CASE STUDY

Connected operational strategies manage complexities and protect endpoints in a cardiovascular megatrial



A KEY QUESTION

How can a CRO create global enrollment momentum, maintain operational control and protect a megatrial's critical endpoints?

KEYWORDS Cardiovascular Megatrial, Global Patient Recruitment, Site Enablement, Data Management, Patient Retention, Long-Term Follow-Up, Endpoint Protection

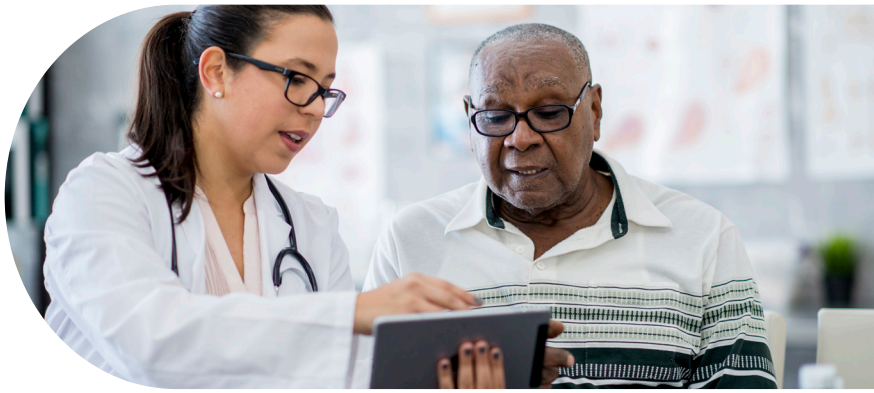
Fortrea was awarded a large cardiovascular outcomes trial (CVOT) to study a sponsor's intravenous investigational medicinal product (IMP). This case study shares how Fortrea managed significant operational complexity to accelerate global site activation across more than 1,000 sites in 40+ countries, enroll 18,000+ patients, maintain high participant retention and deliver high-quality data.



Recognizing the challenges of delivering at scale

Tasked with enrolling participants who had experienced acute coronary syndrome following myocardial infarction (MI), Fortrea needed to enable exceptional operational precision across the full delivery lifecycle. The team faced several hurdles:

Limited screening window to enrollment	Participants needed to be identified and enrolled **within five days** after experiencing MI; the first IMP infusion had to be administered while they were still hospitalized
Managing variability in the standard of care	The study design required administration of four IMP infusions on top of standard of care **within 30 days** after MI
Addressing the participant burden and the risk of loss to follow-up	Numerous in-hospital and outpatient visits were required **within a four-week period**, along with **12 months of follow-up**; differing privacy requirements and geopolitical instability in some countries further increased risk
Adjudicating a high volume of multi-faceted endpoints	Event types requiring adjudication spanned multiple therapeutic areas (major adverse cardiovascular events [MACE], as well as additional endpoint types in cardiology, neurology and hepatology)
Coordinating numerous stakeholders	Fortrea needed to work with two Academic Research Organizations (AROs), multiple technology platforms (EDC, IRT, RBM, Investigator LMS/CTMS Platform, Document Sharing App), central laboratory, adjudication and payment providers, all while managing the sponsor functional team members and sponsor affiliate contacts representing each country where the study was conducted
Meeting a strict requirement for last-patient-last-visit (LPLV)	The protocol required each participant's final visit to occur exactly on day 365 post-randomization, adding a strict scheduling constraint across 18,000+ participants



Applying a combined strategy to meet milestones

Fortrea implemented several cardiovascular clinical trial management strategies to address the trial's challenges. This involved:

Fortrea's strategy	Action taken
Protecting protocol endpoints	**Disciplined risk assessment:** Monthly reviews of Quality Tolerance Limits (QTLs) enabled actionable mitigations and remediation actions **Systematic protocol deviation (PD) review process:** A central review process, focused on Critical-to-Quality factors, promoted consistency in PD handling and oversight, supported by high sponsor engagement **Surveillance monitoring of endpoint reporting:** A Risk-Based Monitoring (RBM) process was established to identify high-risk sites for potential underreporting of endpoints
Proactively handling retention	**Identified at-risk participants before they were lost:** A dedicated Participant Retention Task Force was established early, supported by centralized surveillance and data signals **Implemented multiple retention strategies:** Fortrea developed tailored informed-consent language, site and clinical research associate (CRA) education, participant-recovery vendors, sponsor intervention and formal escalation pathways. A robust prevention and recovery plan was established to re-engage sites and participants to meet endpoint survival data collection requirements **Addressed risk as soon as it emerged:** The team actively challenged and escalated potentially withdrawn consent and lost-to-follow-up cases
Managing a sizable stakeholder ecosystem	**Coordinated the sponsor, AROs, vendors and internal teams:** Fortrea used technology, system integration and customized reporting to manage stakeholder communication **Managed functional risks and performance while aligning culture:** Focused sub-teams managed functional risks and performance, while face-to-face stakeholder engagement and deliberate culture alignment helped establish aligned ways of working and transparent decision-making
Implementing continuous improvement in clinical trial data management	**Progressively increased EDC batch-freeze success:** Routine reviews followed every interim batch cleaning cycle, with clear stakeholder accountability and lessons incorporated into subsequent cycles, leading to database lock being ready three weeks ahead of schedule **A structured adjudication workflow management plan:** This improved the readiness of adjudication data for Data Monitoring Committee (DMC) review, strengthened cooperation between the adjudication and operational teams on aging events and prioritized critical documents and information when required records were unavailable. The plan helped the team consistently maintain 95%+ adjudicated events after two cycles of the workflow management plan implementation
Engineering precision into LPLV	**Targeted communication and preparation:** CRA and site readiness for database cleaning activities and milestones were prepared in advance of LPLV to support alignment on goals, timelines and expectations. LPLV preparation instructions were provided to both CRA and site staff to mitigate late scheduling of the final participant visit **Mapped and tracked participant final visits in advance:** The team planned ahead for every participant's Day 365 visit. Critical path sites were proactively identified and alerted to support on-time completion of the final participant visit. CRAs and sites received targeted preparation, while clinical trial leads (CTLs) followed up ahead of scheduled visits and provided near real-time visit confirmation. Electronic data capture (EDC) entry enabled the team to identify risks before they affected the milestone

Reviewing the results of the collaborative efforts

With Fortrea's support, the program demonstrated sustained performance under exceptional operational volume and complexity.

Met global site activation and recruitment goals

- Reached 50% and 85% site-activation one to two weeks ahead of schedule
- Averaged recruitment of 1.0 patient/site/month, exceeding the projected 0.6
- Achieved >96% compliance for required IMP infusions

Demonstrated robust participant retention and recovery

- Achieved 99.5% participant retention at database lock
- Recovered 66% of 264 withdrawal of consent (WDC) participants to provide MACE and/or survival status, including eight participants recovered more than 1,000 days after randomization
- Recovered approximately 99% of the 212 potential lost to follow-up (LTFU) participants, leaving only two confirmed LTFU cases
- Delivered LPLV on time across all 18,000+ randomized participants



Enhanced data management

- Achieved and sustained 90%+ success rates through database lock, improving from much lower success range in early cycles

Maintained high-volume endpoint adjudication

- Maintained 95%+ adjudication threshold for 32 consecutive months
- Improved case-closure cycle time from 80 days to 30 days
- Completed endpoint adjudication three weeks ahead of database lock
- Exceeded case-closure targets at every interim analysis: 82% actual vs. 80% target at IA1, 99% vs. 85% at IA2, 99% vs. 95% at IA3 and 100% at database lock

Reflecting on lessons learned

The trial demonstrated that megatrial operations must be intentionally designed into the operating model, rather than developed in response to problems. Key lessons learned included:

- **Early intervention and broad retention strategies improve recovery:** Fortrea found success with early education, risk surveillance and intervention, which proved critical to preventing WDC and LTFU. A broad toolkit of retention strategies, combined with decisive investigator and sponsor engagement, also improved recovery
- **Proactive data management reduces risk:** To manage data and endpoints, the team found that rolling data-cleaning milestones, interim freezes and routine reviews created compounding efficiency rather than concentrating risk at database lock
- **Proactive collaboration helps protect timelines:** Transparent, early communication to sites on planned milestones, paired with simple instructions and clear expectations, enabled on-time delivery of the database lock and other interim data-cleaning milestones and significantly contributed to meeting study goals and study-team cohesion

Overall, Fortrea demonstrated its ability to deliver operational excellence in a global cardiovascular trial, from site activation through endpoint protection, under sustained volume pressure. As a result of the coordinated strategies, the team achieved a low LTFU rate, accelerated data readiness, maintained a high adjudication event rate, delivered on-time LPLV across 18,000+ patients in more than 40 countries and was database lock ready three weeks ahead of schedule.



Want to learn more?

Get more information about Fortrea's cardiovascular experience and how it can help protect your trial's timelines and endpoints at fortrea.com

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