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Cancer: Unpronounceable Drugs, Incomprehensible Prices

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GUEST POST WRITTEN BY

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Cancer drug prices keep rising. The industry says this reflects the rising costs of drug development and the business risks they must take when testing new drugs. I think they charge what they think they can get away with, which goes up every year.

	Xalkori	Zykadia
Approval date	26-Aug-11	29-Apr-14
Indication	First line	Second line
Approval required RCT	NO	NO
Number of pivotal trials	2	1
Total sample size	255	163
Proof of concept approval	NO	YES
Time to complete trial	1.5 years	3.5 years
Cost ($2013, at approval)	$11,375	$13,276
Cost ($2013, current)	$11,562	$13,276
Frequency	twice per day	once per day
Companion diagnostic	YES	NO
Outcomes (Xalkori: Study A, Study B; Zykadia: investigator assessment/BIRC assessment)		
ORR	50% (42%, 59%) 61% (52%, 70%)	54.6% (47, 62) 43.6% (36, 52)
Duration of response (months)	9.7 (1.4+, 9.7+) 11.1 (0.9+, 17.7+)	7.4 (5.4, 10.1) 7.1 (5.6, NE)
Toxicities (grades 3/4, measures reported in both labels only)		
Diarrhea	<1%	6%
Nausea	<1%	4%
Vomiting	1%	4%
Abdomional Pain	<1%	2%
Constipation	<1%	0%
Esophageal disorder	1%	1%
Fatigue	2%	5%
Decreased appetite	1%	1%
Rash	0%	0%

Let's consider the two arguments, and how the latest new drug for lung

cancer supports each.

The drug is Zykadia, Novartis' pill for a sub-type of lung cancer caused by a defect in the Alk gene, approved by the FDA in April of this year. The company charges $13,200 per month for it. Its competitor is the older drug Xalkori, Pfizer's pill that has the same mechanism of action and targets the same type of lung cancer. Approved in 2011, it costs $11,500 per month. In other words, Zykadia costs almost $2000 more per month.

The industry talks about the risk that a drug they develop may not work. True, there are large risks, as clinical research often fails to pan out. Novartis took that risk with Zykadia. But Zykadia is a me-too drug. Xalkori, the drug it imitates, was the first of its kind. So whatever Novartis' risk, Pfizer's was greater. Yet Zykadia costs more.

The industry says that clinical research costs a lot of money because the FDA requires large human studies. True. Novartis had to run a trial of 163 patients to convince the FDA about Zykadia. But Pfizer had to run two studies with 255 patients in total. More studies with more patients means Pfizer spent more than Novartis on clinical research. The pricing of the two drugs suggests the opposite.

The industry cites the challenges of bringing new classes of drugs to the market. They have to educate doctors about them and the disease sub-type they target. Here again, Pfizer did the work back when few doctors knew about Alk associated lung cancer. Three years later Novartis enters a mature and educated market.

In the case of these two drugs, figuring out whether a lung cancer patient should get either requires determining if a lung cancer patient even has the defect in the Alk gene. That requires a special genetic test that did not exist commercially a few years ago. So Pfizer (not Novartis) partnered with Abbott Labs to develop the test in tandem with Xalkori. The FDA approved Pfizer's Xalkori and the test, what experts call a companion diagnostic, on the same day. Novartis, well, didn't have to take on that task either.

Differences in clinical outcomes in some cases might explain this pricing paradox, but the two drugs have not been directly compared. Anyway, the FDA says Xalkori, not Zykadia, is the first choice for this subgroup of lung cancer patients. Zykadia is for what experts call 'second line treatment'. The response rates, a measure of the drug's effectiveness, seem about the same. Side effects are hard to compare, but a number of them occur more often with Zykadia – both the minor ones and the life threatening ones.

So, we're left with only one explanation that actually fits the data, and it's mine. The pricing of Zykadia has nothing to do with what it took to bring it to market, it has to do with when it came on the market. Today's tolerance for high drug prices is just greater than it was three years ago and much greater than it was a decade ago when the median price of cancer drugs was about $5,000 per month (in today's dollars).

This rapid rise in prices has put cancer drugs near the top of the list of growth categories in healthcare spending. Nearly $30B on cancer drugs last year, up 9% from the year before. The phenomenon has bled into other diseases more recently. A new drug for cystic fibrosis called Kalydeco costs $26,000 per month. It needs to be taken for life.

Gilead's drug Sovaldi for Hepatitis C is $30,000 a month and $84,000 for a treatment course. One health executive posited that the annual pricetag for Sovaldi could reach $300B because so many people have this infection. That's more than all spending on all drugs in the United States currently. A more realistic number might be between $7B and $12B a year. Even that amount is roughly five times the amount Gilead spends each year on research.

Regardless of the estimate, the pricing of new drugs for cancer and now other common diseases has come unglued from the rationale the industry has long espoused. Instead, pricing is explained by a phenomenon of increasing boldness by the industry against a backdrop of regulators and insurers who have no legal authority to dictate or even propose alternative pricing models.

We are going to have to take some difficult steps, and do so at a time when the healthcare dialogue is polarized not only over the Affordable Care Act's implementation, but over whether or not there is a distinction between rationality and rationing.

One way forward would be to ensure that when me-too drugs come on the market, even high priced ones for life threatening diseases, the manufacturer's have incentives, and insurers have payment mechanisms, that support those companies undercutting their competitors on price in order to gain market share. Right now our system doesn't do that, but that's what a normal market would look like.

Or we could stick with the current expensive model, in which case we should ask the drug industry to connect the dots for us between the societal goals they aim to achieve, the costs they incur, and the profits they should reasonably be earning. They might as well start by explaining why Zykadia costs more than Xalkori.

Dr. Bach is The Director of Memorial Sloan Kettering's Center for Health Policy and Outcomes. His work is regularly featured in major scientific and lay press outlets such as the NEJM, JAMA, and the New York Times. Dr. Bach is a member of the Institute of Medicine's Board on Health Care Services and National Cancer Policy Forum and the Committee on Performance Measurement of the National Committee on Quality Assurance.