IDDI'S ORGANIZATION AND TOOLS OVERCOME TRIAL DESIGN CHALLENGES IN A PHASE I/II MYELODYSPLASTIC SYNDROME STUDY

IDDI CASE STUDY

STUDY DESCRIPTION

A phase I/II open-label, multi-center, dose-finding, safety, efficacy study on patients with higher risk myleodisplastic syndrome (MDS) and untreated acute myeloid leukemia (AML) who are ineligible for induction chemotherapy.

The Phase I part of the study consists of a dose exploration administered in 18 patients at a starting dose once every 2 weeks in a 28-day cycle. The dose is escalated and evaluated for the occurrence of dose limiting toxicities using a standard 3+3 dose escalation design. This dose exploration phase of the study established the safety and tolerability and the recommended Phase II dose and schedule in adult patients with higher risk MDS.

The Phase II part enrolls 175 patients and employs an open-label 2:1 randomized design to evaluate the effect of treatment at the recommended Phase II dose determined in Phase I.

INDICATION	PATIENT POPULATION	STUDY DURATION	REGIONS
Myeloid malignancies	193 patients Both phases: Adult patients with a documented diagnosis of relapsed/refractory MDS or higher risk MDS previously untreated. Phase II only: Bone marrow with myeloblasts constraints.	32 months	6 US centers

SITUATION

IDDI as the Biometry Partner to Ensure Data Quality

- IDDI had been selected earlier for the review of previously collected outputs and for the Biostatistics support of the Sponsor's program including the generation of trial statistical designs, protocols and statistical analysis plan development. In this particularly important phase, the Sponsor benefited from IDDI's consultants rich experience in oncology, trial design and relationship with regulatory authorities including pre-IND meeting package submission.
- The Sponsor selected IDDI as the full biometric partner including eClinical tools (EDC & RTSM), data collection, data cleaning and data analysis. It was important to have these tasks executed by one vendor to ensure data quality and coherence with trial design.
- Sponsor selected another vendor for Clinical and Medical monitoring, ensuring a clear separation of tasks.

IDDI TASKS

MULTIPLE CHALLENGES

Fast access to all collected data including eCRF, lab data, RTSM, external systems, etc.

Complex protocol design and specific data collection requirements combined to ease site burden

- Implementation of the dose escalation algorithm in the eCRF was particularly important to the Sponsor as it would determine the recommended Phase II dose
- eCRF ease of use for tumor and radiological assessments – importance of consistent lesions identification throughout the study
- Drug supply management system (RTSM) to be correlated with eCRF
- Payment sheets linked to schedule visits

Covid-19 Implementaton

- COVID-19 could create missed visits, missed data – Sponsor wanted a mechanism to ensure study goals would still be met
- Importance of risk-based monitoring – Need to apply a monitoring plan directly in the EDC to direct CRAs in Source Data Verifying the required fields

SOLUTIONS (1)

IDDI
PASSION. SCIENCE. EXPERIENCE.

IDDI offered to deploy its fully integrated eClinical suite consisting of ID-base (EDC) and ID-net (RTSM)

Webservices allow IDDI's EDC system to communicate with other systems whether internal to IDDI (such as RTSM) or external systems.

Adhoc reporting allows users to build their own reports based on their own needs content wise and timewise.

Use of calculation functionalities to copy the target and nontarget lesions documented at screening into the post treatment visits, ensuring consistency in lesion identification across the entire study, reducing data entry by sites.

Dose escalation algorithm implemented into eCRF to allow determination of Phase II dose.

SOLUTIONS (2)

Clear separation between monitoring and biometry teams
Clinical Data Management (CDM), RTSM and Biostatistics teams coordination

CDM linked to Biostatistics Services and kept separated from monitoring, allowing two completely independent views of the data (Monitors and Biometry team); the link between CDM and Biostatistics ensured collected data met the requirements of the study objectives.

The main element is the expertise of the Clinical Data Manager. When it comes to eCRF design the combination of Lead Clinical Data Manager / EDC specialists is the key to success.

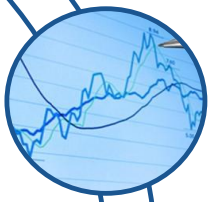
Key Data Management and Biostatistics milestones integrated in the planning: SDTM part of the CDM team allows to start programming the datasets as soon as eCRF is finalized. Biostatistics team works on ADaM datasets and clear any data issues directly with the CDM team.

Seamless protocol amendment implementations: Lead CDM, Biostatisticians and MD all reviewed protocol (schedule of assessments and data to be collected).
Once protocol was finalized and eCRF developed, the Biostatisticians review ensured collected data could be easily analyzed and all endpoints were included.

RESULTS

IDDI has successfully delivered!

FAST IMPLEMENTATION OF A COMPLEX DESIGN THANKS TO INTEGRATED TECHNOLOGY



EASY AND PRECISE DETERMINATION OF PHASE II DOSE

COORDINATED IDENTIFICATION AND RESOLUTION OF MISSING DATA DUE TO COVID-19

COHERENCE BETWEEN SDTM AND ADaM DATASETS

CONTACT US

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For more information on IDDI's Trial Design - Randomization - Clinical Data Management & Biostatistics services for Pharmaceutical and Biotech companies contact us at:

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ABOUT IDDI

COMBINING PASSION, SCIENCE AND EXPERIENCE TO ENSURE YOUR CLINICAL DATA IS READY FOR SUBMISSION

International Drug Development Institute (IDDI) is an expert organization in biostatistical and integrated eClinical services that is committed to assisting pharmaceutical, biotech, medical devices, and Cooperative Groups in several disease areas, with a special focus on oncology and ophthalmology.

IDDI optimizes the clinical development of drugs, biologicals, biomarkers and devices thanks to proven statistical expertise and operational excellence. Founded in 1991, IDDI has offices in Belgium, Boston (MA) and Raleigh (NC).