PRA Health Sciences

CASE STUDY

Successful Adaptation to the Evolution of Complex Dose Escalation Within a Large Master Protocol Basket Design Across IO Co-Therapies

Efficient management of frequent data analyses and timely quality driven monitoring in support of Recommended Part 2 Dose (RP2D).

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ABSTRACT

The sponsor presented PRA with frequent shifts in strategy for the Part 1 escalation cohorts, including changes in prioritization for the [at times] competing Part 1 cohorts (e.g., monotherapy, combination therapy, triple combo therapy, special interest patients, etc.). Despite these challenges, the PRA team stayed flexible with site and amendment coordination, collaborated to optimize strategies, exemplified strong cross-functional leadership to maintain overall high-quality monitoring, and successfully met all data deliverables. Throughout the timeline changes, PRA PMs modeled enrollment scenarios to assist the sponsor in their drug development planning.

STUDY DESCRIPTION

A Phase I dose escalation and cohort expansion study of an immune checkpoint inhibitor, in patients with advanced solid tumors.

Endpoints of Interest
Anti-tumor activity as monotherapy and/or combination therapy according to RECIST v1.1 and irRECIST.

Indication
Melanoma, Colorectal, and Non-Small Cell Lung Cancer (NSCLC)

Study Phase
Phase I

Business Segment
Product Registration Services

Drug Class
Immune checkpoint inhibitor (monoclonal antibody)

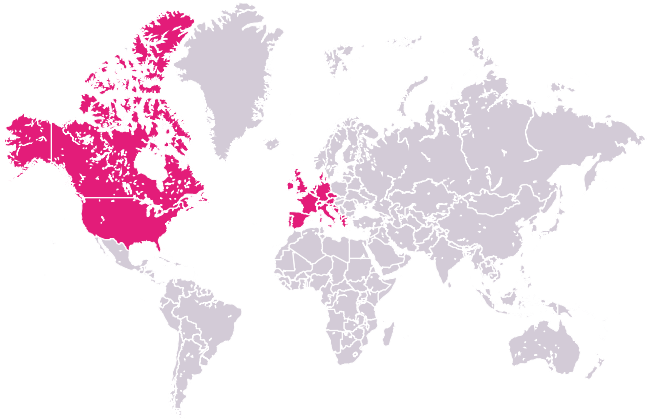
PRA Services
Project Management
Clinical Operations/Monitoring
Site Recruitment and Management
Regulatory (outside of US)
Drug Safety (Submission of SUSARs to sites and IRB)
DMC Services

Study Duration
Approximately 6 years

No. of Clinical Sites
69 sites in total across Parts 1 (escalation) and 2 (expansion), taking place in 2 regions (United States and Europe)

Patient Population
400 patients in Parts 1 and 2 combined, across Melanoma, Non-Small Cell Lung Cancer (NSCLC), and Colorectal Cancer; all-comers enrolled in early dose escalation cohorts

Regions
North America
Europe



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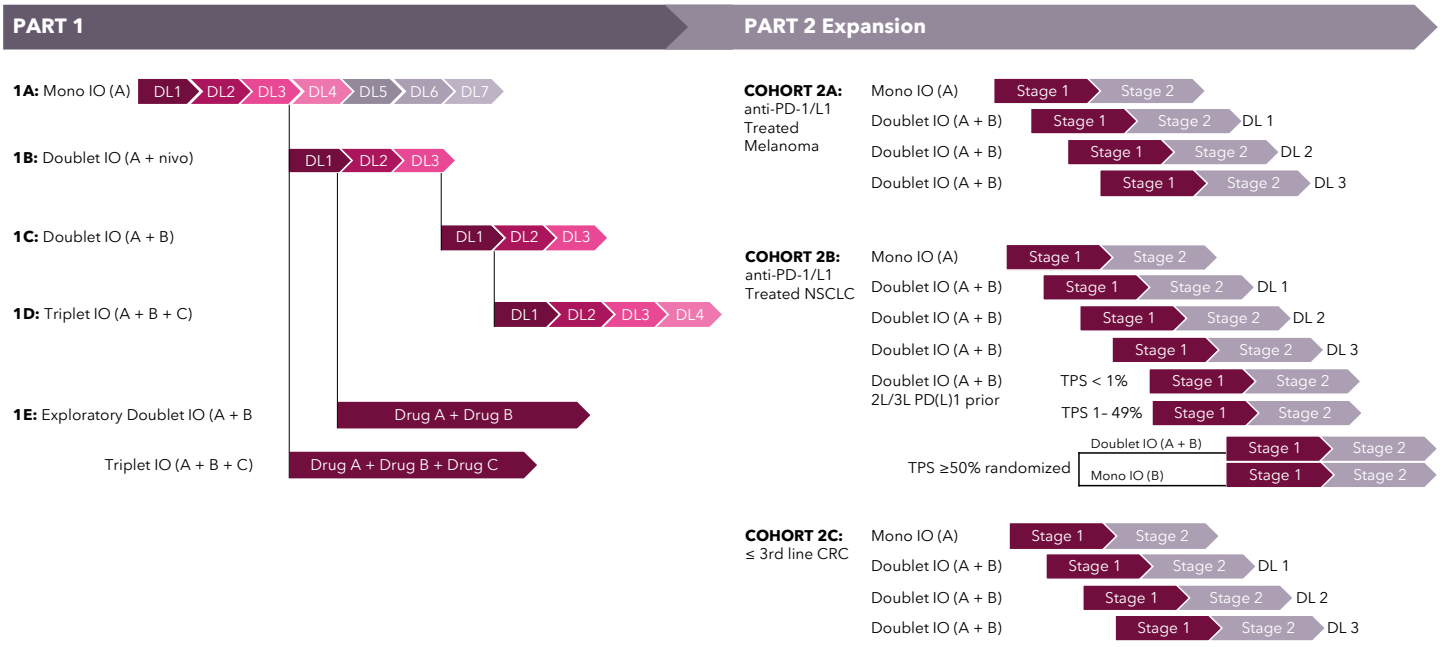
Situation

PRA was initially awarded the work in 2015 from the sponsor, a mid-size biotech company. Mid-study, the sponsor was acquired by a large pharma company to which PRA has efficiently supported the transition to the evolving sponsor business model and operations.

Challenges

The primary study challenges related to frequent changes to patient population, enrollment timelines (including protocol amendments), cohort prioritization, timing for Part 2 expansion (impacting Part 2 start-up), and short notice on data cleaning deliverables to meet evolving development objectives.



Solutions

The PRA team worked with the sponsor to ensure 30-day notice on all data cleaning deliverables to adequately prepare and plan with sites. Changes in study population (e.g., anti-PD1/L1 vs IO-naïve) for new cohorts were addressed by conducting thorough feasibility with active sites, consulting with PRA scientific leadership on therapeutic landscape assessment, and modeling enrollment rate scenarios for new populations by region. PRA recommended additional sites when needed and adjusted site start-up and enrollment timelines based on aforementioned evaluations.

Through heightened site communication and an IRT system, PRA effectively and successfully managed the slot assignments across this highly complex cohort design. Enrollment for the overlapping Part 2 expansion cohorts was achieved ahead of the agreed timelines. The team also rigorously orchestrated data entry and cleaning efforts across the Part 1 and Part 2 cohorts to achieve cleaning deliverables for IB updates, cohort review meetings, and DMC meetings. These were achieved with high quality and within the required timelines.

Results

As a result of the solutions noted above as implemented by PRA, enrollment for the various cohorts (and Part 2 expansion) has been met in advance or within all agreed timelines. Data cleaning activities and deliverables have been met with great collaboration, transparency, and most importantly with utmost quality within the agreed timelines. As a result, the client has been able to identify the optimal dose level and indication for continued testing of their investigational product.

"Thanks for making our project a success!"

Sponsor Director, Clinical Operations

"I deeply value your collaborative, flexible, and proactive approach to execute high quality projects with efficiencies. We've certainly shared and overcome challenges together, but we've celebrated even more successes, thanks to your strong leadership and support."

Sponsor Clinical Development Director, Oncology