Ora The Ophthalmology Research Company™

CASE STUDY

Global Execution of Phase 3 Clinical Trials in Geographic Atrophy

Expanding therapeutic horizons in Dry AMD

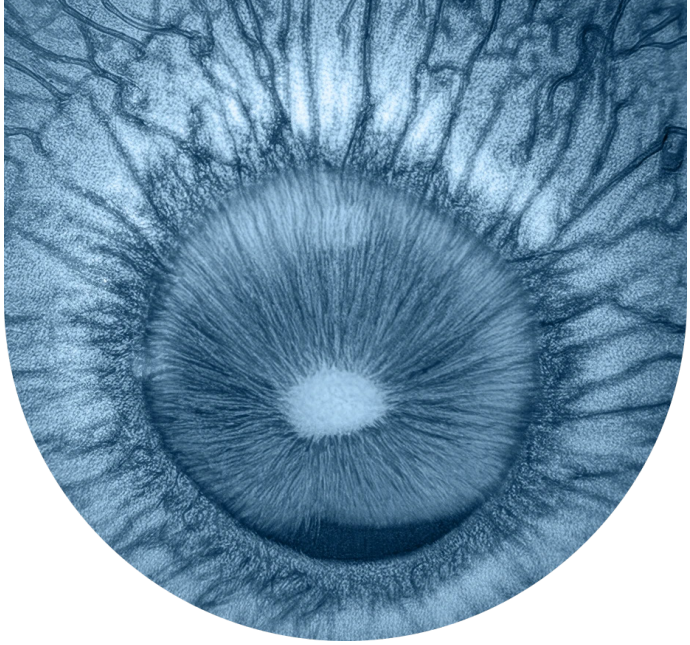
Global phase 3 pivotal GA trial

In early 2024, Ora partnered with a biotechnology company to initiate a global Phase 3 registration trial for Geographic Atrophy (GA). The study targeted enrollment of 360 subjects to be followed for a two-year treatment period with optional roll over into an open-label extension. With an anticipated screen failure rate of approximately 45%, the team would need to screen 655 subjects within a one-year period to achieve enrollment goals and maintain timelines. This scope required tight regulatory coordination, active site engagement, and strong recruitment strategies.

The following sections outline the challenges encountered in this global study and the approaches Ora implemented to achieve success.

The burden of Geographic Atrophy

Geographic Atrophy (GA), the advanced form of dry age-related macular degeneration (dAMD), is a leading cause of irreversible central vision loss worldwide. Recent estimates suggest that there are over 200 million people globally living with AMD[1]. In the United States, there are two FDA-approved therapies for slowing the progression of retinal pigment epithelium (RPE) and photoreceptor loss. In the United States, there are two FDA-approved therapies for slowing the progression of retinal pigment epithelium (RPE) and photoreceptor loss. While the FDA has accepted anatomical outcomes,



these companies also sought approvals in Europe but regulators did not deem the functional benefits of either treatment to be sufficient for approval. In contrast to wet AMD, for which anti-VEGF therapies have transformed outcomes, there are no curative options for GA. Patients face an inevitable decline in visual function, marked by progressive loss of retinal tissue and the inability to carry out everyday tasks, such as reading, driving, and recognizing faces[2].

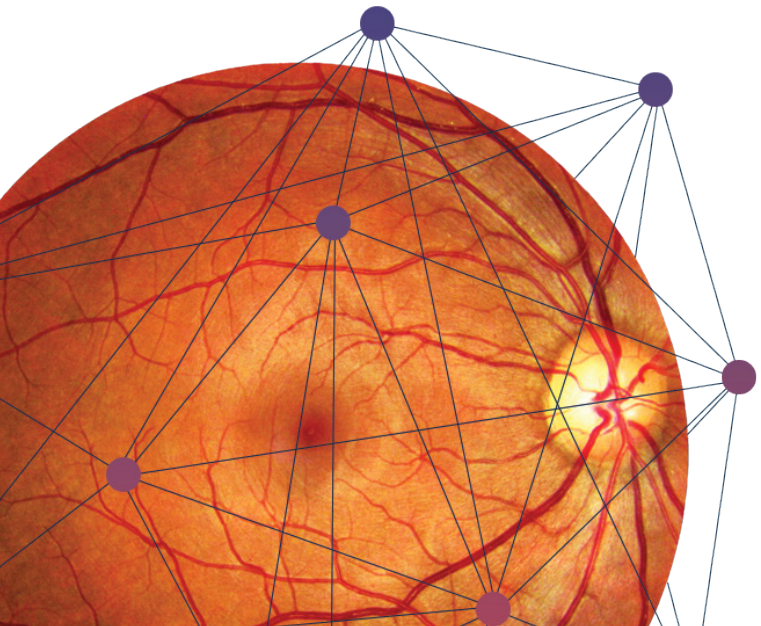
The impact of GA extends well beyond visual acuity. Individuals frequently experience impaired mobility, reduced independence, social isolation, and depression. The burden also extends to caregivers and healthcare systems. In the US, population-based data suggest GA prevalence is 0.48–0.56% among older adults, translating into hundreds of thousands of affected individuals in Medicare populations[3]. In European clinical practice, GA accounts for roughly 60% of advanced AMD cases, with about one-fifth of AMD eyes meeting criteria for GA due to advanced dry AMD[4].

Natural history studies document an average GA lesion expansion rate of approximately 2 mm^2 per year, significant given the human fovea area is ~1.7 mm^2 and the macula is ~23 mm^2 and underscoring the urgent need for therapies to slow or halt progression[5].

Challenges in Phase 3 GA trials

Designing and conducting pivotal Phase 3 studies in GA is inherently complex. Long study durations are required to capture the natural course of disease[5]. Patients, often elderly and with comorbid conditions, must travel to the clinic for long visits with frequent functional and imaging assessments, including best-corrected visual acuity (BCVA), low-luminance BCVA, and photography endpoints. Recognizing potential retention risks, Ora worked closely with sites to identify eligible patients and sustain engagement throughout the trial.

The program focused on enrolling subjects with less advanced GA, relative to previous clinical programs. This population is critical for assessing disease-modifying interventions but recruitment comes with challenges. Inclusion of very small lesions opened access to patients often excluded from GA trials; however, early-stage cases were limited in the clinical setting in several European countries, where late-stage diagnosis is often more common[6]. This resulted in recruitment challenges and higher than expected screen failure rates.



To mitigate this, Ora introduced practical recruitment strategies, including regular touchpoints with sites to exchange approaches for finding eligible patients, and a centralized image prescreening service to reduce screen failures.

The requirement for daily subcutaneous injections also raised concerns about patients' willingness to participate and dosing compliance. Investigators worried that elderly GA patients might struggle with self-administration or object to a daily dosing regimen. Ora mitigated these concerns by sharing strong adherence data from the Phase 2 trial, emphasizing the drug's unique bilateral ocular benefit, and also by providing targeted training and educational materials for both sites and subjects. This built investigator confidence and enabled productive conversations with potential participants.

Finally, the regulatory complexity of a global trial added another layer of difficulty: approvals were required across four regions and multiple ethics committees. Ora streamlined this process by running global and regional workstreams in parallel and ensuring close communication between the sponsor's regulatory team and country experts, minimizing delays despite divergent local requirements.

Ora successfully launched this pivotal Phase 3 GA trial across...

8 countries | **63** sites | **680** patients

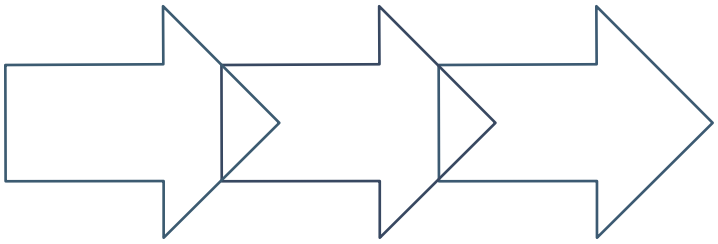
Global execution at scale

Despite these challenges, Ora successfully launched this pivotal Phase 3 GA trial across eight countries: the United States, United Kingdom, Germany, Hungary, Italy, Spain, the Czech Republic, and New Zealand. This program marked a milestone for Ora, as its first global retina initiative, demonstrating expansion into large-scale posterior segment development.

A total of 63 sites were activated within an accelerated start-up window, enabling more than 680 patients to be screened and enrollment completed in just over one year. Despite asynchronous approvals across four regions, Ora's coordinated model kept timelines on track. To maintain momentum across staggered activations, Ora hosted two regional Investigator Meetings and monthly coordinator calls. These sessions reinforced training, aligned procedures, and created forums for investigators and coordinators to exchange strategies for identifying eligible patients.

Taking advantage of rolling activations, Ora adopted a continuous improvement mindset, refining study tools, source documents, and patient-facing materials in real time. The team quickly incorporated feedback from initial activations so later sites benefited from smoother workflows and stronger patient-engagement resources. Additionally, Ora established utilization of central image prescreening, which reduced the risk of image-based screening failures. This improved efficiency and saved valuable site and participant time.

From the first subject enrolled, Ora worked closely with sites to minimize attrition, sustain subject motivation, and ensure dosing success. Tailored site training and patient-support tools helped address the challenges of daily injections in a visually impaired population. These patient-first strategies, combined with tight operational oversight, allowed the study to progress smoothly despite the inherent demands of a global, high-volume Phase 3 trial.



Lessons for the future

This global GA program demonstrated that large, complex retina trials will succeed when operational excellence is paired with scientific rigor and patient-first execution. Key takeaways for future Phase 3 programs include demonstrating that, with a combination of deep expertise, a trusted network, and proven processes, whatever your challenge Ora is here to ensure success.

1

Build a broad global network early and broadly

Secure geographic coverage across both established and emerging retina centers. Balance academic hubs with private clinics to accelerate enrollment and reach diverse patient populations.

2

Keep sites engaged

Sustain momentum with recurring communication touchpoints: investigator meetings, coordinator calls, and recruitment updates. Regular sharing of best practices helps sites stay motivated during long and complex trials.

3

Iterative improvement

Use rolling activations to your advantage. Incorporate feedback from early-activated sites to refine workflows and tools creating smoother execution for sites that follow.

4

One team mindset

Maintain transparency and proactive communication so sponsor and CRO function as a unified team. Shared accountability helps protect trial integrity and ensures patient retention.

Future GA trials will demand not just operational rigor, but trust, foresight, and innovation. Ora's success in this pivotal program shows how an engaged network, continuous learning, and sponsor alignment can overcome global execution challenges and advance the field toward approval of next generation GA therapies.

References

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