

**Table S1: Ethics Committees (EC)**

<b>UNITED KINGDOM</b>
<b>Name of EC</b>
NHS Health Research Authority
Office for Research Ethics Committee Northern Ireland (ORECNI)
<b>GERMANY</b>
<b>Name of EC</b>
Ethikkommission Universität Tübingen
Landesärztekammer Rheinland-Pfalz
Ethikkommission der Universitätsmedizin Göttingen
Ethikkommission Med. Fakultät, Universität Würzburg
Ethikkommission Med. Fakultät, HHU Düsseldorf
Ärztekammer Westfalen-Lippe
<b>REPUBLIC OF IRELAND</b>
<b>Name of EC</b>
University Hospital Waterford Research Ethics Office
<b>CANADA</b>
<b>Name of EC</b>
CIRBI (Centre for IRB Intelligence)* - a central IRB institution

**Table S2** Eligibility criteria for the GA and non-GA groups in a cross-sectional study conducted in 17 sites in the United Kingdom, Germany, Ireland, and Canada

<b>GA group</b>		<b>Non-GA group</b>	
<b>Inclusion criteria</b>	<b>Exclusion criteria</b>	<b>Inclusion criteria</b>	<b>Exclusion criteria</b>
Bilateral symptomatic GA (physician confirmed)	Participated in an interventional study ≤12 months before study inclusion date	Had no ophthalmic condition that in the opinion of the investigator affected visual function. Conditions allowed in the study included (but were not limited to): early/intermediate AMD, dry eye, choroidal nevus, epiretinal membrane, a history of cataract surgery	Participated in an interventional study ≤12 months before study inclusion date
Aged ≥70 years at study inclusion	Participated in the Genentech, Inc. Mahalo study (NCT01229215)	Aged ≥70 years at study inclusion	History of GA, CNV, DME, and/or RVO

Provided informed consent <sup>a</sup> allowing contribution of patient data into the study	Participating in the Roche Chroma (NCT02247479), Spectri (NCT02247531), Proxima A (NCT02479386), or Proxima B (NCT02399072) trials	Provided informed consent <sup>a</sup> allowing contribution of patient data into the study	Decreased cognitive function such that the patient was unable to understand the interview at time of visit (in the opinion of physician/research nurse)
	History of CNV, DME, and/or RVO		
	Decreased cognitive function such that the patient was unable to understand the interview at time of visit (in the opinion of physician/research nurse)		

**Note:** <sup>a</sup>No identifiable information is reported in this study. Patients consented for their data to be used in this study, including completion of patient questionnaires. Patients were given the option to also provide additional consent for their data to be linked to other available electronic medical record data sources and agree to being contacted post study for follow-up, which was optional and dependent on gaining approval from ethics and other regulatory authorities in participating countries (not a consideration for this study, and separate documentation will be submitted).

**Abbreviations:** AMD, age-related macular degeneration; CNV, choroidal neovascularization; DME, diabetic macular edema; GA, geographic atrophy; RVO, retinal vein occlusion.

**Table S3** Sociodemographic, vision-specific, disease characteristic, and patient-reported outcome variables (GA and/or non-GA groups) in a cross-sectional study conducted in 17 sites in the United Kingdom, Germany, Ireland, and Canada

<b>Variable</b>	<b>Description</b>
<b>Sociodemographics (GA and non-GA groups)</b>	
Age	Continuous ( $\geq 70$ years)
Sex	Male, female
Ethnicity	White, Asian, Chinese, Black/African/Caribbean, mixed, other
Marital status	Single/never married, married/domestic partnership, divorced, widowed, separated
Living status	At home alone, at home with family or friends, in an assisted living facility (private or public), in a nursing home/residential care home (private or public)
No. of people living in household, including patient	Including number of people in household such as spouse, dependent children, and elderly parents
Highest level of education	Graduate degree (eg, master's degree, doctoral degree, or PhD), university or college degree, university or college qualification below a degree (eg, diploma), upper secondary school qualification (eg, A levels), lower secondary school qualification (eg, standard grade, intermediate), none of the above
Occupation	Paid full-time, paid part-time, self-employed, voluntary work, homemaker, retired, unable to work
Insurance status	Insured or not insured
<b>Disease characteristics (GA and non-GA groups)</b>	
VA measures	Measured $\pm 14$ days from date of study inclusion. Included type

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(eg, ETDRS or Snellen) and distance (eg, 4 meters, 6 meters)

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**Disease characteristics (GA group)**

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Year of GA diagnosis                      The month and year of first affected eye and where applicable second affected eye

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Tests at GA diagnosis                      Tests conducted  $\pm 14$  days from the date of GA diagnosis were recorded and included FAF, FFA, OCT, VA, color fundus photography, etc<sup>a</sup>

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Condition of eyes                              Included fellow eye status, center foveal involvement, and lesion size

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Lesion size                                      Measured  $\pm 14$  days from date of study inclusion. Based on broad categories (eg, 1 DD, 1–2 DD, 2–3 DD) and method of assessment (clinical examination, color fundus photograph, FFA image, FAF region finder, infrared image, OCT image, FAF image)

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Central retinal thickness and macular volume (OCT)                      Measured  $\pm 14$  days from date of study inclusion. Date of measurement, center point thickness measurement, and macular volume (mm<sup>3</sup>)

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Involvement of the fovea<sup>a</sup>                      Any foveal involvement, non-foveal involvement

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Blindness                                        In the clinician's opinion, was the patient eligible to be registered as legally blind at the time of study inclusion: yes/no

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**Disease characteristics (non-GA group)**

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Reason for visit                                Early/intermediate AMD, dry eye, choroidal nevus, epiretinal membrane, history of cataract surgery, other

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**Other clinical information (GA and non-GA groups)**

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Comorbidities                                  Ocular and non-ocular comorbidities such as cataract, glaucoma, and diseases in Charlson Comorbidity Index such as diabetes<sup>a</sup>

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**Interviewer-administered patient-reported outcomes (GA and non-GA groups)**

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NEI-VFQ-25<sup>1,2</sup> Interviewer-administered disease-specific vision-related functioning and QoL questionnaire. Includes one item on general health and 25 items that comprise 11 vision-related subscales: near activities, distance activities, dependency, driving, general vision, ocular pain, social functioning, mental health, role difficulties, color vision, and peripheral vision. In this study, an additional six appendix items were included for the near activities and distance activities subscales. The composite score and subscale scores range from 0–100, with higher scores indicating better vision-related functioning

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Global Rating of Change Scale<sup>3</sup> Paper-based questionnaire administered by the interviewer at the study inclusion visit. The patient was asked to assess their current vision status compared with a previous time point, and rate whether their vision had improved or deteriorated over the last year. The score was aggregated into the following categories: worse (–7 to –2), the same (–1 to +1), and better (+2 to +7)

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**Disease characteristics (GA and non-GA groups)**

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VA measures Measured  $\pm 14$  days from date of study inclusion. Included type (eg, ETDRS or Snellen) and distance (eg, 4 meters, 6 meters)

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**Vision-specific details (GA group)**

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Legally blind Yes (registered as legally blind in the applicable country), ongoing (currently going through the process for blindness classification and/or registration process pending completion), no

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Driving license Yes, no

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Driving confidence (day/night)	During the day (yes, no), during the night (yes, no)
Eye rehabilitation services used	Services used ≤24 months before study inclusion: none, low-vision clinics, physical/occupational therapist, support groups, other
Vision-related equipment used	Equipment used ≤24 months before study inclusion: portable lighting, glasses, magnifiers, binoculars, reading aids (eg, electronic books, larger-print paper copies), independent living aids (eg, talking clock, talking remote control), computer and communication tools (eg, voice-activated phone, braille printer), cane/white cane/walking stick, guide dog, other
Transport regularly used	Do not use transport, drive own vehicle, public transport, taxi, travel with paid caregiver, travel with partner/friend
Adjustment(s) made to the patient's home due to GA	Yes, no (eg, bright lighting, installation of railings, installation of ramps)
Time off due to vision (if working)	Days per month
Assistance with activities of daily living	Yes receives assistance (unpaid assistance, paid assistance), no assistance required
Support/benefit from government	Yes, no (eg, disability benefit)
Home health care services	Services used ≤24 months before study inclusion: community nurse/occupational therapist, counseling, support from charities, other
Participation in support group(s)	Yes, no

**Note:** <sup>a</sup>Fovea is defined as a small area of the retina of ~1.5 mm in diameter situated within the macula lutea.

**Abbreviations:** AMD, age-related macular degeneration; DD, disk diameter; ETDRS, Early Treatment Diabetic Retinopathy Study; FAF, fundus autofluorescence; FFA, fundus fluorescein angiography; GA, geographic atrophy; NEI-VFQ-25, National Eye Institute Visual Function Questionnaire-25; OCT, optical coherence tomography; QoL, quality of life; VA, visual acuity.

**References:**

1. Sivaprasad S, Tschosik E, Kapre A, et al. Reliability and construct validity of the NEI VFQ-25 in a subset of patients with geographic atrophy from the phase 2 Mahalo study. *Am J Ophthalmol.* 2018;190:1–8.
2. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD; National Eye Institute Visual Function Questionnaire Field Test Investigators. Development of the 25-item National Eye Institute Visual Function Questionnaire. *Arch Ophthalmol.* 2001;119(7):1050–1058.
3. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials.* 1989;10(4):407–415.



**Table S4** Health care resource use variables for the GA group in a cross-sectional study conducted in 17 sites in the United Kingdom, Germany, Ireland, and Canada

<b>Variable</b>	<b>Operational definitions</b>
<b>Direct ophthalmologic resource use</b>	
Ophthalmological-related patient visits	Number of visits was recorded. Visits were identified as subspecialist, general ophthalmologist, or nurse/optometrist/other allied health care professional, and as first visit or subsequent visits
Ophthalmological tests or procedures	Number of tests was recorded. Tests included VA, OCT, FAF, FFA, eye pressure test, ophthalmoscopy, ICG angiography, microperimetry, cataract surgery, etc
Drugs or other treatments related to eye disease	Number of prescriptions/treatments was recorded and included prescriptions, over-the-counter vitamins, etc
<b>Indirect ophthalmologic resource use<sup>a</sup></b>	
Treatment for falls and other medical occurrences	Included care provided by physicians, hospital admissions, procedures/treatments including elective or emergency treatment, etc

**Note:** <sup>a</sup>Information on treatment for depression/anxiety was collected but not included in analysis due to minimal associated costs.

**Abbreviations:** FAF, fundus autofluorescence; FFA, fundus fluorescein angiography; GA, geographic atrophy; ICG, indocyanine green; OCT, optical coherence tomography; VA, visual acuity.

**Table S5** Visional functioning based on NEI-VFQ-25 subscales<sup>a</sup> – GA and non-GA groups in a cross-sectional study conducted in 17 sites in the United Kingdom, Germany, Ireland, and Canada

Variable	GA group (n=137)	Non-GA group (n=52)	P-value
General health			
Mean (SD)	48.0 (24.5)	49.0 (25.7)	
[95% CI]	[43.9–52.1]	[42.0–56.0]	
Median (IQR)	50.0 (25.0–50.0)	50.0 (25.0–62.5)	
Missing	1	0	
General health: in general would you say your overall health is, n (%)			
Excellent	11 (8.1)	5 (9.6)	
Very good	20 (14.7)	8 (15.4)	
Good	59 (43.4)	22 (42.3)	
Fair	39 (28.7)	14 (26.9)	
Poor	7 (5.1)	3 (5.8)	
Missing	1	0	
General vision			
Mean (SD)	45.9 (19.3)	78.5 (10.4)	
[95% CI]	[42.7–49.1]	[75.7–81.3]	
Median (IQR)	40.0 (40.0–60.0)	80.0 (80.0–80.0)	
Missing	1	0	

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General vision: at the present time

would you say your eyesight using both

eyes is, n (%)

Excellent	0	5 (9.6)
Good	17 (12.5)	38 (73.1)
Fair	38 (27.9)	9 (17.3)
Poor	49 (36.0)	0
Very poor	32 (23.5)	0
Completely blind	0	0
Missing	1	0

Ocular pain

Mean (SD)	86.6 (19.9)	92.8 (11.2)	0.173 <sup>b</sup>
Median (IQR)	100.0 (75.0–100.0)	100.0 (87.5–100.0)	
Missing	1	0	

Near activities

Mean (SD)	25.6 (16.2)	46.4 (10.8)	<0.001 <sup>b</sup>
Median (IQR)	22.8 (13.8–38.4)	46.8 (42.5–50.5)	
Missing	1	0	

Distance activities

Mean (SD)	26.4 (16.7)	46.3 (10.8)	<0.001 <sup>b</sup>
Median (IQR)	25.4 (14.3–38.2)	48.5 (42.3–50.5)	
Missing	1	0	

Social functioning

Mean (SD)	64.7 (30.7)	98.6 (4.0)	<0.001 <sup>b</sup>
Median (IQR)	62.5 (43.8–100.0)	00.0 (100.0–100.0)	

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Missing	1	0	
<b>Mental health</b>			
Mean (SD)	53.1 (25.4)	91.6 (10.9)	<0.001 <sup>b</sup>
Median (IQR)	56.3 (31.3–75.0)	93.8 (87.5–100.0)	
Missing	1	0	
<b>Color vision</b>			
Mean (SD)	78.9 (27.7)	99.0 (4.9)	
Median (IQR)	100.0 (50.0–100.0)	00.0 (100.0–100.0)	
Missing	3	0	
<b>Peripheral vision</b>			
Mean (SD)	62.8 (32.6)	98.1 (6.7)	
Median (IQR)	50.0 (25.0–100.0)	00.0 (100.0–100.0)	
Missing	6	0	

**Notes:** <sup>a</sup>Subscale scores range from 0–100, with higher scores indicating better vision-related functioning. <sup>b</sup>Because the parametric assumptions were not met (ie, equal group variance and distributions consistent with a normally distributed population), the comparison between groups was conducted using a Wilcoxon rank-sum test. Note: percentages, means, medians, and 95% CIs are based on non-missing values.

**Abbreviations:** GA, geographic atrophy; IQR, interquartile range; NEI-VFQ-25, National Eye Institute Visual Function Questionnaire-25.

**Table S6** Medical and nonmedical resource utilization in the GA group – costs associated with direct and indirect ophthalmologic resource use in a cross-sectional study conducted in 17 sites in the United Kingdom, Germany, Ireland, and Canada

Variable	Costs per patient (GA group) (N=137) Annual
Direct ophthalmologic resource use (€), mean (SD) <sup>a</sup>	
Patient visits <sup>b</sup>	188.3 (169.8)
Tests or procedures	1070.9 (1294.6)
Drugs/other treatments <sup>b</sup>	116.4 (641.6)
Eye rehabilitation services	14.4 (30.6)
Home health care services	319.2 (2397.2)
Vision-related equipment <sup>c</sup>	62.9 (111.0)
Mean total for direct cost (€)	1772.1
Indirect ophthalmologic resource use (€), mean (SD) <sup>d</sup>	
GP (or equivalent) visits	176.6 (270.2)
Visits to emergency department	11.9 (43.8)
Inpatient admissions	38.6 (236.00)
Outpatient admissions	6.9 (41.03)
Mean total for indirect cost (€)	234
Mean total for direct and indirect costs (€)	2006.1

**Notes:** <sup>a</sup>For each patient, a cost was calculated for each test/procedure or treatment per period. Costs were adjusted if the patient had <24 months of history. The currency used to estimate costs was euros. The reference year for the unit cost was 2017 and the following 2017 average currency exchange rates were used: 1 British pound sterling = 1.1413 euros and 1 Canadian dollar = 0.6826 euros.

<sup>b</sup>The unit cost per prescription was defined as the mean cost of all available prescriptions for each treatment, regardless of use. For Canada, a cost per pill was collected for amoxicillin and because it is generally prescribed for depression with a long duration of treatment, costs for its use were calculated for 6 months of treatment with a posology of one pill per day.

<sup>c</sup>Only one piece of equipment per period was considered to calculate the cost of vision-related equipment. Because the cost of reading aids was very different between the United Kingdom and Germany, the cost collected in the United Kingdom was applied to Germany.

<sup>d</sup>For each patient, a cost was calculated for each type of visit and admission per period. For admissions, because the length of stay was not collected in the questionnaire, the unit cost (cost for 1 day) was applied for inpatient admissions. Costs for outpatient admissions were adjusted if the patient had <24 months of history. No adjustment of cost was applied on inpatient admissions. Treatment prescribed for falls/other medical occurrences or prescribed medication related to visits were not collected in eCRFs.

Note: means are based on non-missing values.

**Abbreviations:** eCRF, electronic case report form; GA, geographic atrophy; GP, general practitioner.