CASE STUDY · ONCOLOGY

Pivotal Phase III Comparison of an Oral Chemotherapeutic Against the Leading Metastatic Breast Cancer Therapy

5,500+ radiological reads · 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. This pivotal Phase III trial compared the safety, tolerability and tumor response of a new oral chemotherapeutic against the leading therapy for metastatic breast cancer. Because the comparator was an established standard, the margin the sponsor needed to demonstrate was narrow, and any systematic bias or noise in central tumor assessment could obscure a real difference between arms.

With more than 5,500 radiological reads across a mixed population of measurable soft-tissue disease and non-measurable bone disease, the sponsor required blinded reads that were insensitive to treatment arm, consistent handling of bone-only progression, and a review process whose documentation would stand up to regulatory inspection of a comparative efficacy claim. The distinction between measurable soft-tissue response and progression in bone is especially important in a comparative trial, where unequal interpretation could influence the apparent treatment contrast. A skeletal abnormality must be assessed within its imaging context rather than treated as equivalent to a change in target-lesion dimensions.

Intrinsic Imaging's Solution

Intrinsic Imaging developed the imaging charter with acquisition standards for CT, MRI and bone scintigraphy, qualified sites before enrollment and trained site staff on timepoint scheduling and the submission requirements for correlative imaging of bone lesions. Image transfer and processing were centralized with quality control at receipt. Correlative imaging requirements address the limited specificity of an isolated bone-scan finding for progression. Consistent scheduling and complete submissions also support comparison of skeletal and soft-tissue findings within the intended assessment period, without assuming that different modalities measure the same biological process.

Oncology radiologists from the company's 12-member oncology team performed blinded independent double reads under RECIST 1.1, with adjudication on discordant response categories and progression dates. The charter specified how new bone-scan lesions would be confirmed on CT or MRI, how flare would be distinguished from progression, and how non-target disease would be assessed for unequivocal progression. The confirmation and flare rules provide a defined basis for interpreting skeletal changes that may otherwise be ambiguous. Keeping non-target progression distinct from target-lesion measurement is essential because these findings contribute differently to the overall response determination. Adjudication resolves the classification used for analysis without eliminating the underlying uncertainty of an individual lesion.

Reader blinding to treatment arm was protected through image de-identification and randomized case presentation, and reader agreement was monitored throughout, with recalibration where needed. The locked imaging dataset was reconciled with the sponsor's clinical database before each analysis. Blinding safeguards address expectation bias, while agreement monitoring addresses consistency between readers. Database reconciliation serves a different purpose: maintaining correspondence between imaging assessments and the clinical records used for analysis. None of these controls alone establishes comparative efficacy, which remains dependent on the trial's overall evidence.

Intrinsic Imaging’s Results

- More than 5,500 blinded independent reads completed across 95 sites in 17 countries with adjudication on every discordant assessment
- Bone-only progression handled under a documented confirmation rule, with roughly 18% of progression events requiring correlative confirmation
- Reader agreement on overall response held above 85% across the trial with two recalibration sessions documented
- Imaging dataset reconciled with the clinical database and locked on schedule for the primary analysis under an FDA-audited quality system

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Read the full study online: https://intrinsicimaging.com/case-studies/oncology-mbc-oral-chemo-2015

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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