cancernetwork
home of the journal ONCOLOGY

PRACTICE & POLICY

Challenges to the FDA Review Process: Cost Considerations and Long-Term Benefit Benchmarks

Interviewed by Anna Azvolinsky, PhD | February 22, 2012

In this interview we discuss the current challenges of the US Food and Drug Administration (FDA) review process as it relates to oncology therapeutics and upcoming changes to the Prescription Drug User Fee Act (PDUFA). The goal of the FDA review process is to provide an effective but efficient process to allow access to medical products that better the health of the population. I am joined by Christopher-Paul Milne who is the associate director of the Tufts Center for the Study of Drug Development and Kenneth Kaitin, a professor at the Tufts School of Medicine and Director of the Tufts Center for the Study of Drug Development.

Christopher Milne (left) and Kenneth Kaitin (right), Tufts Center for the Study of Drug Development

AUDIO:

Download podcast (mp3)
Subscribe in iTunes

CANCERNETWORK: So let's start with your recent publication—you both **recently published an analysis of the challenges within the FDA review process**[1] for both the reviewers and the drug sponsors. Could you describe some of these challenges?

CHRISTOPHER MILNE: We decided to take a novel approach to this analysis that really hadn't been done, or done rarely—and now we know why, cause it's kind of difficult—to look at the experience that an FDA sponsor or sponsors submitting applications to the FDA can expect in terms of the review divisions. Over the years we had heard drug sponsors had issues with the consistency of their experience with the different review divisions, so we decided to take a look at that. And again what has been one of the challenges is the process of ironing out issues with the process. There have been changes obviously in the types of drugs that are being reviewed, in the types of organizational changes that the FDA has had to go through to deal with them. Our paper took all of those issues into context, and actually, the oncology review division came out very well. So in terms of oncology, I think things are going reasonably well, but certainly challenges remain.

CANCERNETWORK: What are some of the novel challenges that were not on the radar say 5 to 10 years ago. Is there anything new that has come up recently in terms of the process?

CHRISTOPHER MILNE: There are always new things that are coming out. And again, to refer back to our paper, we talked about the process having to improve because we have to get to these content challenges. Things have changed so we have to be able to deal with those in terms of personalized medicine, which is obviously a very big issue for cancer drugs. Patient-centered care and trying to bring in and involve patients in the critical risk-benefit analysis. Again, especially for cancer patients this is critical. The process is trying to involve the patients in these decisions, not only in the review stage, but in the design stage in terms of the end points that particular programs are going to look at. Also the reimbursement issues in terms of how payers establish and look at the value of a particular drug. These are all things that we didn't really see a lot of 5 or 10 years ago. I am sure that Ken has his own views on that.

KENNETH KAITIN: There is no question that the economic environment has changed dramatically over the last few years. The cost consciousness of payers and those that reimburse drugs has put pressure on the FDA. Although the FDA's mandate says that it is not required to look at the cost-effectiveness of individual medications, there is much more of an acceptance of the fact that it is no longer sufficient of developers of products to simply demonstrate safety and efficacy. They have to demonstrate some sort of cost value. And I think, although the FDA is not mandated to review that information they still feel that pressure.

CANCERNETWORK: Could we get your take on that cost measure in terms of oncology because, specifically for oncology drugs, it seems that costs keep rising with new treatments and innovations.

KENNETH KAITIN: There is a lot of activity in the oncology space, and there is no question that across the board oncology leads all other therapeutic areas in terms of research and development activity. In fact, overall worldwide about one-third of all research and development activity is in the oncology area. I think that is stimulated by several factors. One of them being that there is a lot of scientific advances in the oncology area in terms of understanding disease mechanisms and in particular the genetic basis of oncology. There is a lot of benefit within the FDA in terms of review process and accelerated approval, but most significantly, reimbursement has not traditionally been an issue in the oncology space so most manufacturers of oncology products get the reimbursement and coverage for their drugs. Now, I think we are beginning to see that that is slowly eroding and that in fact, more health plans are saying, "We are not just going to blindly reimburse for an oncology product, but we are going to look for some evidence that it is superior to what's already out there or that it does represent value over other types of treatments."

CANCERNETWORK: And part of that value is, let's say, in an overall survival benefit, right? Or a significant extension in life rather than just, say, progression-free survival for a few months?

KENNETH KAITIN: Exactly. And I think the FDA itself is looking at that more closely. Their decision with bevacizumab (Avastin) was certainly a bellwether is some respects about the FDA's current posture on this. They are not going to simply allow drugs to be on the market if they meet some

interim benchmark, but rather they have to increase survival or show long-term benefit.

CANCERNETWORK: So there are new PDUFA V recommendations that are coming, and they seem to support an enhanced transparency of drug development and the review process. Maybe you could describe the types of changes that we can expect for next year?

CHRISTOPHER MILNE: One thing that is very positive—and again, has to do with ironing out these process issues so that we can move on to the more difficult content issues—is putting in this 2 month pre-review period where the clock won't necessarily start in terms of first-cycle action, which I think is a net benefit for both sides. So there is going to be some give and take. More communication before the clock actually starts, and the pressure is on for the FDA to make some sort of commitment within 6 months or 10 months. I think that was kind of a disenfranchisement on both sides so I think that this will help with dealing with some of these particularly thorny new applications or applications for new technologies that are going to be coming up during the reign, if you will, of PDUFA V.

CANCERNETWORK: Do you feel that it is really the increase in the number of new drug applications and new technology innovations that is the bottleneck in the review process?

CHRISTOPHER MILNE: Again, there have been a variety of problems that have been pointed to over the years. But even the FDA itself says, when they talk about their initiatives to improve regulatory science that they themselves admit that they need to enhance their expertise for dealing with these new technologies. Not only personalized medicines but also stem cells and nanotechnology. We are getting a lot of overlap now with drug device combinations as well as new drug delivery vehicles. So there is just an expansion and they are not only going to have to enhance their in-house capacity but I think they are going to have to look to improve, sort of, the policy network so that they can extend their expertise outreach too.

CANCERNETWORK: Do either of you think that PDUFA V will create a more efficient to-market process and allow earlier access to breakthrough therapies, which is especially important for cancer patients?

KENNETH KAITIN: I think going all the way back to the AIDS epidemic era in the late 1980s and early 1990s, there has been a slow move over the last 2 decades to speed access to life saving drugs. I think that the new version of PDUFA is certainly going to have something along those lines as well. Clearly there is going to be an expansion of the FDA's accelerated approval program which many cancer drugs will fall into, allowing for a targeted subpopulation as the basis for the intended clinical effect of the drug. In other words, approval will be based on effect of a biomarker as opposed to an end point.

There is also an expanding emphasis within the agency on pharmacogenomics and biomarker activity so that more of this can be used for making determinations about disease mechanisms and early surrogate end points for drug approval. And hopefully, this will create a success rate for products that enter clinical testing. There is even an emphasis on speeding access to drugs for orphan diseases. There is a program that has been suggested called ULTRA for "Unlocking Lifesaving Treatments for Rare diseases," and it is based on approval based on surrogate end points, but it is worth noting that both the national organization for rare diseases and members of Congress are against this because there really is a need for more clinical evidence in making approval determinations. So I think it really emphasizes that at the end of the day, it is a balance between getting access to drugs quickly and demonstrating, providing some evidence of efficacy for these products. And that is a challenge that the FDA has been struggling with and dealing with essentially since its founding. Balancing that need to provide access to medicines, but at the same time ensuring that the drugs that reach the market represent the best benefit to risk ratio possible.

CANCERNETWORK: Thank you so much both for joining us today.

CHRISTOPHER MILNE: OK, thank you.

KENNETH KAITIN: You're welcome, bye.

References

1. Milne CP, Kaitin KI. FDA review divisions: performance levels and the impact on drug sponsors. Clin Pharmacol Ther. 2012;91:393-404.