Disruptive Immunology

The term "disruptive innovation" was coined in 1995 by Clayton Christensen and refers to a process by which a product relentlessly overtakes a market (1). Approval of the checkpoint inhibitors pembrolizumab and nivolumab, seen as the vanguard of immunotherapy, has been considered by many to be just such a disruptive innovation, but it falls short of a strict definition because, in truth, checkpoint inhibition cannot reach the entire "market" of patients with cancer (see Fig. 1). Indeed, we cannot yet predict the subset of patients who will receive benefit, and it is unlikely that we are just one more checkpoint or another immune approach away from benefiting the rest. The history of oncology, and indeed, of medicine itself, would suggest that we are not just one discovery away. In this CCR Focus section, we look at the rapidly evolving field of immunotherapy beyond checkpoint inhibitors—some of the targets, strategies, and technologies that are in development. These include dendritic cell and neoepitope vaccines, chimeric antigen receptor T cells, and strategies for monitoring checkpoint inhibition. Guest Editors Ignacio Melero and Theresa Whiteside have assembled a panel of experts to review new strategies and think about life "after" the immunotherapy approvals. We hope we are just one step away for the whole population, but it is not likely.

Still, there is reason to be cautious in the wholesale embrace of this disruptive innovation. Although we have seen these agents bring results where none were had before, experience teaches that there will be limits, downsides, and possible harm, and those must be identified and evaluated. Too many times, the medical profession has created paradigms that later required enormous effort to undo. Examples in recent decades of paradigms we were confident were correct include bone marrow transplantation for breast cancer, screening mammography, early detection with PSA, and various versions of adjuvant chemotherapy. In Ending Medical Reversal: Improving Outcomes, Saving Lives, the authors write that our optimistic human nature is part of the problem (3). They also observe that medical research too often emphasizes how things work, thereby discounting the importance of determining how well they work. Unfortunately, many of our patients already have to reconcile the disconnect between the headlines and their own bottom line. Here is an opportunity to stay focused on the bottom line—putting clinical trials and evidence first before translating the unproven to real-world practice.

References
Clinical Cancer Research

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