only thing I wouldn't like was if they were both done together." (P10)
	(-) Discomfort of clip/speculum during injection procedure	5. "What will put me off is this thing that they put in [the speculum]. That's the worse thing anyway." (P22) 6. "I am having injections in my other eye... it is very painful because of that clip they put on." (P3)
	(-) Long waiting times in clinic	7. "If it can be done more quickly, it would be much better. Because you come here ready for your injections and waiting makes you more nervous... So making it quicker will make it absolutely better." (P22)
Burden: "The perceived amount of effort that is required to participate in the intervention"	(+) Proximity to hospital	8. "I don't mind to come in as many times as required. I live very close, 10 minutes [away]." (P5)
	(+) Ease of travel to hospital	9. "I can get to the hospital quite easily. If my wife can't do it, I've got close family that would do it so there's no expense like taxis, et cetera." (P13)
	(-) Regular travel to hospital	10. "[A disadvantage is] having to come to hospital every so often... Just travelling, coming here." (P24) 11. "Coming to hospital if it's once in 6 months is ok... If it's frequent, that's going to be a problem." (P11)
	(-) Frequent treatment intervals	12. "I think if it is [an injection] every month, it is too much." (P29)
	(-) Impacts on accompanying relatives/caregivers	13. "There's the fact of getting here - I can't rely on my daughter all the time. She is trying to run a business. And it's not easy for me, I can't drive anymore." (P14)
	(-) Concerns about side effects	14. "Disadvantages would be the side effects... One thing is haemorrhage. And the other thing is the intraocular pressure going up." (P11)
(-) Increased risk of wet AMD	15. "I would want to have longer vision, but I am concerned about risk of wet AMD." (P5)	
Ethicality: "The extent to which the intervention has a good fit with an individual's value system"	(+) Belief that GA injections will help preserve independence	16. "My family would benefit knowing I can still use my eyesight. It will help me to maintain my independence. I am sure my family will be pleased about that." (P17)
	(-) Concerns about scarce NHS resources	17. "I wouldn't want to bother the [clinical] team. Because I'm sure that the team are so worried about everything... Injections every two months would be ideal, but it depends on the resources." (P30)
Intervention coherence: "The extent to which the participant understands the	(+) Clear understanding of anticipated treatment effects	18. "You want to keep your eyesight as long as possible. Even if it's not going to reverse it, you know you're going to be able to have sight that bit longer." (P16)
	(+) Understanding of the intravitreal injection process due to previous wet AMD treatment	19. "If it had been the first time then there would be a lot more questions to ask. But I know the routine would be the same as what I'm having now anyway, so I wouldn't be worried at all." (P9)

intervention and how it works (i.e. the 'face validity' of the intervention for the recipient)"	(-) Confusion regarding improvement of vision	20. "[After treatment] I think I will be able to read, I cannot read now... If I could keep whatever sight I have that would be very excellent - if you can stop it there and it doesn't get worse." (P28)
	(-) Queries regarding treatment timeline	21. "How long will treatments go on for? I think the treatments going on for a lifetime would be a concern for some patients." (P2) 22. "Can I withdraw from injections if I am not happy?" (P10)
	(?) Need for further information before treatment uptake	23. "Of course when I come to injections I am going to ask more about it and then decide if I take it." (P7) 24. "I would like to know for how long this treatment will be? And the success rate? ... How certain it will maintain my eyesight for longer?" (P17)
Opportunity costs: The extent to which benefits, profits or values must be given up to engage in the intervention	(+) Lack of time pressure	25. "There aren't really disadvantages unless your time is used 24/7 and it's taking time for something else. But it doesn't, it wouldn't impact me in that way." (P28)
	(+) Injections free at point of use for patients in the UK	26. "I can't see any disadvantages to be honest with you. I mean if I was living in [United States of] America, it would probably cost me a £1000 a pop to have the injection. But I can't see the disadvantages." (P13)
	(-) Waiting at eye clinic takes time away from valued activities	27. "The waiting around is the most bothering. If I came in and out, I would be fine. I love the comfort of my home." (P19)
Perceived effectiveness: The extent to which the intervention is perceived as likely to achieve its purpose	(+) Anticipated benefits due to having vision for longer	28. "If it's going to slow down the process, give me better quality of life, better vision, I will have it... I might go blind in future but every little bit helps. So give me two to three years [more] of vision so I can watch TV, read books." (P25)
	(-) Belief that extra time with vision may not be worth it	29. "In six years, I will be nearly 90. Will I still be here? So from a time perspective it might not be worth it... How would I benefit really at my age?" (P15)
	(-) Belief that vision is currently good, therefore no perceived urgency for treatment	30. "At the moment, I'm quite happy... I can read the newspapers and everything. I feel much better. So, there's no point in taking injections." (P4)
	(-) Belief that vision-related quality of life has already deteriorated too much to benefit from treatment	31. "It will not bring back the lost vision... I have always been an avid reader.... I can still read, not bad. Sometimes, when I read, the end of the word goes - but I am getting used to that. So as the treatment will not bring back any of those, no, I think I will not benefit from it." (P3)
	(-) Difficulty of perceiving benefits of treatment first-hand	32. "I saw the benefits of having the [wet AMD] injections, but I am not sure if I will get the benefit of this new one." (P24)
Self-efficacy: The participant's confidence that they can perform the behaviour required to participate in the intervention	(+) Confidence to regularly attend eye clinic	33. "I would rather come here [to the eye clinic] for treatment. I just feel confident when I come here." (P15)
	(-) Concerns about feasibility of longer-term commitment to treatment	34. "In another year, I don't know how it is going to be. So I don't know how long I can commit for treatment." (P7)

237 **Qualitative findings beyond the TFA**

238 Themes were also generated inductively from aspects of participants' accounts which
239 fell outside the constructs of the TFA, but were still relevant to GA treatment acceptability.
240 These themes and associated quotations are presented in Appendix 6.

241 **Discussion**

242 Our study findings suggest that a majority of GA patients would be accepting of
243 intravitreal treatment for GA, whilst recognising potential burdens and inconveniences. The
244 key concern for people with GA, which emerged in our study as the central motivation for
245 treatment, is the high priority placed on ability to continue with vision-specific activities,
246 particularly for those in worse self-reported health. For 60% of the study participants, despite
247 acknowledging potential drawbacks, the possibility of extending the time they have to
248 engage in vision-specific activities and remain independent was deemed a worthy trade-off,
249 and they would therefore opt for 'treatment at any cost'. The factors limiting acceptability
250 were largely clustered around concerns about magnitude of treatment efficacy, fear of wet
251 AMD and side effects (and to a lesser extent, the injection procedure itself), and logistics of
252 regular eye clinic visits for treatment. Specifically, reducing the frequency of injections from
253 monthly to every other month increased the proportion of participants that were extremely
254 likely to accept these treatments if offered now.

255 Interestingly, as explored within the TFA's Perceived Effectiveness construct, there
256 were a number of participants with better visual acuity than the sample average who saw no
257 value in treatment, because they perceived their vision as currently good and thus saw no
258 rationale for treatment. However, natural history studies demonstrate a progressive decline
259 in vision over time, with almost two-thirds of eyes observed to have foveal involvement
260 associated with moderate or severe sight loss within 4-5 years (16,32). Additionally, the
261 current treatments in late-stage trials have been suggested to have higher efficacy the
262 further the lesion is from the fovea (5,33), thus extending time of foveal preservation.
263 Therefore, there is a challenge here to accurately identify and robustly support patients at

264 risk of foveal involvement in future whilst their visual acuity remains good, in order to
265 maximise potential to preserve vision with these treatments.

266 Given the heterogeneity of GA in terms of progression, observation of recent
267 progression over time with multi-modal retinal imaging could be a useful way to demonstrate
268 the potential likelihood for the individual patient to benefit from these treatments. Further
269 work is required to develop precise and robust risk stratification tools and to determine the
270 time-difference in progression that patients will perceive as meaningful. Data from Colijn and
271 colleagues' analysis of four population-based cohort studies (16) suggests that delaying
272 progression to foveal involvement by at least 0.8 years could allow the average individual
273 with non-foveal GA to retain central vision and avoid severe vision loss for the rest of their
274 life.(34) As such, even a modest reduction in rate of progression could deliver clinically
275 meaningful benefits to a large number of patients.

276 Within the Burden construct, the increased acceptance of every other month
277 injections is worth highlighting, particularly given recent 24-month outcome data from the
278 DERBY and OAKS phase 3 registration trials. These trials demonstrate a marginal
279 difference in GA growth reduction between the monthly and every other month treatment
280 regimen (19% reduction for eyes treated monthly vs 16% reduction for eyes treated every
281 other month in DERBY; 22% reduction for eyes treated monthly vs 18% reduction for eyes
282 treated every other month in OAKS) (35). On the other hand, monthly injections in these
283 trials were associated with a near doubling of the rate of exudative choroidal
284 neovascularisation (11.9% in monthly versus 6.7% when treated every other month). Similar
285 rates of choroidal neovascularisation have been reported in the avacincaptad pegol trials
286 (36). An every-other-month regime could thus deliver increased adherence and persistence,
287 a better safety profile (almost 50% reduction in neovascularisation risk) and greater cost-
288 effectiveness for healthcare funders, with only a minimal reduction in efficacy.

289 Furthermore, participants' fear of wet AMD risk commonly emerged as an off-putting
290 aspect of treatment, although for some participants this was less of a concern because of

291 the availability of a more efficacious treatment for wet AMD, or if they were already being
292 treated for wet AMD. Even for study participants generally accepting of the GA treatment,
293 the prospect of injections on the same day for wet AMD and for GA was burdensome
294 (although there was one participant – P26 – who welcomed the convenience of consecutive
295 same-day injections). A 2-3 fold increased risk of wet AMD as demonstrated in the phase 3
296 trials (33,36) may necessitate regular monitoring with retinal imaging for these patients
297 associated with increased costs to payers. Innovative patient pathways and service delivery
298 will be required to rollout these treatments. Shared-care models involving monitoring by
299 community optometrists may help expand capacity and reduce time spent in hospital clinics.

300 Listening to our study's participants, it is vital that patients are effectively counselled
301 on the natural history of GA and accurate expectations of treatment effects; including the fact
302 that they are unlikely to perceive treatment benefits directly, and can expect their GA to
303 continue to progress, albeit at a slower pace. Treatment initiation should follow a shared
304 decision-making process involving the patient and their eye care team (37,38). Since
305 participants also noted that their stance on treatment may change over time, counselling on
306 treatment expectations will need to take place regularly to support adherence (10).

307 Our results confirm that longer-acting therapies which slow progression to a higher
308 degree or halt atrophy remain an unmet need and must be the focus for future drug
309 development. In the meantime, more frequent ocular assessment may well be welcomed by
310 many GA patients, who are currently discharged from eye clinics in the UK, with no targeted
311 psychosocial support for what is a progressive and debilitating disease (39,40).

312

313 **Strengths and Limitations**

314 Initially conceived as an exploratory pilot study, our study has a number of limitations.
315 Firstly, as a relatively small-scale study involving patients from two London-based sites,
316 there is limited generalisability to other contexts, for example other geographies in the UK

317 (e.g. rural populations) or other countries with different eye care systems. Secondly, our
318 system of categorisation of participants into three acceptability groups was undertaken in
319 response to emergent patterns in our framework matrix, but did not follow a standardised
320 method that had been predetermined in our protocol. This categorisation could variously be
321 considered too subjective or reductive, and our forthcoming larger, multi-site quantitative
322 study will provide a more robust, generalisable quantification of GA treatment acceptability.
323 Thirdly, while the TFA was used to analyse the data, our interview topic guide was not
324 systematically developed from the TFA; instead, more open-ended questions were used to
325 explore participants' hopes, beliefs and concerns around treatment, based on our literature
326 review and the insights of our study's patient advisory group. This meant that for certain TFA
327 constructs (e.g. Ethicality and Self-efficacy), there was less rich discussion than there may
328 have been, had the TFA been used expressly to shape the topic guide.

329 Nonetheless, this is the first study systematically exploring prospective acceptability
330 of GA intravitreal therapy among a diverse sample of patients, recruited using maximum
331 variation sampling to try to ensure participants were representative of the broader GA
332 population. The quantitative element helps to corroborate and (tentatively) quantify
333 interpretations made on the basis of the qualitative data; indeed, there was close alignment
334 between responses to the Likert-type scale questions and patterns in the qualitative data.
335 Analysis of the qualitative data using the robust Theoretical Framework of Acceptability
336 allowed us to make sense of a rich and complex dataset, and to identify the key motivating
337 factors driving acceptability and what most concerns GA patients and could be modified in
338 future.

339

340 **Conclusion**

341 In summary, a majority of participants (~60%) were positive about GA treatment,
342 despite the potential inconvenience and burdens. Participants' key concerns related to the
343 modest efficacy of treatment, the risk of wet AMD and side effects, and logistical issues

344 associated with frequent, potentially lifelong treatment. We observed a sharp increase in
345 patient acceptability when considering an every-other-month treatment regimen in
346 comparison to monthly treatment. Given encouraging efficacy and safety outcomes for the
347 every-other-month regimen, this may be an optimal dosing label for patients, payers and
348 health services.

349 Further research in a larger population of patients with GA is required to confirm our
350 findings, and identify any correlations between patient acceptability and structural and
351 functional biomarkers of GA severity. We expect such research to aid patient education,
352 selection and individualisation of treatment regimes.

353

354 **Summary**

355 What was known before

- 356 • Intravitreal injection treatments for Geographic Atrophy (GA) are currently showing
357 promising results in Phase 3 clinical trials, significantly slowing down (although not
358 stopping or reversing) GA progression.
- 359 • The acceptability of emerging treatments to patients is a vital consideration, in order
360 to support design and delivery of interventions that patients will adhere to and persist
361 with in the real world.

362 What this study adds

- 363 • Sixty percent of participants would opt for the intravitreal treatments to slow GA
364 progression in spite of potential treatment burdens.
- 365 • Participants' key concerns related to the modest efficacy of treatment, the risk of wet
366 AMD and side effects, and logistical issues associated with frequent, potentially
367 lifelong treatment.
- 368 • Our study illustrated a sharp increase in patient acceptability when considering an
369 every-other-month treatment regimen in comparison to monthly treatment.

370 • Common misunderstandings regarding the workings and likely effects of the
371 intravitreal treatments demonstrate a need for clear, accessible patient education
372 tools.

373

374 References

- 375 1. Owen CG, Jarrar Z, Wormald R, Cook DG, Fletcher AE & Rudnicka AR. The
376 estimated prevalence and incidence of late stage age related macular
377 degeneration in the UK. *Br J Ophthalmol* **96**, 752-756 (2012).
- 378 2. Dinah C, Enoch J, Ghulakhszian A, Taylor DJ & Crabb DP. Intravitreal
379 treatment for geographic atrophy: coming soon to a patient near you? *Eye* **36**,
380 1121-1123 (2021).
- 381 3. Varma R, Souied EH, Tufail A, Tschosik E, Ferrara D, Zhang J, et al. Maximum
382 reading speed in patients with geographic atrophy secondary to age-related
383 macular degeneration. *Invest Ophthalmol Vis Sci* **59**, 195–201 (2018).
- 384 4. Krezel AK, Hogg R, Lohfeld L, Chakravarthy U & Azuara-Blanco A. Core
385 outcomes for geographic atrophy trials. *Br J Ophthalmol* **104**, 1196–1202
386 (2020).
- 387 5. Lally DR, Heier JS, Sadda S, Eichenbaum DA & Danzig C. Progression of
388 Atrophy in AMD: Post Hoc Analysis From the GATHER1 Study. 2022.
389 [https://investors.ivericbio.com/static-files/4341199c-b031-45a0-bc6f-](https://investors.ivericbio.com/static-files/4341199c-b031-45a0-bc6f-a032a44a8021)
390 [a032a44a8021](https://investors.ivericbio.com/static-files/4341199c-b031-45a0-bc6f-a032a44a8021) [cited 2022 Sep 1].
- 391 6. Heier J, Singh R, Wykoff C, Steinle N, Boyer D, Monés J, et al. Efficacy of
392 intravitreal pegcetacoplan in geographic atrophy: 24-month results from the
393 phase 3 OAKS and DERBY trials . In 2022 [cited 2022 Nov 28]. Available from:
394 [https://investors.apellis.com/static-files/78d1b209-7324-4c4c-8b20-](https://investors.apellis.com/static-files/78d1b209-7324-4c4c-8b20-bf7778493bae)
395 [bf7778493bae](https://investors.apellis.com/static-files/78d1b209-7324-4c4c-8b20-bf7778493bae)
- 396 7. Loewenstein A & Trivizki O. Future perspectives for treating patients with
397 geographic atrophy. *Graefe's Arch Clin Exp Ophthalmol* (2022).
398 <https://doi.org/10.1007/s00417-022-05931-z>
- 399 8. Hutton D. Industry leaders react to FDA's pegcetacoplan approval.
400 Ophthalmology Times [Internet]. 2023; Available from:
401 [https://www.ophtalmologytimes.com/view/industry-leaders-react-to-fda-s-](https://www.ophtalmologytimes.com/view/industry-leaders-react-to-fda-s-pegcetacoplan-approval)
402 [pegcetacoplan-approval](https://www.ophtalmologytimes.com/view/industry-leaders-react-to-fda-s-pegcetacoplan-approval)
- 403 9. Ehlken C, Ziemssen F, Eter N, Lanzl I, Kaymak H, Lommatzsch A, et al.
404 Systematic review: non-adherence and non-persistence in intravitreal
405 treatment. *Graefe's Arch Clin Exp Ophthalmol* **258**, 2077-2090 (2020).
- 406 10. Droege KM, Muether PS, Hermann MM, Caramoy A, Viebahn U, Kirchhof B, et
407 al. Adherence to ranibizumab treatment for neovascular age-related macular
408 degeneration in real life. *Graefe's Arch Clin Exp Ophthalmol* **251**, 1281-1284
409 (2013).
- 410 11. Finger RP, Daien V, Eldem BM, Talks JS, Korobelnik JF, Mitchell P, et al. Anti-
411 vascular endothelial growth factor in neovascular age-related macular
412 degeneration - a systematic review of the impact of anti-VEGF on patient
413 outcomes and healthcare systems. *BMC Ophthalmol* **20**, 294 (2020).
- 414 12. Boyle J, Vukicevic M, Koklanis K, Itsiopoulos C & Rees G. Experiences of
415 patients undergoing repeated intravitreal anti-vascular endothelial growth factor

- 416 injections for neovascular age-related macular degeneration. *Psychol Health*
417 *Med* **23**, 127-140 (2018).
- 418 13. Senra H, Ali Z, Balaskas K & Aslam T. Psychological impact of anti-VEGF
419 treatments for wet macular degeneration: a review. *Graefe's Arch Clin Exp*
420 *Ophthalmol* **254**, 1873-1880 (2016).
- 421 14. Thier A & Holmberg C. The patients' view: age-related macular degeneration
422 and its effects—a meta-synthesis. *Disabil Rehabil* **44**, 661-671 (2022).
- 423 15. Fleckenstein M, Mitchell P, Freund KB, Sadda S, Holz FG, Brittain C, et al. The
424 progression of geographic atrophy secondary to age-related macular
425 degeneration. *Ophthalmology* **125**, 369-390 (2018).
- 426 16. Colijn JM, Liefers B, Joachim N, Verzijden T, Meester-Smoor MA, Biarnés M, et
427 al. Enlargement of Geographic Atrophy From First Diagnosis to End of Life.
428 *JAMA Ophthalmol* **139**, 743-750 (2021).
- 429 17. Sekhon M, Cartwright M & Francis JJ. Acceptability of healthcare interventions:
430 An overview of reviews and development of a theoretical framework. *BMC*
431 *Health Serv Res* **17**, 88 (2017).
- 432 18. Klaic M, Kapp S, Hudson P, Chapman W, Denehy L, Story D, et al.
433 Implementability of healthcare interventions: an overview of reviews and
434 development of a conceptual framework. *Implement Sci* **17**, 1-20 (2022).
- 435 19. Klassen AC, Creswell J, Plano Clark VL, Smith KC & Meissner HI. Best
436 practices in mixed methods for quality of life research. *Qual Life Res* **21**, 377-
437 380 (2012).
- 438 20. Enoch J, Ghulakhszian A, Crabb DP, Dinah C & Taylor DJ. Acceptability of
439 intravitreal injections in geographic atrophy: protocol for a mixed-methods pilot
440 study. *BMJ Open* **11**, e049495 (2021).
- 441 21. Liao DS, Grossi F V, El Mehdi D, Gerber MR, Brown DM, Heier JS, et al.
442 Complement C3 Inhibitor Pegcetacoplan for Geographic Atrophy Secondary to
443 Age-Related Macular Degeneration: A Randomized Phase 2 Trial.
444 *Ophthalmology* **127**, 186–95 (2020).
- 445 22. Jaffe GJ, Westby K, Csaky KG, Monés J, Pearlman JA, Patel SS, et al. C5
446 inhibitor Avacincaptad pegol for geographic atrophy due to age-related macular
447 degeneration: a randomized pivotal phase 2/3 trial. *Ophthalmology* **128**, 576–
448 86 (2021).
- 449 23. Freeman WR, Bandello F, Souied EH, Guymer RH, Garg S, Chen FK, et al.
450 Phase 2b Study of Brimonidine DDS: Potential Novel Treatment for Geographic
451 Atrophy. *Invest Ophthalmol Vis Sci* **60**, 971 (2019).
- 452 24. UK Government. Regional ethnic diversity [Internet]. 2020 [cited 2022 Sep 9].
453 Available from: [https://www.ethnicity-facts-figures.service.gov.uk/uk-population-](https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity/national-and-regional-populations/regional-ethnic-diversity/latest)
454 [by-ethnicity/national-and-regional-populations/regional-ethnic-diversity/latest](https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity/national-and-regional-populations/regional-ethnic-diversity/latest)
- 455 25. Sandelowski M. Sample size in qualitative research. *Res Nurs Health* **18**, 179-
456 183 (1995).

- 457 26. Holz FG, Ho A, Khanani AM, Chang A, Bliss C, Sharp D, et al. Efficacy of
458 Pegcetacoplan in Subgroups Defined by Distance from the Foveal Center Point
459 in the Phase 3 OAKS and DERBY studies of Patients with Geographic Atrophy.
460 In: The Macula Society 45th Annual Meeting, Berlin, Germany. 2022. Available
461 from: [https://investors.apellis.com/static-files/adcd2696-44f6-41f2-bbb8-](https://investors.apellis.com/static-files/adcd2696-44f6-41f2-bbb8-4cb517cdd67c)
462 [4cb517cdd67c](https://investors.apellis.com/static-files/adcd2696-44f6-41f2-bbb8-4cb517cdd67c) [cited 2022 Sep 13]
- 463 27. Richardson SJ, Carroll CB, Close J, Gordon AL, O'Brien J, Quinn TJ, et al.
464 Research with older people in a world with COVID-19: identification of current
465 and future priorities, challenges and opportunities. *Age Ageing* **49**, 901-906
466 (2020).
- 467 28. Ritchie J & Spencer L. Qualitative data analysis for applied policy research. In:
468 Analysing qualitative data. (Routledge, London, 1994) 173–94.
- 469 29. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework
470 method for the analysis of qualitative data in multi-disciplinary health research.
471 *BMC Med Res Methodol* **13**, 117 (2013).
- 472 30. Guest G, MacQueen KM & Namey EE. Applied Thematic Analysis. (Sage,
473 Thousand Oaks, 2012).
- 474 31. Künzel SH, Möller PT, Lindner M, Goerd L, Nadal J, Schmid M, et al.
475 Determinants of quality of life in geographic atrophy secondary to age-related
476 macular degeneration. *Invest Ophthalmol Vis Sci* **61**, 63 (2020).
- 477 32. Keenan TD, Agrón E, Domalpally A, Clemons TE, van Asten F, Wong WT, et
478 al. Progression of geographic atrophy in age-related macular degeneration:
479 AREDS2 report number 16. *Ophthalmology* **125**, 1913-1928 (2018).
- 480 33. Goldberg R, Heier J, Wykoff CC, Staurengi G, Singh RP, Steinle N, et al.
481 Efficacy of intravitreal pegcetacoplan in patients with geographic atrophy (GA):
482 12-month results from the phase 3 OAKS and DERBY studies. 2022.
483 [https://investors.apellis.com/static-files/ed761716-e969-4d23-a352-](https://investors.apellis.com/static-files/ed761716-e969-4d23-a352-541fa01fd557)
484 [541fa01fd557](https://investors.apellis.com/static-files/ed761716-e969-4d23-a352-541fa01fd557) [cited 2022 Aug 31].
- 485 34. Sadda SR & Sarraf D. Therapeutic Margin for Geographic Atrophy: The Race
486 Between Longevity and Disease Progression. *JAMA Ophthalmol* **139**, 751-752
487 (2021).
- 488 35. Singh RP, Boyer DS, Lad EG, Holz FG, Bliss C, Wong JG, et al. Efficacy of
489 Intravitreal Pegcetacoplan in Geographic Atrophy: 24-Month Results from the
490 Phase 3 OAKS and DERBY Trials. 2022. [https://investors.apellis.com/static-](https://investors.apellis.com/static-files/a1ec9fdb-ef70-49c1-ae6e-5ad7caa63abe)
491 [files/a1ec9fdb-ef70-49c1-ae6e-5ad7caa63abe](https://investors.apellis.com/static-files/a1ec9fdb-ef70-49c1-ae6e-5ad7caa63abe) [cited 2022 Oct 24].
- 492 36. Iveric Bio. Iveric Bio Announces Positive Topline Data from Zimura® GATHER2
493 Phase 3 Clinical Trial in Geographic Atrophy [Internet]. Parsippany, New
494 Jersey; 2022 Sep [cited 2022 Sep 9]. Available from:
495 [https://investors.ivericbio.com/news-releases/news-release-details/iveric-bio-](https://investors.ivericbio.com/news-releases/news-release-details/iveric-bio-announces-positive-topline-data-zimurar-gather2-phase)
496 [announces-positive-topline-data-zimurar-gather2-phase](https://investors.ivericbio.com/news-releases/news-release-details/iveric-bio-announces-positive-topline-data-zimurar-gather2-phase)
- 497 37. Bouaziz M, Cheng T, Minuti A, Denisova K & Barmettler A. Shared Decision
498 Making in Ophthalmology: A Scoping Review. *Am J Ophthalmol* **237**, 146-53
499 (2021).

- 500 38. Scheffer M, Menting J, Roodbeen R, van Dulmen S, van Hecke M,
501 Schlingemann R, et al. Patients' and health professionals' views on shared
502 decision-making in age-related macular degeneration care: A qualitative study.
503 *Ophthalmic Physiol Opt* **42**, 1015-1022 (2022).
- 504 39. Taylor DJ, Jones L, Binns AM & Crabb DP. 'You've got dry macular
505 degeneration, end of story': a qualitative study into the experience of living with
506 non-neovascular age-related macular degeneration. *Eye* **34**, 461-473 (2020).
- 507 40. Carlton J, Barnes S & Haywood A. Patient Perspectives in Geographic Atrophy
508 (GA): Exploratory Qualitative Research to Understand the Impact of GA for
509 Patients and Their Families. *Br Ir Orthopt J* **15**, 133 (2019).

510

511 **Figure and table legends**

512 Figure 1. Summary of study procedure

513 Figure 2. Responses to questions on acceptability of GA treatment at different intervals

514 Table 1. Responses to Likert-type scale questions on acceptability of GA treatments

515 Table 2. Select ocular and demographic characteristics of participants, with overall
516 acceptability levels

517 Table 3. Participant reflections on prospective acceptability of GA treatment, categorised
518 within the seven component constructs of the TFA

519

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524

525 **Author Contribution statement**

526 All authors contributed to the study conception and design. Material preparation, data
527 collection and analysis were performed by authors JE, AG, DJT and CD. Expert support
528 regarding treatment acceptability and the Theoretical Framework of Acceptability was
529 provided by MS. Supervision was provided by DPC and CD. The first draft of the manuscript
530 was written by JE and all authors commented on several draft versions of the manuscript. All
531 authors read and approved the final manuscript.

532 All named authors meet the International Committee of Medical Journal Editors (ICMJE)
533 criteria for authorship for this article, take responsibility for the integrity of the work as a
534 whole, and have given their approval for this version to be published.

535

536 **Conflict of Interest**

537 Jamie Enoch, Arevik Ghulakhszian and Mandeep Sekhon declare that they have no
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549 Christiana Dinah has served on advisory boards for Novartis, AbbVie, Ora Clinical, Roche
550 and Apellis. CD is on the scientific advisory board for Ora Clinical, has received speaker fees
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552

553 **Data Availability Statement**

554 The raw datasets generated during and analyzed during the current study are not publicly
555 available, because the in-depth and specific information they contain could compromise the
556 privacy of the participants, given that most participants were recruited from a single London-
557 based site. However, elements of the anonymised raw data may be shareable on
558 reasonable request; in which case, please contact the corresponding author for further
559 information.

560

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566 **Appendices**

567 Appendix 1: Study questionnaire

568 Appendix 2: Codebook for coding qualitative data

569 Appendix 3: Demographic and clinical characteristics of study participants

570 Appendix 4: Primary language(s) spoken, as self-reported by participants (n=30)

571 Appendix 5: Extended results with additional quotes

572 Appendix 6: Themes relating to GA treatment acceptability outside the TFA constructs