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Pursuing Global Equity in Access to Cancer Drugs:

Lessons Learned From the HIV Epidemic

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Enzalutamide, sold under the brand name Xtandi, is a breakthrough, life-extending medication for castration-resistant prostate cancer.[1] Although most nonresected prostate cancers initially respond to chemical or physiological castration, nearly 100% will eventually gain castration resistance, thus falling into the therapeutic niche of enzalutamide. For patients whose cancer is rapidly growing but has not yet metastasized, treatment with enzalutamide has been shown to increase metastasis-free survival times by almost 350%.[1] Among patients whose cancer has already metastasized, enzalutamide is associated with a 33% reduction in mortality compared with placebo.[2] Enzalutamide represents a particular potential benefit to the developing world, where the burden of prostate cancer is increasing precipitously[3] and a greater proportion of cancers are discovered in later stages owing to low screening rates. Unfortunately, the drug is also very expensive. In India, enzalutamide is sold at $65 000 per year, which is half the $130 000 price in the United States, but still represents roughly 40 times the annual income of the average person in India.[4]

In 2016, the IndianPatent Office denied patent protection for enzalutamide, paving the way for production of an affordable generic.[4] In response, the patent holder, the University of California, LosAngeles (UCLA), pursued legal action in the Indian courts on behalf of the licensees Pfizer and Astellas. That action has had the effect of halting generic production while a legal battle ensues. This phenomenon—in which a groundbreaking drug is marketed at inaccessible prices, patent protection is denied, and a decade-long lawsuit results—has played out for numerous medications in India. For example, the patent for the leukemia medication Glivec (imatinib mesylate)was rejected in 2006, and the patent holder, Novartis, was able to delay generic production with a 7-year legal battle.[5]

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This state of affairs, ultimately, does a disservice to patients in the developing world in several ways. Although the tendency of the Indian government to reject the patents for very expensive medications is an understandable effort to improve access, it has the unintended effect of disincentivizing pharmaceutical innovation. More importantly, this model also fails to quickly provide access to these medications for the Indian people because lengthy lawsuits provide a form of de facto patent protection that can last a decade or more. The legal battle over enzalutamide has already delayed generic production for 3 years, during which time nearly 70 000 men in India, and almost 1 million men in low- and middle-income countries, have died of prostate cancer, the vast majority of whom could never afford enzalutamide at its current price.[3]

A better model for the equitable distribution of life-saving medications already exists, and has been used most notably for the treatment of HIV. Between 2000 and 2015, the global percentage of individuals living with HIV infection who received antiretroviral treatment rose from very low levels to over 40%, fueled in large part by tremendous advances in access to treatment in developing nations.[6] That progress would not have been possible without a sliding scale fee system, wherein high-income countries continue to pay tens of thousands annually per patient, while low- and middle-income countries pay a fraction of that cost. That model increases access to medications while still incentivizing drug development. For medication patent holders, early partnerships with generic manufacturers, especially those that include volume guarantees, represent a reliable source of royalty income.[6] Nevertheless, pharmaceutical companies in the developed world appear unlikely to enter into those agreements without pressure from civil society and government. In the case of treatments for HIV infection, the successful implementation of a sliding-scale system could not have been accomplished without the sustained efforts of activists, governmental, and nongovernmental groups.[6]

Public support for increasing access to HIV medications was galvanized by the growing recognition that the burden of HIV was reaching epidemic proportions in the developing world. Yet the epidemiolocal data suggest that cancer in the developing world could now be considered in similarly epidemic terms. At the peak of the HIV epidemic, just under 2 million people died per year from HIV and AIDS.[3] Today 9 million people die annually from cancer, which is forecasted to reach 15 million people by 2040.[3] Considering only individuals age 15 to 49 years, we can expect 1.2 million cancer deaths per year by 2040, which is double the projected rate of HIV mortality in 2040 for the same age group.[3] Furthermore, substantial infrastructure now exists to treat HIV and other infectious diseases in the developing world, but services, access to medications, and funding mechanisms for cancer treatment are very underdeveloped.

The role of public universities and public funds in the development of cancer drugs represents a key point of leverage over pharmaceutical licensing policies. Enzalutamide was developed at UCLA—a public university—using public research funds. Yet that same public university is currently suing the government of India, resulting in a delay in affordable access. Officials at UCLA have resisted calls from activists and student groups to withdraw the institution’s lawsuit, arguing that the university is contractually obligated to protect the interests of the pharmaceutical companies. The current pharmaceutical development

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paradigm brings in huge profits for corporations and their shareholders, as well as for universities themselves; enzalutamide sales reached $1.7 billion US dollars in 2017 alone, and are forecasted to grow precipitously, while the University of California earned a $1.14 billion lump sum for leasing the patent rights. There is little incentive in this model, however, for inventors or pharmaceutical companies to ensure global access to medications, and many new drugs are accessible only to the wealthiest.

When facing public outcry over high drug prices domestically and abroad, pharmaceutical companies and their partners at academic institutions have tended to point to charity programs established to give low- or no-cost access to a set number of individuals. Those programs represent a poor solution because they typically provide medications for only a small fraction of patients, drug shortages are common, and the programs are not reliable for long-term care.[7] Nevertheless, they are favored by drug manufacturers because they often allow the companies to subtract the market value of the donated medications from their tax burden, further limiting the public benefit derived from the invention of medications created using public dollars.[7]

Yet in HIV, we have seen that public universities do have the power to build early generic partnerships for developing countries into their licensing agreements for new drugs. An encouraging example can be found in the case of stavudine, an HIV medication for which social pressure from researchers and students compelled Yale University to renegotiate its patent agreement with Bristol-Myers Squibb, resulting in a 34-fold price reduction in South Africa.[6] The scale-up of HIV medications in the developing world is one of global health's greatest success stories. We must adopt a similar sliding-scale approach—implemented by mobilizing the same kind of broad-based support among students, academicians, policy makers, activists, and patients—to treat the next wave of health challenges in the developing world, especially cancer. Those agreements will not be a panacea; they will do nothing to fix the issue of very high drug prices in developed countries. Nevertheless, such partnerships can bring access for billions of individuals in the developing world, using mechanisms that have already been proven effective in the global health arena.

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