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From the editor

Phase I Clinical Trials: Overcoming Barriers

A medical student, upon hearing an explanation of a Phase I clinical trial, remarked that the first patients to enroll in first-in-human Phase I trials were, in effect, "jumping on the grenade" for those who would come later. There are more drugs in development for cancer indications than ever before – 861 according to PhRMA, yet our ability to carry out Phase I trials is increasingly constrained. This issue of CCR Focus is dedicated to those patients who, for every drug currently on the market, have jumped on the grenade. Multiple factors have coalesced to increase barriers to effectively testing all of these agents. The need for extensive preclinical testing, outlined by Senderowicz, is the first daunting task. Next, the nature of the Phase I trial itself – and concerns about sub-therapeutic dosing – leads patients and their oncologists to delay enrollment in Phase I trials. Exacerbating this, as detailed by Ivy and coauthors, the community has failed to embrace novel, more efficient trial designs that might get to effective doses faster, in favor of the traditional 3 + 3 cohort design. Further, we are victims of our own success: in bringing new therapies to market we have increased the number of salvage options, again reducing enrollment in clinical trials. The complexities of selecting patient populations who are most likely to benefit from a new agent – personalized medicine – also limits our ability to execute Phase I studies effectively. Dancey and colleagues provide some guidance in this area. To help in the steadily growing regulatory burden for data collection and reporting, Rock and colleagues have outlined critical data collection components, providing in essence a GCP primer for the academic oncologist. Of course these issues are not unique to drug development in the United States, as well documented in Calvert's European/Asian perspective. We have the pipeline. What we don't have are fast, straightforward methods of getting the drugs through the Critical Path to market and also personalizing what novel drug is best suited for a specific patient. In the following pages, Guest Editors LoRusso and Seymour have brought forward an important collection of papers. Along with guidelines generated by the NCI Investigational Drug Steering Committee's working groups to improve and speed both Phase I and II trials, they offer the researchers' own insights into, and ways of managing, the obstacles that impede our progress in this area that is so critical to our collective enterprise. As always, we hope that this issue of *CCR Focus* will challenge those expert in the field and prove valuable to the interested non-expert.

Susan E. Bates, M.D.
Deputy Editor
CCR Focus

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