CASE STUDY · ONCOLOGY

Global Phase III Oral Chemotherapeutic Trial in Metastatic Breast Cancer

110 sites in 20 countries · CT, MRI, bone scan · RECIST 1.1 BICR

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. A global pivotal Phase III trial of a new oral chemotherapeutic for metastatic breast cancer required blinded independent central review of thousands of radiological examinations. Metastatic breast cancer frequently involves bone, where lesions are non-measurable under RECIST 1.1 and progression judgments depend on consistent interpretation of bone scans and correlative CT or MRI, and across 110 sites in 20 countries acquisition practice varied considerably.

The sponsor needed a central review that handled mixed measurable and non-measurable disease consistently, maintained reader blinding across a long follow-up period, and sustained throughput as enrollment accelerated, all under a quality system suitable for a registration submission. A mixed disease population creates an interpretive asymmetry: measurable lesions can be followed quantitatively, while skeletal and other non-target findings may require categorical judgments supported by correlative imaging. Consistency therefore depends on preserving the distinction between evidence of change and the specific evidence sufficient to declare progression under the charter.

Intrinsic Imaging's Solution

Intrinsic Imaging developed the imaging charter with a standardized acquisition protocol for CT, MRI and bone scintigraphy, qualified each site before first patient imaging, and provided training on timepoint scheduling and bone-scan correlation. Image transfer and quality control were centralized, with acquisition deviations returned to sites with specific corrective guidance. Qualification and acquisition feedback address technical variability before it propagates through longitudinal comparisons. Bone-scan correlation is particularly relevant because a newly visible skeletal focus does not, by appearance alone, resolve whether the finding represents progression or a treatment-associated change. Complete, appropriately timed submissions support interpretation without guaranteeing that every skeletal abnormality can be classified definitively.

Two oncology radiologists performed blinded independent reads under RECIST 1.1 at every timepoint, with adjudication on discordant response categories and progression dates. The charter defined how new bone lesions would be confirmed, how flare phenomena would be handled, and how non-target disease would contribute to progression determinations. The charter's separate treatment of new bone lesions, flare and non-target progression constrains judgments that are not reducible to target-lesion measurements. Independent reads expose differences in interpretation before an adjudicated result enters the analysis dataset. A documented progression date is consequential for time-to-event analysis, even when the underlying imaging evidence includes uncertainty.

Reader agreement was monitored across the trial and recalibration sessions were held when drift was detected. Data management delivered a locked imaging dataset aligned with the sponsor's statistical analysis plan at each planned analysis. Agreement monitoring and recalibration address the possibility that interpretive thresholds change during prolonged follow-up. Alignment with the analysis plan connects the imaging output to its intended statistical use, but does not determine the magnitude or clinical relevance of a treatment effect. Timely delivery and methodological consistency are distinct from the efficacy conclusions drawn from the completed trial.

Intrinsic Imaging’s Results

- Approximately 7,200 blinded independent reads completed across 110 sites in 20 countries
- Unevaluable timepoints held under 3% through site qualification and rapid feedback on acquisition deviations
- Adjudication on roughly 15% of timepoints with documented rationale, supporting a defensible progression-free survival analysis
- Imaging datasets delivered on schedule for interim and final analyses under an FDA-audited, ISO certified quality management system

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Read the full study online: https://intrinsicimaging.com/case-studies/oncology-mbc-phase-iii-2016

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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