Case Study:

STRATEGIES TO OPTIMIZE PHASE I OPEN-LABEL STUDY FOR CAR-TREG CELL THERAPY IN RHEUMATOID ARTHRITIS

A Phase I, open-label study evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and activity of a single-dose autologous CAR-Treg cell product in adult patients with rheumatoid arthritis (RA) who experience inadequate long-term disease management with other available treatments.

Population: Adults (18-70 yrs.) diagnosed with moderate-to-severe RA who have previously failed at least 3 prior biologic or targeted synthetic disease modifying anti-rheumatic drug therapies with different mechanisms of action.

18	10	1
PATIENTS	SITES	COUNTRY (US)

CHALLENGES

- CAR-Treg cell therapies are becoming a more common treatment in oncology and hematology fields but are considered novel to other therapeutic areas, such as inflammatory and auto-immune diseases, making this treatment a pioneering, first-in-human therapy. The mechanism of the therapy itself (CAR-Treg) is unfamiliar to many rheumatologists, thus requiring the recruitment of an additional co-investigator on the study with experience in CAR-Treg cell therapies.
- The regulatory requirements for a cell therapy study are more stringent and require International Biosafety Committee (IBC) review in additional to approval by an Institutional Review Board. IBC requirements pose risks of start-up timeline delays as the IBC is not a regulatory body familiar to most rheumatologists, meaning site staff with prior submission experience may not be readily available to support IBC submissions.
- There was significant potential for delays in patient recruitment due to the treatment being higher-risk than other available treatments for RA, which has a plethora of lower-risk treatment options.
- Due to the first-in-human nature of this trial, the FDA set a requirement that safety data from day 1 to day 28 for each patient be fully reviewed by an independent Safety Monitoring Committee (SMC), prior to initiation of dosing of the next patient.

THE SOLUTIONS

- A cross-functional Medpace team with backgrounds in both rheumatology, oncology/hematology, and cell therapies was created to ensure there would be an experienced Medpace team member available for all possible post-dose outcomes.
- Sites with both strong rheumatology, and oncology/hematology cell therapy programs were targeted during the feasibility process. All sites were required to identify both an oncology/hematology investigator experienced with cell therapies, and a rheumatology investigator willing to work together as co-investigators to be considered for site selection.
- Biweekly calls focused on regulatory submissions were scheduled with all sites to ensure all necessary safety review committee and IRB submissions were on-track with the site's proposed timelines. A subject matter expert (SME) for the IBC was assigned to the study to facilitate the creation of submission documents designed to proactively address potential IBC queries and reduce IBC approval timelines.
- A large focus was placed on patient education and information, especially regarding CAR-Treg cell therapies and other cell therapy specific procedures (e.g. apheresis), while designing patient and site materials.
    - A patient educational video was created to clearly emphasize what it means to participate in a first-in-human clinical trial, further elaborate the study procedures patients would be partaking in, and explain the process of CAR-Treg cell therapy in patients with RA. This video included more granular details on the role T cells play in autoimmune diseases, the process of harvesting T cells via the apheresis procedure, how the T cells are genetically modified into CAR-Treg cells during the IP manufacturing process, and the impact this medication may have on the patient's health.
    - A study website was developed with further information for potential patients interested in this treatment that included patient FAQs, treatment procedures, and trial clinic locations interested individuals could contact for participation or further information.
- Granular timelines were created for each patient, related to IP manufacture, dosing, and follow-up with close communication and follow-up between Medpace, the Sponsor, and study sites to ensure all SMC meeting deliverables (e.g., patient profiles, clinically significant vital signs and lab findings, etc.) were available for review promptly after each patient reached Day 28 to ensure timely and efficient review by the SMC with approval to dose the next patient without significant delay.

RESULTS

The selection of sites with experienced cell therapy teams required minimal on-site training pre-infusion and resulted in no infusion-related reactions in any dosed patients.

There were no observable delays with respect to IBC submissions and approvals.

Patient Recruitment initiatives ensured a qualified patient was ready to begin dosing at the earliest possible date to both comply with FDA requirements and allow for efficient enrollment of subsequent patients.

All SMC meetings were held successfully within two weeks of each patient's D-28 visit and resulted in positive outcomes with no delays to study timelines.

FULL-SERVICE CLINICAL DEVELOPMENT

Medpace is a scientifically-driven, global, full-service clinical contract research organization (CRO) providing Phase I-IV clinical development services to the biotechnology, pharmaceutical and medical device industries. Medpace's mission is to accelerate the global development of safe and effective medical therapeutics through its high-science and disciplined operating approach that leverages local regulatory and deep therapeutic expertise across all major areas including oncology, cardiology, metabolic disease, endocrinology, central nervous system and anti-viral and anti-infective.