

INCTR Progress Report

AGM and Governing Council Meeting
6th March 2004

Public Relations and Communications

Newsletter

The INCTR newsletter continues to be published quarterly, and is also available from INCTR's website both in HTML and as a downloadable pdf file. Specific types of article will also be made accessible via the new Portal. We receive many compliments about the newsletter, and occasional requests to reprint articles. Publication tends to be behind, since the Newsletter is produced by staff who all have other major assignments. The Newsletter could be made even better if we had an individual with medical knowledge to assist with relevant research and perhaps produce a regular feature article about cancer in a developing country, or news from outside INCTR. Marcia Landskroener continues to layout the Newsletter and write certain feature articles (e.g. Cancer Medicine Profile, Forum) for the newsletter but we are considering having the layout done in Brussels, which would save time and resolve present problems relating to file compatibility with Marcia, the printer and the website. The identification of a sponsor for NETWORK would significantly aid its production by permitting more staff time to be assigned, and potentially bringing publication largely in-house.

NewsFlash

From time to time, a one page Newsflash is sent by e mail to INCTR Associate Members. This is not a regular feature, but is used to provide recent news and to remind members of meeting dates, report meetings etc.

Web Site

The web site continues to be updated regularly. We continue to work with The Magazine Group (based in Washington, DC) and are satisfied with their services. The number of "hits" has continued to increase, and occasional enquiries (e.g., relating to assisting with the development of a cancer program in Ethiopia) are precipitated by it. We hope finally to be able to create an area for educational materials accessible to INCTR members and potentially others through the Portal.

Portal and Data Bases

INCTR now has a fine Portal, through the generosity of CTIS (and particularly Raj Shah), which has worked with INCTR staff (largely, Melissa) to design it to meet INCTR's needs. The Portal will be a project in continuous evolution, and will serve a variety of needs, including communications among the various elements of INCTR (it can be accessed via internet, and is password protected), project management and education. Staff members/committee members and Associate members will be given varying degrees of access to documents and information of relevance to them. The Portal will

include a universal calendar, an information section, and the main member data base. This site could become the premier site for information pertaining to cancer in developing countries, as well as providing relevant educational materials, but this will require at least part time editorial assistance. In addition, the Portal will provide secure access to INCTR's new clinical trials data base, currently being developed, again, by CTIS, according to CTO (Melissa) specifications. The first version of the Portal has been completed, and training of INCTR staff by CTIS is in progress. INCTR thanks CTIS for this valuable donation which will elevate the level and efficiency of INCTR's activities significantly.

A New Telemedicine System

A TELESYNERGY® Global Medical Consultation Work Station has very recently been installed at the NCI Liaison Office in Brussels. The TELESYNERGY® system, which was developed from commercially available hardware and software by the Radiation Oncology Sciences Program and Oncology Outreach programs of the NCI, is a multi-image diagnostic quality medical research workstation that allows for the collaboration of multiple professionals using many different technologies. It allows face-to-face consultation among multiple participant sites (3 via direct linkage, maximum of 10 via hierarchical links and 30 if connected via NCI in Bethesda). It can transmit information and images from several different sources including a microscope, patient examination camera, document camera, color video printer, DVD player/recorder, PC, etc. The system can conduct live, or transmit recorded transmissions of case presentation, seminars, rounds and lectures, and distance education of all kinds, and will thus present an important tool for education and training. INCTR will have access to this system, and plans to use it for planning, implementation and management of a number of projects as well as for education. A separate document outlining preliminary plans has been written. INCTR is grateful to Dr Norm Coleman, Associate Director, NCI, and Director, Radiation Oncology Sciences Program, and Frank Govern, Deputy director, Radiation Oncology Sciences Program and Chief, Oncology Outreach Program, for providing INCTR with access to this system.

New Staff and Contractors

Three new staff members have joined INCTR since the last meeting. Lolita Lantican joined the Clinical Trials Office as a Clinical Data Manager in April. Corinne Claes also joined the clinical trials office as a data entry clerk in June, after working as a stagiaire during the spring. Suzanne Elout replaced Michel Caprasse approximately a year ago in the Administrative Office.

INCTR will shortly be dispensing with the cIMIS membership management system it has used via a contractual arrangement with GIC. This system proved to be cumbersome, and the service provided by GIC was unsatisfactory. cIMIS will be replaced by the Portal, described above.

GIC also manages INCTR's Annual Meeting. Although Wessel Niewenweg, the primary contact has provided excellent service, this is expensive (\$30,000 per annum, not including expenses and VAT) and INCTR will now employ for a similar (probably lower) sum an individual who will manage all of INCTR's increasing list of meetings (including strategy groups, committee meetings, workshops, symposia and Annual Meeting). A candidate, Cedric Petitmusin, has been identified. Cedric worked closely with INCTR on the three occasions that the Annual Meeting was held at the Brussels Hilton hotel, his former employer. It is anticipated that Cedric will commence his duties in July, in time to assist in the management of this year's annual meeting, which will, for the last time, be primarily

managed by GIC.

Discussion will take place in this GC meeting regarding the appointment of a palliative care physician, Stuart Brown, to head INCTR's rapidly developing palliative care program, discussed below. This program can be closely interdigitated with a telemedicine program, and for this reason, it would be logical to situate Stuart at the NCI Liaison office, where space is available and the TELESYNERGY® system, provided by NCI is located.

Stuart's wife, Alison could also serve INCTR in several capacities. She is a dentist who has conducted epidemiological work on oral cancer in Saudi Arabia. It is envisioned that she could take on a multifaceted post relating to INCTR's communications and educational program, in part, performing a research role with respect to the collection of information pertinent to cancer in developing countries to feed both the Portal and Newsletter (with a specific focus on the availability of resources in specified countries and regions), potentially developing a liaison with IARC with respect to cancer registration efforts (e.g. that presently going on in Lahore, Pakistan) and also editing educational materials (e.g. derived from telesynergy or actual meetings and workshops). Additional tasks might include editing a Member's directory (which would include pertinent information about institutional members) and assisting with the production of an annual report. This would greatly boost INCTR's ability to collect and disseminate information rapidly and would function as an embryonic "Communications and Information" office reporting to the Director. There may also be advantages in locating this office, if possible, at the NCI Liaison office, and it may be possible to develop partial funding, at least, of Alison's salary, through the Telesynergy program.

Given the close liaison between INCTR and the NCI's OIA, this geographical situation will also aid communications, and take advantage of the administrative assistance relating to educational programs that is provided by Liaison Office staff in the context of joint projects involving INCTR and OIA.

Branches and Offices : An INCTR Charter

The existence of a number of Branches and offices (France, UK, USA, Brazil, Egypt, India, Nepal and Tanzania) and requests from several countries interested in the establishment of additional branches (Kuwait, Turkey and Iran) has focused attention on the role of branches within the network, and how to ensure optimal functioning of what is truly an international network. Branches are established as legal not-for-profit entities within the country in which they are located such that they may raise and disburse funds in support of the INCTR mission. Branches establish and maintain linkages with cancer centers or units, relevant professional organizations or elements of national or regional governments, and assist the coordination of ongoing INCTR programs and projects (including education) within the country or region. The precise role will depend upon available expertise within the branch. INCTR Branches work at a national or supranational (regional) level with respect to furthering the INCTR's mission and those in developing countries are anticipated to become a part of the cancer control capacity of the country or region in which it is situated. Each Branch will require an administrative structure consistent with the scope and extent of its activities and may employ medical, scientific and support staff. This may include, in the context of clinical projects, the appointment of individuals such as data monitors, for quality control of clinical trials and education of data managers. These individuals could also provide training in data

management within the region, and some branches may ultimately take on the guise of a regional data center. Similarly, translational research laboratories might best be established in the context of regional or national branches, since this would avoid many of the problems relating to the transportation of human tissues and fluids across national boundaries.

Clearly, in the context of the INCTR network, it is not desirable for branches and offices to function independently (although individual branches may initiate projects, or contribute the bulk of the professional expertise in any given project), but to work in a "network-wide" context, participating in and contributing resources (human or financial) to what should be considered as "INCTR" projects. The goal is for INCTR to function as a whole, not a series of separate parts, and to ensure that resources from wherever they are available in the network are maximally utilized. In addition, all INCTR projects need to be processed in an identical fashion, e.g., disease-specific projects arising from strategy groups and undergoing independent scientific/medical review as well as ethical review at INCTR and national levels, and management being supervised by the Clinical Trials Office. This *modus operandi* will be greatly aided by the web-based Portal, and will be guided by an INCTR Charter, also to be discussed at this meeting, which, when completed, will clearly delineate the responsibilities of branches and the circumstances whereby the INCTR name can be used. The Charter will also establish guidelines for the creation of new branches and oversight.

USA Branch

With respect to INCTR's existing branches and offices, it is of note that Phil Schein recently resigned as President of INCTR(USA) and also from the Governing Council. Bobbie Scheffler, Treasurer of the US Branch resigned at the same time, as did Bo Aldige. The INCTR Executive Committee, whose task it is, has approved the appointment of four new Board Members for the US Branch, Chandra Venkatesh, Joe Simone, Jimmie Holland and Shivraj Singh. A new President and treasurer will be appointed at the next Board meeting and approaches whereby the US Branch can contribute to the overall network discussed.

UK Office

At the London Office, soon to become a branch (i.e a legal entity within the UK), Tom Lister has replaced Margaret Cresswell as administrator.

Programs and Projects

Clinical Trials Office: Strategy Groups and Disease-Specific Activities

The Clinical Trials Office supervises and performs data management for INCTR clinical research studies. These studies fall into two main categories: 1. Information seeking. e.g. why patients present late for treatment (retinoblastoma), or a retrospective cross-sectional profile of a disease (breast cancer). Such information is likely to be of great value to developing strategies for disease control and may also provide epidemiological information. 2. Prevention or treatment studies. Some studies are largely directed to the provision of an acceptable prevention or treatment regimen in

a disciplined fashion, via the conduct of standardized treatment protocol, and associated with outcome data (a process that contrasts with use of guidelines, which is an undisciplined process that is not associated with formal outcome measurements or continuing education). Thus, patients entered into such studies benefit greatly while investigators and research personnel undergo continuing education and training in the conduct of clinical trials. Moreover, the collection of information about the disease as well as the outcome of treatment provides a basis from which improved approaches to cancer control can be developed in the future.

Osteosarcoma Strategy Group

The project of the Osteosarcoma Strategy Group, which is a Phase II study of the treatment of newly diagnosed patients with metastatic osteosarcoma has accrued far fewer patients (6, to date) than anticipated. At the next meeting of this strategy group, it will be decided whether to close this study, or to open it to all patients with osteosarcoma. Of interest is the overestimate of participants with respect to the numbers of metastatic patients seen at participating centers, and the fact that the anticipated Brazilian contribution has not materialized. In the few patients who have been treated on this protocol, toxicity has been minimal suggesting that this is a feasible regimen to conduct in developing countries. At the next meeting a decision will be taken as to whether there are sufficient prospects of increasing accrual to justify keeping the study open, or whether there is an interest in broadening the therapy to all patients with osteosarcoma.

Retinoblastoma Strategy Group

The survey study entitled, "Understanding Problems Faced by Parents of Children with Retinoblastoma Prior to Treatment" has enrolled over 241 participants from six institutions in 4 countries. This study will be expanded to other countries, Nigeria and Tanzania and to another center in India. Several institutions that were involved in the development of the study have not as yet contributed any data that can be included. The reasons for this include: the departure of Principal Investigators from the participating institutions (2), submission of the pilot version of the questionnaire (2), the use of an institutional questionnaire instead of the standardized "protocol" questionnaire (1), incomplete data (1), and the inability to establish a local ethical review committee (1). The CTO is currently conducting an audit of collected.

In addition to characterizing the presenting features of patients, and access to specialized care, this study may well reveal interesting information concerning cancer in the families of patients with retinoblastoma, and the frequency of consanguineous marriages in these patients. Such results are likely to provide publishable information and also to provide the basis for epidemiological studies.

Several of the participating countries have developed approaches to early detection of retinoblastoma: INCTR assisted in the printing of posters to be used in Mexico, and a film drawing attention to retinoblastoma has been prepared in Brazil (in many languages). This film can be viewed on INCTR's website.

The treatment sub-committee of the Retinoblastoma Strategy Group has yet to finalize a protocol for the treatment of locally advanced retinoblastoma. A further meeting of this group is planned

in the near future to make final decision regarding this project.

INCTR has assisted in the establishment and participated in the first meetings of the Retinoblastoma Group of Mexico. Under the leadership of Dr Carlos Leal, this group appears to be flourishing.

Leukemia Strategy Group

Plans for the continuation of studies in the treatment and characterization of acute lymphoblastic leukemia (ALL) in India are well underway. A new protocol has been completed and final approval from the Indian Council for Medical Research (ICMR) is awaited (this will allow data to be sent to the CTO and tumor tissue to INCTR collaborators). This process has taken longer than expected, due to the large number of documents required, but it is hoped that final approvals will be obtained in time for a start date of the study of April 1st 2004. In the meantime, a data collection system is being designed with the assistance of CTIS and plans are being developed for a quality control system, entailing the employment of at least one data monitor in India, supervised locally by an Indian oncologist who has practiced in the USA and is familiar with clinical trial auditing processes (Dr Shivaji Gunale) who will work closely with the CTO. It is anticipated that some aspects of the management of this study (e.g., the implementation meeting) can be conducted by teleconferencing using the new Telesynergy facility at the NCI Liaison Office. This will save considerable time and money.

This study will be partially supported by a grant of \$250,000 from the Sir Ratan Tata Trust, but its conduct would be greatly enhanced if funds (an estimated \$100,000) could be made available to support patients in the participating Indian centers who may not be able to participate because of the lack of funds for the purchase of drugs. At present, local funds are available to support some of these patients, but the increased cost of the new protocol may stress the reserves of the participating institutions. Possible contributions of drugs by pharmaceutical companies will be discussed at the next corporate collaboration committee meeting to take place next week.

Whilst awaiting commencement of this new study, to be accompanied by the coordinated development of a cooperative group which will initially use the protocol presently in use (MCP841), accrual on MCP841 continues. An analysis of 1048 patients treated between 1993 and 1997 is being prepared for publication, along with a review of ALL studies in India in the last decade, and it was decided at the last meeting of the Leukemia Study Group of India (coordinated by INCTR as its Indian chapter of the Leukemia Strategy Group) that took place in early February 2004, that a review of patients entered on study since 1997 will be undertaken. Individual centers reported further progress in reducing toxic death rates, and corresponding improvements in survival rates at the joint INCTR/Chennai leukemia update meeting also held in February of 2004.

Dr Kishor Bhatia of the King Faisal Specialist Hospital & Research Centre (KFSHRC) and his team have continued to coordinate the molecular profiling studies. Data from several of the participating centers indicates a difference from patients with ALL in the US or Europe - specifically, the good prognosis (in western studies) 12;21 translocation, that creates a TEL-AML1 fusion gene occurs in

less than 10% of Indian patients studied in these series (over 300 cases have been analyzed), as opposed to 25% of western patients (from published literature). Poor prognosis lesions, such as BCR-ABL (t9;21) are, correspondingly slightly increased. This is relevant to therapeutic strategies. Studies on epigenetics (methylation patterns) and single nucleotide polymorphisms relating to predisposition and response to therapy continue to progress and a number of manuscripts have now been published from the transnational research group. KFSHRC continues to provide the resources for training scientists from India and elsewhere (Dr Bu, from China has already completed 3 years as a post-doctoral fellow).

In April, 2004, an additional meeting of the Middle East Children's Cancer Association (MECCA) be held in Kuwait. The group will discuss the use of the Indian ALL protocols in at least some of the participating countries.

At the meeting in Chennai, representatives from centers from Egypt and China were also present, and discussions are ongoing about their participation in INCTR ALL studies.

Breast Cancer Strategy Group

The last meeting of the Breast Cancer Strategy group took place in Egypt in the autumn. The data collection forms for the cross sectional study of breast cancer in several developing countries (anticipated to include 8-10,000 patients) has been finalized and a grant proposal submitted to the Susan Komen Foundation. Although preparations for the initiation of this study, including the appointment of data managers and the creation of a data base that will be used are continuing, we should hear the results of the grant application in March.

It is anticipated that once data managers have been trained, a clinical trials infrastructure for breast cancer studies will have been developed in participating centers. In anticipation, a protocol for the treatment of locally advanced breast cancer is in preparation by a small group of physicians agreed upon by the strategy group. A draft proposal has been prepared and will be discussed at the next meeting, scheduled for the summer of 2004.

Dr Leclercq of the Belgian study group has proposed participation in molecular aspects of breast cancer studies with his group at the Jules Bordet Institute. Discussions are underway.

Cervical Cancer Strategy Group

Projects in direct visualization cervical cancer screening have been initiated in Nepal and Tanzania via a collaboration with the IARC. These studies are going well, and thousands of women have been screened to date. Discussions will take place as to how these model programs can be replicated, and some training at least, be undertaken by telemedicine. Existing centers will also be used as regional training centers.

INCTR is also arranging for training of individuals from Nigeria in India, in order to develop direct visualization cervical screening programs in the southern part of this country, where no organized

screening programs currently exist. Plans are being made for two gynaecologists and several nurses from Lagos and Ile Ife to be trained. Lagos, for example, is a city of 13 million persons with essentially no screening programs except occasional cytological examination in wealthy persons.

A Clinical Trial Examining the Treatment of Locally Advanced Uterine Cervical Cancer, Conducted in Partnership with Eli Lilly Corporation.

Accrual (over 500 patients) on this study has now been completed and finalization of the initial data base and follow up proceeds. INCTR has been asked by Eli Lilly to prepare a report of the results of this study (toxicity and preliminary treatment results). Audits of the CTO by Lilly went well, and Lilly has expressed an interest in working more closely with INCTR in the future. This too will be discussed at the Corporate Collaboration Committee meeting next week. It is to be noted that 10 centers from developing countries participated in this study, and INCTR is now working with up to 20 centers capable of conducting high quality clinical trials in developing countries. Since many of these centers see very large numbers of patients, the potential for undertaking relevant trials is large.

Lymphoma Strategy Group

The planning phases of the study of the treatment of Burkitt's lymphoma in several African countries are also nearing completion. The protocol has undergone ethical approval, and the next step is an implementation meeting for training of data managers and investigators in Africa. It is anticipated that this will take place in August.

It will be essential to develop a means of providing funding for the treatment of these patients. A survival rate of at least 50% is anticipated, and the cost of treatment per patient (using drugs purchased from India) is in the region of \$150-200. It is expected that 250 patients per year will be accrued. A grant proposal was submitted to Cancer Research UK, but this organization indicated that it is unable to fund clinical studies outside the UK. Attempts will therefore be made to obtain funding for the drugs from the pharmaceutical companies concerned.

An approach is also being made to Cancer Research UK to support a study comparing gene expression in African Burkitt's Lymphoma with that occurring in the West. The latter can only be done in the context of the clinical trial, thus an amended grant proposal for the 2 studies will be submitted to Cancer Research UK.

Two additional studies in Burkitt's Lymphoma are also being explored by Ama Rohatiner:

- (1) An evaluation of liposomal ara-C for intrathecal use in patients with CNS involvement
- (2) A Phase II study of Fluoxetine (Prozac) which is active against Burkitt's Lymphoma cell lines at concentrations known to be achievable with conventional oral doses, and could be investigated in the African setting initially, in patients in whom other therapies have failed.

An additional meeting of the lymphoma strategy group was held in Cairo in the autumn. Various studies were discussed, including the molecular characterization of chronic lymphocytic leukemia in various world regions and discussion about a collaborative study in diffuse large B cell Lymphoma to compare the conventional regimen 'CHOP' with the same regimen given with Rituximab (provided funding or free drug can be obtained from Roche). The possibility of using a different, more intensive regimen including additional drugs, as is currently under study in the UK (based on results achieved in adult patients with Burkitt's lymphoma) was also discussed.

The status of all INCTR trials is shown below:

Protocol No.	Title	Status	Total Accrued
INCTR 01-01	Phase II Study of Previously Untreated Metastatic Osteosarcoma with a Combination of Chemotherapy (cisplatin, doxorubicin, ifosfamide) and Surgery	Active patient accrual. Note: patients accrued by 2 of 5 participating institutions.	4
INCTR 01-02	Adult and Pediatric Lymphoma Loss to Follow Up Study	Single institutional study. Closed to new subject enrollment. Enrolled subject follow up only.	196
INCTR 01-03	Understanding Problems Faced by Parents of Children with Retinoblastoma Prior to Treatment	Multi-institutional questionnaire study. New subject enrollment continues. Participants enrolled by 6 of 14 participating institutions	241
INCTR 02-04	The Treatment and Characterization of Acute Lymphoblastic Leukemia in Children, Adolescents and Young Adults	Multi-institutional study. Accrual has not begun pending ICMR approval. Accrual is anticipated to begin in April, 2004	0
INCTR 03-05	The Treatment of Locally Advanced, non-Metastatic Retinoblastoma	In development	0
INCTR 03-06	The Treatment and Characterization of Burkitt's Lymphoma in Africa	Multi-institutional study. Local ERC approval required by 3 of 5 participating institutions	0

INCTR 03-07	The Treatment and Characterization of Acute Lymphoblastic Leukemia Using a Standard Treatment Protocol	Approved by INCTR ERC with stipulations. Re-submission pending revisions and review by Indian Principal Investigators	0
INCTR 03-08	A Retrospective Survey of Presentation of Breast Cancer and Risk Factors for Treatment Outcome	Approval by INCTR ERC and local ERCs. Awaiting database development prior to activation.	0

Note: All INCTR protocols undergo INCTR ERC review prior to distribution to participating institutions for local ethical review and approval. Once protocols are approved by the INCTR ERC, all undergo annual continuing reviews.

The possibility that pharmaceutical companies may be willing to provide drugs for at least a fraction of patients who participate in INCTR trials will also be addressed in the Corporate Liaison Committee to take place this week.

Education Program

INCTR Meetings Held in the last Year

Pediatric Updates and Training

Two pediatric updates were held respectively in Dubai, on 4th and 5th October (jointly with Shaukat Khanum in the course of its Annual Meeting, and in Chongqing, China, on 21st November (as a component of the Chinese Pediatric Oncology Society's Annual Meeting. Approximately 50 people attended the meeting in Dubai, and 150 people, the meeting in Chongqing. Both workshops included presentations and discussions on the management of common pediatric neoplasms, the role of bone marrow transplantation, limb sparing surgery and palliative care and were organized by Aziza Shad, Chairperson of the sub-committee on Pediatric Oncology. Both were also supported by the OIA, NCI.

Two additional meetings were held in 2003 at the King Hussain Cancer Center, Jordan to discuss improving care for children with cancer in Iraq. A variety of organizations (including INCTR) were involved as well as oncologists from many Middle East countries.

Cancer Nursing Education, Cameroun, 6th Mar, 2003

A one day course for oncology nurses was organized in Cameroun by Sabine Perrier-Bonnet of INCTR's French Branch, AMCC immediately following the second Euro-African Cancer Congress, in Yaounde. Topics covered included communications with patients and families, administration of

chemotherapy, secondary effects of cytotoxic drugs and techniques relevant to cancer nursing and palliative care.

Lymphoma Workshop at NCI, Cairo, Nov 16th to 18th, 2003

A 3 day Workshop, attended by more than a hundred Medical Oncologists and Haematologists-in-training was organized as a collaborative venture between the UK and Egyptian offices of the INCTR. The Faculty, comprising physicians and scientists, engendered lively discussion with the audience on areas of controversy in lymphoma treatment and research. The Workshop was funded jointly by the OIA (NCI Bethesda), INCTR and the pharmaceutical industry.

Meeting for Cancer Nurses at NCI, Cairo, Nov 16th to 18th, 2003

A 3 day meeting for Egyptian and Palestinian Cancer Nurses organized took place concurrently with the Lymphoma Workshop. Nurses from St. Bartholomew's Hospital and the Royal Marsden Hospital, London, together with those from the School of Nursing at the NCI Cairo comprised the Faculty, teaching about recent developments in cancer nursing. The meeting was funded by the OIA (NCI Bethesda) and the Special Trustees of St. Bartholomew's Hospital.

Acute Lymphoblastic Leukemia in India, Feb 9th and 10th, 2004

A meeting focused on the characterization and management of acute lymphoblastic leukemia (ALL) in India was held on 9th and 10th January, 2004, immediately after the Jubilee Meeting of the Cancer Institute, W.I.A in Chennai, India. In the course of the meeting, presentations were made from the major centers cooperating with INCTR (or its Anlage) for over 2 decades, as well as from other centers throughout India which have used the protocol MCP841, now by far the most widely used ALL treatment protocol in India. Gratifying improvements in results were clearly demonstrable throughout this period, and it was also apparent that clinical data was being presented and analyzed in a standard fashion by INCTR collaborating centers, but not by others. Approximately 150 people attended the meeting. Data was also presented on characterization of ALL in India using PCR detection of chromosomal translocations, strongly suggesting that Indian patients have a higher likelihood of having a "poor risk" translocation than western patients.

Additional Meetings planned for 2004

Clinical Trials Workshops similar to that held in Beijing in 2002 are being planned to take place in Brazil and in India. The Brazilian workshop will be partly sponsored by Eli Lilly, and is anticipated to take place before the end of the summer (the meeting was originally planned for April, but had to be postponed for local reasons). The meeting in India is tentatively scheduled for November 2004 and is likely to be jointly sponsored by the Indian Council for Medical Research, the State of Andhra Pradesh, and probably CTIS.

A further course in cancer nursing organized by Sabine Perrier-Bonnet will take place in Sétif, Algeria, immediately following the international Forum on Cancer, which will be held on March 15th

and 16th.

Through the Pediatric Oncology Education sub-committee, training workshops will be organized for Iraqi pediatric oncologists. The first one will be held in April 2004 and will focus on hematopoietic malignancies and supportive care. The second one will be held in the autumn of 2004, with a focus on solid tumors.

An additional Pediatric Oncology workshop is being proposed to be held in Karachi, Pakistan, to which pediatric oncologists from Afghanistan, Iran and Pakistan would be invited.

Visiting Expert Program

The purpose of the visiting expert program is to make possible a visit by mutually agreed upon experts to centers in developing countries. Experts may come from anywhere in the world, including other developing countries. They will spend one to several weeks in selected centers, participating in daily activities in addition to providing educational sessions. Such experts provide a means of exchanging ideas, enhancing knowledge, assessing capabilities and needs of recipient centers, promoting the conduct of an ongoing INCTR project, undertaking discussions regarding new projects, and improving communication within the network. The program was initiated in 2002. To date, it has focused on ongoing INCTR projects, retinoblastoma and palliative care.

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 2 weeks at the Shaukat 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 doing Out-patient Clinics and ward rounds, and teaching undergraduates and postgraduates at Allama Iqbal Medical College.

Other Educational and Training Activities

A total of 9 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.

Dr Corina Gonzales visited Panama to discuss the development of a pediatric oncology and nurse training program in 6 Central American countries. Such a program would be a joint effort of St Jude, INCTR and AHOPCA, the Central American Association for Pediatric Cancer.

Translational Research Program

The translational program of the INCTR is housed in the Research laboratory of the King Fahad National Children's Cancer Center and Research. Resources from the KFSHR&C support this program. At the present time the program is staffed by 3 Senior Scientists, 2 postdoctoral scientists, one graduate student and one technician in addition to 2 administrative assistants.

A pilot program was initiated with the purpose of coupling laboratory-based studies to clinical studies conducted by the INCTR. In order to rapidly assimilate laboratory data from such clinical trials, a translational project in childhood acute lymphoblastic leukemia was designed to assess genetic heterogeneity of leukemia cells and normal cells in patients. This peer reviewed project was initiated in 2001. Since then, several technology platforms have been set up and validated, including real time PCR tools for molecular sub classification, a platform for epigenetic analysis and pharmacogenetic analysis of the patient DNA. We have recently acquired an Affymetrix DNA chip system and the laboratory should be able to provide information on gene expression profiles of ALL samples. In the last two years, the program has trained 5 scientists from INCTR affiliates in India, Egypt and Turkey and has analyzed over 500 leukemia samples. Emerging data supports the hypothesis that the overall composition of molecularly defined poor and good prognosis ALL subclasses differ in India compared to that in the US or Europe

Committees

Education Committee

A core group of the education committee met in December 2003, particularly to discuss the coordination of educational meetings within the INCTR network. It was decided that a process of application for meetings is necessary, as INCTR is receiving many requests to hold educational meetings. An application form has been developed. It was also decided that MoU's would be prepared for all meetings other than committee/strategy group meetings, so that all parties, including sponsors and organizers, agree in advance to their role and funding sources are assured.

Ethical Review Committee

The INCTR Ethical Review Committee (ERC) is currently chaired by Francis Crawley who is also the Chairman of the European Forum for Good Clinical Practice. The ERC met in July and October of 2003 to discuss newly submitted protocols and to review on-going studies. Members of the ERC actively participated in Annual Meeting 2003 through an ethics workshop. This session was very well attended and generated much discussion. Therefore, members of the ERC have expressed a willingness to participate in Annual Meeting 2004 in a similar session pertaining to ethics in clinical research.

Corporate Liaison Committee

The next meeting of the CLC is planned for 10th March. Topics to be discussed include future clinical studies with the pharmaceutical industry, particularly Eli Lilly, and the development of a mechanism for providing at least some treatment costs, or the direct provision of drugs, for patients who might be prevented from having therapy for financial reasons.

Further training workshops and other educational support in Clinical Trials and Data Management in collaboration with the pharmaceutical industry will also be discussed.

Associate Membership

Some expansion of associate member corporations and institutions has been accomplished since the last meeting of the governing council. A full list of associate members is provided separately. In addition, a new type of associate membership has recently been initiated - individual associate membership. This is associated with a variable fee of \$100 (euros) to \$5000. Its purpose is similar to that of the corporate associate membership, i.e., it provides additional income, but also creates contacts with individuals who may be able to assist the INCTR in other ways, e.g. fund raising (Amber Valletta), new contacts, or perhaps provision of voluntary services (e.g. functioning as a cancer expert in the educational program). Individual members may come from all walks of life, e.g., health professionals, most of whom are likely to live in affluent countries, celebrities, or prominent members of the community. Of particular interest is the potential role for individuals from developing countries working as oncologists in western countries. Associate members are INCTR Associate members, regardless of the country of origin, or means of recruiting them.

Collaboration with other Organizations in the Field of Cancer Control

Collaboration with IARC, which has considerable expertise in cancer registration, epidemiology, particularly geographic epidemiology, and some specific early detection programs will be within two major areas, cancer registration and cervical cancer screening. The IARC is one of the recipients of a Gates Foundation award to further the detection of pre-invasive uterine cervical cancer, the predominant cancer in women in underprivileged societies, such that funding for training and the provision of limited equipment (speculae and colposcope) is presently available for joint projects through this route. Discussions regarding longer term collaborations have begun, in particular, how INCTR can further the replication and increased population coverage of projects initiated with IARC. INCTR is specifically involved, via Dr Sankaranarayanan, with cervical screening projects in Tanzania and Nepal.

INCTR is also working with IARC to establish a population based registry in Lahore. An expert in cancer registration well known to Dr Parkin, and based in Karachi, visited Lahore last year and a detailed budget is being prepared based on her recommendations.

INCTR has also been approached by Dr Cecilia Sepulveda of WHO who is interested in working with INCTR in a spectrum of cancer control activities, a particular priority being palliative care in Africa,

where WHO has already conducted a needs assessment. WHO is unlikely to be able to provide funding directly, but may have access to funds given by Governments for specific projects - e.g. 15% of US Government funding for AIDS in Africa has been dedicated to palliative care, and this may be administered via WHO.

INCTR has also had preliminary discussions with Dr Bhadrasain Vikram of the International Atomic Energy Agency of the United Nations. Dr Vikram is in charge of the clinical element of this agency relating to radiation oncology, and is involved with training and education of radiotherapists and nuclear physicists as well as in assisting to establish more radiation therapy programs in countries where there is a major shortage. Dr Vikram is also involved in clinical trials, although has limited access to clinical trials management. Further discussions will doubtless be held.

Funding - Sponsorships, Donations and Grants

INCTR continues to receive core funding from NCI, Bethesda. The value of this funding has been significantly affected by the devaluation of the dollar against the euro. However, this has been offset by support received from the Office of International Affairs for educational projects. Additional sources of income include Associate Memberships, sponsorships of meetings and donations and in kind support from CTIS and the NCI.

NCI OIA Support for Training and Education

INCTR has been strongly supported by the NCI Office of International Affairs, Directed by Joe Harford. Funds have been provided for a number of educational activities, including the pediatric updates in Dubai and Qingong, the oncology nursing course in Cairo and INCTR's Annual Meeting. INCTR anticipates a continuation and strengthening of this relationship, which will be greatly assisted by the administrative help of Susanne Radtke of NCI's Liaison Office in Brussels, through whom requests for support of educational activities will, from henceforth, now be directed. Dr Harford has promised support in 2004 for a workshop for Iraqi and Jordanian pediatric oncologists to be held in April, for training of Afghani physicians in the provision of cancer services, and has expressed a particular interest in working closely with INCTR in the area of palliative care.

CTIS Support for IT Development and INCTR Projects

CTIS has donated services and software use to INCTR in developing its Portal, described above, and clinical trials management programs. These donations are worth hundreds of thousands of dollars, and considerably more if normal licensing fees for software (e.g. TrialBridge) are taken into consideration. CTIS has also pledged \$200,000 towards INCTR projects this year, has provided \$30,000 for INCTR's palliative care projects, and has expressed a willingness to continue to support the development of the latter.

Sponsorships from the Pharmaceutical Industry

INCTR received approximately \$20,000 in sponsorships in 2003, and has already received \$50,000

from Eli Lilly in support of the Clinical Trials workshop to be held in Brazil.

TELESYNERGY®

INCTR has been given use of a powerful telemedicine system, just installed at the Liaison Office in Brussels. Some funds will be made available through the Liaison Office for telephone linkage (the system requires up to 30 ISDN lines), but discussions with respect to the development of telemedicine programs are ongoing.

Project Specific Funding/Grant Proposals/Contracts

INCTR received a grant of \$30,000 from the Lymphoma and Leukemia Society of America for a workshop on lymphomas in developing countries, that took place at its annual meeting 2003.

INCTR was successful in applying for a grant from the Sir Ratan Tata Trust for \$250,000 (over a three year period) towards its leukemia studies in India.

A grant application, also for \$250,000 has been made to the Susan S Komen Foundation for its study in breast cancer. The result of this application will be known this month.

A grant application for funding of the characterization of Burkitt's lymphoma will be re-submitted to Cancer Research (UK).

INCTR has assisted Eli Lilly in the conduct of a randomized trial for the treatment of locally advanced cervical cancer in 10 centers in countries with limited resources. This experience has produced income, while being entirely consistent with INCTR's mission. It has also ensured that INCTR's Clinical Trials Office meets industry standards (an audit and a visit have been made by Lilly staff).

Associate Membership

This program continues to be successful. Fees secured from corporations range from \$10,000 to \$100,000 per year, but corporate members are few. The individual associate membership program is a potential source of significant revenue, and many new invitations have recently been sent out. Further efforts will be made in 2004 to increase the number of Associate Members in all categories, since this both provides income, and enriches the human resources available to INCTR in the conduct of its mission. It is hoped that branches will participate more vigorously in attracting new INCTR members.

More precise information relating to income and expenditure is provided in the budget documents.

Annual Meetings

This year (2004), the annual meeting will take place at the Conrad Hotel in Cairo between October

2nd and 5th. Winners of INCTR awards for 2004 are Franco Cavalli (Paul P. Carbone Award in International Oncology) and Mohammed Mafous (Nazli Gad-el-Mawla Award). The program is in draft form and the first announcement has been sent out.

The Annual Meeting, 2005, will probably take place in Chennai, India (to be finalized shortly). The location of the 2006 meeting will be discussed at the next meeting of the Special Panel of the Advisory Board, to be held at the 2004 Annual Meeting. On this occasion, the winners of the 2005 INCTR awards will also be chosen.