PRA Health Sciences

CASE STUDY

Early Phase Innovative Pediatric Oncology Program Achieves Successful First Multiple Solid Tumors Study

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STUDY DESCRIPTION

An early-phase, multicenter, open-label basket study of the study drug's safety and pharmacokinetics in pediatric and young adult patients with previously treated solid tumors.

Primary Endpoint:

Primary Efficacy Endpoint

- Objective Response Rate
- Progression-Free Survival

Safety Objective

To evaluate the safety and tolerability of the study drug in pediatric and young adult patients–focusing on the nature, frequency, and severity of serious and non-serious adverse events, as well as effects on laboratory values and vital signs.

Pharmacokinetic Objective

To characterize the pharmacokinetics of the study drug.

Immunogenicity Objective

To evaluate the immune response to the study drug on the basis of the incidence of anti-therapeutic antibodies (ATAs).

Client Type:

Top 15 Pharmaceutical/Big Biotech

Drug Class:

Monoclonal antibody of IgG1 isotypeagainst the protein programmed cell death-ligand 1 (PD-L1)

Study Phase:

Phase I/II

Business Segment:

Product Registration Services

Therapeutic Area:

Pediatric Oncology Solid Tumors

Indication

Previously treated solid tumors/ children and young adults

Study Duration

5 years, 6 months (2014-2020)

No. of Clinical Sites

2 consortia:
POETIC, NA and ITCC, EU

35 Phase I (activated)

21 Phase II (not activated)

Patient Population

115 patients screened

90 enrolled

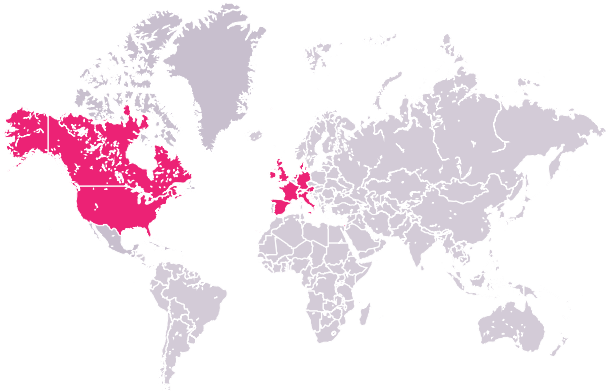
87 treated

Regions

North America :
USA, Canada

Western Europe:
Austria, Denmark, France, Germany, Ireland, Italy, Netherlands, Spain, Switzerland, UK

Middle East:
Israel



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Situation

PRA partnered with the sponsor's new pediatric oncology department on an innovative pediatric oncology program. The program provided early evaluation of oncology treatments on children with relapsed or refractory solid tumors, fulfilling an unmet need in the industry.

The enrollment in several solid tumor cohorts on the first study of the program was very successful, with a higher rate than initially anticipated. The sponsor's enrollment intermediate goal (SMT goal) was achieved three months in advance for the first 60 patients. The cause of this high enrollment was due to a few factors:

- Involvement of parallel tumor cohorts in the study design
- Immense need and high expectations for the study drug
- Engaged PIs in high profile pediatric institutions with the right patient population

All intermediate data analysis was completed on-time or ahead of schedule. The study team successfully mitigated the quality risks related to very high enrollment.

All interim analyses were completed successfully and on-time, as well as the primary analysis, with a primary clinical study report published in Aug 2018. All of the pediatric investigational plan (PIP) regulatory requirements were fulfilled and the sponsor early-terminated the study in 2019.

Challenges

In EAPA, 46 Innovative Therapies for Children with Cancer (ITCC) sites were selected, with a split of phase I and phase II sites. The phase II sites remained on standby, planning to come onboard if the study was expanded.

The study had high enrollment from the beginning, while all cohorts were enrolling in parallel (up to 10 times the expected enrollment rate in Q1 and Q2 2016). It became clear that the phase II sites would not be needed.

Solutions

Sites were regularly informed of the study progress on an ongoing basis, and they were notified immediately when it was decided the phase II sites would not be activated. These sites were reimbursed for their start-up effort. Patients from the phase II sites could be referred to activated sites.

The PRA team adapted quickly, exhibiting flexible management of resources. They provided a several-day visit plan and a team of CRAs on-site to maintain the study's quality and ensure the source data verification (SDV) backlog was contained. All data cleaning milestones for interim analysis were achieved on-time per data quality review plan. For example: first, second and third PK analysis, independent data monitoring committee (IDMC) meetings.

The PRA team successfully controlled enrollment in the cohorts and management of the site communications for slot assignments. The sites felt supported by the team—all of their questions were answered within 24 hours, and each subject's eligibility was reviewed within 24 hours. The study was an overall excellent collaboration between PRA's clinical team and the sponsor's pediatric oncology drug development team.

Results

Although response to the study drug was restricted,

- the study results collected on several solid tumor types enabled the sponsor to rapidly fulfill all of the pediatric regulatory requirements for the study drug
- the study findings have the potential to help define future development strategies for immune checkpoint inhibitors.

Operations

This study kicked off a successful working partnership between PRA and the sponsor's pediatric oncology drug development team. PRA was awarded the new studies of the program in a non-competitive way. The success and lessons learned from this first study can be referenced when other studies are performed, whether in this program, global pediatric oncology studies, basket trials, or trials working with pediatric consortia.