CASE STUDY · CENTRAL NERVOUS SYSTEM

# ARIA Safety Monitoring in an Anti-Amyloid Alzheimer's Trial

110 sites · 3T MRI with FLAIR and T2*-GRE/SWI · ARIA-E and ARIA-H severity grading

## Challenge

Intrinsic Imaging supported this study’s imaging activities, addressing the scientific and operational considerations that inform the work of an imaging CRO and imaging core lab. Amyloid-related imaging abnormalities are the defining safety signal of anti-amyloid antibody therapy. ARIA with edema or effusion and ARIA with hemosiderin deposition are usually asymptomatic but can be serious, and dosing decisions at each visit depend on knowing whether they are present and how severe they are. In this Phase III trial, protocol-specified safety MRI scans were scheduled before selected infusions, and the investigator could not proceed with dosing until the central read was available.

That made turnaround a safety matter rather than an operational preference. The 110 sites spanned time zones from the Pacific to Eastern Europe; participants who were APOE ε4 homozygous were at elevated risk and required more frequent imaging; and unscheduled MRIs triggered by symptoms had to be read faster still. Severity grading also needed to be reproducible across many readers, because the number and extent of FLAIR hyperintensities and the count of microhemorrhages and superficial siderosis determine whether a participant continues, pauses or discontinues treatment. The sponsor required a safety read service that was fast, consistent at the grade boundaries that govern dosing, and insulated from the efficacy imaging workload.

## Intrinsic Imaging’s Solution

Intrinsic Imaging separated the safety read workflow from the efficacy reads so that ARIA assessment never waited behind volumetric or amyloid PET analysis. A dedicated neuroradiology panel was trained and qualified on the protocol's ARIA severity scales using a standardized training set, with periodic recalibration reads to monitor drift. Each safety MRI was compared with the participant's baseline and most recent prior scan, and every ARIA-positive read was confirmed by a second neuroradiologist before release.

Grading followed the protocol's scales exactly: ARIA-E by the extent and number of FLAIR hyperintensities, ARIA-H by the count of new microhemorrhages and the presence of superficial siderosis, each compared with baseline so that pre-existing microhemorrhages were never counted as incident events. Because asymptomatic mild ARIA-E permits continued dosing while moderate or severe findings do not, the grade boundary received particular attention in training, and borderline cases were escalated to a third neuroradiologist rather than released on a split decision.

We committed to a 48-hour service level for scheduled safety MRIs and 24 hours for symptom-triggered scans, with seven-day read coverage. Site-facing alerts notified the investigator and the sponsor's medical monitor the moment an ARIA-positive result was released, with the severity grade and the protocol-defined dosing recommendation. The acquisition protocol was harmonized across the three scanner vendors in use, with site qualification confirming that FLAIR and susceptibility-weighted sequences met the slice thickness and coverage the grading scale requires.

## Intrinsic Imaging's Results

- 1.6 days median turnaround for scheduled safety MRIs against a 48-hour service level, maintained across 110 sites spanning time zones from the Pacific to Eastern Europe
- 100% of symptom-triggered and unscheduled scans read within 24 hours, supported by seven-day neuroradiology coverage and immediate alerts to investigators and medical monitors
- 95%+ severity grading concordance between the two neuroradiologists for both ARIA-E and ARIA-H, with borderline grades escalated to a third reader
- Zero dosing decisions delayed by an outstanding central safety read over the course of the trial, including among higher-risk APOE ε4 homozygous participants

Read the full study online: https://intrinsicimaging.com/case-studies/cns-aria

## About Intrinsic Imaging, LLC

Intrinsic Imaging is an ISO certified medical imaging CRO and imaging core lab providing comprehensive services in support of Phase I-IV clinical trials and Class I, II, III medical device trials. Intrinsic Imaging is also a world leader in conducting Artificial Intelligence studies. With its team of more than 50 board-certified and fellowship-trained physicians, Intrinsic Imaging's team has sub-specialization in all therapeutic areas, including Cardiovascular, Central Nervous System,Gastroenterology, Musculoskeletal, Oncology and Ophthalmology. Certified by the British Standards Institution (BSI), Intrinsic Imaging is the only company in the world to hold five ISO certifications specifically for providing imaging core lab services on clinical trials. For more information, please visit www.IntrinsicImaging.com.

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