

# Clinical Research Program Report

INCTR Annual Meeting 2007

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# General Description of Program Functions

- Main Functions
  - Coordination of Strategy Groups
  - Management of Clinical Research Studies
  - Education and Training
- Other Functions
  - Administration of INCTR Ethical Review Committee
  - Provision of Data Management Services

# Strategy Groups – A Brief Review

- Comprised of investigators from countries with limited resources
- Disease-specific (African BL, Breast Cancer, Cervical Cancer, Leukemia Study Group of India, Lymphoma, Osteosarcoma, Retinoblastoma)
- Determine the role of INCTR in the control of a specific cancer
- Design of clinical research studies

# Retinoblastoma Strategy Group - Activities

- Public and professional awareness campaigns
  - Mexico
    - Formation of Mexican Retinoblastoma Group
    - Poster Campaign
    - Public Service Announcement for TV
  - India
    - Professional Awareness for Ophthalmologists (role of chemo-reduction)
    - Public Awareness (full length movie of the story of a child with bilateral retinoblastoma)

# Retinoblastoma Strategy Group Activities

- Public and Professional Awareness Campaigns
  - Turkey
    - Retinoblastoma Day (highly publicized)
    - Professional Education
  - Brazil
    - Public Service Announcement on TV
    - Telephone Card Campaign

# Retinoblastoma Strategy Group – Survey Study

- Understanding Problems Faced by Parents of Children with Retinoblastoma Prior to Treatment
- Description:
  - Interview of parents/guardians
  - Recording the child's clinical data
- Objective:
  - To identify the factors contributing to delays in diagnosis and obtaining treatment

# Retinoblastoma Study

- 13 institutions from 10 countries have contributed data to this study
  - Brazil
  - Bolivia
  - Guatemala
  - Mexico
  - Nigeria
  - Tanzania
  - Zimbabwe
  - Turkey (2 institutions)
  - India (3 institutions)
  - Pakistan

# Retinoblastoma Study

	Number (%)	
Fathers	179	46.1
Mothers	176	45.4
Guardians	32	8.2
Patient	1	0.3
Total	388	100

# Retinoblastoma Study – Summary of Findings

- Children from rural areas had higher stages of disease
- Older age children had higher stages of disease
- Lower socioeconomic status was associated with higher stages of disease
- Fathers' education level was associated with St Jude Stage of disease (the lower the education level, the higher the stage)
- Lower education levels of fathers were associated with longer time intervals between time of first symptom and diagnosis

# Retinoblastoma Survey Study

- Detailed results will be presented in the Retinoblastoma Workshop on Saturday, March 3<sup>rd</sup> of the Annual Meeting

# Retinoblastoma Strategy Group Activities

- Treatment protocol:
  - Extraocular retinoblastoma
  - Eligible patients include those with extraocular disease that has not metastasized to the CNS
  - VCR/ETOP/Carb – optic nerve negative or  
IFOS/ETOP/Carb (ICE) – optic nerve involvement
    - with RT for both groups
  - ICE regimen piloted at Ankara University for feasibility

# Leukemia Study Group of India

- Treatment Protocol
  - INCTR 02-04 entitled, "The Treatment and Characterization of Acute Lymphoblastic Leukemia in Children, Adolescents and Young Adults"
- Based upon an earlier treatment protocol used in India for many years called MCP841

# INCTR 02-04 - Objectives

- Characterize the pattern of ALL in India (immunophenotype, DNA index, molecular profiling)
- Correlate laboratory findings with clinical characteristics
- Identify prognostic factors predictive of relapse and survival

# INCTR 02-04

<i>Institution</i>	No. Patients
All India Institute of Medical Sciences	58
Cancer Institute, Chennai	55
Tata Memorial Hospital	61
Jaslok Hospital	50
Total	224

# INCTR 02-04

	Total	No (%)
Gender	Males	163 (66.4)
	Females	61 (33.5)
Age (years)	1 - < 2	8 (4.0)
	2 - 9	113 (53.7)
	10 - 17	75 (27.5)
	18 - 25	28 (14.8)

*Note: In Chennai, patients tend to be older (23.7% are  $\geq 18 - 25$  years old)*

# INCTR 02-04 - Immunophenotype

<i>Center</i>	Precursor B	Precursor T
AIIMS	73.4%	22.4 %
CI	59.6%	34.6%
TMH	78.7%	21.3%
Jaslok	75%	22.6%

## INCTR 02-04: T Cell Disease, Socioeconomic Status, Urban versus Rural

SES	Low	Mod	High	Combined
URBAN	26%	22%	16%	19%
RURAL	40%	22%	-	34%
TOTAL	35%	22%	16%	

# INCTR 02-04 Response

CR	84.4%
PR/NR	2.4%
Not evaluated	
<i>Induction deaths</i>	11.8%
<i>Lost to follow-up</i>	0.9%
<i>Voluntary withdrawal</i>	0.5%

# INCTR 02-04 – Status of CR Patients

Alive in CR	127	71.3%
Remission deaths	20	11.2%
Relapse	17	9.5%
Off-study - other	14	7.8%

*Majority of relapses occurred in one institution 9/17 where multiple problems were documented with supportive care and protocol deviations*

# INCTR 02-04 Summary

- Rural populations with low SES have a higher proportion of T cell disease than urban populations of low SES
- Patients from Chennai differ
  - 24% were 18-25 years of age
  - 60% were from rural regions
  - 35% have T cell disease
  - Account for majority of relapses and off-study patients
- CR rate seems low (84%), but if calculated based upon only patients who could be evaluated for response, CR rate is 97%

# INCTR 02-04 Summary

- Protocol is more intensive than earlier protocol
- Induction and remission death rates *appear* higher than MCP841
- Relapse rate *appears* to be lower than MCP841
- Most patients have not completed treatment and therefore, it is too soon to draw conclusions or make valid comparisons with MCP841
- Data monitoring has been introduced
- Web-based data entry has been introduced
- Study committee comprised of PIs meets regularly

# African Burkitt Lymphoma Strategy Group - Activities

- Treatment protocols
  - INCTR 03-06: "The Treatment and Characterization of Burkitt Lymphoma in Africa" (accrual began in August, 2004)
  - INCTR 06-09: "Phase II Study to Determine the Efficacy and Safety of DepoCyte for the Treatment of CNS Relapse in Patients with African BL" (to be started in 2007)

# INCTR 03-06 - Objectives

- Characterize the presentation features of African Burkitt Lymphoma
- Assess response and survival
- Improve data collection and patient follow-up

# INCTR 03-06: Treatment Plan

- First-Line Treatment
  - Newly diagnosed, previously untreated patients
  - Treatment stratification based upon low or high risk definitions
  - CTX/VCR/MTX with IT Rx x 3 or 6 cycles
- Second-Line Treatment
  - Non-responders or early relapses
  - ETOP/IFOS (mesna), Ara-C with IT rx x 4 cycles

# INCTR 03-06

<i>Institution</i>	Patients
Ocean Road Cancer Institute, Tanzania	77
Kenyatta National Hospital, Kenya	38
Obafemi Awolowo University, Nigeria	29
Ibadan University Hospital, Nigeria	16
Total	160

# INCTR 03-06 – Patient Characteristics

Gender	Males	107
	Females	53
Age (years)	Range	2 - 28
	Median	6
Risk Group	High Risk	160
Total		160

# INCTR 03-06: Patient Characteristics

<i>Site of Disease</i>	(%)
Jaw	58.6
Abdomen/Pelvis	54.0
Lymph nodes	24.5
Orbit	20.7
CNS	10.2
Bone marrow	4.9
Bone	4.5

# INCTR 03-06: Response to First-Line Treatment

CR	75.4%
PR	13.0%
NR	3.1%
Not evaluated	8.5%

*Some PRs may have achieved CR later in therapy*

# INCTR 03-06: Response to Second Line or Repeat First Line

- Second-Line Treatment – 12 patients
  - 6 NR/PD, 2 CR, 4 missing data
- Repeat First-Line Treatment (late relapse) – 7 patients
  - 3 CR, 2 PR, 1 NR and 1 missing data

# INCTR 03-06 – Off-Study Patients

Deaths	27 (16.9%)
Lost to Follow Up	9 (5.6%)
Voluntary withdrawals	6 (3.7%)
Treatment failures	5 (3.1%)
Total Off-Study	47 (29.4%)

# INCTR 03-06: Summary

- Data monitoring visits have taken place in 3 of the 4 institutions
- Problem of “lost to follow up” has significantly decreased (<6%)
- Expert visit in May, 2006 for 6 weeks in one institution led to improvements in supportive care practices
- Participating investigators have been able to present data at national meetings in 2006

# Breast Cancer Strategy Group - Activities

- Survey Study
  - INCTR 03-08 entitled, "Retrospective Survey of Presentation Features and Risk Factors for Treatment Outcome"

# INCTR 03-08

- Retrospective Survey of Female Breast Cancer Patients 1993-2001
  - Presentation features
  - Treatment received
  - Outcome

# INCTR 03-08

- Educational grant support obtained from Susan G. Komen for the Cure
  - Partial data manager salary support
  - Database development
  - On-site data monitoring visits
- Office of International Affairs, NCI

# INCTR 03-08

- Participating Institutions
  - Instituto Nacional de Enfermadades Neoplasicas, Lima, Peru
  - National Cancer Institute, Cairo, Egypt
  - Cancer Institute, Chennai, India
  - Jinnah Hospital, Lahore, Pakistan

# INCTR 03-08: CRF Summary

Institution	Completed	Submitted
INEN, Peru	3,224	3,224
CI, Chennai	1,819	402
Jinnah Hospital	220	120
Total	5,243	3,746

*In CI, 1,952 records to be abstracted, NCI Cairo has just begun to abstract data.*

# Data Management Services for External Organizations

## ■ Cervical Cancer

- Off-site data management for a large randomized trial for the treatment of locally advanced cervical cancer (Eli Lilly)
- Over 500 patients enrolled

## ■ Breast Cancer

- Off-site data management for a large randomized comparison of two methods of radiotherapy in locally advanced breast cancer (IAEA)
- Over 900 patients will be enrolled
- Protocol written and approved by INCTR ERC, accrual to begin in 2007

# Education and Training in Clinical Research

- Protocol-specific Data Manager Training
  - On-line training of data managers
  - On-site training at the time of monitoring visits
- Meet the Expert Sessions
  - Annual Meeting in Chennai, 2005
  - Annual Meeting 2007
    - Investigator Responsibilities in Clinical Research
    - Solutions to Challenges in Data Management

# Thank You

- External Scientific Reviewers
  - Peter Adamson
  - Alfred Reiter
  - Torrey Sandlund
  - Pierre Scalliet
  - Jean-Marie Deneufbourg
- Oncology Pharmacy
  - Paul Jarosinski
- Statistics
  - David Venzon

# Thank You

- Principal Investigators contributing to all studies
- Data managers working with the PI's
- Award for Special Achievements in Data Management
  - Mr Lukman Bhashir, Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Nigeria (African BL study)
    - Improvements in data management practices
    - Training of a new data manager in Ibadan

# Thank You

- INCTR Ethical Review Committee
  - Francis Crawley (Chairperson)
  - Angelo Rosolen (Co-Chairperson)
  - Henning Bredenkfeld
  - Marc Buyse
  - Julia Challinor
  - Nasir El-Lalani
  - Ali Khan
  - Sabine Perrier-Bonnet

# Thank You

- INCTR CTO Staff
  - Lolita Lantican
  - Corinne Claes
- INCTR Consultant
  - Julia Challinor

