CASE STUDY · CARDIOVASCULAR & THORACIC

International Phase III Heart Failure Trial With Central CPET Analysis

48 sites in 11 countries · Cardiopulmonary exercise testing (CPET) · Peak VO2, VE/VCO2 slope, ventilatory threshold

Challenge

Intrinsic Imaging supported this study's cardiopulmonary exercise testing (CPET), applying the scientific and operational discipline of an imaging CRO and imaging core lab to a functional endpoint. An international Phase III trial in heart failure with preserved ejection fraction used change in peak oxygen uptake (peak VO2) from baseline to week 24 as its primary endpoint, with the VE/VCO2 slope and oxygen uptake at the ventilatory threshold as key secondary endpoints. Testing took place at 48 sites in 11 countries using metabolic carts from five manufacturers and both treadmill and cycle ergometers.

The expected treatment effect was about 1 mL/kg/min, comparable in size to the measurement noise introduced by uncalibrated equipment, inconsistent protocols and submaximal effort. Peak VO2 depends on how hard a patient exercises, so a low value may reflect early termination rather than limited capacity. The VE/VCO2 slope varies with the portion of the test used to calculate it, and the ventilatory threshold must be identified by reading gas-exchange curves. Without central control, each of these factors could be resolved differently at every site, adding variability that a trial of this size could not absorb.

Intrinsic Imaging's Solution

Intrinsic Imaging wrote the CPET charter and site manual, specifying an individualized ramp protocol designed to reach symptom limitation in eight to twelve minutes, the same exercise modality at every visit for each patient, daily gas and flow calibration, and averaging of breath-by-breath data over defined intervals. Sites were qualified on calibration records and on a test performed by a healthy staff member, repeated quarterly as a biological quality control check of each metabolic cart. Each patient's exercise modality and metabolic cart were fixed at baseline so that serial tests could be compared directly.

Every test was transferred as raw breath-by-breath data and reviewed centrally for calibration, protocol adherence, signal quality and effort, with a peak respiratory exchange ratio of 1.05 or higher recorded as the objective marker of maximal effort. Two blinded exercise physiologists independently identified the ventilatory threshold with the V-slope method supported by ventilatory equivalents, and a cardiologist adjudicated differences above a prespecified limit. Peak VO2 and the VE/VCO2 slope were calculated by fixed rules for averaging and slope range rather than by local software defaults. Readers were recalibrated whenever agreement drifted outside the charter's limits.

Sites received written feedback within two business days when a test showed technical problems or submaximal effort, while the patient's visit window still allowed a repeat. Results remained blinded to treatment assignment throughout the study, and the final dataset was delivered with a complete audit trail for every derived value, ready for the sponsor's statistical analysis and regulatory submission.

Intrinsic Imaging’s Results

- Approximately 1,900 CPET tests from 48 sites in 11 countries centrally reviewed under one charter
- 94% of tests met prespecified quality and effort criteria for the primary endpoint analysis
- Ventilatory threshold identified in 86% of evaluable tests, with adjudication required in fewer than 10%
- Inter-reader agreement for oxygen uptake at the ventilatory threshold documented with an intraclass correlation of 0.93

Read the full study online: https://intrinsicimaging.com/case-studies/cardiology-cpet-heart-failure

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 IntrinsicImaging.com.

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