

Overcoming Challenges in GVHD Trials

Supporting a Complex FMT Trial for Steroid-Refractory GI-aGVHD Across Europe



Situation

A European sponsor partnered with Caidya to support a global, **multi-center Phase IIa** clinical study evaluating the safety and efficacy of **fecal microbiota transfer** (FMT) in patients with steroid-refractory gastrointestinal acute **Graft-versus-Host Disease** (GI-aGVHD) following allogeneic stem cell transplantation.

The trial aimed to enroll 32 patients across 28 sites in five European countries, with key milestones including first patient in (FPI) in May 2018 and projected last patient out (LPO) in February 2020. Caidya provided a **comprehensive suite of services** including clinical project management, feasibility assessments, regulatory affairs, study start-up and site management, clinical monitoring, data management, biostatistics, vendor management, and medical affairs.



Challenge

The study posed multiple challenges related to **disease rarity, protocol complexity, and regulatory requirements**:

- **Low Enrollment Potential:** GI-aGVHD is a rare condition with unpredictable incidence; pre-screening was not feasible due to narrow eligibility criteria.
- **Stringent Inclusion Criteria:** Complex protocol design increased the risk of incorrect patient selection and dosing.
- **Antibiotics Discontinuation Window:** A mandatory 12-hour washout period for antibiotics prior to FMT heightened infection risk.
- **Regulatory Delays:** The German regulatory authority (BfArM) rejected the study twice due to concerns over the novel drug's manufacturing process and mechanism of action, delaying site activation in Germany.



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Solution

Caidya implemented a series of proactive, risk-mitigating measures to ensure study continuity and compliance:

•**Robust Recruitment Strategy:** A detailed recruitment plan was developed and executed early. Clinical Research Associates (CRAs) maintained bi-weekly contact with sites to assess recruitment barriers and escalate potential patient cases for review. Feasibility was expanded to include new sites in the UK and Italy to increase enrollment potential.

•**Eligibility Review Process:** A formal eligibility approval system was introduced before dosing, involving coordinated review between CRAs, the medical monitor, the sponsor's Chief Medical Officer, and the coordinating investigator. Retraining was conducted to reduce protocol deviations and enhance site understanding.

•**Medical Oversight & Infection Mitigation:** Site staff received enhanced training on infection risk and monitoring procedures. Caidya supported the implementation of strict infection control protocols at each site.

•**Regulatory Navigation:** Caidya's regulatory team worked closely with the sponsor to align submissions with agency expectations. A strategic recommendation was made to organize **face-to-face meetings with BfArM**, which ultimately facilitated approval in Germany after additional documentation was submitted.

32

Patients | 28 Sites | 5 Countries

Successfully managed a complex, multi-center study across Europe for a rare GI-aGVHD indication with novel treatment modality.

Callout

Caidya's full-service, cross-functional approach ensured the successful delivery of a highly complex, high-risk clinical trial involving a novel therapeutic approach in a rare and severe patient population.



Outcome

Caidya's operational and strategic oversight yielded significant study milestones and improved data integrity:

•**Enrollment Success:** Despite the initial delays, the planned recruitment rate of 2–3 patients per month was achieved. The impact of delays in Germany was mitigated through rapid activation of additional sites in the UK and other participating countries.

•**Protocol Compliance:** Following retraining and the introduction of an eligibility review process, only one patient was incorrectly included. No additional errors occurred after February 2019.

•**Patient Safety Maintained:** No infections were reported across enrolled patients. Data Safety Monitoring Board (DSMB) reviews confirmed no safety concerns.

•**Regulatory Approval in Germany:** A sponsor-led face-to-face meeting with BfArM, supported by Caidya's regulatory team, resulted in the study's eventual approval in Germany. No further issues were raised by competent authorities in the remaining four countries.



Regulatory Turnaround in Germany



High Protocol Compliance & Patient Safety



Enrollment Goals Met