CASE STUDY

Maximizing data from a limited patient population through an adapted FIH SAD/MAD design

A KEY QUESTION

How can targeted recruitment and adapted protocols improve efficiency to reduce recruitment time and maximize data in a First-In-Human Cold Agglutinin Disease trial?

KEYWORDS: First-In-Human (FIH), Cold Agglutinin Disease (CAD), Rare Disease, Healthy Volunteers, Single Ascending Dose, Multiple Ascending Dose, Adaptive Protocol Design

Introduction

Fortrea was initially tasked with adding a single cohort of CAD patients to an already approved Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) study in healthy participants, based on promising PD data. The study was designed to assess safety, tolerability, PK and PD.

Following recruitment of the first three patients in the CAD cohort, the scope was expanded to include a second CAD patient cohort with a longer dosing period. This required a number of protocol adjustments, alongside stringent blood sample handling to prevent hemolysis and preserve data integrity.

Challenges

- Executing a study with two different patient cohorts presented several challenges, the most critical being the need to adapt the protocol. This was to enable patients with CAD to be added after initial healthy participant dosing, for viable CAD data collection
- CAD is a rare disease, resulting in a highly limited patient population available for recruitment
- Blood samples required processing and analysis at body temperature (37°C), to prevent damage to samples, necessitating specialized equipment and controlled handling

Fortrea

Actions and solutions

We leveraged Fortrea therapeutic physicians to identify a CAD KOL who worked with the study sponsor to support protocol design decisions.

To facilitate patient recruitment, Patient Identification Centers were identified and established to support referral of patients with CAD to the Fortrea clinical research unit (CRU). We also liaised with the CAD foundation and conducted a webinar to increase awareness of the study.

Ensuring blood sample viability was paramount. Partnerships with specialized laboratory vendors capable of processing and analyzing blood samples at 37°C were established. Portable incubators were used to ensure blood samples remained at the correct temperature during transport.

Protocol design adaptations to add patient cohorts and optimize dosing schedules

The study began with intravenous cohorts of healthy participants, which rapidly progressed from April 2022 through August 2022. An initial subcutaneous cohort of heathy participants followed in November 2022. This enabled protocol amendments and dose schedule optimization, leading to the inclusion of CAD patient cohorts in April 2024.

Dosing expanded gradually from SAD to MAD to include additional CAD cohorts.

The study amendments and dose optimization over time meant that the final protocol included a larger CAD patient population with an extended dosing period (five doses over four weeks).

Outcomes

As a result of the initial study, the cohorts of healthy participants were dosed successfully, generating positive data that supported protocol expansion to CAD patients. The strong collaboration forged by Fortrea with a key clinical investigator facilitated efficient protocol changes and patient enrollment. As a result of meticulous planning and coordination, blood samples were successfully handled and analyzed at controlled temperatures, preserving data quality.

Data from the initial CAD cohort enabled further protocol amendments, allowing enrollment of more CAD patients and longer dosing schedules.

Conclusion

This study demonstrates how KOL-informed protocol adaptations, coordinated recruitment strategies and operational due diligence can support complex FIH, even when patient populations are limited in rare diseases and technical requirements are stringent.

Partner with Fortrea to leverage efficiencies from rare patient populations.

LEARN MORE at fortrea.com

Fortrea