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While We're at It, Let's Whack the FDA

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It's that time, early in the cycle of U.S. presidential campaigns, when candidates try to attract attention by announcing their personal plans for reforming the government. This year's proposals run the strange gamut from building a wall on the Mexican border to keeping out undocumented Hispanic immigrants to banning all Muslims, even Muhammad Ali, Kareem Abdul-Jabbar, and other iconic Muslim-American citizens from entering the U.S. However, my personal favorite is the proposal by Ted Cruz, the presidential contender and Republican U.S. Senator from Texas, who would rush cancer cures into the U.S. from "trusted" countries like Malta, Lichtenstein, and Bulgaria.

In his Reciprocity Ensures Streamlined Use of Lifesaving Treatments (RESULT) bill, introduced into Congress in December 2015, Senator Cruz proposed that the U.S. Food and Drug Administration (FDA) would have 30 days to approve any drug already approved in a "trusted country," a broad descriptor that includes our allies in Europe and Asia, in addition to a number of smaller countries such as the three already mentioned [1]. Under the *RESULT* bill, if the FDA turns down the proposed drug or device, Congress could override that decision. In this observer's opinion, it is unlikely that Congress has the scientific expertise or interest to make such a decision. Even if that expertise were present, would Congress be an unbiased judge, given its heavy reliance on campaign contributions from the health-care industry?

Certainly, the FDA has had its shortcomings. As Vincent De Vita points out in his recently published book, *The Death of Cancer,* for many years in the post-World War II era, the FDA was reluctant to approve new drugs without evidence from phase III trials that proved a drug's life-saving efficacy [2]. For De Vita, the skeptical culture of the FDA was incompatible with the obvious need to push the boundaries as fast as possible.

However, the FDA of 2015 is not your grandparents' FDA. Indeed, the Division of Oncology Drug Products has benefited from the enlightened leadership in Richard Pazdur, a card-carrying academic oncologist who fully understands the need for better drugs and who has hastened drug review during his transformative 16-year tenure at the FDA.

Let's look at the facts.

In 2015, the FDA approved, by my count, 23 different cancer drugs for 27 new treatment indications, most of these being first-time approvals for newly marketed drugs [3]. Of the 18 new chemical entities, 4 received accelerated approval, and 5 decisions were based on phase II trials. In former times, improved overall survival was the gold standard for receiving FDA approval. Not so in 2015. The endpoint for first-time approvals was overall survival in only 5 of 18 actions, whereas for 13 newly approved drugs, response rate or progression-free survival provided the convincing evidence of benefit. Thus, the agency's actions reflect a flexibility and commitment to bringing new drugs to cancer patients hard to reconcile with Senator Cruz's criticism. It is also notable that virtually all approvals were for drugs discovered and developed in the U.S. The biggest problem for our "trusted" neighbors overseas as well as for the U.S. is figuring out how to pay for these new agents, mostly derived from NIH investments in biomedical research.

The recent FDA record is truly impressive, as compared with years ago, when an average drug took 7 to 10 years to reach the market. Five of last year's cancer drugs were approved based on early phase trials, and one was granted Accelerated Approval after only 3 years or less of clinical trials. Some would argue that this sort of speedy approval is unsafe, that the toxicity of these drugs is incompletely understood, but, to date, only one drug, ponatinib, has been withdrawn for safety reasons after receiving Accelerated Approval, and that drug was allowed to re-enter clinical use 1 month later under more restricted prescribing conditions [4]. More new drugs will follow this path to rapid approval as the FDA expedites the review of drugs registered under the visionary Breakthrough Therapies legislation [5].

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In fact, the major limitation in curing cancer is not the FDA. It is our steadily improving but still limited understanding of cancer in all its facets: drug resistance, immunologic tolerance, genomic instability, and so many other properties that make treatment difficult. It is not simply a problem of easing the approval process, encouraging communication between bench scientists and clinical investigators, or, as Vice President Biden proposes, sharing big data; all of these steps are important, but together they are still insufficient.

The greatest obstacle is our fundamental lack of understanding our enemy in biological terms. That will only come with research, with asking the right questions, and bringing new insights into application. I am confident that as we gain this knowledge, industry will make ever more effective drugs, the FDA will approve them, and cancers, one by one, will be prevented and cured.

Rather than opening the floodgates for bogus drugs from overseas, we need Congress to expand support for cancer research and biomedical science here at home. That is the best and, indeed, only answer to the cancer problem.

Disclosures

Bruce A. Chabner: Sanofi, Merrimack, Zeltia (C/A, H), BioMarin, Seattle Genetics, Zeltia, Epizyme, Pharmacyclics, Gilead, Celgene (OI), Eli Lilly (ET).

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

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For Further Reading:

Bruce A. Chabner. Breakthrough Drugs and Turtle Soup. ***The Oncologist*** 2015;20:845–846.

This editorial describes the U.S. Food and Drug Administration (FDA) category of Breakthrough Therapy drug, which was established in 2012, fostered by collaboration between legislators, researchers, industry representatives, and cancer research advocates. This category allows the FDA to designate certain lifesaving drugs for expedited review, and it has been successful in speeding the approval of several new drugs.