

Translating knowledge into action

INCTR Report

April 2005



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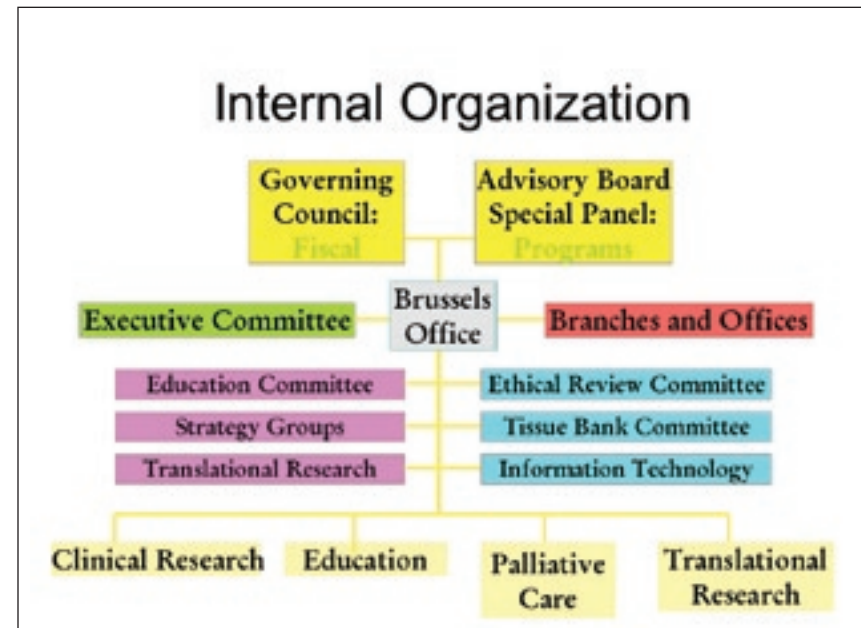
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THE INCTR ORGANIZATION PROVIDES A NETWORK OF EXPERTS WORKING TOGETHER TO BUILD CAPACITY FOR CANCER TREATMENT AND RESEARCH IN DEVELOPING COUNTRIES.

Improving Cancer Control in Countries with Limited Resources

It is just five years since INCTR opened its offices in Brussels, in space kindly provided by the Institute Pasteur. In April 2000, INCTR had a Governing Council and a staff of three. Two strategy group meetings, dealing with childhood cancers, had taken place at its Inaugural Meeting (held in Antwerp in November 1999), but there were no Associate Members or committees and INCTR programs existed only as concepts. In the ensuing years, the organization has grown rapidly. It now has eight employees in Brussels, branches and offices in nine countries, several volunteers who support the administrative staff, and access to a broad range of health and other professionals who give their precious time and knowledge to serve on INCTR committees or work on INCTR projects. Four programmatic areas have been established - Clinical Research, Education, Translational Research and Palliative Care - and there are presently almost 220 Associate Members, (corporate, institutional or organizational, and individual) who support the organization in various ways, including through partnerships in specific areas of endeavor and/or by their financial contributions. There is an Advisory Board, one element of which provides scientific review of INCTR projects, and the other, the Special Panel, comprised of distinguished oncologists and pathologists from developing countries, provides more general advice and

selects INCTR awardees. There are committees dealing with diverse areas such as ethics, education, translational research, tissue banking, corporate collaboration, funding and information technology, and there are eight disease-specific strategy groups. A healthy slate of projects and activities are underway and already, approximately 20 articles have been published in the medical literature. INCTR's newsletter is read around the world, and INCTR is often asked to participate in the activities of major national or international organizations when they involve cancer in developing countries. In addition to its core funding from the National Cancer Institute (NCI), substantially more than \$1.5 million has been raised in grants, contracts, donations and sponsorships. Each year, INCTR holds an annual meeting for health professionals, predominantly from developing countries. There were approximately 400 participants at the Annual Meeting in Cairo in 2004 and future meetings will be held in India and Brazil. One might say that we have made a beginning.

But success should not be measured in terms of programs and committees established, in meetings held, in projects actively underway, or even in publications, although adding to the global knowledge base as well as to the infrastructure and human resources devoted to cancer in developing countries are essential

Our Mission: The INCTR is dedicated to helping to build capacity for cancer treatment and research in developing countries, and thereby to create a foundation on which to build strategies designed to lessen the suffering, limit the number of lives lost, and promote the highest quality of life for children and adults with cancer in these countries, and to increase the quantity and quality of cancer research throughout the world.

to the achievement of INCTR's mission. The ultimate measure of success is the number of cancers prevented or cured, and the number of cancer patients - and their families - whose suffering has been relieved. INCTR has made a significant start in this direction, with clear outcomes of this kind being documented in its ongoing projects. These include cervical cancer screening, in collaboration with the International Agency for Research in Cancer (IARC), early detection of retinoblastoma, treatment protocols in acute lymphoblastic leukemia, Burkitt's lymphoma and osteosarcoma as well as information-gathering projects on which to base future strategies, such as surveys of the characteristics and treatment of breast cancer and the reasons for late presentation of retinoblastoma. Treatment protocols for advanced breast cancer, cervical cancer and retinoblastoma, as well as lymphoma, are in the planning phases. All of these studies are managed by INCTR's Clinical Trials Office, directed by Melissa Adde.

The Educational Program, directed by Ama Rohatiner, has organized a variety of workshops, training courses and symposia. Visiting Experts have spent time in institutions in developing countries, several exchange fellowships have taken place, and a larger agenda is emerging with respect to formal professional education from medical students to oncology nurses and oncologists. Efforts are made to ensure that educational programs, as far as possible, take place in the developing countries themselves.

The Palliative Care Program, directed by Stuart Brown, has been functioning for only a year and a half, but already a coordinated program involving several centers and a home hospice component has been established in Nepal, and plans are being made to develop similar programs in other countries.

The Translational Research Program, directed by Kishor Bhatia, and based within the Research Center of the King Faisal Specialist Hospital, has been highly productive, particularly with regard to studying molecular genetic differences in acute lymphoblastic leukemia in India, and identifying genetic polymorphisms associated with an increased risk for cancer, or treatment outcome.

INCTR has now held four Annual Meetings, and given six awards to persons who have made major contributions to cancer in developing countries. In the

course of planning its projects and activities, numerous committee and strategy group meetings have taken place, in Brussels and in many other countries.

In five years, INCTR has acquired a past. What of the future? With so much enthusiastic support of the concept of INCTR and increasing interest in cancer in developing countries, it seems likely that the organization will continue to grow from strength to strength. INCTR is grateful to NCI for making the vision of INCTR a reality,

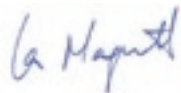
but its future will depend upon the sustainability and size of its funding base and of the nucleus of staff, including health professionals, necessary to stimulate and manage INCTR's activities and projects. It is essential to continue to build credibility and to sustain the progress made if funding bodies and donors are to be convinced that the organization is worthy of support. To be successful, INCTR must function not only as an institution but as a community - a far-flung community of dedicated professionals and volunteers, many of whom work in circumstances that most of their colleagues in more affluent nations cannot even imagine. It must continue to build a multi-dimensional network that includes not only doctors and nurses and allied health professionals, but also advocacy and support organizations, government departments, governmental and non-governmental agencies, academic and professional bodies, corporations, and even the friends and relatives of cancer patients and cancer survivors themselves. And INCTR must ensure that its efforts, and those of its collaborators, remain firmly rooted in the scientific method, for there is no room for assumption in dealing with as devious and malign an enemy as cancer. Attempting to improve the resources available for prevention, diagnosis, treatment and palliative care,



IAN MAGRATH, PRESIDENT, INCTR

and to overcome problems caused by the maldistribution of resources, is central to INCTR's strategy - for without a significant increase in the capacity for cancer control - human, financial and physical - the continuously increasing global burden of cancer, that is shifting more and more to the developing countries, will not only result in greater human misery resulting directly from cancer, but will also create a steadily enlarging economic burden. Conversely, creating more effective means of controlling cancer will become an increasingly important element of economic development.

Cancer is a global problem which will be best overcome by using the global laboratory to understand better the factors which predispose to cancer, and to determine optimal approaches to its prevention and treatment. In this respect, the variations in cancer patterns throughout the world provide both valuable scientific opportunities to understand more about cancer, while at the same time requiring cancer control programs to be tailored to the patterns observed, to the resources available and to relevant cultural differences. Cancer is a deadly set of diseases, but many can be prevented or, particularly when detected early, effectively treated. It is essential that the world unites against this common foe, as is increasingly the case for other global problems such as environmental pollution, climate change, terrorism and nuclear proliferation. Whilst we can be under no illusions with respect to the size and complexity of the problem, these serve only to emphasize the need for a multidimensional, cooperative approach, and one which at times may overlap into more general areas of disease prevention and control. This report demonstrates that by working together we can make a difference. We must now move to consolidate the accomplishments of the last five years and to develop a more sustainable funding base, such that the organization can continue to grow, enabling it to steadily increase its contribution to the reduction of suffering and death caused by cancer.



Ian Magrath
President, INCTR

Cancer in Women and Children

INCTR is particularly focused on cancers in women and children – in part because of the particular vulnerability of these populations in developing countries, in part because of the critical role of women in the family, and of children to the future of developing countries, and in part because there are effective methods for controlling these cancers. Breast and uterine cervical cancer alone accounted for almost one million of the close to



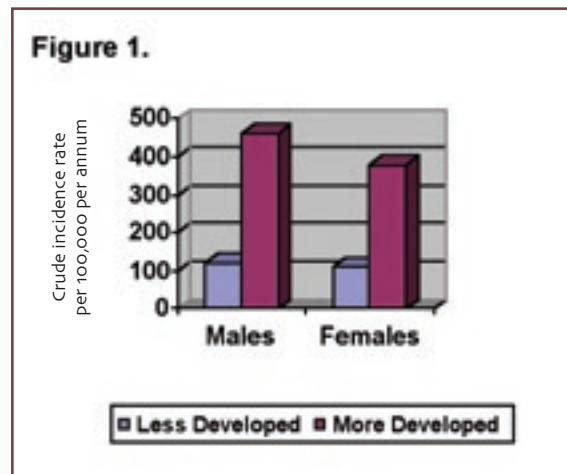
GLOBAL DISTRIBUTION OF CANCER OF THE UTERINE CERVIX, CRUDE INCIDENCE RATE, FROM GLOBOCAN, IARC, 2002, SHOWING PEAK INCIDENCE RATES IN LATIN AMERICA AND INDIA.

six million cancer cases estimated to have occurred in developing countries in 2002, while the high proportion of children in the populations of developing countries ensured that their approximately 134,000 cases of

childhood cancer (age 0-14 years) comprised over 80% of all children with cancer in the world. Both cervical and breast cancer can be cured if detected early. Inexpensive but sensitive screening methods for pre-cancerous lesions are available for cervical cancer, and effective vaccines for Human Papilloma Virus, likely to prevent cervical and other cancers, are in advanced stages of testing. Although rare, childhood cancer has been shown to be highly curable in affluent countries and a child cured of cancer has an entire, potentially highly productive life to lead.

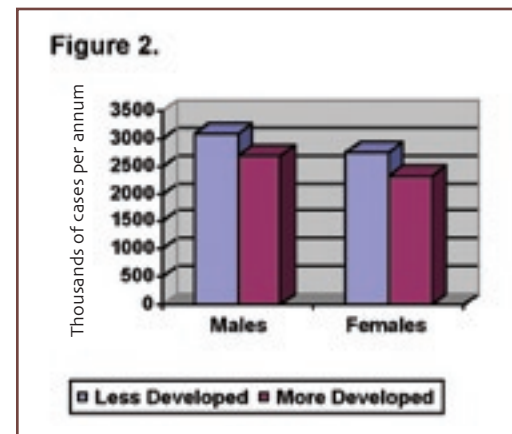
The Growing Cancer Burden in Developing Countries

Communicable diseases have for long been the predominant health problem in developing countries and this remains the case in the poorest countries (such as Africa, where the AIDS epidemic has further tipped the balance), and the most vulnerable populations in low and middle income countries. However, although the burden of infectious disease is high, slightly more people die of cancer in developing countries each year than die of tuberculosis, AIDS and malaria combined. The incidence of cancer overall is markedly lower in developing countries than in affluent countries (see Figure



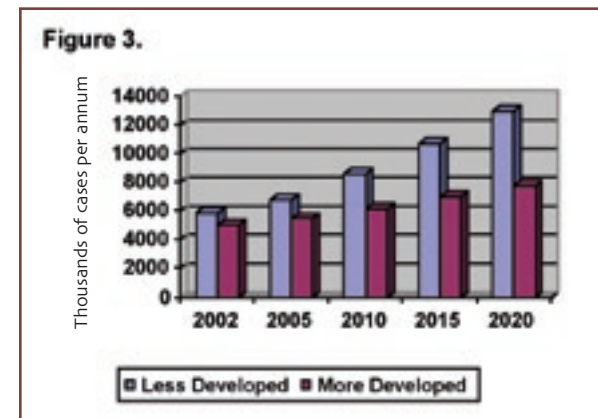
1 for 2002 estimates), largely because of differences in the diet, and smoking rates. However, since over 80% of the world's people live in developing countries, the latter account for more than half of the global cancer burden (see Figure 2 for 2002 estimates). Smoking

rates are at last beginning to decline in many affluent countries, but are increasing in the poorer nations. This, coupled to the fact that population growth is largely confined to developing countries, whose populations are aging as their socioeconomic circumstances improve, means that the global cancer burden will fall progressively upon the countries least able to deal with it (Figure 3). Clearly, the time to act, in order to lessen the impact of this avoidable catastrophe, is now!



Unfortunately, developing countries have limited human capital, facilities, equipment, and drugs, and although the design and implementation of cancer control programs has been advocated by the World Health Organization for some years, and a resolution to this effect is likely to be adopted by the World

Health Assembly in 2005, the effective conduct of such programs will not be possible without major improvements in the available resources for cancer control. Approaches will also need to be developed to counteract the negative impact on capacity building that results from the loss of the most highly trained and educated members of such societies to the more economically privileged countries and to reduce the disparities in health service delivery that exist throughout the world, but which have a much greater impact in countries where a high proportion of the population is already living below the poverty line.



Clinical Research

Because the patterns of cancer, the available resources and the cultural settings differ greatly around the world, the development of effective strategies for cancer control in developing countries must be based upon valid evidence obtained from clinical research studies conducted in those countries. Such studies will generally be closely linked to the provision of health care, so that benefits to patients begin to accrue immediately. Moreover, the requirement for relevant knowledge, skills and discipline in the conduct of clinical research (e.g., accurate diagnosis, effective delivery of care and patient support, and the collection of high quality data) requires that such studies are associated with education and performance monitoring. Thus, they provide highly effective “on-the-job” training in addition to a foundation of knowledge on which future studies or policies can be based. INCTR is collaborating with institutions in many countries in Latin America, Africa and Asia on research studies that are providing valuable disease-specific information while building effective prevention and treatment programs. These studies are focused predominantly on cancer



in women and children as well as leukemias and lymphomas, consistent with its policy of giving the highest priority to preventable or curable cancers.

The Clinical Trials Office coordinates the activities of the Clinical Research Program, including the organization of INCTR Strategy Group meetings, the management of clinical research studies and the administration of the INCTR Ethical Review Committee. A major part of its work is the provision of data management services and education and training in all aspects of clinical research.

Strategy Groups

Strategy groups, comprised of investigators from developing countries working closely with INCTR staff, shape clinical research programs as well as promote public and professional awareness about specific cancers. At present there are strategy groups devoted to acute lymphoblastic leukemia, African Burkitt’s lymphoma, breast cancer, uterine cervical cancer, lymphoma, osteosarcoma and retinoblastoma. Members of these strategy groups represent institutions in Argentina, Peru, Brazil, Bolivia, Mexico, Nigeria, Kenya, Tanzania, Uganda, Egypt, Kuwait, Saudi Arabia, Pakistan, India, Nepal, China, Philippines and Vietnam. It is anticipated that the number of countries and institutions participating in strategy group activities, as well as the number of strategy groups, will expand in the coming years, although the focus in 2005 will be to complete the design of several protocols currently in the planning stages. Ongoing and planned clinical research studies are described in the context of the activities and programs of each strategy group.

THE LEUKEMIA STUDY GROUP OF INDIA MET IN DELHI AT ONE OF ITS EARLY PLANNING SESSIONS (APRIL 2001).

Breast Cancer

Breast cancer is the most common cancer in women worldwide. Unfortunately, there is relatively little published information about the disease in developing countries. INCTR's Breast Cancer Strategy Group has therefore decided to conduct a retrospective survey of breast cancer patients seen in members' institutions. The survey captures hospital registry information about the total numbers of patients with breast cancer seen, and patient data, including basic demographic information, social, reproductive and family history, risk factors such as pathological features, disease stage, treatment administered and treatment outcome. This survey will also provide information on the effectiveness of follow-up. Data collection is already underway in institutions in India and Pakistan and will begin in 2005 in Egypt and Peru. It will be expanded to institutions in other countries – Argentina, Mexico, Tanzania, Kuwait and Nepal after a preliminary analysis of the data.

In addition to the survey, the group is in the process of writing a treatment protocol for patients with locally advanced breast cancer in order to evaluate the role of neoadjuvant chemotherapy in these patients. It is anticipated that the protocol will be implemented towards the end of 2005.

African Burkitt's Lymphoma

A major goal of the African Burkitt's Lymphoma Strategy Group is to try to improve treatment results and patient follow-up through the conduct of a standard chemotherapy protocol, feasible in equatorial African countries. The

protocol entitled "The Treatment and Characterization of Burkitt's Lymphoma in Africa" has been approved by both the INCTR Ethical Review Committee and by four institutions in three African countries – Kenya, Nigeria and Tanzania. It is estimated



BEFORE TREATMENT.



AFTER TREATMENT.



INCTR STAFF AND AFRICAN COLLEAGUES MEET AT THE OCEAN ROAD CANCER CENTER IN TANZANIA TO IMPLEMENT THE BURKITT'S LYMPHOMA PROJECT.

that the primary treatment regimen (first-line treatment) would cost approximately \$150 to \$200 per patient – a tiny fraction of the treatment cost in affluent countries. In August 2004, a training meeting on protocol and data management procedures was held for the investigators and data managers involved in the care of these patients. Patient enrollment began in late 2004. It is anticipated that 200 children will be treated in this study each year.

Two new studies in Burkitt's lymphoma are in development. The first is an evaluation of liposomal ara-C for intrathecal use in patients with recurrent disease in the central nervous system. SkyePharma has generously agreed to supply the drug free of charge. The second study is a Phase II study of Fluoxetine (Prozac), which is active against Burkitt's lymphoma cell lines at concentrations known to be achievable with conventional doses. Investigators in the strategy group believe the effectiveness of this treatment could be investigated in the African setting, in patients in whom all other treatment has failed.

Cervical Cancer

An important goal of INCTR is to expand population coverage for the detection and treatment of CIN (cervical intraepithelial neoplasia) i.e., benign lesions that can evolve into invasive cervical cancer. Demonstration programs using well-established approaches to the detection and treatment of CIN are planned for small selected populations located in close proximity to regional cancer centers that have existing programs for cervical cancer detection. Existing health care infrastructure such as smaller health centers or their equivalents, family practitioners and general hospitals will be used as screening points. Regional cancer centers will provide training and coordination, as well as treatment for women detected with invasive cancer. Success of the screening programs will be measured by the number of women screened expressed as a fraction of women at risk, CIN/cancer detection rates and treatment rates. Professional education about cancer prevention will be provided by the regional cancer centers for medical students, nurses, health assistants, gynecologists and family practitioners. Community involvement will be widened through public awareness campaigns and attempts will be made to enlist local and regional governmental support.

INCTR presently supports demonstration programs for early cervical cancer detection and treatment that are located in Nepal and Tanzania in collaboration with the International Agency for Research on Cancer. To date more than 20,000 women have been screened at four sites.

INCTR is providing off-site data management services for a clinical trial in the treatment of locally advanced cervical cancer. The trial is sponsored by Eli Lilly and is being conducted by ten centers in eight developing countries. Over 500 patients have already been enrolled on the study.

Burkitt's Lymphoma in Africa

Burkitt's lymphoma was first recognized in Africa as a tumor of the jaw occurring at high frequency in children; the first documentation of a child with Burkitt's lymphoma comes from the first missionary hospital in Uganda, founded in 1897. Studies conducted in many University Hospitals, subsequently established in various equatorial African countries, revealed a high frequency of tumors of the jaw and orbit in children. Definitive descriptions by Dennis Burkitt and Greg O'Connor of the clinical features and pathology, respectively, date to the late 1950s and early 1960s. Burkitt's lymphoma accounted for over 50% of the childhood cancers prior to the AIDS epidemic (now, in some African countries, Kaposi's sarcoma occurs more frequently). Many lessons have been learned from the study of this tumor in Africa, including its apparent relationship to the distribution of malaria, its association with Epstein-Barr virus, and the presence of certain characteristic molecular abnormalities in the tumor cells. It was also one of the first tumors shown to be curable by chemotherapy alone (in some cases by a single dose of a cytotoxic drug!). Quite simple, inexpensive combinations of cytotoxic drugs, manageable in the African setting, were shown to result in the cure of approximately half of all patients with this disease in the early 1970s. Unfortunately, little progress has been made in Africa since that era, and today, many patients do not even complete their treatment so that presently achieved survival rates in most countries are largely undocumented. In contrast, in affluent countries, newer, more intensive chemotherapy regimens, combined with improvements in the ability to support patients undergoing intensive regimens, have resulted in cure rates of approximately 90%. The cost and toxicity of such treatment protocols in Africa, however, is prohibitive – even if affordable, such regimens would probably result in many deaths from the treatment itself.

Leukemia Study Group of India

INCTR and the Leukemia Study Group of India – a strategy group dedicated to the treatment and characterization of acute lymphoblastic leukemia (ALL) in children, adolescents and young adults – implemented a new treatment protocol in August 2004. The study is being conducted in four major centers in three major cities in India – Chennai, Delhi and Mumbai – and includes a more prolonged period of intensive therapy with higher total doses of asparaginase. The primary objective is to identify prognostic factors – in the previous protocol, factors common to all participating centers have, surprisingly, not been identified. It is also hoped that survival will be improved and serious toxic complications reduced. Over 40 patients have been enrolled since August 2004 and we anticipate that 150 patients will be entered on the protocol each year. The study is partially being supported by a grant of \$250,000 (over three years) from the Sir Ratan Tata Trust. INCTR is seeking additional funding or gifts-in-kind to support costs of some of the more expensive drugs used in the treatment of patients – asparaginase and cytarabine.

As with all studies, INCTR ensures that the data collected is of the highest quality. INCTR in partnership with Capitol Technology Information Services, Inc. (CTIS) has developed a web-based data entry system for use by the participating institutions so that the study can be monitored closely. Measures of submitted data quality are in place and a data monitor, employed through the INCTR India Office as well as staff members of INCTR's Clinical Trials Office, will be conducting site visits of each of the participating institutions throughout the duration of the study.

Another important goal of the group is to assist additional institutions throughout India to effectively use the prior treatment protocol for ALL, MCP841, used by the major institutions. With the guidance and supervision of the investigators at major centers, it is anticipated that more centers in India will be trained in the conduct of clinical research and improved data management in the context of this earlier protocol which is now widely accepted as standard treatment for ALL in India. We hope that the inclusion of additional

Ongoing INCTR Clinical Trials

- INCTR 01-01. PHASE II STUDY OF PREVIOUSLY UNTREATED METASTATIC OSTEOSARCOMA WITH A COMBINATION OF CHEMOTHERAPY (CISPLATIN, DOXORUBICIN, IFOSFAMIDE) AND SURGERY. Active patient accrual. Patients accrued by two of six participating Institutions. TOTAL ACCRUED: 7.
- INCTR 01-02. STUDY OF ADULT AND PEDIATRIC LYMPHOMA LOSS TO FOLLOW-UP. SINGLE INSTITUTIONAL STUDY. Closed to new subject enrollment. Enrolled subject follow-up only. TOTAL ACCRUED: 196.
- INCTR 01-03. UNDERSTANDING PROBLEMS FACED BY PARENTS OF CHILDREN WITH RETINOBLASTOMA PRIOR TO TREATMENT. Multi-institutional questionnaire study. New subject enrollment continues. Parents enrolled by 10 of 15 participating institutions. TOTAL ACCRUED: 309.
- INCTR 02-04. THE TREATMENT AND CHARACTERIZATION OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS. Multi-institutional study involving four centers in India. New subject enrollment is ongoing. TOTAL ACCRUED: 53.
- INCTR 03-06. THE TREATMENT AND CHARACTERIZATION OF BURKITT'S LYMPHOMA IN AFRICA. Multi-institutional study involving five centers in four countries in Africa. New subject enrollment is ongoing. TOTAL ACCRUED: 27.
- INCTR 03-08. A RETROSPECTIVE SURVEY OF PRESENTATION FEATURES OF BREAST CANCER AND RISK FACTORS FOR TREATMENT OUTCOME. Data collection in process in two of four centers. Two other centers will begin in 2005. TOTAL ACCRUED: >1,000.

A Model Program In Nepal

When resources are particularly limited, palliative care must be a high priority because the majority of patients will have very advanced cancer. Unfortunately, this tends to support the erroneous notion that there is little that can be done about cancer. Thus, it critically important to ensure that the message that cancer can be prevented is emphasized, and to develop programs directed at curing curable cancers at the earliest opportunity. INCTR has worked closely with several institutions and organizations in Nepal, one of the world's poorest countries, in helping to improve cancer control in a stepwise fashion. Palliative care has been considerably enhanced, with new programs in three institutions, and the initiation of a home-care program (see Palliative Care, page ___). Cancer prevention efforts have also been significantly boosted in the Kathmandu valley through public education (primarily of schoolchildren), which has been undertaken by INCTR Nepal (also known as the Nepalese Network for Cancer Treatment and Research) and screening for pre-malignant (cervical intraepithelial neoplasia) lesions which can often lead to invasive

cervical cancer - the most frequent cancer in women with low socioeconomic status - which has been undertaken in conjunction with the International Agency for Research in Cancer (IARC). Cancer of the uterine cervix is deadly if left untreated but easily curable



WOMEN LINE UP FOR CERVICAL CANCER SCREENING AT THE SCHEER MEMORIAL HOSPITAL IN BENEPA, NEPAL.



REGISTERED NURSE VIRGINIA LE BARON, AN INCTR VISITING EXPERT, DISCUSSES THE ROLE OF THE PALLIATIVE CARE NURSE AT KANTI CHILDREN'S HOSPITAL.

if detected early. In collaboration with IARC, INCTR has initiated direct visualization cervical cancer screening programs that have reached thousands of rural Nepalese women. INCTR staff and professional volunteers recently met with Nepalese organizations, such as the Nepalese

Cancer Relief Society, staff of the major Maternity and Gynaecological Hospital in Kathmandu and the teams already undertaking screening at Scheer Memorial Hospital and Bhaktapur Cancer Center to discuss how to extend cervical cancer screening to other parts of the country, and also to introduce other simple measures aimed at preventing other diseases in women who attend for cervical cancer screening. The next step in improving cancer control was taken in meetings with staff of the Kanti children's hospital, which is now participating in the palliative care program, it was decided to develop a formal training program in pediatric oncology in order to ensure that children with potentially curable cancer (79-80% of childhood cancer in affluent countries) are given the opportunity of cure. Meetings were also held with members of the Nepalese government to discuss issues such as opioid availability and the implementation of broader national cancer control strategies.

institutions in MCP841 will lead to the development of a formal cooperative group within India.

A manuscript detailing the results of an analysis of 1,048 patients treated on protocol MCP841 between 1993 and 1997, in which survival rates were markedly improved, and over time, serious toxic complications reduced, has recently been accepted for publication in the European Journal of Cancer.

Lymphoma

Investigators from the Lymphoma Strategy Group have agreed to collaborate in the treatment of newly diagnosed adult patients with diffuse large B cell lymphoma. A standard anthracycline-containing chemotherapy regimen given with anti-CD20 (Rituximab) will be used, and results in patients from different ethnic backgrounds and different geographical areas will be compared with respect both to treatment outcome and molecular characteristics of the tumor cells. Investigators from institutions in Brazil, Egypt, Saudi Arabia, Pakistan and India have agreed to participate in this study. An investigator-initiated proposal is in development and will be formally submitted to Roche, International. Roche has already agreed to donate Rituximab (anti-CD20) for this study.

Osteosarcoma

The Osteosarcoma Strategy Group is comprised of investigators from Brazil, Colombia, Mexico, Saudi Arabia, Pakistan, China and the Philippines. The group is conducting a protocol for the treatment of previously untreated patients with metastatic osteosarcoma. The treatment consists of a combination of chemotherapy – cisplatin, doxorubicin and ifosfamide – and surgery, with preservation of limbs whenever possible. Although patient entry has been low, the protocol has been shown to be feasible and cost-effective and the group will consider developing a similar protocol in which all patients with osteosarcoma will be included.

Planned Studies for 2005 and 2006

- THE TREATMENT AND CHARACTERIZATION OF ACUTE LYMPHOBLASTIC LEUKEMIA USING A STANDARD TREATMENT PROTOCOL. Approval by INCTR ERC with stipulations. Re-submission planned for July 2005 following revisions by Indian Principal Investigators. PLANNED ACCRUAL: 1,000.
- RANDOMIZED TRIAL COMPARING THREE REGIMENS FOR THE TREATMENT OF LOCALLY ADVANCED BREAST CANCER. Multi-institutional study planned with four centers in four countries. Finalization of protocol document planned for 2005. Activation anticipated for late 2005 or early 2006. PLANNED ACCRUAL: 1,500.
- PHASE II STUDY OF LIPOSOMAL ARA-C IN AFRICAN BURKITT'S LYMPHOMA PATIENTS WITH RECURRENT CENTRAL NERVOUS SYSTEM DISEASE. Multi-institutional study planned in five centers in four African countries. Protocol document in preparation. Anticipated activation date – late 2005. PLANNED ACCRUAL: 40.
- PHASE II STUDY OF FLUOXETINE IN AFRICAN BURKITT'S LYMPHOMA PATIENTS. Multi-institutional study planned in five centers in four African countries. Protocol document in preparation. Anticipated activation date – late 2005. PLANNED ACCRUAL: 20.
- THE TREATMENT OF NEWLY DIAGNOSED PATIENTS WITH DIFFUSE LARGE B CELL LYMPHOMA USING AN ANTHRACYCLINE-BASED CHEMOTHERAPY REGIMEN WITH ANTI-CD20. Multi-institutional study planned in eight centers in five countries. PLANNED ACCRUAL: 250.
- THE TREATMENT OF EXTRA-OCULAR RETINOBLASTOMA. Multi-institutional study planned in centers located in Latin America and Asia. PLANNED ACCRUAL: 60.

Retinoblastoma

Retinoblastoma is a disease that is curable in 90% of children in industrialized nations and many children can be treated with preservation of the eye – largely because it is nearly always detected when confined to the eye and with rather limited disease. Unfortunately, in developing countries, where the disease appears to have a higher incidence rate, children with retinoblastoma usually present with much more advanced disease, and a high proportion of children lose an eye, and occasionally both eyes. Some children even present with metastatic disease, such that there is a significantly higher mortality rate than in affluent countries. The major objective of the Retinoblastoma Strategy Group, comprised of investigators from one or more centers in Brazil, Bolivia, Mexico, Nigeria, Tanzania, Zimbabwe, Turkey, India, Pakistan, Vietnam and the Philippines, is to develop a multi-national program for the control of retinoblastoma in which a two pronged approach will be used – 1) public and professional education to increase the likelihood of early detection and 2) the development of treatment for patients with advanced disease. Because of the rarity of retinoblastoma, and particularly of advanced retinoblastoma



in affluent countries, the lead in the development of effective treatment of advanced disease will need to come from developing countries.

In early 2001, the group decided to conduct a survey in an attempt to identify problems faced by parents prior their child's diagnosis and to identify other factors that may have contributed to delays in diagnosis

POSTERS LIKE THIS ONE TEACH PARENTS IN MEXICO TO RECOGNIZE THE EARLY SIGNS OF RETINOBLASTOMA.

and treatment. The survey is designed to obtain information through an interview with parents and to retrieve clinical data relating to the child's illness. A preliminary analysis of the first 289 surveys has been performed. Many statistically significant findings were observed. Children with higher stages of disease tended to be older than children with less advanced disease. Longer intervals between the time when the first sign was noticed to the date of diagnosis were also associated with higher stages of disease. Both findings suggest that the vast majority of tumors arise early in life and grow progressively in the first few years. The father's education level was positively associated with the duration of symptomatic disease – the duration was significantly longer in fathers who were either illiterate or who had primary school education. The children of fathers with lower education levels in general also tended to have children with higher stages of disease. These preliminary findings suggest that public awareness campaigns in which the early signs or retinoblastoma are essential, but it will also be necessary to target fathers, who have the primary decision-making role in families in developing countries, and to emphasize that lives and eyes can be saved by early detection.

Activities related to increasing public and professional awareness have been initiated in many countries represented in the Retinoblastoma Strategy Group. Materials for both health care professionals and the public have been developed. A public service announcement (a brief video) produced in Brazil has been translated into many languages for use in other countries. This announcement is on the INCTR web site (from where it can be downloaded) and also on that of a Brazilian non-profit organization, Tucca (<http://www.tucca.org.br>). Several countries, including Mexico, Turkey and the Philippines, have formed or are in the process of forming cooperative groups of health care professionals interested in the care of children with this disease. The purpose is to improve early detection and standardize treatment approaches.

The Retinoblastoma Strategy Group plans to finalize the design of a treatment protocol for children with very advanced disease in 2005.

The Multiple Benefits of Clinical Trials

Cancer control must, to have any chance of success, be based on evidence derived from clinical research with human subjects. Practice guidelines can be valuable if based on relevant evidence, and when the necessary resources are available, including appropriate knowledge, skills and discipline. Unfortunately, all are in short supply in developing countries. Thus, guidelines devised in more affluent countries may prove to be either not feasible, or inappropriate for particular populations in developing countries. This creates an urgent need for regionally-relevant research including surveys (directed towards investigating such problems as the reasons for late presentation, poor follow-up or current practice), prevention and treatment trials, where useful, in collaboration with experienced clinical researchers – if necessary, from outside organizations or institutions. Such trials, in their simplest form, consist of the disciplined application of appropriate treatment (or prevention) guidelines coupled to outcome measures, but may also involve epidemiological or translational research elements. Treatment studies, especially in the setting of developing countries, generally lead to improvements in patient diagnosis, management and outcome, and provide a focus for hands-on training of a broad range of health professionals, not only in research - which is essential for the improved definition and solution of local problems - but also in good medical practice.

Moreover, clinical research results in the creation of a more scientifically-minded culture and hence more rational medical and public health decisions. Where such trials involve multiple centers, they also lead to greater accessibility to the limited local expertise (as well as international expertise), improved educational and professional opportunities for a broad range of personnel, and the foundation of locally relevant evidence as well as valuable scientific resources, such as tissue banks. The desire for an enhanced professional reputation and the quality assurance built into data collection



THE IMPLEMENTATION MEETING OF THE NEW PROTOCOL OF THE LEUKEMIA STUDY GROUP OF INDIA TOOK PLACE IN _____ 2004 BY VIDEO TELECONFERENCE CONNECTING BRUSSELS, MUMBAI AND DELHI.

methods creates added incentives for improving the quality of care, while the information collected in the course of a series of clinical studies provides a growing foundation of evidence, relevant to national or regional problems, on which ever more efficient cancer control strategies can be built.

Information technology can enhance all aspects of communication, including consultations, education (e.g., through multi-disciplinary telemedicine conferences and a variety of e-learning tools), knowledge assessment, recordkeeping (including registration and clinical trials data management) and access to data and images. Information technology is inexpensive compared to imaging or radiotherapy equipment, and in addition to increased efficiency and reduced costs (from savings on staff time and travel) provides rapid access to a wide range of information. It can also greatly enhance the efficiency of patient tracking and follow-up, improve treatment documentation and reduce errors, e.g., through the use of bar-coded drugs or products, and automatic label generation. Information "on-the-move" can be provided by hand-held "PDA's" connected to the local Intranet or Internet.

Education and Training

INCTR is committed to enhancing knowledge and skills among health care professionals involved in cancer prevention and treatment in developing countries. In addition to the training elements relating to specific projects, a variety of educational activities are undertaken, including meetings, courses, expert visits to specific institutions, and sponsored training or elective fellowships in other institutions. These activities are primarily organized by members of the Education Committee, in concert with INCTR branches and offices. To date, they have been concerned primarily with medical oncology, pediatric oncology and clinical trials design and management. In the coming years, pathology, imaging and radiation therapy training programs will be added, and e-learning, using INCTR's portal, as well as video conferences will be introduced. Educational elements may include a broad variety of health-care providers and trainees, including doctors, nurses, data managers, social workers and medical students. These activities are summarized below:

Clinical Trials Workshops

Thus far, two have been held very successfully in Beijing (2002) and Sao Paulo (2004). Designed predominantly for doctors-in-training, data managers and research nurses, the workshops have covered all aspects of designing and conducting clinical trials, from discussions about the ethics of "informed consent" to GCP guidelines, data management and data analysis. Both workshops were supported by the pharmaceutical industry, in Beijing, by Eli Lilly exclusively, and in Brazil, by Eli Lilly, Novartis, Shering Plough and Aventis. (Please check and put in correct companies).

INCTR Educational Meetings

WORKSHOPS

Clinical Trials

- The Value and Conduct of Clinical Trials in China, Beijing, China, March 29-31, 2002
- An Educational Workshop on the Value and Conduct of Clinical Trials in Latin America, Sao Paulo, Brazil, September 1-3, 2004
- Issues in Clinical Trials and Basic Data Management, Manila, Philippines, June 4-6, 2005

Data Manager and Data Monitor Training

- Date Manager/Data Monitor Training Workshop for Indian Leukemia Study, Brussels, Belgium, November 15-19, 2004

Lymphoma

- Lymphoma Workshop, Brussels, Belgium, May 31, 2003
- Lymphoma Workshop, Cesme, Turkey: April 11-13, 2005

Oncology Nursing Training

- Oncology Nursing Training, Yaoundé, Cameroon, March 6, 2003
- Cancer Nursing Workshop, Cairo, Egypt, October 16-18, 2003
- Oncology Nursing Training, Sétif, Algeria, March 15-16, 2004
- Training for Nurses in Cancer Care, Ouagadugu, Burkina-Faso, November 6-14, 2004
- Cancer Nursing Workshop, Cesme, Turkey, April 11-13, 2005

Palliative Care

- Training in Palliative Care for Nepalese Doctors and Social Workers, Calicut, India, October 13-17, 2003

(continued on page 17)

Training Cancer Nurses

From communicating with patients and families to administering chemotherapy and pain management therapies, nurses around the world bear the brunt of patient care. Their focus is on the needs of the patient rather than the specific disease, yet cancer nurses must be highly skilled, well-trained and knowledgeable about treatment. Such nurses are able to undertake many tasks previously performed only by doctors – thus increasing capacity and influencing patient access to care. They help to improve patients' support by providing more information and counseling to patients – critical to improving follow-up – and have an important role in patient care, including the administration of chemotherapy, care of patients undergoing radiation therapy or surgery, and the management of treatment complications. Research nurses participate in the collection of information needed to evaluate treatment efficacy and side effects, and specialized palliative care nurses help manage symptoms, particularly pain, in the terminally ill, whether in a hospice or community setting. By training cancer nurses in developing countries, INCTR seeks to strengthen the quality and quantity of health care. To date, training courses for cancer nurses have been held, under INCTR's Visiting Expert program, in Algeria, Burkina Faso, Cameroon, Egypt, Nepal and Pakistan.



NURSING WORKSHOPS AND MEETINGS LIKE THIS ONE IN BURKINA FASO (TOP) AND CAMEROON ENHANCE THE QUALITY OF HEALTH CARE IN DEVELOPING COUNTRIES.

with a one-day course for oncology nurses in Cameroon in March 2003. This was a basic course in chemotherapy and palliative care and was intended as a first step in promoting the education of cancer nurses. To assure that as many health professionals as possible could attend, the workshop was held at the same time as the second Euro-African Cancer Congress in Yaounde. Sabine held a similar course in Setif, Algeria, during the first International Forum on Cancer, held in March 2004. Last November, a three-day training course was organized in Ouagadougou, the capital of Burkina Faso, for both doctors and nurses. This course included a workshop on the psychological support of terminally ill patients.

Cancer nurses from St. Bartholomew's Hospital and the Royal Marsden Hospital in London organized a three-day meeting in Cairo, Egypt, for both Egyptian and Palestinian cancer nurses in November 2003. The English nurses, working together with those from the School of Nursing at the National Cancer Institute, Cairo, conducted classes focused on recent developments in cancer nursing. They paid special attention to the nurse's role in caring for the immuno-compromised patient (generally caused by chemotherapy) and the development of cancer nursing protocols. This meeting, which ran concurrently with a Lymphoma Workshop, was funded jointly by the OIA (NCI Bethesda), and the Special Trustees of St. Bart's.

Melanie Ridge, an oncology nurse who works for the MacMillan Fund in London, spent two weeks at the Shaukut Khanum Hospital in Lahore, Pakistan, as an INCTR Visiting Expert. INCTR plans to develop coordinated efforts in the education of cancer nurses through additional short courses of this kind, and arrange longer term exchange programs with centers where cancer nursing is more developed. Nurses in developing countries are often undervalued, and it is important to ensure their participation in local and national medical cancer meetings and conferences of all types. This will also permit the exchange of views on needs and the best approaches to meeting them. A planning session of this kind will be held in Turkey in April 2005.

Workshops and Symposia

A three-day symposium on lymphomas, supported by the US NCI Office of International Affairs (OIA), was held at the NCI, Cairo in 2003. The faculty included both local and international speakers. The symposium focused on areas of debate and controversy and was characterized by lively discussion. After the symposium, a strategy group met to consider possible clinical research projects that might be undertaken by INCTR.

Two pediatric oncology workshops, also supported by the OIA, were held in Dubai and Chongqing, China. Both workshops included presentations and discussion on the management of common pediatric neoplasms, the role of bone marrow transplantation, limb-sparing surgery and palliative care. In addition, a workshop was held in Amman, Jordan, primarily for pediatric oncologists from Iraq. The purpose of this was to identify problems currently being faced in Iraq, to attempt to find solutions, and to update the participants in leukemias, lymphomas (by far the greater part of their patient populations), supportive (including blood transfusion practice) and palliative care.



EGYPTIAN AND PALESTINIAN NURSES ATTENDED A WORKSHOP ON CANCER NURSING DURING THE LYMPHOMA SYMPOSIUM IN CAIRO.

INCTR Educational Meetings (continued from page 15)

Palliative Care

- Palliative Care Training for Nepalese Nurses, Calicut, India, August and September, 2004
- Palliative Care Workshop, Cairo, Egypt, October 3, 2004
- Symposium on Palliative Care, Kathmandu, Nepal, January 9, 2005
- Palliative Care Workshop (with American Cancer Society), Chennai, India, December 11, 2005

Pediatric Oncology

- Pediatric Oncology Update (with Shaukat Khanum Memorial Cancer Hospital and Research Center), Dubai, UAE, October 6, 2003
- Pediatric Oncology Update (with Chinese Pediatric Oncology Society), Chongqing, China: November 21, 2003
- An Educational Workshop for Iraqi Pediatric Oncologists, Amman, Jordan, April 18-20, 2004
- Seminar on the Need for a Multidisciplinary Approach in Pediatric Oncology, Sao Paulo, Brazil, September 1-3, 2004
- Educational Workshop for Iraqi Pediatric Oncologists, Cairo, Egypt, October 3, 2004

SYMPOSIA

Leukemia and Lymphoma

- Pathology and Management of Lymphomas, Cairo, Egypt, October 16-18, 2003
- Management of Lymphoblastic Leukemia, Chennai, India, February 9-11, 2004

Visiting Expert Program 2003 & 2004

Stuart Brown visited Nepal twice in the last year, accompanied on the latter occasion by two colleagues (palliative care specialists) from Canada.

Melanie Ridge, an oncology nurse who works for the MacMillan Fund in London spent two weeks at the Shaikut Khanum Hospital in Lahore, working on the wards and in the Day Unit.

Ama Rohatiner, a medical oncologist, worked with physicians in the Dept. of Medical Oncology at the NCI, Cairo, prior to the meetings there in October, attending multidisciplinary meetings and ward rounds.

Marty Malowar, an orthopedic surgeon from the Lombardi Cancer Center and Washington Cancer Institute, spent time in Shanghai in November, after the Pediatric Oncology update in China, discussing limb-sparing procedures.

Ama Rohatiner recently spent a week at Jinnah Hospital in Lahore conducting Outpatient Clinics and ward rounds, and teaching undergraduates and postgraduates at Allama Iqbal Medical College.

Dr Lynn Murphree, a Los Angeles-based ophthalmologist specializing in the care of retinoblastoma, and currently chairman of the Children's Oncology Group committee on retinoblastoma, spent a week at the Instituto Nacional de Pediatria, Mexico City.

Dr Judith Kingston, a pediatric oncologist from St Bartholomew's Hospital in London. has also recently completed a visit to Mexico, where she attended the first meeting of the Mexican Retinoblastoma Group and participated in activities at the Instituto Nacional de Pediatria.



DR STUART BROWN (FAR LEFT) RECENTLY MET WITH MEDICAL STAFF AT BHAKTAPUR CANCER CARE CENTER IN NEPAL.

Dr Stuart Brown, a specialist in palliative care from the KFSHRC and chairman of INCTR's Palliative Care Sub-committee, traveled to Nepal and India in November 2002. Dr Brown worked with the NNCTR/INCTR office to identify palliative care programs and individuals involved in palliative care in the Kathmandu valley region, and to assess their efficiency and training needs. He

gave lectures on palliative care and will maintain an ongoing relationship with colleagues in Nepal. He plans to provide additional educational materials, arrange for training of Nepalese Health care workers in Calicut, India, and also arrange to send palliative care nurses to Nepal. His next visit is in March.

Workshop for Cancer Nurses

Concurrent with the Lymphoma Symposium held at the NCI, Cairo, a three-day training course entitled New Developments in Cancer Nursing was held for Egyptian and Palestinian nurses (supported by OIA, NCI, USA, the pharmaceutical industry and the Charitable Foundation of St. Bartholomew's Hospital (SBH), London).

In October 2003 Ama Rohatiner was a visiting professor at the NCI Cairo and in February 2004 visited the Allama Iqbal Medical Hospital and Jinnah Hospital in Lahore. She was involved in multidisciplinary team (MDT) meetings, Outpatient clinics and ward rounds, and taught undergraduates and postgraduates. As a result, a sequence of doctors from Pakistan have come to work at SBH, (as well as visitors from Ghana and Uzbekistan).

Educational Activities Planned for 2005

- A Workshop on Research Methodology organized in collaboration with Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH&RC), to be held in Lahore, Pakistan, March 2005.
- A Workshop on Lymphoma, in collaboration with the University of Izmir, and the Middle East Cancer Consortium (MECC), to take place in Cesme, Turkey, April 2005. This will bring together doctors from Israel, Palestine, Jordan, Egypt and the Republic of Cyprus, as well as those from Turkey.
- A three-day training course for cancer nurses will take place in Cesme, April 2005, (concurrently with the Lymphoma Workshop). This will also include nurses from the MECC countries.

Trainees 2003 & 2004

The Instituto Nacional de Pediatria has, with INCTR coordination and support, assisted in the training of a pediatric oncologist from Bolivia in the care of children with retinoblastoma and INCTR hopes to encourage this relationship, which should lead to the establishment of a referral center for retinoblastoma at the Instituto Oncológico del Oriente Boliviano.

Dr Bu, an MD, Ph.D. from China, continues to work in the INCTR-affiliated Laboratories in Saudi Arabia. Initially supported by INCTR, his salary is now paid by KFSH&RC. Upon his return to China, Dr Bu will play a critical role in establishing an INCTR-affiliated laboratory program in China.

Nine individuals, including physicians and nurses, attended a course in palliative care medicine in Calicut, India. Participants were selected by INCTR's Branch in Nepal, NNCTR/IN CTR, which also made all necessary arrangements.

Specific Training Projects

Under the auspices of the INCTR, staff from St. Bartholomew's Hospital (SBH) are helping SKMCH set up high-dose treatment in Lahore. Two senior nurses from SBH have just returned from working alongside the nurses at SKMCH, Ama Rohatiner will help train medical staff there in March.

Elective Fellowships and Continuing Education
Eight final year medical students from SBH will each spend six weeks at INCTR Associate Member Institutions as part of INCTR's student fellowship program. Locations will include the National Cancer Institute, Cairo; Ocean Road Cancer Institute, Dar-es-Salaam; Jinnah Hospital, Lahore; University Hospital, Rio de Janeiro.

The INCTR Annual Meeting

INCTR's Annual Meeting has become an important event which serves to bring together INCTR Associate Members from many different countries to strengthen international collaboration in all aspects of cancer treatment and research, to report progress that has been made in INCTR projects, and to identify focal points for discussion that may lead to the development of new projects.

In addition to its formal content (plenary talks by international speakers, workshops, etc), the Annual Meeting has an inherent educational purpose in providing a forum for doctors and nurses from both developing and affluent countries to exchange ideas. The Meeting also provides an opportunity for younger physicians to present data, as an oral presentation or as a poster. In 2004, 137 abstracts were submitted (considerably more than in previous years), of which 12 were selected for oral presentation and 76 as posters.

The concept of a 'Multidisciplinary Team (MDT) Meeting' was introduced

at last year's Annual Meeting in Cairo and will also be a feature at the 2005 Annual Meeting in Chennai, India.

INCTR Awards

The Annual Meeting also provides an occasion to recognize and honor those working in cancer medicine who have made significant contributions to the field,

even when resources are limited. The Nazli Gad-el-Mawla Award is given for outstanding contributions to cancer control by an individual from a country with limited resources; The Paul P. Carbone Award for International Oncology is made for outstanding contributions to oncology or cancer research by an individual from a resource-rich country.



THE INCTR ANNUAL MEETING BRINGS HEALTH CARE PROFESSIONALS TOGETHER FROM AROUND THE WORLD.

The Paul P. Carbone Award Winners for International Oncology



DR JOHN L. ZIEGLER	DR MAXWELL PARKIN	DR FRANCO CAVALLI
UNITED STATES	UNITED KINGDOM	SWITZERLAND
2002 RECIPIENT	2003 RECIPIENT	2004 RECIPIENT

The Nazli Gad-el-Mawla Award Winners for Cancer Control in a Developing Country



DR V. SHANTA	DR SACKMANN-MURIEL	DR MAHFOUZ
INDIA	ARGENTINA	EGYPT
2002 RECIPIENT	2003 RECIPIENT	2004 RECIPIENT

Translational Research Program

Translational research refers to making use of knowledge derived from studies in the laboratory in improving the diagnosis and care of patients with cancer, or in learning how best to prevent cancer. Much research is focused upon understanding the fundamental processes that transform normal cells into cancer cells and is stimulated by a desire to identify cellular pathways and to unravel the molecular aberrations that lead to cancer. Knowledge derived from such studies nonetheless provides scientific explanations for why some individuals are particularly prone to develop cancer, or why a subset of patients respond to or are cured by a particular therapy, while others, given the same therapy remain unresponsive or have only a temporary response.

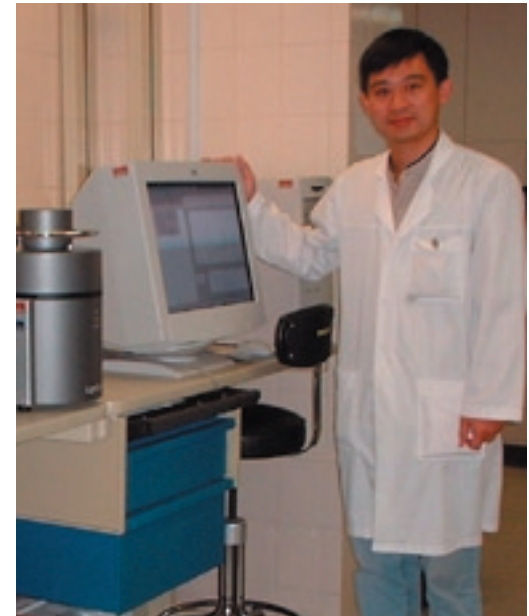
Because of its importance to understanding predisposition to cancer or response to treatment, translational research is a critical component of the overall INCTR initiative. By developing strategies for analyzing tumor specimens in the context of a clinical or biological question, translational research complements clinical research. The diagnosis of cancer is increasingly based on – and refined by - the more objective tests that can be done in the laboratory, and without accurate diagnosis, the results of treatment programs will be misleading. The INCTR Trans-

Ongoing Translational Research

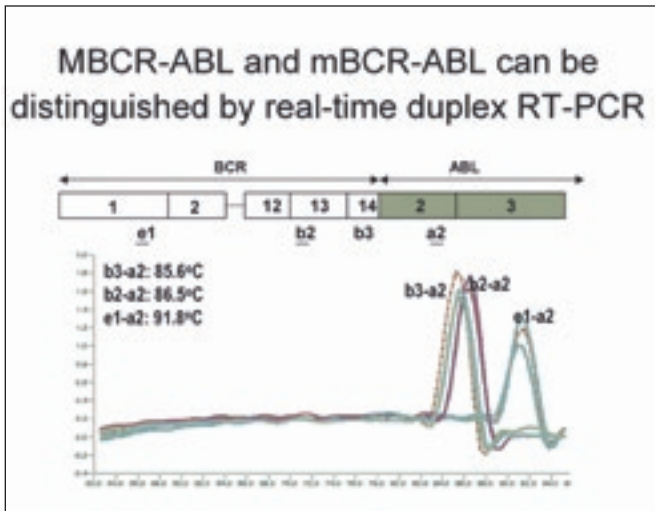
- Development of molecular biomarkers and assays for diagnosis and management of ALL
- Comparison of patterns of molecular subtypes of disease in different populations and environments (Indian leukemia)
- Comparison of molecular patterns (DNA methylation, SNPs) in disease versus control populations
- Training workshops for specific techniques

lational Research Program therefore, strives to integrate capacity building in translational research with clinical needs in the context of the development of new diagnostic approaches and the identification of molecular factors relevant to prognosis. Because it works on an international stage, INCTR is well placed to validate the application of novel diagnostic assays and to compare the patterns of cancer in diverse populations, to assess the clinical impact of established and novel biomarkers in different parts of the world, and to develop programs and resources that will lead to a better understanding of these differences.

With the advent of powerful new techniques, for example, DNA chip technology, that permits the profiling of the gene expression patterns with respect to the entire genome in specific cancers, microfluidics technology for diagnosis, and the use of gene-based assays and pharmacogenetics to identify patterns associated with good or poor responses to therapy, to say nothing of the development of new drugs or other agents specifically targeted at the molecular abnormalities associated with specific cancers optimal treatments for individualized patients will soon be possible.



DR BU WAS SUPPORTED FOR RESEARCH TRAINING AT INCTR'S AFFILIATED LABORATORY AT THE KING FADH CHILDREN'S MEDICAL CENTER IN SAUDI ARABIA, WHERE INCTR'S TRANSLATIONAL RESEARCH PROGRAM IS LOCATED.



Although this sounds expensive and labor intensive, techniques tend to become less and less expensive as time goes by, and the improved diagnostic accuracy should permit the

more efficient use of resources. Moreover, such approaches will become increasingly mechanized, although interpretational skills of the findings will need to be developed.

The main goals of the Translational Research program are to provide support for the development of correlative science studies, to build capacity for optimal practice and integration into patient care of relevant molecular diagnostic and prognostic assays, to accrue information on how the biology of cancers in developing countries both differ from that of corresponding cancers in western countries, and is relevant to their clinical behavior and response to particular treatment approaches, and how differences in the genetics of populations in developing countries, in the context of specific environmental exposures, may influence their risk of developing cancer. Additionally the Translational Research Program is committed to helping build the requisite resources such as Human Biospecimen resources that are necessary for the conduct of correlative science in countries with limited resources.

Much of the work of INCTR's team of laboratory scientists, presently located primarily at the King Faisal Hospital for Cancer Research, has been devoted to

the analysis of molecular subtypes of acute lymphoblastic leukemia in India. Clear differences have been found from results published about patients studied in Western countries. These suggest that Indian patients are less likely to have the leukemia subtypes most amenable to therapy, such that research in India will be essential to optimize treatment results.

Beyond studies related to therapy, INCTR is in a unique position to take advantage of the diversity of populations and environments throughout the world, and to assess epidemiological questions relating to gene-gene and gene-environment interactions, which will help elucidate both differences in cancer susceptibility, and potentially, also, differences in response to treatment.

The projects within the Translational program will be disease/organ site directed, but the formulation of the research projects will be such that they will be highly complementary and interactive. Information obtained in one project is fed into questions addressed by other projects.

Quality assurance will be provided by the central laboratory, but much of the work will be conducted in-country, following necessary technical training. In addition to its role in quality assurance, the central laboratory will lead in the development of novel translational research questions, design and help obtain funding for new scientific proposals, perform standardization of assays that will be required to complement clinical studies and also actively interact with the training and education programs of INCTR. Regional laboratories will translate technologies established by the central laboratory into routine clinical practice and will be responsible for the

BCR-ABL subtypes in childhood ALL (B + T lineage)

	p190	p210	Total
• Germany (N: 648)	2.2%	1.1%	3.3%
• Taiwan (N: 328)	3.3%	0.3%	3.6%
• India (N: 260)	3.1%	4.2%	7.3%

collection, care and documentation of samples, coordinating specimen collection and storage and processing with the clinical investigators and Clinical Trials Office, and preparing samples for investigation.

Palliative Care

With so many cancer patients in developing countries presenting in the late stages of their disease, sometimes the only treatment option available to doctors is to make their patients as comfortable as possible until the end comes. Treatment that relieves distressing symptoms, eases pain and enhances the quality of life during the final days is as beneficial to patients as it is to their families, who find some comfort in facilitating a peaceful, pain-free death. Since 2002 INCTR has been working with the Nepal Network for Cancer Treatment and Research (NNCTR/INCTR), which is INCTR's branch in Nepal, to develop a program for end-of-life care suitable for their country.

Four facilities (Hospice Nepal, Bhaktapur Cancer Care Center, Scheer Memorial Hospital and Kanti Children's Hospital) were chosen as sites where palliative care would be developed. By February 2005, 25 beds had been designated and were functioning. Dr Stuart Brown is the Director of the Palliative Care Program. He, three other palliative care physicians, two nurses and a psychosocial



INCTR IS WORKING TO HELP ESTABLISH HOSPICE CARE FOR TERMINAL CANCER PATIENTS THROUGHOUT NEPAL.

worker have made several trips to Nepal. They have given lectures, conducted clinical workshops and attended ward rounds. The core training elements include modern methods of symptom palliation, the correct use of opioid medication and the psychosocial support of patients and their families. INCTR funded seven physicians and 24 nurses from Nepal to attend intensive courses in Calicut, India, where there is a well-established training program and similar socio-economic circumstances. Clinical guidelines have been written and will be developed further over time. As a consequence, extensive educational gains have been made and the quality of care improved. In particular, the World Health Organization "pain ladder" is now being followed.

Dr Brown has met with government officials and physicians to discuss the changes needed in healthcare policy and legislation in order to improve the availability, prescribing, distributing and dispensing of essential drugs (especially opioids). A home hospice program has begun and INCTR has provided \$10,000 for the purchase of a vehicle, which is essential to the development of this program. Lastly, a number of Nepali physicians and businessmen have formed the "Nepal Palliative Care Group" which meets to discuss collaborative projects.

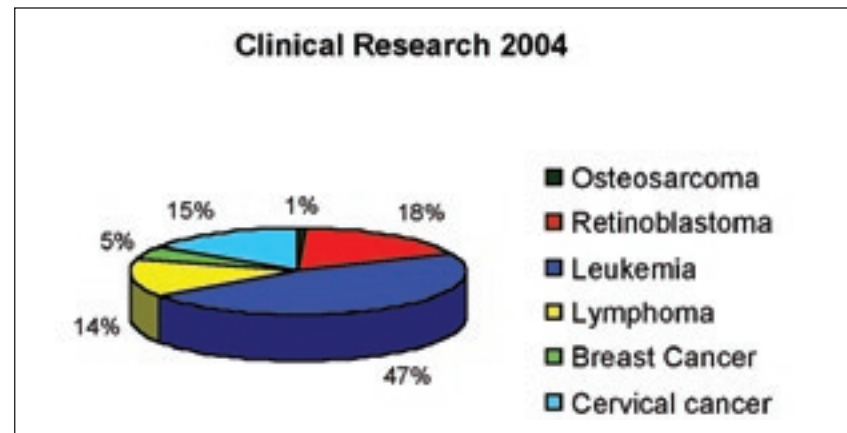
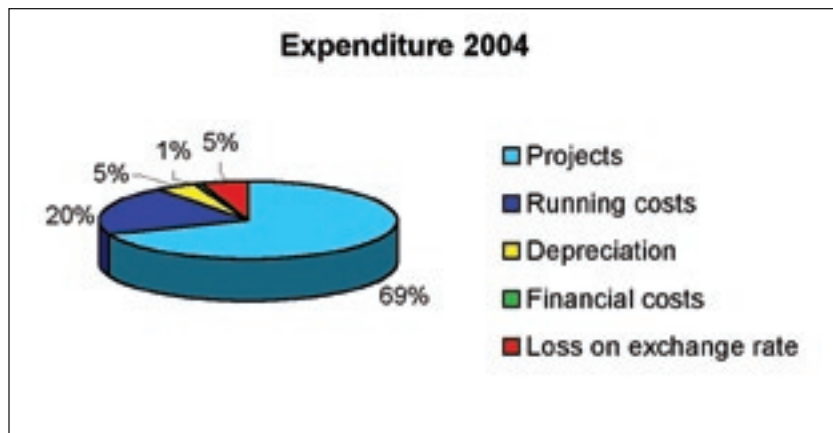
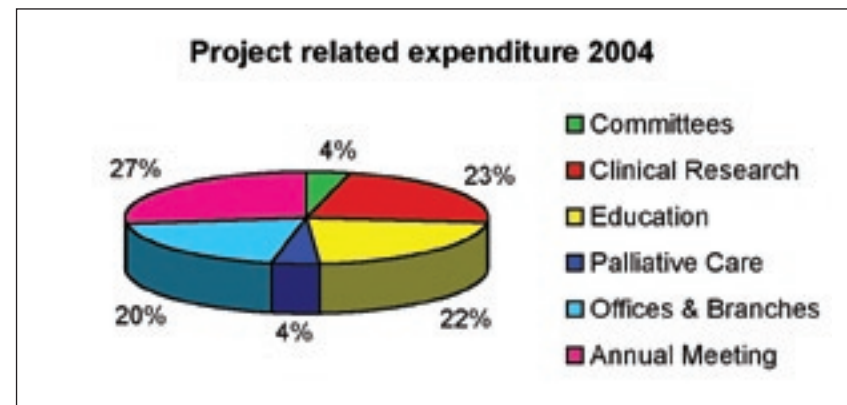
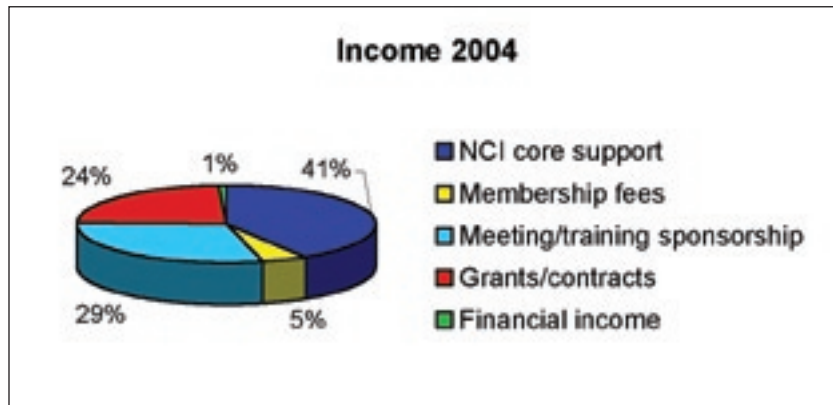
Future plans for Nepal include the establishment of a rural outreach service, expansion of pediatric palliative care, implementation of web-based teaching and support, and extension of the program to other regions.

It has become clear that the success of initiating and sustaining effective palliative care schemes depends on establishing the World Health Organization's foundation measures; that is, educating the public, healthcare professionals and policy makers about palliative care, ensuring the availability of essential drugs, and lobbying government to introduce policies that emphasize the importance of alleviating cancer pain. As a result of INCTR's encouraging progress in Nepal, there are plans to introduce similar palliative care projects to other emerging countries in the course of the next two years. This organization is in a unique position to promote such ventures because of its longstanding partnerships with institutions and societies in many of these countries. If successful, thousands of patients and their families will benefit.

Financial Report

INCTR's annual income and expenditure exceeded a million dollars, in 2003 and 2004. Expenditure (running costs and project costs) were similar. Income and expenditure breakdowns are shown in the pie-charts below.

Project related expenditure and expenditure on clinical research are further subdivided in the pie-charts below.



In addition to monetary income, INCTR has benefited greatly from in-kind contributions. These include the several volunteers that provide administrative support, assistance from the Institut Pasteur in accounting and personnel management, from CTIS, which has developed INCTR's portal and provided programming and software support in the production of clinical trials software, and the numerous individuals who have served voluntarily on INCTR's various boards and committees. INCTR collaborative projects include major contributions by participating institutions.

INCTR is grateful to the following sponsors which have supported numerous educational and training meetings:

- The Office of International Affairs, NCI, Bethesda
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Hôpital 20 Août 1953, Morocco
Ho Chi Minh City Cancer Center, Vietnam
Hospital Albert Einstein, Brazil
Hospital Pédiatrico de Sinaloa, Mexico
Hospital Arco Iris, Bolivia
Hospital Universitario del Valle, Colombia
ICEDOC International Campaign for Establishment & Development of Oncology Centre, Egypt
IGCS - International Gynecologic Cancer Society, USA
Imperial College of Science, Technology and Medicine, United Kingdom
Instituto de Enfermedades Neoplásicas, Peru
Instituto Nacional de Pediatría, Mexico
Instituto Oncológico del Oriente Boliviano, Bolivia
Iraqi Society of Cancer Patients and Their Friends, Iraq
ISPHO - Israeli Society of Pediatric Haematology /Oncology, Israel
Kenya Medical Research Institute, Kenya
KFSH&RC - King Faisal Specialist Hospital & Research Center Saudi Arabia
King Hussein Cancer Center, Jordan

MAHAK - Society to Support Children Suffering from Cancer, Iran
Mbarara University of Science and Technology, Uganda
Ministry of Health-Hussein Maki Juma Cancer Centre, Kuwait
Mofid Children's Hospital, Iran
National Cancer Institute Radiation & Isotopes Centres Khartoum RICK, Sudan
NCI Cairo - National Cancer Institute, Egypt
NCRS - Nepal Cancer Relief Society, Nepal
Netaji Subhas Chandra Bose Cancer Hospital & Research Institute, India
NNCTR - Nepaleese Network for Cancer Treatment and Research, Nepal
Noor Foundation for Cancer, Afghanistan
OAUTHC - Obafemi Awolowo University Teaching Hospitals Complex Nigeria
Ocean Road Cancer Institute, Tanzania
Ospedale San Gerardo, Italy
PGIMER - Postgraduate Institute of Medical Education and Research, India
Philippine Children's Medical Center, Philippines
Queen's University of Belfast, United Kingdom
Rajiv Gandhi Cancer Institute and Research Center, India
Rizk Hospital, Lebanon
SAARC Federation of Oncologist-Nepal
Sanchetee Hospital and Cancer Institute, India
Santa Marcelina Hospital, Brazil
SGRH - Sir Ganga Ram Hospital, India
Shanghai Children's Medical Center. China
Shaukat Khanum Memorial Cancer Hospital & Research Center, Pakistan

Sheba Medical Center, Israel
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Technical University Munich, Germany
Tong-Ji Hospital of Tong-Ji University, China
TUBA - Turkish Academy of Sciences Cancer Committee, Turkey
Tygerberg Hospital and University of Stellenbosch, South Africa
Union Hospital of Tongji Medical College, China
Università di Siena, Italy
University College Hospital - Ibadan Nigeria
University Hospital of Antwerp, Belgium
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