Building a Better FDA

This March, the physician Scott Gottlieb resigned from his post as commissioner of the FDA to spend more time with his family. Dr Gottlieb's appointment, which lasted less than two years, represented a departure from those of his predecessors because of his work as a venture capitalist in addition to his clinical and academic work. He received a great deal of criticism regarding his industry connections and the potential for these to impact his decision-making. What ended up happening, in my opinion, is that these prior connections provided him with experiences that in some cases made him better at his job.

One of the FDA's roles is to protect public health by regulating potentially harmful commercial products, an area in which industry ties could be very problematic. Demonstrating his adherence to the principles of his job and refusing to bow to industry, Dr Gottlieb pressed for extensive regulations governing tobacco and e-cigarette products. He also addressed the opioid epidemic head-on by confronting the producers. As Dr Gottlieb stated in his first remarks to the FDA staff on May 15, 2017, "FDA always faces big challenges because of where it sits at the intersection of so many critical concerns. By virtue of the fact that people's lives—quite literally—depend on what we do. Patient and consumer protection are at the heart of what we do. And I believe deeply in that fundamental mission of this agency."

In oncology, the FDA is discussed primarily as it relates to drug approvals. In the past, oncologists could prescribe an approved drug for off-label use as long as they could medically justify it to themselves, and there was typically very little pushback from insurance companies. The use of rituximab in CLL serves as an example. When rituximab was approved for use in lymphoma in 1997, it gained widespread use in CLL as both a single agent and in combination with chemotherapy—although it did not receive approval for use in CLL until 2010. In the current payer environment, FDA approvals and compendium listings are almost obligatory in determining coverage for cancer therapy.

Dr Gottlieb's quote speaks to the "big picture" governing the FDA's mission. In reality, the devil is always in the details. Dr Gottlieb worked to help bring more generics to market in an attempt to help control prices. Although the introduction of generic medications plays an important role in cost containment, it potentially "robs" us of the benefits seen with novel drug development. The earnings reaped from sales prior to generics is meant to fund costly research endeavors. In this month's edition of *Clinical Advances in Hematology & Oncology*, we see an example of an agent that has obtained approval in a disease with an incidence perhaps too low to even qualify for an orphan indication. In his interview, Dr Naveen Pemmaraju discusses treatment options for patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN), including the recent approval of tagraxofusp-erzs, a diphtheria toxin–IL-3 fusion protein that predominantly targets CD123-expressing cells. BPDCN is a hematologic neoplasm that is remarkably difficult to study, given its rarity and the difficulty in making a diagnosis. Its high expression of CD123 makes it amenable to being targeted with biologic therapy, as was capitalized on with tagraxofusp-erzs. We need more rationally designed therapeutics, even if they are directed to a small number of patients, because they represent proof of principle. My hope is that the FDA will use its authority to help enable and direct efforts to identify drug targets in rare diseases and produce agents that address them.

A second area that the FDA can become involved in relates to a multitude of agents that work via the same mechanism and are approved for different indications, such as PD-1 inhibitors (the subject of our interview with Dr Michael Postow). We have multiple effective PD-1 inhibitors for a large number of different cancers, and many more are being developed. Unfortunately, the FDA limits competition among comparable agents by requiring new agents to be proven superior to already-approved agents, and indication-specific approvals further prevent approved agents from competing with one another. If the drugs are otherwise equivalent, the only force governing which one to use in a particular patient is reimbursement. Focusing on a drug class such as PD-1 inhibitors could serve as a good testing ground for the FDA to clarify its role, which must balance the twin goals of encouraging drug development through protective indications and controlling prices through competition and generics.

Whether your patient has a rare condition or a common one, effective treatment is essential. Our goal should be to continue to facilitate the development of agents for rare cancers yet avoid burdening the system with large numbers of redundant drugs. As the FDA looks for a new commissioner, this would be an opportune time for it to re-examine its mandate.

Sincerely,

Richard R. Furman, MD