Master protocols

Accelerating drug development with master protocols

Enhancing clinical efficiency through master protocol trial design

There is growing interest in accelerating drug development by creating master protocol trial designs that simultaneously evaluate multiple investigational products and various disease subpopulations under a single overarching protocol and infrastructure, eliminating the need for individual trial protocols. Master protocols, also known as complex clinical trials, offer adaptive design flexibility. This allows researchers to modify the study by eliminating less promising treatments or advancing treatments that show better performance to different phases of the study.

Common types of master protocol studies include:

- **Basket trials:** Evaluate a single investigational drug or a drug combination across multiple disease populations
- **Umbrella trials:** Evaluate multiple investigational drugs within a single disease population
- **Platform trials:** Evaluate multiple medical products for a disease or condition continuously, with products entering or leaving the trial as needed
- Other trial designs that may include a hybrid combination

Master protocol studies can provide potential opportunities to shorten R&D timelines, reduce R&D costs, and improve the probability of success — if designed and implemented properly. The distinct feature of the master protocol design is its flexible start, which gradually adjusts based on the likelihood of success. For instance, adding new treatment arms, changing the standard of care arm, adding or removing disease populations, and changing eligibility criteria are achieved by utilizing more frequent interim data reviews and decision-making that relies significantly on data currency and quality. However, the master protocol design has dramatically increased implementation complexities because of the frequent substantial protocol amendments and or protocol adaptations. As a result, questions about what, why, when, where, who and how have become critical to answer.

Skilled in multi-phase master protocol management

In the past five years, our expert master protocol/complex clinical trial team has supported:

88+
Master protocol/ complex clinical trials

8,394+
Patients

32+
Indications

67+
Countries

2,440+
Global sites

Proven delivery across multiple master protocol types

We have managed and delivered multiple indications across different types of master protocols, including:

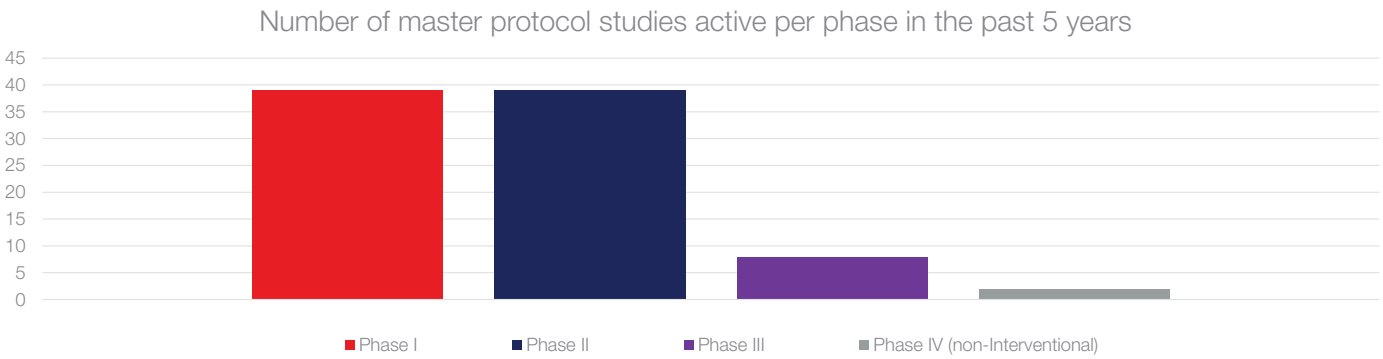
Basket	60
General Medicine	**1**
Rheumatic Diseases	1
Hematology/Oncology	**57**
Acute Myeloid Leukemia (AML)/ Myelodysplastic Syndrome (MDS)	1
Carcinoma, Non-Small-Cell Lung	1
Carcinoma, Squamous Cell	1
Carcinoma, Triple Negative Breast	1
Colorectal Diseases	2
Hematologic Diseases	2
Leukemia, Chronic-Phase Myeloid	1
Leukemia-Lymphoma, Precursor B-Cell Lymphoblastic	1
Lymphoma, Large B Cell Diffuse	2
Lymphoma, Non-Hodgkin	1
Multiple Myeloma	2
Neoplasms, Breast	1
Neoplasms, Head and Neck	1
Neoplasms, Ovarian	1
Osteosarcoma	1
Solid Tumors	38
Neuroscience	**1**
Parkinson Disease	1
Vaccines	**1**
Carcinoma, Non-Small-Cell Lung	1

Platform	20
General Medicine	**2**
Dermatitis, Atopic	1
Obesity	1
Hematology/Oncology	**5**
Cancer, Gastric	1
Carcinoma, Non-Small-Cell Lung	1
Melanoma	2
Neoplasms, Lung	1
Infectious Diseases	**7**
Asthma	1
Coronavirus	4
Hepatitis B, Chronic	1
Respiratory Distress Syndrome, Adult	1
Neuroscience	**1**
Stress Disorders, Post-Traumatic	1
Vaccines	**5**
Coronavirus	**5**

Umbrella	8
Hematology/Oncology	**7**
Breast Cancer, Relapsed Metastatic	3
Carcinoma, Non-Small-Cell Lung	1
Leukemia, Chronic Lymphocytic	1
Solid Tumors	2
Infectious Diseases	**1**
Human Immunodeficiency Virus (HIV)	1

Driving global trial efficiency through unified, adaptive master protocols

Our past 5 years of experience have encompassed various phases of clinical trials:



The master protocol approach allows for the efficient assessment of several interventions, often for the same disease, using a shared infrastructure and control group. Key features include:

1. **Adaptive design:** The master protocol can be fixed design or be adapted based on interim results, allowing for the addition of new treatments or the discontinuation of ineffective ones.
2. **Shared control group:** Multiple treatments are compared against a common control group, improving efficiency and reducing the number of participants needed.
3. **Continuous learning:** Data is continuously analyzed, enabling quicker decision-making about the efficacy and safety of treatments.

These trials are particularly useful in fields where rapid testing of multiple therapies is needed, such as oncology, rare or infectious diseases.

Master protocol studies are typically large-scale, global efforts that span numerous countries and investigational sites, each with its own set of requirements and processes for protocol review. These sites also have varied systems for managing patient data, labs, contracts, finance, etc. In addition to sponsors and contract research organizations (CROs), many vendors are involved in providing clinical supplies, processing lab samples, analyzing data, and reviewing imaging data. These entities often use different systems for data capture and analysis, leading to significant data overlap and integration challenges.

Master protocol studies are dynamic and can undergo frequent changes, affecting downstream activities carried out by regulatory affairs, ethics committees, institutional review boards (IRBs), sponsors, CROs, vendors, and sites, ultimately impacting the patient. In the current R&D model, these activities are performed by different organizations using varying processes and systems, necessitating careful assessment of interoperability. Protocol development and amendments are managed by the sponsor or a contracted company or consultant.

To ensure data consistency and integrated process flow, extensive planning, data transfers, and reconciliation agreements are established, requiring considerable time and effort during the trial's pre-planning and start-up phase. Any protocol amendments or adaptations necessitate repeating these development and setup activities, which can be more challenging during ongoing patient enrollment or when many patients are active in the study.

While master protocol studies offer flexibility and adaptability, traditional protocol models can appear rigid, slow, and unclear. Implementing master protocol studies using an orchestrated, cross-functional, risk-based approach can address many concerns associated with traditional methodologies. The ICH E6 (R3) principles outlined in our current SOPs provide opportunities to effectively tackle these challenges while ensuring clinical trial subject protection and data reliability throughout the clinical trial lifecycle.

The PPD™ clinical research business of Thermo Fisher Scientific is committed to delivering excellence. We continually refine the way we deliver master protocols through collaborative innovation with our clients, introducing new tools, service offerings, system enhancements, reporting features and processes to reduce the inherent complexity and burden on sites and subjects.

Learn more at **ppd.com**