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Master Protocols Can Kickstart Clinical Trials

By Bill Myers

Master protocol designs have taken on new significance as sponsors, sites and regulators have come to recognize that decision points must be reached sooner—and the FDA is planning to issue new guidance on them in the coming weeks.

Master protocols are an effort to test more than one or two treatments in more than one patient type or more than one disease. They can offer sponsors and sites enormous flexibility because they aren't as rigorously tied to the traditional Phase I, II, III trial approach and they sometimes enable researchers to launch expansion cohorts or otherwise scale up their efforts.

There are three major types of master protocol design:

- Platform trials—study multiple, targeted therapies for a single disease more or less perpetually, with treatments allowed to drop in or out of the platform depending on how well they perform in the trial;
- Umbrella trials—study several therapies for a single disease but focus on various subgroups (usually determined by biomarkers) of a disease; and
- Basket trials—study a single, targeted therapy for several diseases or disease subtypes (for instance, by focusing on a cancer mutation and seeing how a given drug treats the mutation when it appears in different types of cancers).

For all their advantages, master protocols also have to be managed carefully and each different type of design has its own special problems, says Lindsay McNair, chief medical officer at WCG.

A platform study, for instance, requires absolute commitment—and rapid—communication.

"You have so many moving parts," McNair says. "You may have randomization schemes that are adaptive and if you have multiple sites and multiple partners, you have to make sure that you're getting data back quickly and that, for example, your IRBs are getting safety data to be able to assess whether risk and benefit expectations are changing, and to ensure that information in informed consents is current."

A basket study can challenge an organization, especially if—like so many large institutions—the research organizations are divided by specific disease areas, McNair says. "It may mean that they have to make changes to their infrastructure to conduct those studies," she notes.

As for umbrella trials, the multiple areas of focus mean they can quickly become a combination of drug and diagnostic tests at the same time.

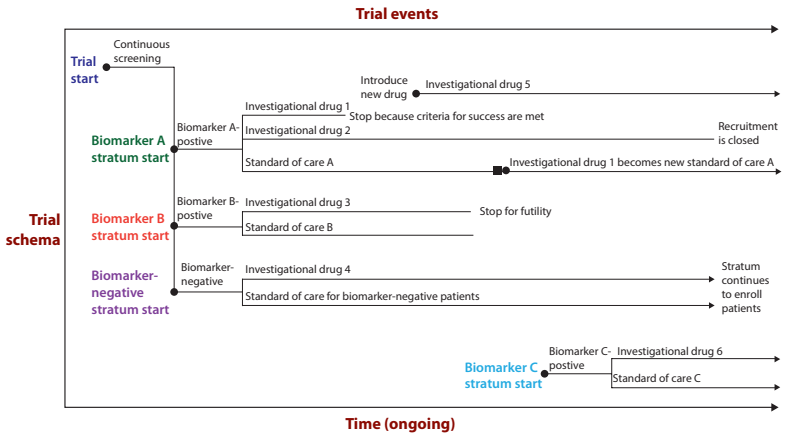
"It's not just comparing drugs for tumor A against drugs for tumor B. It's testing the device that detects the tumor mutation and then assigns a treatment," McNair says.

That may mean that sponsors have to be aware of device regulations—and not just regulations for the drugs they're testing.

Platform Trials

- Objective: To study multiple targeted therapies in the context of a single disease in a perpetual manner, with therapies allowed to enter or leave the platform on the basis of a decision algorithm

- "We need to make clinical trials more like laboratory trials-so that we can look at the data coming in and respond and change the experiment, rather than waiting years to find out we had the question wrong."



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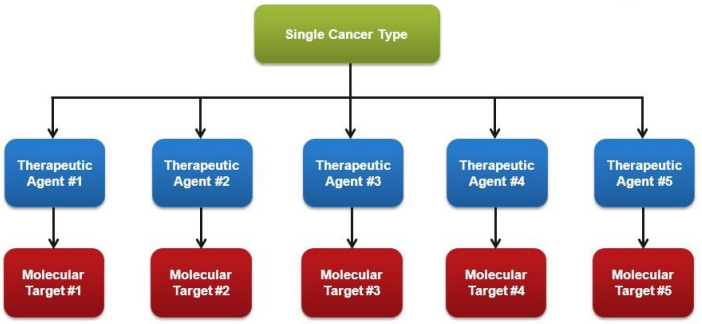
Umbrella Trials

- Objective: To study multiple therapies in the context of a single disease
  - Evaluates various subgroups (often defined by biomarkers) within a larger group with conventionally-often anatomically-defined disease
  - Design may be randomized or may use external control group, depending on the disease



Basket Trials

- Objective: To study a single targeted therapy in the context of multiple diseases or disease subtypes
  - Participants are screened for a molecular target, regardless of the location of disease
  - The study population could include participants with many different diseases of histologic features