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Transforming Trials: Reducing Cost and Risk

It is evident that costs and excessive risk are holding back drug development. The total sponsor cost per new drug compound approved in the US now exceeds $2.5 billion, including nearly $1.5 billion for clinical development – a significant 145 per cent jump in just 15 years, according to the Tufts Center for Drug Development. (1). However, only seven percent of first-in-human drugs gained FDA approval in the same period, representing not only great financial cost and great risk, but also a toll in human terms - high drug costs often restrict patients' access to needed therapies, leading to poorer health and possibly, financial hardship.

This inefficiency largely results from a traditional drug development system of three discrete, fixed trial phases. It lacks the flexibility, analytical power and efficiency required to develop complex new therapies targeting the smaller and often heterogeneous patient populations increasingly seen today (2). Antiquated clinical trial processes can slow drug development and force abandonment of promising drug candidates when development costs exceed projected revenues.

Bending the drug cost curve requires more than efficiency gains: we must remove risk from the process entirely. Much of the innovation needed to transform clinical development exists today, and enjoys explicit regulatory support. ICON is addressing this need through our Transforming Trials initiative. This comprehensive rethinking of the entire clinical trials process uses new approaches coupled with existing, tested technologies to substantially reduce the risk and cost of clinical drug development.

DRIVING CHANGE WITH BIG DATA

Big data insights play a major role. For example, developing study protocols with patient inclusion criteria that are shaped by actual

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patient data, automatically harvested from EMRs, reduces the risk of launching a study with unrealistic patient recruitment potential. Access to de-identified live patient data also reduces recruitment costs by knowing how many patients match a trial protocol and where they are located. Automated site monitoring greatly reduces site management costs while ensuring that data are properly collected and validated – reducing the risk and cost of patients lost to protocol deviations.

Remote data links enable data collection directly from patients at home. This not only reduces the number of costly interim office visits required for a trial, it can yield valuable insights into how patients respond to therapy 24/7 in the real world. EMR data allow automated post-market surveillance in Phase IV trials that can vastly expand study populations while actually lowering costs.

Rapid data collection and processing make possible mid-trial insights that support planned adaptive trial changes. These might include homing in on the most effective dose, or enriching a later phase sample with patients who are more likely to respond, or increasing or decreasing sample size to accommodate a drug that has a larger or smaller therapeutic effect than predicted. Real-time data validation technologies support quick data lock for interim analysis and protocol revisions, which is a requirement for successful adaptive design trials.

HARNESSING ADAPTIVE DESIGN

Adaptive approaches also are more efficient and are encouraged by regulatory agencies in Europe and the US. They can be used at every phase of clinical drug trials: modifying study protocols in predetermined ways based on interim patient data and have the potential to eliminate many unanticipated risks that undermine efficacious drugs and unnecessarily extend development timelines. In a single two-year combined Phase II/III trial, adaptive trials can often deliver information that might otherwise require three or more consecutive conventional trials over three or more years. These seamless trials reduce the total sample size needed by using the same patients in more than one stage. We estimate that optimal use of adaptive trials across a portfolio could reduce trial costs by 25 per cent. ICON has successfully designed and executed almost 200 adaptive trials and has an international staff capable of translating and validating patient-centric trial protocols anywhere in the world.

RADICAL PATIENT FOCUS

Improving patients' lives is the ultimate goal of clinical trials. Insight from real-world data supports everything from defining outcomes that matter most to patients, to offering trials to patients identified through EMR in their physicians' office, to minimising control arms using advanced statistical methods and providing study results as soon as they are available.

All of these innovations are already in use sporadically, and their individual potential proven. When implemented fully in a systematic way, we believe they could significantly cut clinical trial costs and reduce time to market by months, if not years.

Expertise in each area, as well as excellent change management skills, are required to fully implement this reimagined clinical trial process. What will make it all worthwhile will be the accelerated delivery of more new drugs to market, saving and improving more patient lives.

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1 DiMasi et al., Tufts Center for the Study of Drug Development, 2014
2 Jones DS et al. The Burden of Disease and the Changing Task of Medicine. N Engl J Med 2012;366:2333-2338 June 21 2012, DOI: 10.1056/NEJMp1113569