

Trend shifts away from phase I ‘healthy volunteers’

Looking to stretch their research dollars beyond phase I safety determination and catch early glimpses of efficacy, sponsors and CROs are pursuing patient populations to provide those first signs, rather than depending on “healthy volunteers” for safety and then launching phase II trials.

This shift comes as phase I and phase II development cycles increasingly are being combined into single proof-of-concept designs. The goal is to dose targeted patient populations as early as possible to find signals of both product safety and efficacy—a combination that sharply reduces the historical approach to using healthy volunteers.

“Permanent changes are taking place in the [clinical trials] business,” said [Parexel International](#) CEO Josef H. von Rickenbach in a conference call with Wall Street analysts, explaining why the company is cutting up to 30% of its early-phase capacity and laying off 300 employees. “We believe that the market for healthy volunteers is not going to be growing much, whereas the market for patient studies is growing more... Clients are conducting studies as needed to get to the next stage.”

Parexel’s restructuring has put a spotlight on this phase I transition, which works best if the proposed drug formulation is well-known or approved for other medical indications. New chemical entities—for

which little is known about the pharmacokinetics and potential side effects—are always tested with healthy volunteers.

“If you can use targeted patients, you can get a more accurate assessment of the safety, along with some signs of efficacy—an overall better picture than from a group

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—Derek Grimes, Senior Director of Clinical Research, TKL Research

of young and healthy university student volunteers,” said Jonathan Isaacsohn, M.D., [Medpace](#)’s executive vice president for regulatory and medical affairs. For example, he said for an obesity drug phase I trial, it would be more helpful to have otherwise healthy, obese patients—the patient population—than lean, healthy volunteers.

As for input from the FDA, there is very little, noted Derek Grimes, senior director of clinical operations at [TKL Research](#). “They are not opposed as long as it does not interfere with the safety data collection,” he said.

A phase I clinical trial usually involves a small number of people (at times less than 12)

who go through the same sequential process and complete a series of medical tests to determine the maximum tolerated dose and define the toxicities of the proposed treatment.

By dosing patient populations as early as possible in proof-of-concept trials that link phase I and phase II, sponsors and CROs benefit by also finding signs of product efficacy and identifying non-viable compounds much earlier. Thus, sponsors can make better “go/no go” decisions earlier and decrease the risk of failure during late-stage trials, saving considerable development costs.

“We are seeing the use of patient populations in combination with phase I and II trials across the board—this is what the industry is looking for,” said Lynn R Webster, co-founder and chief medical director at [Lifetree Clinical Research Center](#) in Salt Lake City. “Sure, it’s easier and faster to recruit healthy volunteers, but sponsors and CROs see the long-term value in working with disease-state populations.”

—Ronald Rosenberg