

CANCER IN THE DEVELOPING WORLD

Drugs Are Scarce As Mix of Programs Aims to Ease Access

By Vicki Brower

Anwer was 35 years old and had been having high fevers for about 6 months when he visited Zeba Aziz, M.D., head of oncology at the Allama Iqbal Medical College in Lahore, Pakistan. Aziz diagnosed Anwer with stage IV Hodgkin's lymphoma. By that time, he had five dollars in his pocket. He had exhausted his life savings, had had to sell his wife's jewelry and household items, and had taken a loan on his house and grocery shop to support his family. "The cost of chemotherapy was \$260 per cycle and he needed to get six cycles," said Aziz. "We started treatment from our own funds, and Anwer gradually improved." By the end of chemotherapy, he had gone into complete remission, but Aziz knew that his chances of recurrence were high, and neither he nor the hospital could afford second line therapy.

Stories like Anwer's are common in the developing world. Cancer incidence and mortality are expected to rise steeply in low- and middle-income countries in the next decades, and will overtake heart disease as the world's number one killer, according to a December 2008 report by the World Health Organization's International Agency for Research on Cancer, or IARC. "Five billion people live in countries with low or no access to cancer drugs, a situation much worse than that of other diseases," said Andreas Ullrich, M.D., the health organization's cancer control officer.

For many patients in low-income nations, cancer drugs are unavailable or unaffordable. And in middle-income countries like Brazil, India, and China, basic drugs may be available but targeted treatments are out of reach for most.

A patchwork of groups and programs are working to improve the situation. Local hospitals raise funds for individual patients as do charitable groups, like the Cancer Patients Aid Association in India. Non-governmental organizations (NGOs) and local health authorities work with drug companies to donate drugs or slash prices. Clinical trial networks are testing low-cost treatment strategies. And legal action to provide access to generic drugs is making a dent in the problem. But such scattershot efforts will be insufficient to address the rapidly growing needs, experts say.

NGOs and Donations

Some of the best-established efforts are charitable programs, such as the 22-year old La Mascota twinning program which matches pediatric oncologists in Switzerland and Italy with counterparts in Managua, Nicaragua. The cure rate of leukemia was zero when Franco Cavalli, M.D., head of oncology at the Ospedale San Giovanni in

Bellinzona, Switzerland, and formerly president of the International Union Against Cancer, started the program. It is now 50–60%, he said. "We treat patients with good, older drugs, with excellent results," said Cavalli. The program, which also brings oncologists to Switzerland and Italy for training, costs about \$150,000 to \$200,000 a year and is proof that a lot can be done without spending a lot of money, he said. Its funding comes entirely from private donations.

Another NGO, L'Association Solidarite Chimiotherapy/Union Contre Cancer or SOCHIMIO, was started in 1999 in Cameroon by French-trained oncologist

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Paul Ndom, M.D., chief of medical oncology at Yaound General Hospital. SOCHIMIO, which works with the International Network for Cancer Treatment and Research (INCTR), enables patients to purchase cancer drugs for 50% less than at private pharmacies, which often don't carry these drugs. Membership dues, charitable contributions, and fees for services help reduce prices.

Axios, a partnership started in 1997 to get HIV drugs to a patients in the developing world, now aims to do the same for cancer patients. Working with AstraZeneca and the Ethiopian Ministry of Health, Axios began tackling rising rates of breast cancer in 2005 with few cancer drugs, no mammography, one oncologist and one radiotherapy unit. By early 2009 the Tikur Anbassa hospital in Addis Ababa had become a center of excellence and referral site for women countrywide, according to Joseph Saba, M.D., Axios' founder and CEO. In addition to developing care guidelines, getting new equipment, and training caregivers, the center receives some drug donations from AstraZeneca. Axios plans to extend its efforts to rudimentary chemotherapy for other cancers, also with drug company donations. Over 3,600 patients have now been screened, diagnosed, and treated at the center.

Saba said he has found that it is vital to work with local governments to determine needs and priorities and to lay the foundation for delivering cheaper drugs. This means establishing infrastructure—laboratories, radiotherapy machines, cancer registries, trained technicians. It is then possible to interest drug companies in donating drugs or reducing prices, he said.

Axios now works with three other companies in addition to AstraZeneca. One is Novartis, which established the Glivec (imatinib) International Patient Assistance Program, or GIPAP, which provides drugs to individual patients with chronic myelogenous leukemia or gastrointestinal stromal tumors. Saba estimates that Novartis has supplied imatinib to about 20,000 patients in 85 countries. Another NGO, the Max

Foundation, an American philanthropy focused on blood cancers, administers the program. Axios also works with Pfizer to supply sunitinib (Sutent) to patients with advanced renal cell cancer and gastrointestinal stromal tumors who pay what they can afford for that drug, and with Merck, which has donated 3 million doses of its human papillomavirus vaccine to prevent cervical cancer.

Clinical Trials

On another front, clinical trials are helping to bring drugs to small numbers of patients. The National Cancer Institute in the United States, for instance, has cooperative agreements for trials with Bangladesh for advanced breast cancer and with Morocco for inflammatory breast cancer.

One goal of trials is to determine whether less costly treatments—shorter courses of therapy and/or less expensive drugs—can be effective. Scot Remick, M.D., director of West Virginia University's Mary Babb Randolph Cancer Center, recently reported that low-dose chemotherapy in AIDS-related non-Hodgkin's lymphoma in Ugandan and Kenyan patients showed promise in a small trial. The team chose a low-dose regimen to avoid the myelosuppression seen in conventional doses, important for resource-challenged areas.

"We plan to conduct trials now at a few more sites with oral, reduced-dose chemotherapy and will try to build an African network of sites," said Remick, who heads the International Working Group of the NCI's AIDS Malignancy Consortium.

In Brazil, a middle-income nation, where 80% of citizens are covered by national insurance and basic drugs are available, the higher cost of newer, targeted therapies is the most pressing issue, said Jose Bines, M.D., of Brazil's National Cancer Institute in Rio de Janeiro. Working with the Breast Health Global Initiative (BHGI) at the Fred Hutchinson Cancer Research Center in Seattle, Bines is conducting trials to determine whether treating HER2-positive patients with trastuzumab (Herceptin) in a shorter regimen can yield comparable results to conventional, longer-term treatment.

Generics and Legal Action

Drug companies are also responding to legal pressure by countries like India and Thailand. Under the World Trade Organization's 2001 Doha Declaration, developing nations can produce generic versions of patented drugs under conditions of "extreme emergency" and "urgency." Called compulsory licensing, this provision allows nations to determine what constitutes an emergency. When repeated negotiations with companies recently failed to lower drug prices, these governments issued compulsory licenses for four cancer drugs: letrozole, docetaxel, erlotinib, and imatinib. They had strong support from patient advocacy groups and international NGOs. As of March 2008, Indian advocacy groups had sought compulsory licenses for 20 other drugs. Facing India's threat of generic production of imatinib, Novartis agreed to supply 97% of needy patients gratis instead of charging the normal price of \$20,000 or reducing its price, according to Saba.

With chemotherapy cost one of the most formidable obstacles to care, getting companies to reduce their prices on patented drugs is vital. In general, drug companies have preferred donating drugs to reducing their prices in third-world countries, fearing the pressure that lower prices might create elsewhere, where the same drugs cost more. No company contacted would speak about this issue.

Until relatively recently, the pharmaceutical industry did not view the developing world as a lucrative market and had little incentive to reduce prices except for the threat of generic competition. This may be changing, however, according to IMS Health, an international pharmaceutical forecasting and consulting company in Norwalk, Conn., which tracks drug sales. IMS has reported that with sales projected to decline for the first time in 50 years, doing business in the developing world at lower prices is starting to look more attractive to drug companies. In 2008, sales in developing markets had increased to \$152 billion from \$67.2 billion in 2003. IMS projects it will rise to \$265 billion by 2013.

Legal actions to obtain access to drugs have often followed patient activism. The idea that access to drugs is a human right dates to the late 1990s when Brazilian HIV/AIDS patient groups sought the right to produce antiviral drugs locally when drug companies refused to sufficiently reduce prices. "Using that notion, Brazil has been a model for other [middle-income] nations' efforts to gain access to other essential medicines," said Alessandra Durstine, vice president of regional initiatives and director of Latin America programs at the American

Cancer Society. Many of Brazil's HIV/AIDS strategies are being adapted in other countries to de-stigmatize cancer and gain support for treatment programs, she said.

Patient activism also played a key role in Israel, a middle-income nation like Brazil, where virtually all citizens are covered by national insurance. Originally, it did not cover newer, targeted treatments, but in a few short years, local advocacy groups organized and successfully pressured the Knesset to pay for these drugs, said Benjamin Corn, M.D.,

an oncologist at the Tel Aviv Medical Center.

Durstine and others see a link between such advocacy movements and societal health. "For cancer, there is a correlation between healthcare quality, services, and strength of civil society," said Cristina Parsons Perez, Ph.D., manager of Latin America initiatives at the American Cancer Society. "There is a lot of work to be done to strengthen civil society and push cancer treatment to the top of national agendas."

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