A Case Study: What MD Anderson Requires for its Complex Studies and the Boutique CRO that Provides the Perfect Model

Clinical Operations in Oncology Trials

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Challenges of Oncology Studies: Infrastructure of Academic Institutions

- Diverse group of stakeholders
  - Different goals, responsibilities, tools
  - “One-off,” narrowly-focused fashion vs. collaborative approach
- Academic center with potential for delay:
  - Funding
  - Budget approvals
  - IRB approvals
  - Clinical trial and material transfer agreements
  - Patient recruitment, complicated ICFs, sicker patients
  - Securing protected research time from medical school departments
  - Multiple review cycles
- Standards of Care - Medical vs. research vs. multinational
  - Multinational across wide geographic locations

Examples of the Impact of Challenges on Trial Design, Execution and Outcomes

- Recruitment
  - Restrictive eligibility criteria
  - Competitive enrollment
- Safety
  - Inconsistency and incompleteness of adequate reporting of adverse clinical events or laboratory toxicological findings
- Quality of data
  - Eligibility criteria influences run-in periods excluding patients prone to adverse effects
  - Greater treatment discontinuation rates in clinical practice
  - Patient selection bias, inadequate reporting of AEs and lab trends due to stake holder influence

MD Anderson Initiative: Moon Shots Program, IACS

- Moon Shots Program
  - To dramatically reduce the incidence and mortality of cancer, so that the disease in all its forms is preventable, detectable, treatable and forgettable
- Created Institute for Applied Cancer Science IACS (2011)
  - **IACS** is a biotech-like organization within MDACC with the mission to “bring novel, more effective therapeutics to patients”
- The first IACS trial is **IACS-010759**, an inhibitor of oxidative phosphorylation for the treatment of acute myeloid leukemia

MDACC Moon Shots Program. Institute for Applied Clinical Science. http://www.cancermoonshots.org/platforms/institute-for-applied-cancer-science/

Partnering Sponsor CRO Model: Large or Boutique??

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What are the General Questions?

- Who will give you undivided, high-touch attention?
- How will feedback be given on the study design to avoid later issues?
- Are they willing to deep-dive into the study design complexities?
- Are they willing and able to assign highly-qualified resources ("A-team") to provide the level of detail needed up- front?
- Will they collaborate on the key findings and messages for:
  - Safety and efficacy in the preparation of Safety Review
  - Safety Summaries / Regulatory Reports
  - Clinical Study Reports / Publications?

What are IACS Specific Questions

- Who will efficiently and effectively execute the phase 1 trial?
- Who will bring it to the next inflection point (positive or negative)?
- Who will present a suitable dataset for an external organization to evaluate if the compound is a suitable asset for future development?
- Who will provide a rapid delivery for trial status and responses for external funding?

Why a Boutique CRO is a Good Fit

- Staff with academic and industry backgrounds
- Independent organization with full CRO support services and Oncology experience
- The team will work through all phases of the trial
- Exclusive attention for consultation expertise → extension of MDACC with strategy advice / recommendations
- EDC partnership– Approved and Certified
- Customized solutions demonstrate flexibility
- Responsiveness, respect, quality and performance focus

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Challenges and Solutions: Study Start-up

MDACC Challenge	PROMETRIKA Solution
Drug supply import requirements to achieve set FPI	• Seasoned, competent and qualified Clinical Supply Expert • Select broker with history
Working with multiple stakeholders/ vendors to engage the best outcome	• *Meet* the vendor; √ chemistry • Establish a seamless working relationship • Flexible and rapid response
Limited Research Staff time, balancing care for patients, investigator responsibilities	• Streamline sponsor reviews • Prioritize “need to” vs. “nice to” • Identify back-up resources • Condense list of questions • Working meetings via webinars
Protocol approved a few days before FPI	• Maintain timeline plan • Back-up timeline plan

Challenges and Solutions: Study Execution and Conduct

MDACC Challenge	PROMETRIKA Solution
Complex protocol design • Requiring changes (e.g., ↑↓dosing, additional sites, frequency of detecting DLT, etc.) • Conflicting standards of care	• Protocol review and input pre-IRB • Unity of clinical & research practices • Data collection tool flexibility • eCRF dynamics for natural data collection flow and scientific output • Customized reporting
Frequent review of safety data	• Enable sponsor access • User friendly reports
Local lab use and timeliness for key decision making	• Workarounds with EMR • Automated data transfers
Recruitment	• Feasibility assessments/pre-qual • Community practitioner in research • Engage community

Challenges and Solutions: Management

MDACC Challenge	PROMETRIKA Solution
Staying connected with long distance relationship	• Upper management support • Creative remote meetings • Communication plan • Face-to-face interactions→visibility
Envisioning a scalable solution for one study program	• Efficient design data collection tools • Retain agility • Continual evaluation
Utilizing technology for effective management of clinical and site needs of the trial	• Affordable CTMS • Out of box vs. customization
Sponsor's focus - availability limited for ClinOps, Biostats, Data Mgt	• CRO lists deliverables • Review prior to Sponsor sign-off

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Challenges and Solutions: Quality and Safety

MDACC Challenge	PROMETRIKA Solution
Key messaging and reporting	• Audience criteria • Assemble Clinical Research with Clinical Practice
Full participation for regularly scheduled Safety Review Committee Meetings	• Include Safety Review Committee meetings in Timeline for each milestone • Schedule with SRS members in advance
Reconciling Clinical with Safety	• Develop agreements on reconciling data points
Unexpected Results of Study Outcomes	• Data Triggers – DLTs, Deviations, Discontinuations, Missed doses & Visits

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Challenges and Solutions: Budget

MDACC Challenge	PROMETRIKA Solution
Fiscal efficiency / planning to ensure drug affordability	• Collect data wisely and minimize potential for ↑data queries • Select meaningful tools • Maximize remote accessibility • Regional CRAs
Insufficient financial reimbursement for patient care	• Test the budget • Sort reimbursable from non-reimbursable
Anticipated and unanticipated delays	• Proactive, qualitative risk assessment into every stage of development • Mitigate risks (e.g., staffing, recruit-ment, drug supply delay, regulatory delays, effective communication) • Back-up plans

MDACC's CRO Selection

- The PROMETRIKA Advantage
  - Core values centered on caring and compassion
  - Focus on end goal and impact on patients with cancer
  - Seamless integration to become extension of sponsor team
  - Use seasoned staff to minimize risks of out of scope budgets and extended timeline
  - Establish a collaborative cross-functional approach for successful delivery of quality data
  - Provide a quick start for full-service

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Thank you!

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