Worldwide Clinical Trials

Case Study

Adapting to Oncology Study Needs: Flexibility in Phase I ADC Drug Development

A sponsor approached Worldwide with a Phase I study to investigate the safety, efficacy, tolerability, pharmacokinetics (PK), and preliminary antitumor activity of an antibody-drug conjugate (ADC) in advanced/metastatic solid tumors. These novel treatments can present various challenges during development, meaning the sponsor needed a CRO partner with the expertise and flexibility to adapt during the development and delivery of their study.

Study Details

Sponsor
Small biotech start-up

Indication
Solid tumors, specifically non-small cell lung cancer

Study Type
Phase I, multi-center, open-label, multi-dose, first-in-human

Study Design
3+3 maximum tolerated dose (MTD)-escalation study with multiple ascending dose levels

Sites
15

Country
United States

Primary Objective
Safety and tolerability, MTD or recommended Phase II dose (RP2D)

Secondary Objective
Preliminary antitumor activity, PK, & immunogenicity

Study Challenges

3+3 Cohort Management

01

The study required a short timeline for First Patient In (FPI) and rapid cohort enrollment. Closing a cohort requires three patients to be screened within a tight time frame, and since these are very sick patients with a high potential for screen failures, having backup patients ready to screen is imperative. Strong relationships are additionally required with the sites to enable the interactions needed across multiple departments involved in delivering the complexities of a Phase I study. Data entry is also needed in real-time to align with the frequent protocol amendments typical in 3+3 studies and to ensure data is available for the safety review committee to enable cohort dosing decisions. It's necessary to receive weekly updates from the sites during the dose-limiting toxicity period to collect and note safety events.

Frequent Protocol Adjustments

02

As the data became available while the cohorts progressed, study protocols were frequently adjusted to optimize study design and ensure patient safety. These changes required operational flexibility and challenged sites to adhere to protocols as they changed.

Site Identification and Patient Recruitment Changes

03

Based on the evidence arising throughout the trial, the study shifted from recruiting all 'solid tumor' patients to enrolling patients with more specific tumors or with particular mutations, including HER2 + BC, castration-resistant prostate cancer, head and neck cancer, EGFR mutations, and KRAS for non-small cell lung cancer. This change also meant the study required identifying and onboarding additional or new sites capable of enrolling these new patient populations to meet enrollment goals.

Investigator Hesitance

04

More than half of the study investigators had no prior experience working with ADCs due to the novelty of the treatment. Additionally, the tumor indications had a high number of other studies running at their institutions for which the patients could be eligible, thus presenting these investigators with easier participation options for their patients. These factors led to initial hesitance in working with the compound and the need for additional implementation support.

Worldwide's Solutions

This complex oncology study required a very involved project team that could actively manage the daily operations and adapt to rapidly changing study needs to meet cohort enrollment goals. The solutions that contributed to our success included:

1 Site Selection Strategy

For 3+3 studies, access to sites capable of enrolling quickly as the study progresses into new cohorts is paramount. Additionally, with the shift in focus from all-comer solid tumors to more specific tumor types and biomarkers, the sites selected needed to have access and recruit from a wider range of cancer patients.

Utilizing our global Site Alliance Collaboration, we tapped into our existing relationship with experienced sites to ensure the study met enrollment goals. Worldwide strategically selected sites capable of managing studies with an aggressive timeline and changing protocol. Due to the existing relationships and infrastructure, onboarding timelines were kept to a minimum, allowing the subsequent cohort to begin dosing as rapidly as possible.

2 Strong Relationship Building

Worldwide's strong relationships with the sites and sponsor were a leading contribution to our success. Worldwide's study teams focused on cultivating communicative and open relationships with sites, which smoothed the acceptance of the study's frequent protocol amendments. At times, the sites were asked to meet very short deadlines. Due to the strong relationships and support provided by Worldwide, such as the contact from the CRAs, they prioritized meeting deadlines and felt comfortable requesting more time if the deadline was not achievable.

Worldwide additionally cultivated a mutually beneficial relationship with the sponsor through consistent communication, fast-paced enrollment strategies, knowledge of day-to-day operations, expedited processes, and flexibility.

> *At all times with Worldwide, we felt supported and had access to information we needed — even very specific information we are not used to receiving from a CRO. Our senior management team has high expectations for communication and issue resolution, and we could not have been more pleased with how Worldwide has handled this study. We could trust them completely.*
>
> ***Executive Director, Clinical Trials and Project Management at the Sponsor***

3 Investigator Empowerment & Engagement

To achieve enrollment targets, Worldwide met directly with investigators before the study began to understand what may hinder their enrollment and then worked with the sponsor to tailor the protocol accordingly to ensure recruitment was as successful as possible. Once enrollment began, if investigators were hesitant, the sponsor and Worldwide provided education about ADC trials and helped the investigators understand the benefits for their patients enrolling in the study.

Once onboard, the sponsor and Worldwide held monthly meetings with the investigators to discuss protocol changes and solicit their feedback before implementing any amendments. If a site was not performing as expected from feasibility, we provided support and preclinical information to boost investigator confidence in recommending the study and novel agent to their patients.

Study Outcomes

Our comprehensive solutions allowed us to optimize enrollment success, thereby reducing timelines.

Key Successes

1. We achieved FPI within **six weeks** of starting the study, meaning site identification, start-up activities, and finding a patient occurred seamlessly in half the industry's standard time.
2. Phase I cohorts (from cohort 3 and onward) achieved accelerated timelines, enrolling within **two days** due to the collaboration with sites.
3. Our strategic selection and proactive communication with sites resulted in **expedited site activation**. Successes included:
   - First site activated in three weeks.
   - All 17 sites activated ahead of schedule or on target.
   - Minimum site declines during initial outreach.
   - Sponsor released an additional 15 cohort slots that were rapidly enrolled.
4. Our adaptive protocol permitted the study to pivot intentionally as more data became available. The modified protocol allowed us to study the novel ADC in specific tumor indications.
5. Our investigators were empowered and more educated about ADC clinical trials.
   - Increased comfort and involvement of investigators with each protocol amendment
   - Greater communication between sponsors and investigators
   - More confidence in recommending the study as a treatment option for their patients

Worldwide, as a global CRO, is perfect for a company like us — a small, fast-paced, innovative company. Worldwide has strong SOP processes and their team is tailored to work with a small start-up. They're flexible and able to move quickly to help their customers. Even if their customers may not have adequate funding, Worldwide finds a way to support their clients and make the studies work.

Executive Director, Clinical Trials and Project Management at the Sponsor

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Work with Worldwide Clinical Trials for Your Next ADC Study

As ADC clinical trials continue to gain momentum, make sure to partner with a CRO experienced at managing the complexities of these trials and one that's flexible enough to adapt to frequent changes in protocol. The insights gained from this study will help inform future ADC trials and our approach to targeted immune-oncology drugs. Contact us today to learn more about our full-service oncology capabilities.

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