Development of a Breast Cancer Treatment Program in Port-au-Prince, Haiti: Experiences From the Field

Purpose The nonprofit Project Medishare launched a breast cancer treatment program in Port-au-Prince in July 2013 to address the demand for breast cancer care in Haiti. We outline the development of the program, highlight specific challenges, and discuss key considerations for others working in global oncology.

Methods We reflected on our experiences in the key areas of developing partnerships, building laboratory capacity, conducting medical training, using treatment algorithms, and ensuring access to safe, low-cost chemotherapy drugs. We also critically reviewed our costs and quality measures.

Results The program has treated a total of 139 patients with breast cancer with strong adherence to treatment regimens in 85% of patients. In 273 chemotherapy administrations, no serious exposure or adverse safety events were reported by staff. The mortality rate for 94 patients for whom we have complete data was 24% with a median survival time of 53 months. Our outcome data were likely influenced by stage at presentation, with more than half of patients presenting more than 12 months after first noticing a tumor. Future efforts will therefore focus on continuing to improve the level of care, while working with local partners to spread awareness, increase screening, and get more women into care earlier in the course of their disease.

Conclusion Our experiences may inform others working to implement protocol-based cancer treatment programs in resource-poor settings and can provide valuable lessons learned for future global oncology efforts.

INTRODUCTION
Breast cancer is the leading cause of cancer mortality among women and was responsible for 521,000 deaths worldwide in 2012 alone.1 Over the last 5 years, breast cancer incidence has increased by nearly 20%, with disproportionate growth in low-income countries.2,3 Breast cancer mortality rates are highest in low- and middle-income countries (LMICs), in which rapid socioeconomic changes have led to an increase in breast cancer diagnosis with comparatively little promotion of early detection and affordable treatment.4 In fact, the age-standardized mortality rates from breast cancer in developing nations are three times those in developed countries.5,6 These trends highlight the disproportionate growth and impact of breast cancer in the developing world and emphasize the need for a commensurate growth in treatment programs.

Like many other LMICs, Haiti struggles with the growing burden of breast cancer while lacking the health care infrastructure required to identify, diagnose, and treat the disease. Treatment options that do exist are often prohibitively expensive, and care is often fragmented because of the absence of centralized and coordinated health services.

In an effort to expand accessibility to treatment, the nonprofit Project Medishare in partnership with Hospital Bernard Mevs and the University of Florida launched a breast cancer treatment program in July 2013. Through an innovative mix of private, public, and research-related funds, the Project Medishare breast cancer initiative has provided care to 139 patients with breast cancer in nearly 2 years, becoming an integral part of the oncology community in Port-au-Prince. Project Medishare has worked in Haiti since 1994 and has partnered with Hospital Bernard Mevs since 2010 to provide...
trauma and critical care services, making the location an ideal place to implement a program involving chemotherapy. Before the implementation of this program, neither Project Medishare nor Hospital Bernard Mevs provided any kind of breast cancer care apart from mastectomies. The program has also helped provide the necessary infrastructure to begin collecting data on the epidemiologic profile and tumor biology of breast cancer in Haiti.7

In this article, we outline the key steps in the implementation of Project Medishare’s breast cancer treatment program: building and maintaining partnerships with the local oncology community; securing laboratory services abroad while building local laboratory capacity; using experts in oncology, nursing, and research to establish treatment algorithms and train local staff; and purchasing and importing safe, effective, low-cost chemotherapy and hormone therapy. We also discuss costs and other practical barriers to treatment, and we critically reflect on our own objective performance as a program.

METHODS

Building Partnerships

Project Medishare’s breast cancer treatment program focused on developing strong local partnerships, which were crucial for the program to gain acceptance in the local medical community. Before launching the project, Project Medishare physicians and organizers met with clinicians and administrators from the Haitian Ministry of Health and the oncology program at the University Hospital of Haiti to discuss the scope of the program and request their input. Project directors asked them to review and approve all of the program’s initial patient staging and treatment protocols before they were submitted to the Haitian Ministry of Health for governmental approval. Project Medishare also sent patients to local health care providers for verification of the clinical staging in an effort to ensure quality control in the new program.

In addition, Project Medishare partnered with the Support Group Against Cancer to offer counseling and social services to the program’s patients and help raise awareness of the program through local television and radio campaigns. This partnership increased the program’s credibility in Port-au-Prince among both patients and providers and helped reach more patients than would otherwise have been possible.

Pathology and Laboratory Capacity

The challenge of limited pathology services in Haiti is being addressed via a step-wise approach. Because the immunohistochemical studies for estrogen receptor (ER), progesterone receptor, and human epidermal growth factor receptor 2 biomarkers cannot currently be performed at any laboratory in Haiti, it was necessary to turn to international pathology laboratories. As an initial stopgap measure, tissues from breast biopsy and excision specimens were placed in formalin and sent directly to partner laboratories in the United States for processing, paraffin embedding, and staining. The specimens were hand carried at regular intervals via travelers from Port-au-Prince to Florida, which requires no special importation documentation.

Specimens were previously collected via open biopsy, but core needle biopsies were implemented as part of the program launch. Four Haitian doctors were trained in obtaining samples via three passes with core needle biopsy, typically using 16- to 20-gauge needles. After finding a high false-negative rate in tumors that were clinically apparent cancer, the program switched to six quality samples with the core needle and increased the needle gauge to 14 or 16.

To set up a permanent and reliable system for ascertaining the pathology, Project Medishare partnered with a local pathology laboratory in Haiti to process the formalin-fixed specimens into paraffin-embedded blocks. All samples were then evaluated by breast pathologists in the United States, and all invasive carcinomas were graded according to the Nottingham Histologic Score system. Electronic copies of pathology reports were sent to the treating physicians by e-mail. All specimens with ductal carcinoma in situ or invasive carcinoma of the breast were assayed for ER, progesterone receptor, and human epidermal growth factor receptor 2.8

In conjunction with the Haitian Ministry of Health and several US universities, a reference laboratory will soon be established in Port-au-Prince that can perform immunohistochemistry for ER status for all specimens originating in Haiti, and two new pathology laboratories distributed geographically throughout Haiti will open in the next 12 months.

Clinical Training and Treatment Algorithms

Another critical step in the development of the program was training clinicians in cancer care. At the inception of the program, there were only two
trained subspecialty hematologists in Haiti and no medical oncologists. Chemotherapy options for postmastectomy patients in Port-au-Prince at that time were limited to private clinics and University Hospital of Haiti, where patients had to purchase chemotherapy at high prices and often received substandard chemotherapy regimens such as cyclophosphamide/doxorubicin/fluorouracil. By using educational models similar to those developed for addressing the HIV/AIDS epidemic in sub-Saharan Africa, local health care providers were trained to use curative chemotherapy and palliative care.9 Training at the Project Medishare oncology program was initiated by a US board-certified internist who had previous international experience helping to develop the national cancer treatment program in Rwanda.

Because gynecologists in Haiti were typically the first medical interface for patients with breast cancer, they were selected as the clinicians for the Project Medishare breast cancer treatment program. They received 40 hours of intensive classroom education on breast cancer pathophysiology, presentation, diagnosis, and treatment. In addition, they were trained to use chemotherapy treatment algorithms and were required to discuss all patients individually with the program director for the first 6 weeks of clinical application.

The development and use of treatment algorithms was a crucial part of the oncology training. As mentioned previously, the Project Medishare team worked in conjunction with oncologists from the University of Florida and the University of Miami to develop treatment protocols specifically for Haiti. The protocols included basic staging guidelines, timing of surgical interventions, chemotherapy regimens, hormonal therapy, and radiotherapy recommendations. The two intravenous chemotherapy regimens are four to six cycles of docetaxel/cyclophosphamide or four cycles of doxorubicin/cyclophosphamide followed by four cycles of paclitaxel given once every 3 weeks. These regimens are standard regimens in the United States and do not require growth factor support. Of note, dose-dense scheduling of chemotherapy is not possible in Haiti because of the unavailability of growth factor support, and weekly dosing with paclitaxel is impractical because of significant issues with transportation. Trastuzumab is also not available because of its prohibitive cost. Tamoxifen and letrozole are available and were used by the program in the neoadjuvant, adjuvant, and metastatic settings. The exact algorithm changed depending on the stage, degree of lymphatic invasion, and hormone sensitivity.

Mastectomies and other surgeries, such as bilateral salpingo-oophorectomies for premenopausal women with ER-positive, advanced-stage tumors, were performed by surgeons at Hospital Bernard Mevis. Surgical and anesthesia capacity are less frequently barriers to basic breast cancer care in urban hospitals in developing countries than chemotherapy and other medical treatments. Nevertheless, it is important to note that existing surgical capacity at Hospital Bernard Mevis was key to the rapid scaling up of the Project Medishare breast cancer treatment program.10

Unfortunately, radiotherapy is not available in Haiti, making it impossible to offer breast conservation for those without the resources to pay $2,000 for private treatment in the neighboring Dominican Republic. Moreover, 80% of the women treated by the program in the first 2 years were not candidates for breast conservation therapy because of tumor size, chest wall invasion, skin ulcerations, or the presence of metastasis.7 Nonetheless, radiotherapy was recommended as part of the treatment algorithm for all women with stage IIB to IIIC disease after chemotherapy and mastectomy.11 Going forward, the Haitian government has articulated a long-term plan to build a radiotherapy center in Haiti, and Project Medishare continues to rely on close contacts in Dominican Republic radiotherapy centers to help direct clinical care decisions for qualifying patients.

For breast cancer cases that fall outside the established treatment algorithms, breast oncologists from the University of Florida advise the team on the ground via e-mail and telephone. Roughly 10% of patients required consultation from these oncologists, with the remainder being managed by the Haitian gynecologists alone. Discussion regarding these patients and consistent communication with the University of Florida breast oncologists provided Haitian clinicians with an ongoing education in cancer care.

Nursing protocols were developed for mixing and administering chemotherapy. Nurses in Project Medishare were trained in chemotherapy mixing, administration, and extravasation protocols by Haitian pharmacologists and Haitian-American chemotherapy infusion nurses from Miami. The Haitian compounding pharmacist provided oversight in mixing the chemotherapy to ensure staff and patient safety. After the initial week-long training, the nurses received continued training on a regular basis from visiting infusion nurses who confirmed that the quality of care remained at a consistently high level. All staff wear personal protective equipment when mixing and administering
chemotherapy, ensuring a safe environment for the nurses, pharmacists, and patients.

After 12 months of experience, the Project Medishare nurses designed and implemented an in-service training program for the chemotherapy nurses at the public University Hospital of Haiti to raise the level of care and improve patient and staff safety at the country’s largest public hospital. With trained nurses at the two sites, the “train the trainer” model has proved useful in the Haitian context, although periodic quality control by US-based nurses still occurs at present.

All providers and staff were trained to document clinical encounters on an electronic record system that was principally online but that could be used offline during the frequent power outages. Wireless USB jump drive modems provided Internet via mobile networks. In addition to adapting the treatment protocols to local resources, Project Medishare also adapted consent forms, including those for biopsy and receiving chemotherapy treatments, to adhere to local standards.

Chemotherapy Supply

A critical challenge to the development of the Project Medishare oncology program in Haiti was the inadequate supply of chemotherapy drugs. Project Medishare initially attempted to source chemotherapy drugs locally from each of three pharmacies in Port-au-Prince, but the prices were prohibitively high, selection was small, and quantities were limited and subject to frequent stock outages. Generic drugs were purchased from a manufacturer (Angel Biogenics, Gujarat, India) that had WHO approval. Oncologists from the University of Florida and the University of Miami, in consultation with the team in Haiti, selected drug regimens that were easy to administer, did not require growth factor support, and required the fewest patient visits possible. We estimated the quantities of each drug needed through demand forecasting from partners, based on the local population needs and the financial resources available.

As often happens in countries with poor infrastructure, the imported medications were significantly delayed in customs. The maximum customs delay was 6 weeks, which delayed patients receiving chemotherapy by as much as 1 month. During this time, Project Medishare was again unsuccessful in its attempt to purchase drugs locally. The nursing staff implemented an intensive inventory system at Project Medishare to track usage of the different drugs and ensure timely reordering with the par level set at 3 months, allowing for a buffer of 1 month for customs delays. The local design and ownership of the inventory tracking by the nursing staff contributed to the success of the system and helped avoid stock outs of medications in the second year of the program.

A significant proportion of patients with breast cancer in Haiti do not finish their prescribed chemotherapy sessions because of drug costs, and many more are forced to delay treatment while saving money for future sessions. Because Project Medishare purchased generic drugs in bulk, our patients’ costs were considerably lower than the costs for patients at the University Hospital of Haiti, who purchased drugs individually from private pharmacies. Project Medishare now partners with the University Hospital of Haiti and the Support Group Against Cancer (Groupe de Support Contre le Cancer) to offer chemotherapy to the poorer patients on a sliding scale according to means, thereby increasing access to care. Patients are able to receive the generic drugs from the Project Medishare program, occasionally with financial assistance from Support Group Against Cancer, and bring those drugs to the public University Hospital to be infused. Through this partnership, the University Hospital of Haiti has continued to treat patients, demonstrating the capacity of the public health care system to effectively treat patients when the necessary resources are available.

Costs

The average cost of treatment per patient was initially calculated to be $1,500 per patient: $550 for mastectomy, $450 for chemotherapy, and $500 for the combined cost of pathology, laboratory, radiology, and operating costs. In practice, the cost per patient to Project Medishare was approximately $750 when dividing the total amount of money spent by the total number of patients treated. The cost was lower because of less care given per patient as a result of advanced disease or untimely death. Mastectomy was performed in only 70% of patients (DeGennaro et al, manuscript submitted for publication). The remaining 30% of patients presented after they had already had a mastectomy at another institution or with stage IV disease, which did not clinically warrant a mastectomy. In addition, the curative chemotherapy regimens included more expensive drugs such as docetaxel and paclitaxel than the palliative regimens, which consisted of monotherapy with less expensive agents such as doxorubicin or cyclophosphamide. We plan to calculate the cost-effectiveness of the program as we go forward.
The program has enrolled 139 patients and offers care at an average cost of $750 per patient. However, outcome data are limited and are strongly influenced by poor predictors at time of presentation. For example, the initial data from the first year of our program show that 80% of patients presented with stage III to IV disease, and 50% had a tumor in their breast for 12 months at the time of presentation. The mortality rate for the 94 patients for whom we have complete data, including those who had been diagnosed before the start of the program, was 24% with median survival time of 53 months. Barriers to seeking clinical diagnosis and treatment for breast cancer in LMICs and in Haiti specifically have previously been investigated. Failure to recognize that a lump in the breast might signal illness and fear of the cost of treatment were found to be the most significant contributors to delays in seeking care.12,13

For women receiving intravenous chemotherapy, adherence to 21-day administration intervals for the entire four- to eight-cycle regimen is recommended to all patients.14,15 Traditionally, this has been difficult in Haiti. In efforts to achieve the best possible outcomes, clinic staff were taught to emphasize the importance of timely administration of chemotherapy cycles, and patients were provided with social services, including transportation costs and nutritional support. A retrospective review of our data shows that more than 77% of chemotherapy cycles were delivered on time and 85% were delivered within 1 day of the desired treatment date. All women who received either curative or palliative intravenous chemotherapy and had completed at least two cycles at the time of the investigation were included. Results can be seen in Table 1.

The reasons for treatment delay were reviewed in hopes of finding modifiable factors. Medical reasons for delaying chemotherapy included fever, hemoglobin below 7 g/dL, and an absolute neutrophil count below 1,000. Patients who presented with these adverse events were given treatment for the symptoms, and chemotherapy was resumed as soon as it was safe to do so. Supply-chain delays in importing chemotherapy drugs and/or procuring chemotherapy drugs locally led to more significant delays.

A safety review showed that in 273 chemotherapy administrations, there were no instances of extravasation. There were three instances of chemotherapy drugs being spilled on the floor, which were addressed with preapproved clean-up protocols. There were seven allergic reactions, all to docetaxel, and those quickly went to zero after implementing prednisone pretreatment and administering dexamethasone no more than 1 hour before chemotherapy initiation.

CONCLUSION

Strong local partnerships, significant commitment by the staff of Project Medishare, collaboration with oncology institutions and laboratories abroad, and lessons learned from similar initiatives all helped to make the breast cancer treatment program possible. Despite these efforts, there is significant room for improvement. Most importantly, an increase in cancer awareness nationally is needed to create a shift in cancer stage at presentation and an increase in the cure rate.7 Project Medishare is working with the Haitian Ministry of Health to expand access to pathology, surgery, and chemotherapy for breast cancer nationally by using these same techniques. Project Medishare staff are hopeful that this cancer treatment program will demonstrate new possibilities for hospitals in resource-poor settings and that our lessons learned highlight important considerations and solutions for advancing cancer care in the developing world.

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Table 1 – Rates of Treatment Schedule Adherence

| Dosing Schedule                  | No. of IV Chemotherapy Doses Administered (%) (N = 273) |
|----------------------------------|--------------------------------------------------------|
| Given every 21 days exactly      | 211 (77.3)                                              |
| Given every 21 days ± 1 day      | 234 (85.8)                                              |

NOTE. Total No. of patients for this analysis was 58.
Abbreviation: IV, intravenous.
AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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