

DCRI's PTN Builds Efficiencies to Improve the Enrollment, Design and Conduct of its Studies

DCRI's PTN Applies CTTI's Pediatric Trials in Antibacterial Drug Development Recommendations

SUMMARY

The Duke Clinical Research Institute (DCRI) Pediatric Trial Network (PTN) wanted to optimally conduct studies that improve labeling of medications and devices for children. CTTI's Antibacterial Drug Development (ABDD) recommendations, which help trialists identify and address barriers in conducting antibacterial drug trials in the pediatric population, were foundational to PTN's efforts.

GOAL(S)

Children should have access to antibacterial drugs that have undergone appropriate evaluation for safety and efficacy, yet many trial sponsors have challenges enrolling and completing pediatric antibacterial drug trials. The PTN wanted to conduct efficient studies that improve the labeling of medications and devices in children in a way that used finite resources and minimized burden to patients.

CHALLENGES

Despite legislation enacted to facilitate pediatric drug development, such as the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), many of the antibacterial drugs commonly used in children lack adequate pediatric use information in drug labeling for all age groups, particularly neonates. The time between the approval of a new antibacterial drug for use in adults and pediatric labeling has recently been 5 years or longer, and pediatric studies have yet to be completed for a number of antibacterial drugs more than 5 years after approval in adults.

SOLUTION(S)

CTTI's ABDD recommendations point to four key strategies the PTN used for overcoming these challenges: 1) establish master protocols to expedite the availability of evidence regarding the safety and efficacy of antibacterial drugs in children; 2) engage early with the FDA; 3) minimize the burden of participation; and 4) broaden eligibility criteria to be as inclusive as possible.

TAKING ACTION

The PTN began by exploring where it could build in efficiencies with master protocols that leverage existing pathways to accomplish the most with finite resources. For example, the PTN was interested in looking at several antimicrobials that treated the same type staph infections in neonates. Using CTTI's master protocols guidance, the PTN studied all three anti-staph antibiotics under a single protocol (the dosing of drugs differed, but procedures, pharmacokinetic (PK) sampling, safety, follow-up, and case report forms were identical). Sites initially used whichever drug they preferred and were only asked to switch when data for their preferred drug was complete. As a result of the master protocol approach, the PTN enjoyed efficiencies around total cost and time. Enrolling kids in a study that is not going to meet the PTN's overall goal to inform a label wastes time, money, and-- perhaps most importantly-- exposes kids unnecessarily to drugs. That's why the PTN also applied CTTI's recommendation to collaborate early with the FDA to discuss the science from the regulatory standpoint of what FDA needs to make label changes. Hearing from FDA allowed the PTN early input to structure its protocols so that it can maximize the amount of information given to regulatory bodies, such as endpoints, sample size, and PK sampling strategies. Many of the compounds the PTN evaluates are older drugs that the FDA has had a lot of experience with developing studies. FDA also often has experience with other molecules in a similar class that is valuable to the PTN's protocol development. The PTN also explored ways to minimize patient burden. For example, one particularly burdensome activity in pediatric studies is a high amount of blood draws. Many of the studies the PTN conducts are pharmacokinetic studies that require blood, so the PTN tries to use relatively small volume blood sampling. A 200 microliters sample can be drawn by a heel stick or finger prick rather than through the vein, which is more invasive and can be more painful for the child. (This is very important in premature infants who don't have that much blood to begin with.) The PTN also designs its studies to minimize PK samples as much as possible. Population PK analyses allow the PTN to get what it needs from 3-4 PK samples rather than a dozens. PK samples are also timed with other blood draws, so the child doesn't have to undergo an extra stick. One of the issues with doing studies in children is that there aren't as many sick children as sick adults, so the sample size available for enrollment is relatively small. When possible, the PTN follows CTTI's guidance to make inclusion/exclusion criteria as broad as possible to maximize the potential eligible study population. For example, in one study the PTN conducts, the children are already getting the study drug per standard of care, so there are almost no exclusion criteria. The principle the PTN follows is that there is no reason to add exclusion criteria if you don't have a good scientific or safety reason to justify it.

IMPACT

The PTN has taken advantage of the efficiencies that it has developed, and the group has become expert in looking to see what sponsors and funders need done and then using lessons learned and efficiencies gleaned from CTTI's ABDD recommendations to execute on its projects.

ADVICE

There is always a tension to navigate when the PTN works with investigators to make sure the protocol is as lean as possible while answering critical research questions. While keeping the focus on the primary outcomes of the study, the PTN engages in many discussions with stakeholder to produce feasible protocols with the highest likelihood of answering the research question.

ORGANIZATION

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ORGANIZATION TYPE

Academia
Clinical Investigator/Site

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