



# Optimizing Global Early Phase Oncology Trials

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Early development strategies in oncology trials are constantly evolving in response to regulatory guidance, such as the U.S. FDA's Project Optimus initiative or its draft guidance on Multiregional Clinical Trials in Oncology.<sup>1,2</sup> These ongoing changes require a solid understanding of the requirements and potential challenges, along with a strong command of the solutions needed to mitigate risks and optimize trial outcomes. Below are suggested strategies to ensure successful operations in global early-phase oncology trials.

## Managing Dose Optimization & Complex Study Designs

The Project Optimus initiative pushes for a more comprehensive approach to dose optimization in early phase oncology trials, moving beyond exclusive reliance on maximum tolerated dose to incorporate pharmacokinetic and pharmacodynamic parameters. Expanding the methodology, while ultimately beneficial for cancer patients, introduces greater complexity to study protocols, requiring increased participant enrollment and broader international site networks. Consequently, pharmaceutical sponsors and contract research organizations (CROs) face the challenge of ensuring rigorous data generation. They must do so while navigating the operational realities of recruiting and maintaining patient participation across varied geographical locations and regulatory frameworks.

## Tackling Operational Execution on a Global Scale

The operational execution of Phase I trials demands careful coordination of multiple elements throughout study startup and planning phases. Regulatory requirements form the foundation of this work, though teams can ensure seamless trial initiation and advancement only by having a comprehensive understanding of these mandates and strict adherence to local laws. Patient information remains protected, and trust is preserved, when teams demonstrate thorough knowledge of regional data privacy regulations.

Managing enrollment and cohorts across global trials presents unique challenges. Sites scattered throughout diverse regions and time zones require sophisticated

coordination. Teams operating on a global scale must master intricate protocol details, including multiple treatment arms, dose variations, and adaptive trial designs, all of which demand expert handling.

Beyond enrollment, sites face substantial infrastructure requirements. Cohort-specific needs dictate the presence of specialized personnel, medical equipment, and materials, making careful coordination a requirement. Phase I trials introduce additional layers of complexity, including risk-based monitoring, safety review processes, vendor management, investigational product oversight, and sample handling. Success hinges on effective communication and coordination among all relevant stakeholders.

## Planning for Trial Success, Adapting to Changes

From the outset, trials require comprehensive clinical study mapping, a critical factor for small biotech companies operating with constrained budgets. This context means that a CRO's accumulated knowledge and practical experience become invaluable assets for the trial when making decisions. Risk mitigation strategies deserve equal attention in early planning stages, with provisions for unanticipated events ranging from natural disasters to shifting geopolitical landscapes.

Administrative efficiency improves dramatically when teams deploy automated document management tools, accelerating study startup timelines. Master service agreements offer similar advantages. By streamlining site contract negotiations, these agreements positively influence global startup schedules.

Adaptability stands as a non-negotiable requirement in Phase I oncology trials. Given that change is the only constant in oncology drug development, protocol amendments occur regularly, making flexible setup processes that accommodate adjustments essential. Oftentimes, a trial can launch as a first-in-human study in a single country, then gradually expand its reach across the globe. When teams invest in meticulous advanced planning, they position themselves to anticipate necessary amendments, navigate transitions smoothly, and more accurately forecast trial milestones.

## Planning Strategic Country- & Site-Level Decisions

Phase I trials require sophisticated expertise across multiple domains. Teams must demonstrate mastery of country- and site-level feasibility, ethics committees, and informed consent procedures, all while remaining sensitive to cultural nuances and regional regulatory expectations. The landscape has shifted considerably; global startup timelines now reflect the influence of European Clinical Trial Regulation (EU CTR) 536 and the move toward the Clinical Trial Information System (CTIS).<sup>3,4</sup> We see progress emerging through enhanced collaboration, illustrated by strengthened partnerships with investigators and higher site feasibility efforts. Additionally, targeted outreach, focused on protocol-specific complexities, sharpens the ability to identify optimal sites for participation and better secure the trial, enabling smoother, on-time enrollment.

Strategic groundwork, such as understanding disease prevalence, assessing competitive landscapes, and cultivating relationships with country-level experts and key opinion leaders (KOLs), collectively strengthens study design and streamlines startup processes. The Asia-Pacific region illustrates this principle clearly, because success requires deep knowledge of each country's unique landscape paired with credible local experts. Demographics matter, and so does population diversity. These factors determine protocol adoption rates and levels of acceptance. The equation has one more critical variable: identifying sites equipped with the necessary technology and staffed by knowledgeable investigators accelerates both activation and patient enrollment.

Data-driven approaches offer significant advantages. Predictive analytics enable faster, more informed country selection decisions, while incidence rates and prescribing histories pinpoint suitable sites with precision. One caveat remains, that next-generation,

novel oncology treatments often face heightened regulatory scrutiny, resulting in extended review periods that protocols should account for at the outset.

## Selecting Sites & Engaging KOLs

Recruiting the right sites and patients determines your trial's success. The selection process encompasses several evaluation criteria, including:

- Experience levels
- Specific expertise areas
- Historical performance records
- Identification of key opinion leaders

Through qualification assessments, teams confirm that sites possess appropriate capabilities, including the facilities, staffing, and infrastructure necessary to sustain trial demands. Geographic factors are part of the equation alongside patient demographics and healthcare accessibility.

Successful trial delivery demands strong, collaborative site partnerships. Sponsors and CROs can build these relationships effectively by streamlining feasibility questionnaires through direct conversations, whether during qualification visits or coordinator calls. This approach yields multiple benefits, such as reduced site burden, enhanced engagement, accelerated startup timelines, and lower costs.

The value of early KOL engagement cannot be overstated. These leaders prove instrumental in identifying promising sites and viable countries for trial conduct. Knowledge gathered through KOL and patient engagement offers another strategic advantage by helping teams sidestep protracted regulatory negotiations. Patient advocacy groups serve a complementary function, bridging the gap between CROs, sponsors, and patient communities to illuminate perspectives on existing treatments and to better understand the patient's journey<sup>5</sup>, needs, and wants. Online forums and message boards provide additional insights, and patient voices in these digital spaces should help inform trial design and protocol considerations.

## Coordinating Clinical Trial Logistics

Clinical trial logistics are increasingly intricate, and operational success hinges on two foundational elements, flexibility and comprehensive upfront planning. Central supply is the currently recommended approach, though teams must thoroughly assess trial-specific needs before committing to any strategy.

For comparator drugs, centralized supply offers distinct advantages, primarily by de-risking the supply chain. Yet rigid adherence to any single model invites problems. Flexibility becomes essential when shortages emerge. Geographic expansion introduces additional variables, including new countries that often necessitate local supply arrangements. These configurations shift from one region to another, sometimes even between hospitals within the same area, and each option carries its own cost implications.

Beyond economics, systems must withstand rigorous audits and maintain meticulous pill-level tracking; failures here trigger recalls and compromise patient safety. Reimbursement cards streamline certain processes while simultaneously introducing complexity into drug reconciliation workflows. One emerging alternative is promising, using real-world data arms to potentially eliminate the need to purchase comparators altogether.

Regulatory landscapes vary dramatically. Each country and region imposes distinct approval protocols and packaging specifications, creating a maze of requirements that even experienced teams struggle to navigate. Your strategy should anticipate these complexities and prepare for potential shortages.

## Innovating Oncology Trials With AI

We are seeing increasing use of AI-powered platforms that automate routine tasks and entire workflows, simultaneously reducing site burden and resolving administrative bottlenecks. Document workflow

automation has gained traction, along with forecasting tools. Both technologies align multiple data points to drive operational efficiency.

AI extends its value across multiple trial dimensions, streamlining processes, enhancing data acquisition and analysis, and optimizing overall performance. Early indicators and emerging trends enable proactive planning for downstream protocol decisions. Real-world data arms combined with AI tools may substantially reduce required patient numbers by mining historical datasets. Creating the collective impact of enhanced clinical trial efficiency, reduced costs, and improved outcomes.

Improvements in automation mean that teams must possess deep familiarity with disease prevalence, comprehensive knowledge of local regulations and cultural customs, established regional relationships, and active engagement with KOLs and patients. They must be proficient in local enrollment, cohort management, and coordination of clinical trial logistics. Thorough planning and preparation, augmented by AI, enable informed decision-making and seamless trial execution, but human-in-the-loop oversight by a knowledgeable team is an absolute requirement.

The path forward requires us to collectively embrace change, leveraging deep expertise, and deploying cutting-edge technologies. This allows early phase oncology teams to position themselves to generate reliable data that strengthens regulatory submissions and accelerates drug development.

## References

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The company's flexible service model - spanning full-service trial management to functional service partnerships through Worldwide Flex - is powered by a people-first, partnership-driven outsourcing approach that strengthens collaboration, enhances data transparency, and supports more informed decision making. This provides sponsors with tailored, adaptable solutions that keep pace with the evolving demands of clinical research.

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