WHY SYNTERACTHCR?

A full-service CRO, SynteractHCR has a proven track record of success in all phases of clinical development.

Shared Work – Shared Vision: This is a promised standard, the way we do business. It conveys our collaborative, customized approach to conducting trials tailored to your needs, which meet or exceed your expectations.

Case Study: DNA Therapy RAC Submission and IND Application

Introduction

In January 2013, SynteractHCR began working with Tacere Therapeutics (A Benitec Biopharma company) to prepare for an NIH Recombinant DNA Advisory Committee (RAC) meeting prior to submitting an Investigational New Drug (IND) application to the FDA for its TT-034 Hepatitis C therapy.

TT-034 is a transformative therapeutic intended to provide a "one dose cure" with a single injection. In preclinical studies it has shown that it specifically targets and transfects liver cells without causing toxic effects. However, because DNA therapies are relatively new and complex, the FDA seeks additional guidance with regard to human safety, which is the purpose of the RAC. The RAC committee consists of multiple independent reviewers, all of whom are experts in their respective fields and all of whom can ask questions during the presentation.

Preparing for a RAC presentation requires an intense focus to develop all the deliverables required in a very condensed time period; in this case, the primary project had to be accomplished in just 3 months. Benitec asked SynteractHCR for help in managing the RAC process, planning the protocol, preparing the RAC briefing documents and presentation, and prepping the principal investigator, Keyur Patel, M.D. from Duke University Medical Center, who gave the actual presentation. Our role required working very closely with the sponsor and investigator, and included anticipating any questions or concerns that might be asked by the RAC members.

Challenges

A RAC review is not typical for most INDs, but in the case of extremely complex therapies, such as biologics, the FDA can ask the sponsor to submit to the RAC for review. This requires a team at the CRO that is familiar with the RAC process and conditions, that understands biologics and has the ability to review and distill down vast amounts of information to its most important components. Clear and open communications are critical to the success of working with both the sponsor and the principal investigator. Multiple departments at SynteractHCR were involved in the planning process: medical writing; clinical development, regulatory, project management and biostats included. Our project manager kept all groups updated and engaged as the planning and document development progressed.

The RAC requires the protocol, informed consent form, response to Appendix M questions, and other documentation to be submitted to the committee prior to being invited to a review. This gives them time to review the data and details in order to develop questions and comments. That necessitated our team to develop all potential questions that could be asked, based on the briefing package, so as to help the PI be prepared to answer whatever would be asked.

The protocol was quite complex because this was a first-in-man dose-escalation study in chronically ill Hepatitis C patients. In addition, the plan is to follow the patients for 4.5 years following dosage, using a total of 14 patients (5 cohorts: 2 subjects in the first cohort and 3 subjects in each of the other 4 dose cohorts).

Timing was also of the essence. While the team began protocol development in January 2013, the RAC submission needed to occur in early April in order to meet the RAC meeting planned for June. Once presented, the final responses to the RAC member questions had to be re-

Case Study: Tacere Therapeutics

sponded to within approximately 14 days. And last but not least, budget was tight, so there was no room for error.

Our Solutions

Due to the dedication and expertise of the sponsor and our team, all deadlines were met. The SynteractHCR cross-functional team proved its ability to coordinate and manage the components in rapid order.

In addition to developing the protocol of 98 pages, the team also put together the following:

- Investigator brochure – info on the conduct of the study and background of the project (66 pages)
- Informed consent form for patients (20 pages)
- Appendix M responses
- FAQ, including anticipated medical/regulatory questions and responses

The team prepared the full package and shipped it to the National Institutes of Health (NIH) RAC committee. After the initial materials were submitted, the committee had 15 working days to review them. At the end of the 15 days Dr. Patel was notified about the initial review results and was invited to attend the June RAC meeting to present the protocol. During the time from invitation to the RAC and the actual meeting, the principal investigator and sponsor worked closely with the SynteractHCR team to refine the presentation and prepare for questions. We proceeded to prep Dr. Patel for the presentation, often role-playing the tough questions so that he would be prepared for anything they could ask.

The meeting, which includes a presentation for approximately 20 minutes, is public; the presentation is delivered openly over a live feed. It is followed by a comment and Q/A session. Members of both the RAC and FDA attended the meeting, held at the NIH in Washington, D.C. We attended and took notes so that we could help prepare responses that could be required after recommendations from the RAC were received.

At the end of the session, there were no significant alterations to the protocol requested and we received a unanimous "YES" vote for the human trial to be able to proceed.

Results

A happy client is its own reward! Benitec was extremely happy. We received a letter of praise and thanks from Per Lindell, SVP Corporate Development at Benitec Ltd., stating that TT-034's presentation received very positive reviews from the committee, including complimentary comments such as, "This informed consent form should be a model for all future applications."

The review was watched over the live feed by several of the sponsor's investors and, therefore, also helped Benitec in its financing efforts.

The IND was filed in Dec 2013. And SynteractHCR received the contract to conduct the phase 1 study. Human trials are expected to begin in 2014.

"I am absolutely delighted with this outcome. The meeting went as well as we could have hoped. The generally supportive comments from the reviewers are a testament to the quality of the program and the hard work that has been put in by all."

- CEO, Benitec Biopharma
Dr. Peter French

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