On Drug Development, Chance, and the Prepared Mind

This CCR Focus section examines lessons learned in drug development, focusing on specific examples of agents or targets that have hit roadblocks during development. In some cases, the hurdles have been surmounted; others are still a work in progress. Much has been written about the need to increase the success rate of drugs transitioning from phase II to phase III trials; about half of the drugs that enter phase III testing do not ultimately receive regulatory approval. Even fewer drugs, about 1 in 5, that enter phase I trials are registered. The loss of these agents through the drug development process is costly, both in terms of money and time; for some drug sponsors, a failure in phase III can be devastating. This Focus series shares insights that investigators have gained from experience, so that we can in turn be prepared when chance favors our work. Although the 4-year development of crizotinib for lung cancers with echinoderm microtubule-associated protein-like (EML)–anaplastic lymphoma kinase (ALK) translocations, resulting in simultaneous approvals for both assay and agent, stands as a model, it is clear that lessons learned in a decade developing tyrosine kinase inhibitors helped lay the groundwork.

Guest Editors Susan Bates and Giuseppe Giaccone have joined experts in the field to illustrate lessons learned in drug development and highlight strategies for success. Marzuka Alcalá and Flaherty discuss the development of B-Raf as a target, culminating in the success of vemurafenib; Pollak discusses the difficulties and the surprises encountered in the development of IGFR-I inhibitors and identifies the importance of finding tumors in which the target is critical; Komlodi-Pasztor, Sackett, and Fojo discuss the problems of developing highly specific agents for targets that are tightly cell cycle regulated; and Neckers and Workman describe challenges and progress in developing therapeutic agents against the Hsp90 chaperone, noting new agents in the pipeline. With Amiri-Kordestani, Bates and Giaccone provide an overview of the challenge of finding the right target, the right drug, the right assay, and the right trial design. We hope, as with every CCR Focus section, that this series of articles stimulates and challenges those working in clinical translational oncology, highlights important concepts for future research, and proves valuable to the interested nonexpert.

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Dans les champs de l’observation le hasard ne favorise que les esprits préparés.
“In the fields of observation, chance favors only the prepared mind.”
—Louis Pasteur, University of Lille; December 7, 1854

Figure 1. Portrait of Louis Pasteur on a Polish stamp, issued December 10, 1959.
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