CASE STUDY · MUSCULOSKELETAL

Phase III Knee Osteoarthritis DMOAD Trial

24-month follow-up · Knee MRI, radiographs · JSN and WORMS

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. Demonstrating disease modification in knee osteoarthritis requires reproducible measurement of submillimeter change in joint space width over extended follow-up. The sponsor required radiographic readings precise enough to register these minute structural changes, together with consistent WORMS scoring across 24 months of serial MRI. Because the primary structural endpoint rested on longitudinal comparison, any drift in reader interpretation or measurement technique over the study's duration would bear directly on its conclusions.

Acquisition consistency mattered as much as interpretation. Joint space width on radiographs depends heavily on knee positioning and beam alignment, and modest visit-to-visit variation can produce apparent narrowing or widening unrelated to disease. MRI assessments likewise required consistent sequences and coverage so that cartilage, bone marrow lesions and other WORMS features could be compared reliably over time. The sponsor therefore needed positioning, imaging technique and reader performance treated as interdependent components of a single longitudinal measurement system sustained across two years. Structural progression must be interpreted against the repeatability of the measurement method. An apparent difference in joint space or MRI score may otherwise reflect positioning or scoring variability rather than a corresponding alteration in the underlying joint tissues.

Intrinsic Imaging’s Solution

Intrinsic Imaging provided sites with detailed positioning and acquisition guidance for radiographs and MRI, supported by training before activation and ongoing quality feedback. Each submission was reviewed for positioning, coverage and image quality, and sites were contacted promptly when repeat imaging was required within the protocol's visit windows.

Fellowship-trained musculoskeletal radiologists conducted paired longitudinal reviews of high-resolution knee MRI and radiographs, assessing all timepoints for each subject together while blinded to chronological order to reduce expectation bias. Calibrated measurement tools and a detailed reading charter defining measurement landmarks and scoring conventions governed every assessment, and periodic re-qualification against reference cases confirmed that reader precision was preserved as the study progressed.

Quality metrics, including positioning compliance, repeat-imaging rates and reader performance on re-qualification exercises, were reviewed with the sponsor throughout the study. These reviews allowed targeted support to be directed to individual sites and confirmed that the measurement system remained stable as follow-up accumulated. Precise reading cannot compensate for inconsistent knee positioning, and consistent positioning cannot overcome reader drift over two years; controlling both allowed the trial to measure structural change with the sensitivity its endpoint demanded, and to attribute observed change to disease and treatment rather than to the measurement process itself.

Intrinsic Imaging’s Results

- Reader intraclass correlation above 0.94 for joint space width and WORMS scoring, sustained without degradation across the full 24-month longitudinal follow-up period
- Submillimeter joint space narrowing measured on serial radiographs with the precision required to evaluate a disease-modifying hypothesis rather than symptomatic benefit alone
- Central imaging assessments supported the primary structural endpoint without exclusion of any timepoints on grounds of knee positioning error, beam alignment or reader variability
- Consistent longitudinal scoring, confirmed by periodic re-qualification against reference cases, allowed structural progression to be interpreted in relation to treatment rather than measurement

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

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 650 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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