Case Study:

STRATEGIES TO MITIGATE RISK AND REDUCE ENROLLMENT PERIOD BY 6 MONTHS IN PHASE III STUDY FOR OSTEOARTHRITIS OF THE KNEE

A PHASE III DOUBLE-BLIND STUDY INVESTIGATING A NEW THERAPEUTIC AGENT ADMINISTERED BY ULTRASOUND-GUIDED, INTRA-ARTICULAR (IA) INJECTION IN THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE.

531	36	1
PATIENTS	SITES	COUNTRY *US Only*

CHALLENGES

- Investigational Product (IP) with strict shipping, storage, and handling requirements creating significant blinding challenges.
  - Different shipping conditions were required for IP vs placebo (normal saline), with the potential for site staff to be unblinded at the time of receipt of shipments.
  - Complex preparation requirements meant IP took significantly longer to prepare than placebo creating a potential for staff unblinding.
  - Once prepared, IP could not be easily blinded, requiring the availability of an unblinded injection team.
  - IP required storage in liquid nitrogen, which created a limited window of useability, as IP was required to be used within 10 days of receipt at the site.
- Screen Failure (SF) rates in Osteoarthritis of the knee trials can be very high, increasing the cost of the trial, and creating a significant burden on site staff due to the additional effort required to manage a complex screening process in a high number of patients.

RESULTS

Steps taken with IP transport and receipt reduced the risk for potential unblinding events and appropriate on-site IP handling and management. **Over 98% of patients were dosed without any incidents related to the study blind.**

When compared to a sister study conducted with the same IP in the same target patient population, Medpace achieved a **decrease in the overall enrollment period of 6 months,** saving the client significant time and money in conducting the study.

THE SOLUTIONS

A multipronged approach was implemented to protect the study blind.

- A site-specific blinding plan was developed, outlining each site's process for maintaining the blind and to provide clear communication and escalation pathways for site staff.
- To address potential for unblinding at time of IP receipt, shipments were packaged identically during transport and designated unblinded site personnel received shipments upon arrival.
- As IP took significantly longer to prepare than placebo, pharmacy staff were required to allocate equal time for preparation of both active treatment and placebo to avoid accidental unblinding.
- Syringe covers were provided to the pharmacy to be applied after IP preparation to avoid unblinding of patients during administration.
- IP was administered by a specially trained IP injection team in a pre-specified location, which was off limits to blinded staff during IP administration.
- IP was shipped "just-in-time" for patient dosing to provide the maximum window for dosing using a main courier and a back-up courier to support timely deliveries.
- Medpace assigned an unblinded team including a Clinical Trial Manager, Project Coordinator, Lead CRA, and CRAs to support unblinded site staff with any issues over the life of the study.

A thorough risk assessment related to screening procedures was completed, and multiple mitigation strategies were put in place to allow for a more efficient screening process.

- To decrease the likelihood of SF due to imaging criteria, in patients with bilateral OA knee pain, x-rays were completed for both knees and a flow chart created to guide sites on selection of the first-choice index knee to be treated during the trial to allow for same day MRI imaging.
- The protocol required washout of medications for treatment of pain and inflammation, with some medications requiring longer washout durations than length of screening period outlined in protocol. The protocol was amended to allow an extension to the screening period in cases where long-acting medications needed to be discontinued. Additionally, Medpace Medical Monitors worked closely with investigators to guide proper management of medication washout.
- To decrease burden on patients, and mitigate the impact of a longer screening period, sites were encouraged to collect safety labs the same day as initial screening, and to schedule X-rays and MRI scans to occur on the same day, decreasing the number of clinic visits required of patients during screening and decreasing the overall screening period.
- To avoid site staff becoming overwhelmed with managing too many patients at once, Medpace CTMs and CRAs worked closely with Site Staff to determine how many patients could be accommodated at a time, while ensuring all required assessments were completed, and patients were moving efficiently through screening process. Additionally, site staff were encouraged to pre-schedule additional screening assessments and develop an organized process to keep track of appointments, and results from screening labs and imaging to ensure all assessments were completed within screening window or to confirm an extension window with the Medpace team.

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Medpace's expertise and proven track record of success offer the flexibility to meet the unique needs of rheumatology research. Our in-house board-certified rheumatologists have a thorough understanding of the complex conditions that cause these diseases, as well as the medical complications faced by patients. Experts collaborate across therapeutic areas to create effective and efficient study designs for Sponsors of all sizes, ensuring the successful execution of your trial.