CASE STUDY · CARDIOVASCULAR & THORACIC

Rare Disease Cardiomyopathy Trial With Echo and Cardiac MRI

80 sites in 16 countries · Echocardiography, cardiac MRI · LVOT gradient, wall thickness and LVEF

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. Obstructive hypertrophic cardiomyopathy is a rare disease in which the imaging measurements are the endpoints. In this Phase III trial, the primary efficacy measure was the change in left ventricular outflow tract gradient at rest and with Valsalva provocation, assessed by echocardiography, while cardiac MRI quantified left ventricular mass and maximal wall thickness in a sub-study. At the same time, the mechanism of the investigational drug carried a known risk of reducing systolic function, so the protocol required that any left ventricular ejection fraction below a defined threshold be reported promptly to guide dose adjustment.

Gradient measurements are notoriously operator-dependent. Provocation technique, Doppler alignment and the choice of beat vary between sonographers, and with 80 sites in 16 countries enrolling a few patients each, few sites had deep experience with the disease. Slow enrollment also meant that sonographer turnover at a site could erase the training investment before the next participant visit. The sponsor needed central measurements precise enough to detect the treatment effect, a safety read fast enough to protect participants between visits, and a mechanism for sustaining acquisition quality at low-volume sites over the life of the trial.

Intrinsic Imaging's Solution

Intrinsic Imaging built the echocardiography protocol around the measurements that mattered, with explicit instruction on Valsalva technique, continuous-wave Doppler alignment across the outflow tract, acquisition of multiple beats and the exclusion of mitral regurgitation contamination from the gradient signal. Each site's sonographers completed protocol training and submitted a qualification study reviewed by our cardiology team before enrolling, and feedback on acquisition quality was returned on every examination for the first three studies from each site.

Central measurements were performed by cardiologists with expertise in hypertrophic cardiomyopathy, with each participant's serial studies measured by the same reader against baseline to control longitudinal variability and a second reader on every primary-endpoint timepoint. Cardiac MRI mass and wall-thickness analysis followed a standardized contouring protocol with reader reproducibility documented in the charter.

For safety, LVEF was measured on every echocardiogram as a priority read with a 24-hour reporting commitment, and a result below the protocol threshold triggered an immediate alert to the investigator and medical monitor with the protocol's dose-adjustment guidance. Because the trial enrolled slowly at most sites, the core laboratory also served as a continuity point: when a site's trained sonographer left, we re-qualified the replacement before the next participant visit, so that acquisition quality did not reset with staff turnover.

Intrinsic Imaging’s Results

- 100% of LVEF safety results reported within 24 hours of image receipt, with no dose-adjustment decision delayed by central review at any of the 80 sites
- Inter-reader variability of resting and Valsalva LVOT gradient measurements held within the charter's prespecified limits across every primary-endpoint timepoint in the trial
- More than half: the reduction in echocardiography protocol deviations between the first and second quarters of enrollment following site-qualification feedback and sonographer re-qualification
- Cardiac MRI mass and wall-thickness measurements delivered complete for the sub-study, with reader reproducibility documented in the charter for the clinical study report

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

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.

Contact:
Intrinsic Imaging, LLC
580 Main St., Suite 210
Bolton, MA, 01740, USA
+1 978-616-4650
Contact@IntrinsicImaging.com