



ADVANCING CANCER RESEARCH WITH

LATIN AMERICA LATINA

FOMENTO DE LA INVESTIGACIÓN DEL CÁNCER CON

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***US-Latin American Cancer Research Network: An
Opportunity to Collaborate on Quantitative Image
Research***

Lung Cancer Workshop VIII
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NCI's Global Mandate

The National Cancer Act of 1971 directs that NCI “support research in the cancer field outside the United States by highly qualified foreign nationals which can be expected to benefit the American people; collaborative research involving American and foreign participants; and training of American scientists abroad and foreign scientists in the United States.”



Top 5 Cancers in U.S. Hispanic Men as Compared to Argentina, Brazil, Chile, Mexico and Uruguay[^]

AGE-ADJUSTED MORTALITY RATES (1999-2003*)



	US Hispanic	Non- Hispanic White	Argentina	Brazil	Chile	Mexico	Uruguay
Lung and bronchus	37.2	73.8	29.8	18.6	17.8	13.4	48.4
Prostate	22.1	26.7	15.6	16.3	16.8	12.2	26.1
Colon and rectum	17.5	23.7	15.2	6.5	8.8	4.3	19.6
Liver and intrahepatic bile duct	10.7	6.3	4.4	5.8	5.8	6.4	3.0
Pancreas	9.2	5.4	8.2	4.3	5.1	4.2	8.9

*Annual Report to the Nation on the Status of Cancer 1975-2003, Featuring Cancer Among U.S. Hispanic/Latino Populations. *Cancer*. October 15, 2006. Vol. 107, Issue 7.

[^]Data derived from Globocan 2008

Top 5 Cancers in U.S. Hispanic Women as Compared to Argentina, Brazil, Chile, Mexico and Uruguay[^]

AGE-ADJUSTED MORTALITY RATES (1999-2003*)



	US Hispanic	Non- Hispanic White	Argentina	Brazil	Chile	Mexico	Uruguay
Breast	16.3	25.4	20.1	12.3	11.0	10.1	24.3
Lung and bronchus	14.7	42.0	8.8	7.4	8.1	5.3	8.1
Colon and rectum	11.4	16.4	9.4	5.8	6.9	3.7	13.8
Pancreas	7.5	9.0	5.9	3.3	5.1	4.0	7.4
Ovary	6.0	2.7	4.5	3.0	3.7	3.6	5.0

*Annual Report to the Nation on the Status of Cancer 1975-2003, Featuring Cancer Among U.S. Hispanic/Latino Populations. *Cancer*. October 15, 2006. Vol. 107, Issue 7.

[^]Data derived from Globocan 2008

In the US: All Cancers in Latinos

- All cancers combined, :
 - Highest Prostate/Breast/Colorectal/Lung; but,
 - **Incidence & mortality lower than in NHW**
 - Although lower but much higher than NHW
 - **Stomach/Liver/Cervix/ALL/Gallbladder**
- 2nd leading cause of death in the US after cardiovascular diseases
- Not different than in LA countries

Understanding Cancer in the U.S. and Latin America - The Research Need is Great

- Hispanics will become the largest minority group in the United States
- Cancer rates increase for first-generation Hispanics in the United States compared to cancer rates in their country of origin (*Pinheiro et al, Cancer Epi Biomarkers Prev 2009;18(8). August 2009*)
- Limited data and understanding of cancer burden by Hispanic subgroups in the United States (*Howe et al, Cancer Causes Control. DOI 10.1007/s100552-009-9398-8. July 2009. Howe et al, Annual Report to the Nation, DOI 10.1002/cncr.22193. Sep 2006*)
- Reducing the cancer burden in the United States will depend on our ability to understand and control cancer at the cultural, behavioral, and molecular level

Common Beliefs and Observations

- Hispanics in the US: lower incidence and death rates
- Diagnosed with advanced stage
- Lower survival rates for most cancers (acct age/stage)
- Less access to health care
- Less use of screening
- Larger size tumors
- More likely to die from cancer when diagnosed
- Less adherence to treatment
- >45% have less than HS education (15% in NHW)
- >20% live below the poverty line (8% in NHW)
- ~25% do not speak English fluently
- Temporary workers (% unknown), but how it affects health care coverage?
- >30% do not have health insurance
- Other risk factors: < tobacco and alcohol use; >overweight

Additional Issues that need to be considered

- Factors of acculturation should be carefully studied
- Genetic ancestry as a method of studying risk
- Other susceptibility genes should also be studied
- Environmental factors should be systematically measured
- Place/Region of Origin presents challenges:
 - Mexico
 - Central America
 - South America
 - Caribbean
 - Recognizable sub-categories among all four regions
- Only a 2% of all participants in NCI clinical trials are Latinos
 - Social Responsibility and Scientific Interest/Curiosity
 - Who is responsible for initiating and sustaining this debate?
- Who is Latino/Hispanic? A very contentious issue...
 - Anthropologists should be part of the discussion...
- Dr. Olopade: "stressful to admit that there are biological differences"...concerns about practicing "race medicine"

Office of Latin American Cancer Program Development

- Addressing the cancer burden in Latin America as a means of understanding cancer in the US Latino population
- Closing the research gap in Latin America
- Fulfilling NCI's role as a global cancer research leader through knowledge sharing



OLACPD Vision and Mission

Vision

- To advance local and global initiatives to prevent, diagnose, and treat cancer by facilitating the development of a comprehensive cancer research infrastructure in Latin America

Mission

- To advance the mission of NCI by collaborating with government agencies, researchers, and organizations to further cancer research in Latin American countries



Guiding Principles

- **Advancing Science**

Initiating research projects based on common interests and high bioethical standards will elevate the quality and credibility of cancer research conducted in Latin America.

- **Capacity Building**

Building research capacity in Latin America will lead to independent, sustainable infrastructure to support first-rate clinical research around the globe.

- US investigators will have more capable partners

Model for Partnerships and Collaborations



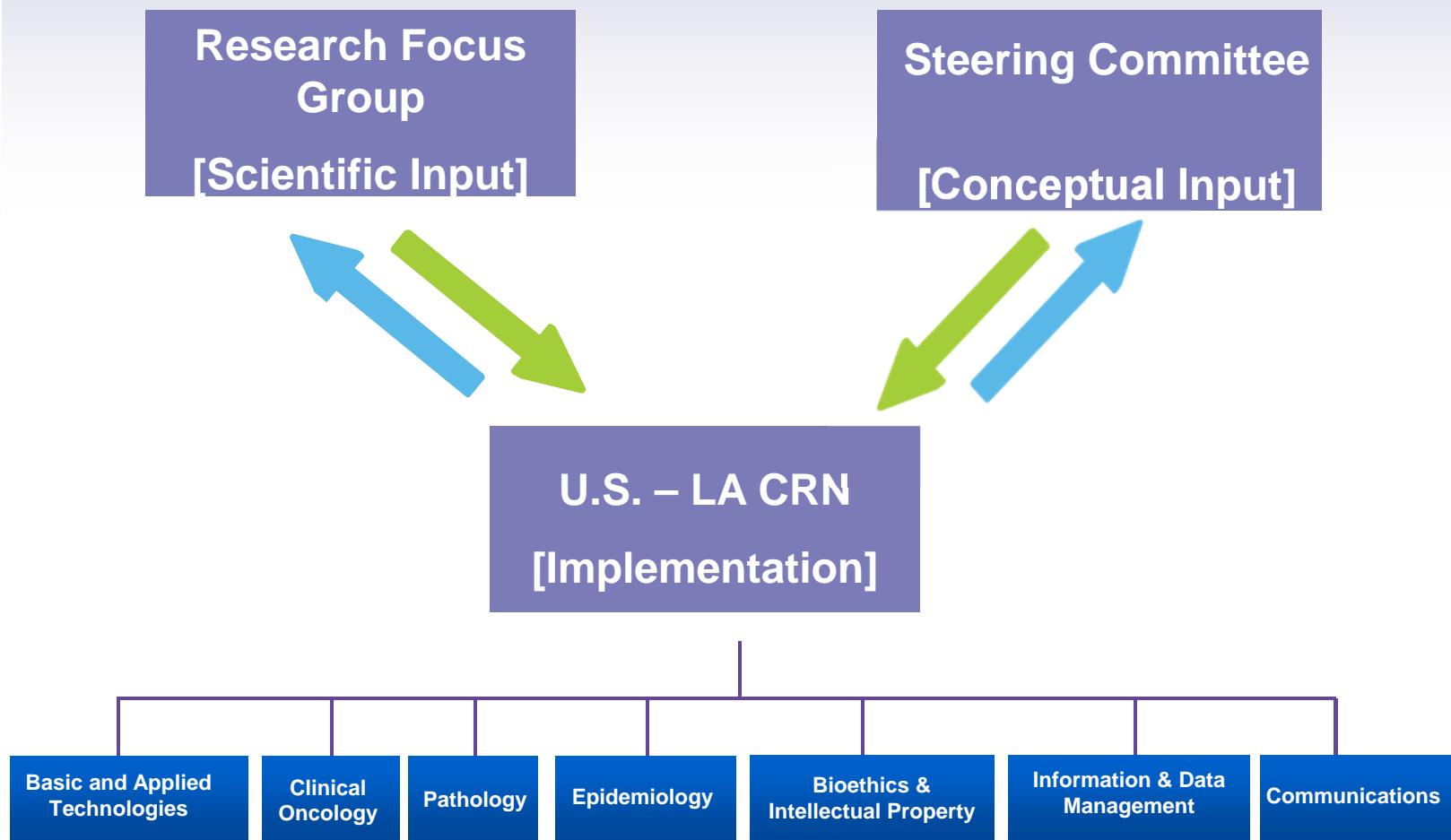
United States-Latin America Cancer Research Network (US-LA CRN): *A New Model for International Cancer Research*



US-LA CRN At a Glance

- Launched in March 2009
- Unprecedented Bilateral Partnership Connecting:
 - Governments
 - Institutions & Researchers
 - Non-Governmental Organizations
- Multi-Phased Strategic Approach
- Governed by a Steering Committee with input from an External Research Focus Group
- Co-Developing Pilot Projects
 - Selecting research areas based on disease burden
 - Breast Cancer: first pilot project

US-LACRN Governance



Infrastructure for Working Together



First Project: Breast Cancer Study

- Addressing the high breast cancer incidence in Latin America
- Providing data to advance cancer management for United States Hispanic population
- Focusing on 21st century biomedical concepts
 - Molecular Profiling of Breast Cancer
 - Understanding/Improving Early Detection
 - Clinical Trials
- Improving biobanking process in Latin America
- Establishing sustainable infrastructures and cancer research networks

Molecular Profiling Breast Cancer Study

Primary Objective

To characterize the distribution of invasive breast cancer stage II and III molecular profiles (luminal type A, luminal type B, HER2-like, basal) in Latin American women

Molecular Profiling Breast Cancer Study

Secondary Objectives

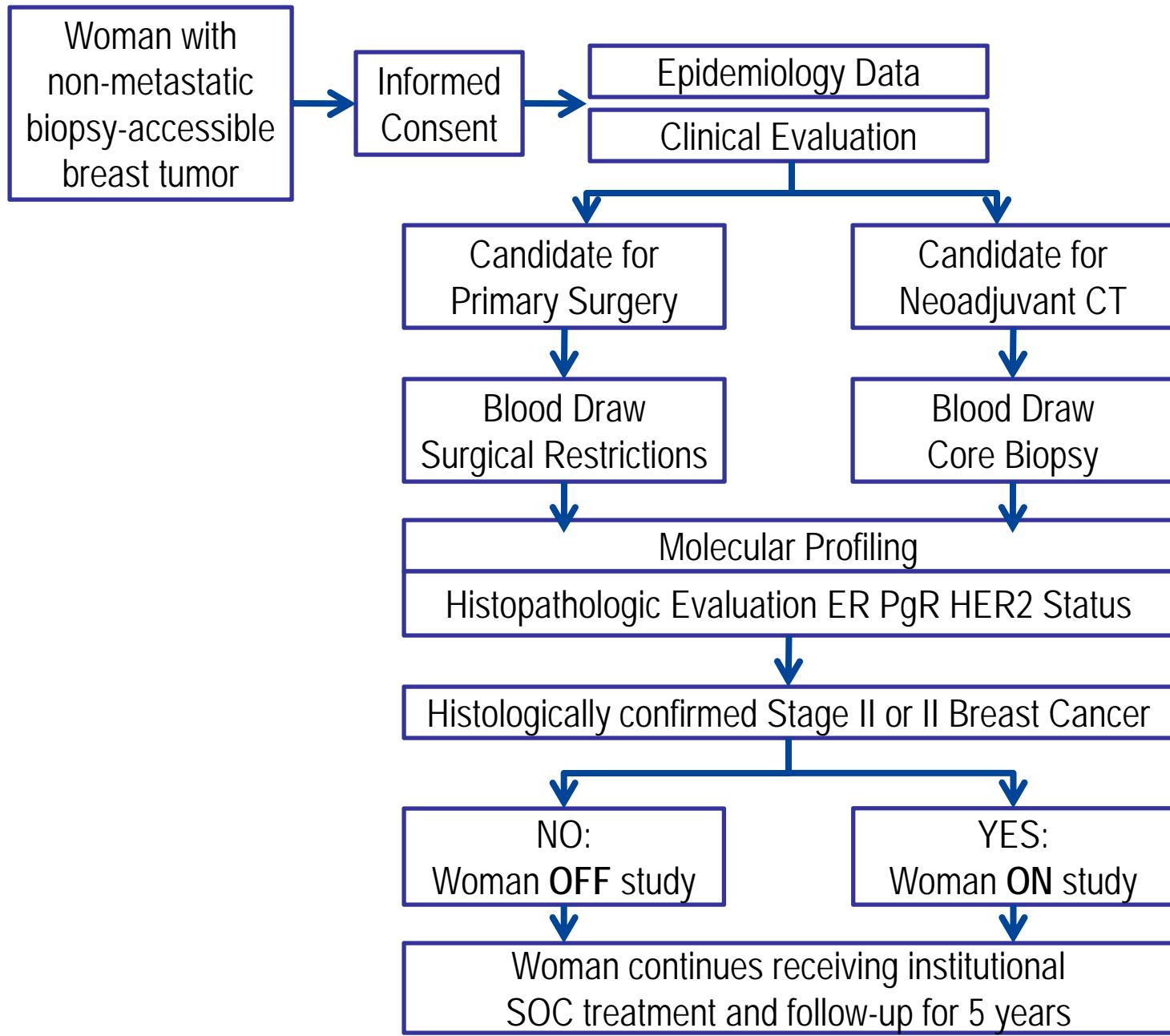
- To find an association between the molecular profiles and the histopathologic characteristics of the tumor prior to treatment including histological type, size, lymph node involvement, and surrogate markers
- To estimate the rate of pathologic complete response (pCR) to neoadjuvant chemotherapy in each of the breast cancer molecular subtypes and to evaluate any differences in success rates among the molecular subtype cohorts
- To discover and develop predictive and prognostic gene expression signatures

Molecular Profiling Breast Cancer Study

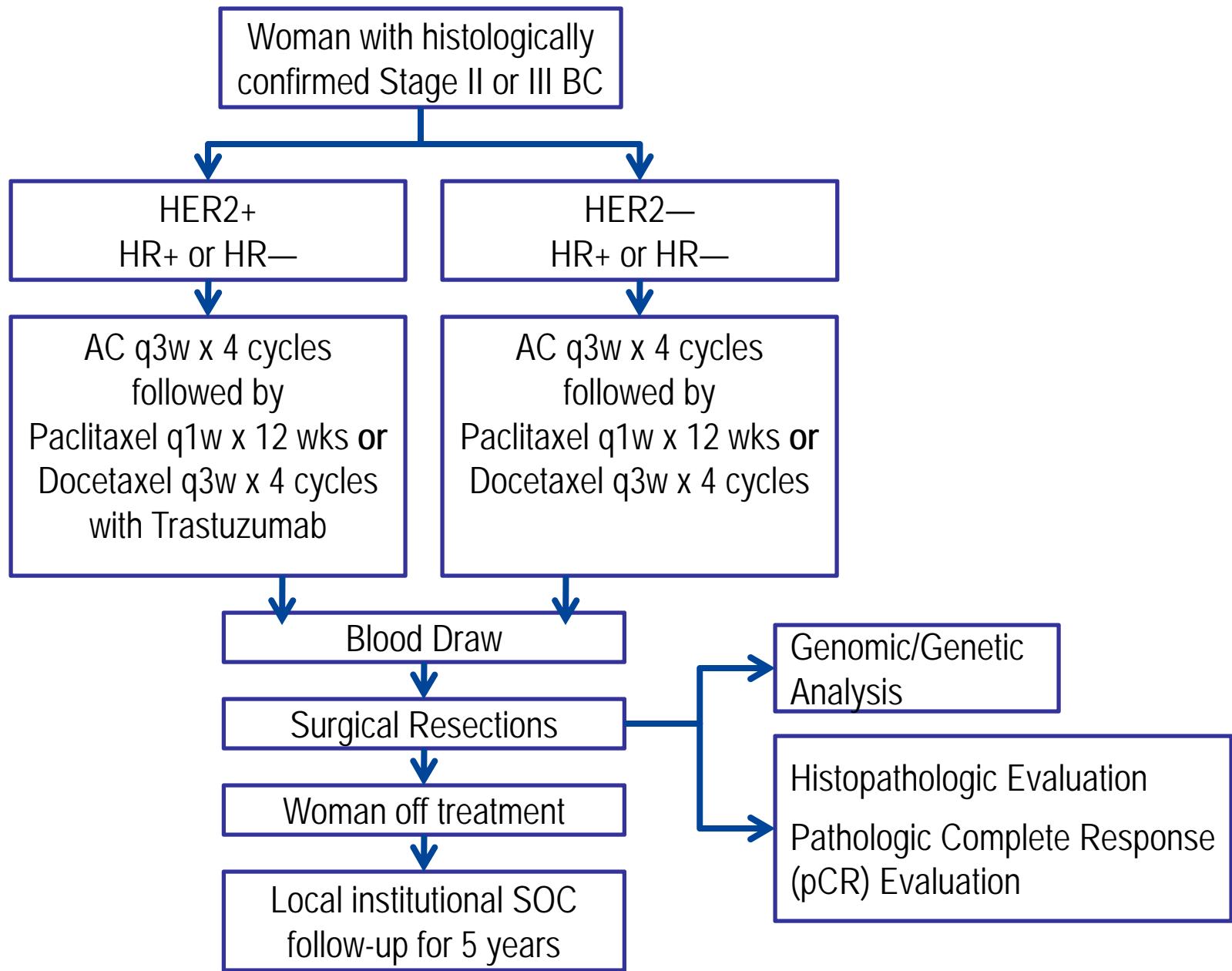
Secondary Objectives *(continued)*

- To determine three- and five-year overall survival (OS), time to first failure (TFF) and disease-free survival (DFS) for each molecular subtype and to evaluate any differences in those parameters among the subtype cohorts
- To document the demographic and epidemiologic characteristics of each molecular subtype.

Breast Cancer Study Protocol Schema



Breast Cancer Study Protocol Schema *(continued)*



Standardization and Harmonization Effort

Key elements in multi-national clinical study/trial design

- Harmonization of Clinical/Oncologic Procedures
- Standardization of Pathology Procedures
- Standardization of Basic Research Procedures
- Development of Case Report Forms (CRFs)
- Development of Epidemiology Questionnaire
- Integrated Biospecimen banking procedures
- Integrated Bioinformatics tools
 - OpenClinica™ (CDMS)
 - BSI-II™ (biospecimen inventory & management tool)
 - Biospecimen labeling (scanner & printer)
 - caArray (caBIG tool)
 - calIntegrator 2 (caBIG tool)

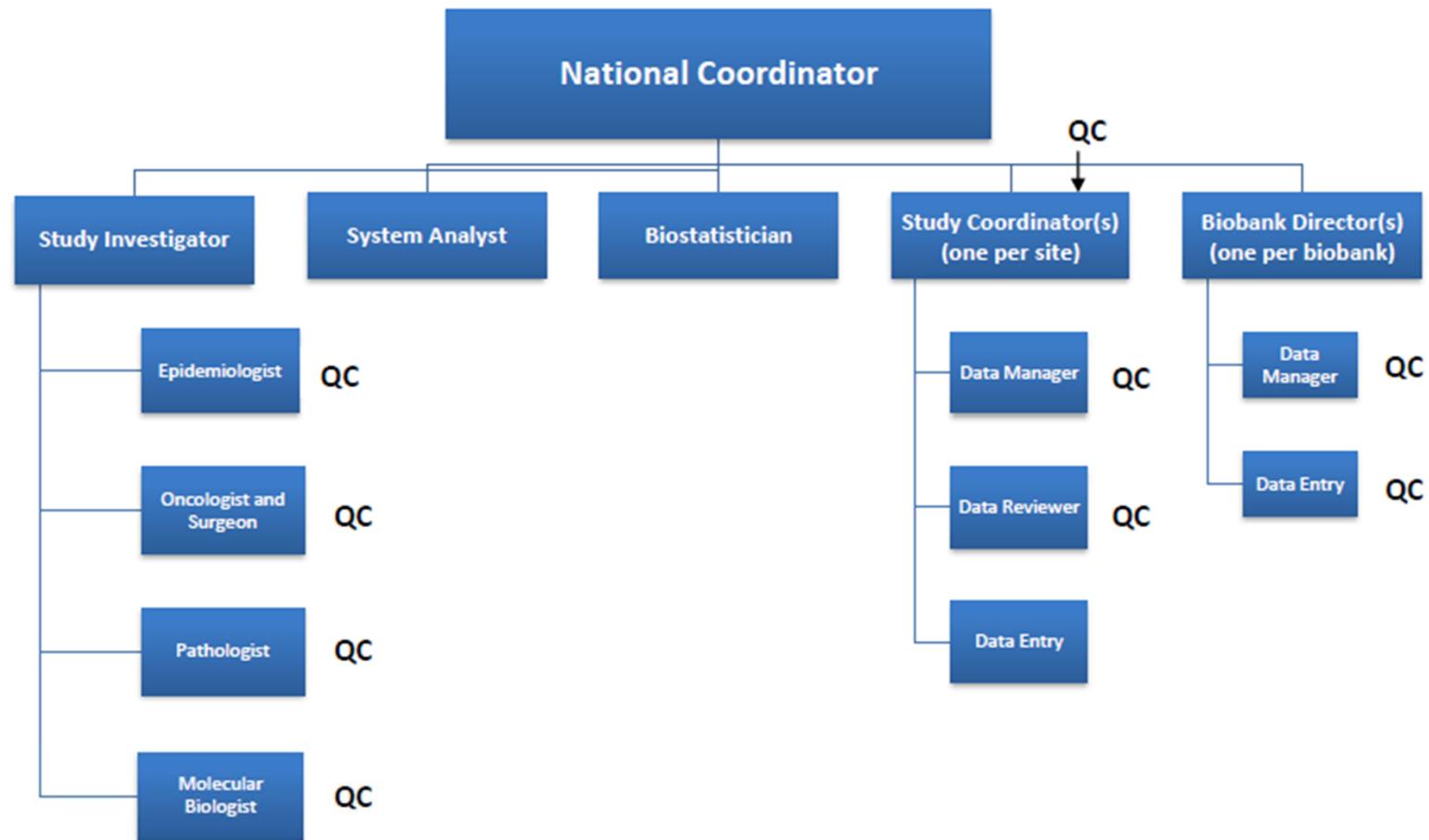
Standardization of Pathology Procedures

- Standard operating procedures (SOPs) for collection, handling, processing and storage of biospecimens (whole blood, biopsy and surgical resections)
- SOPs for ER, PgR, HER2 and Ki67 tumor status assessment
- Unified reagent vendors for formalin and IHC/ISH kit lot numbers
- Harmonization on assay results interpretation
- Participation in US College of American Pathologists Proficiency Testing

Standardization of Clinical/Oncology Procedures

- Development of clinical protocol through a collaborative effort among pathology, oncology, surgery, epidemiology, basic research and steering committees.
- Harmonization on neoadjuvant chemotherapy
- Harmonization on patient evaluation procedures
- Harmonization on diagnostic procedures
- Surveys to assess current infrastructure and capabilities

Study Organization for Quality Control Checkpoints



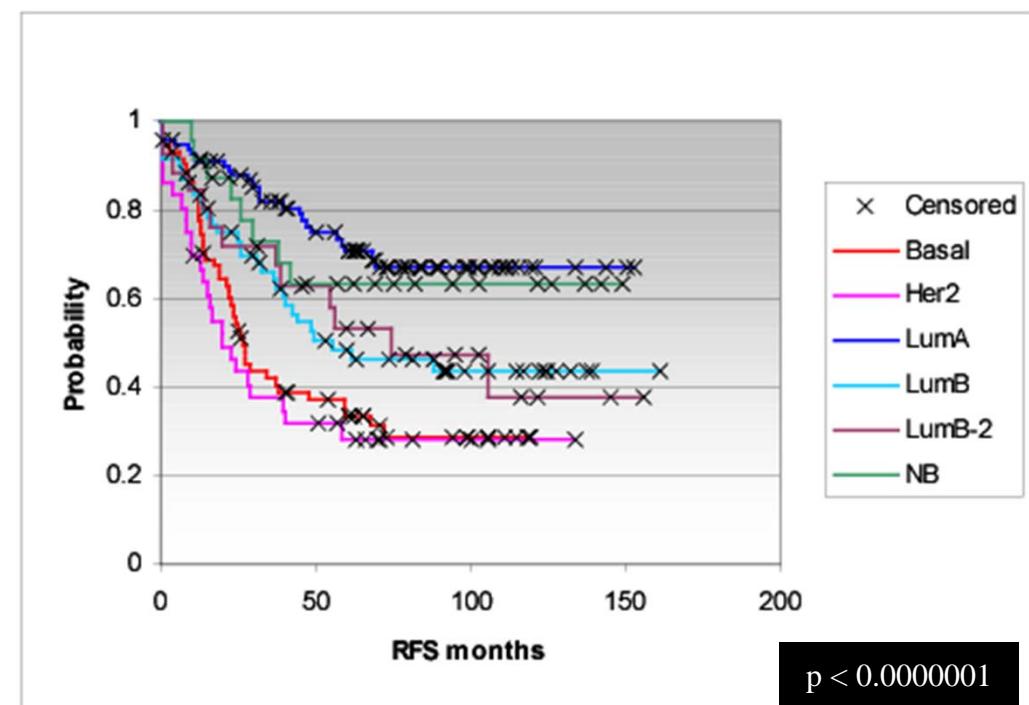
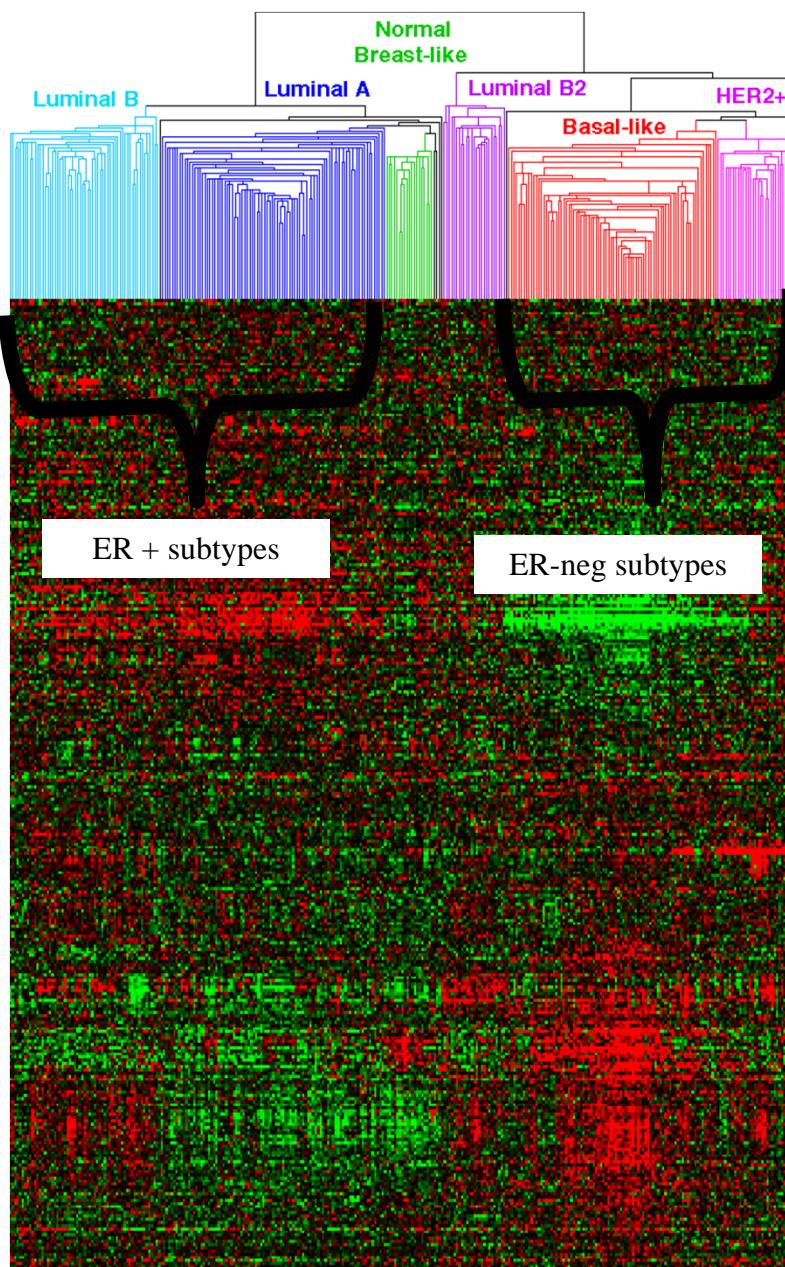
Impact of the Breast Cancer Study

- Improve breast cancer diagnosis and effective treatment by elucidating the molecular profile of breast cancer in Latin American women
- Investigate the association between the molecular profiles and tumor characteristics including histological type, size, lymph node involvement and surrogate markers
- Identify the correlation between the molecular profiles with long term survival and response to therapy
- Identify subpopulations of cancer patients with indolent disease which may permit more “personalized” management and reduce unnecessary exposure to CT

Impact of the Breast Cancer Study *(continued)*

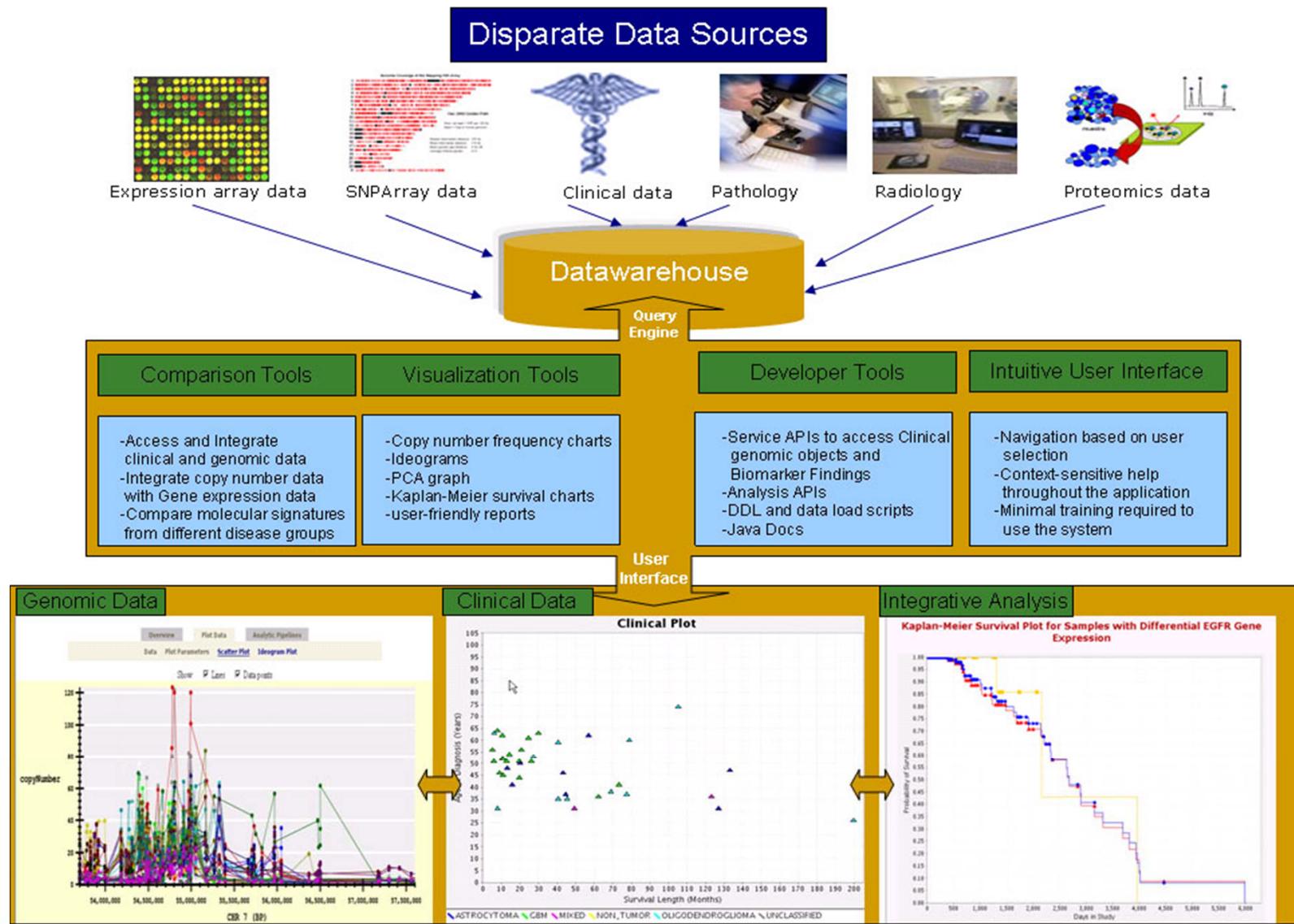
- Bring state-of-the-art cancer research to Latin America:
 - Tissue annotation, storage, management
 - Use of informatics and data management
 - Adherence to high ethical standards
- Create better partners in Latin America for international cancer research
- Increase the pool of Latin American investigators and provide greater visibility at international cancer meetings

Breast Cancer Molecular Profiling

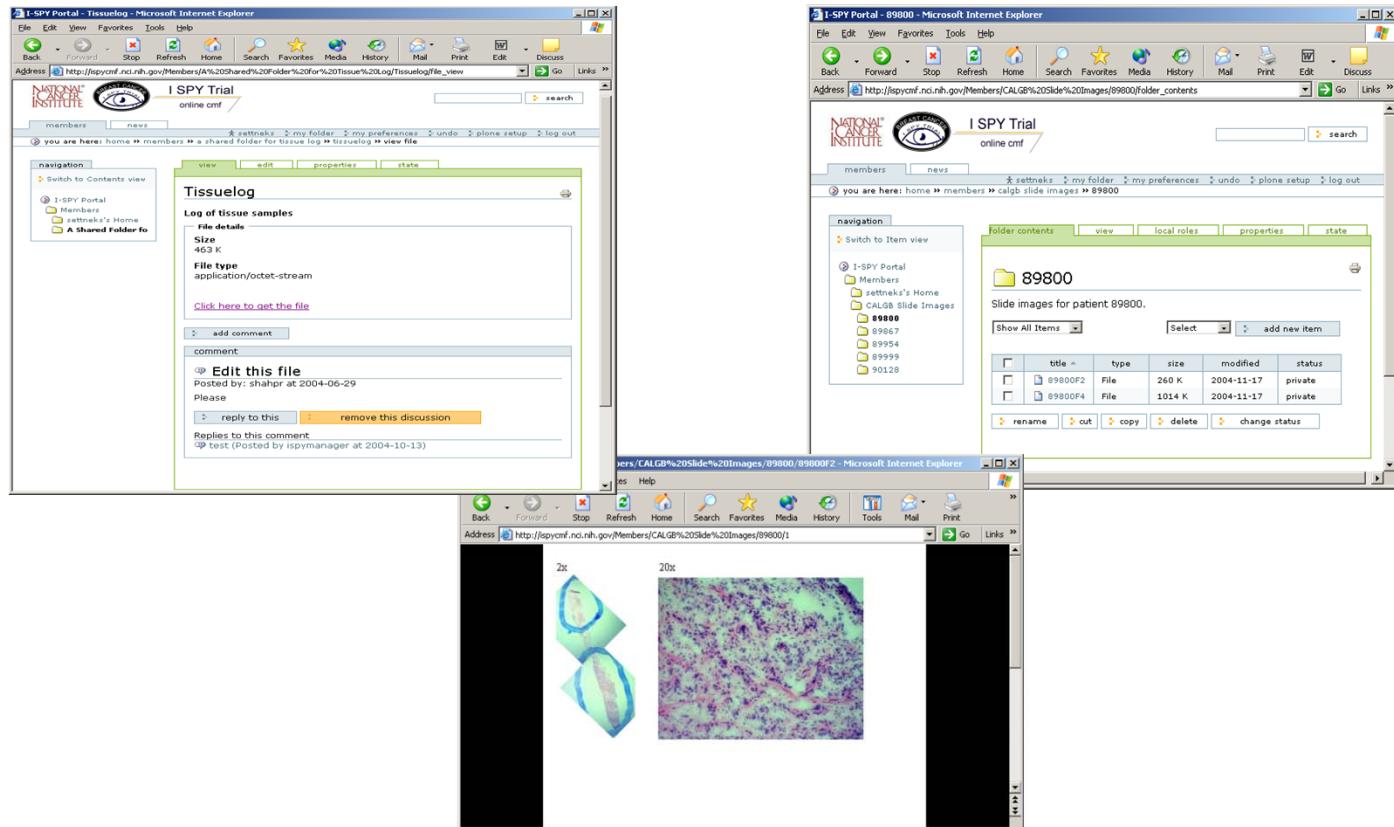


Courtesy Chuck Perou

National Cancer Institute



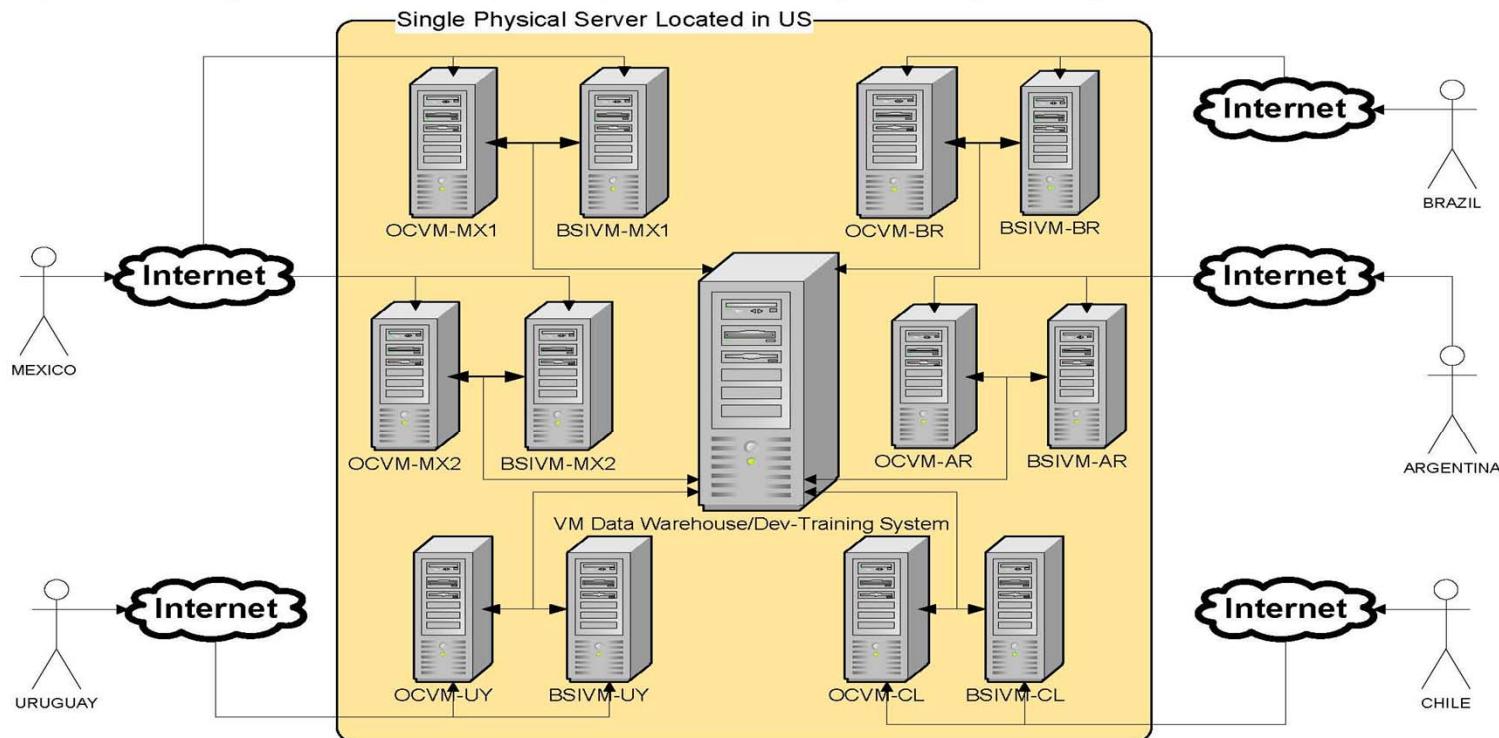
File Sharing – slide images and tissue logs, meetings



Phase I: OpenClinica™ + BSI™

Initial Phase – OpenClinica + BSI

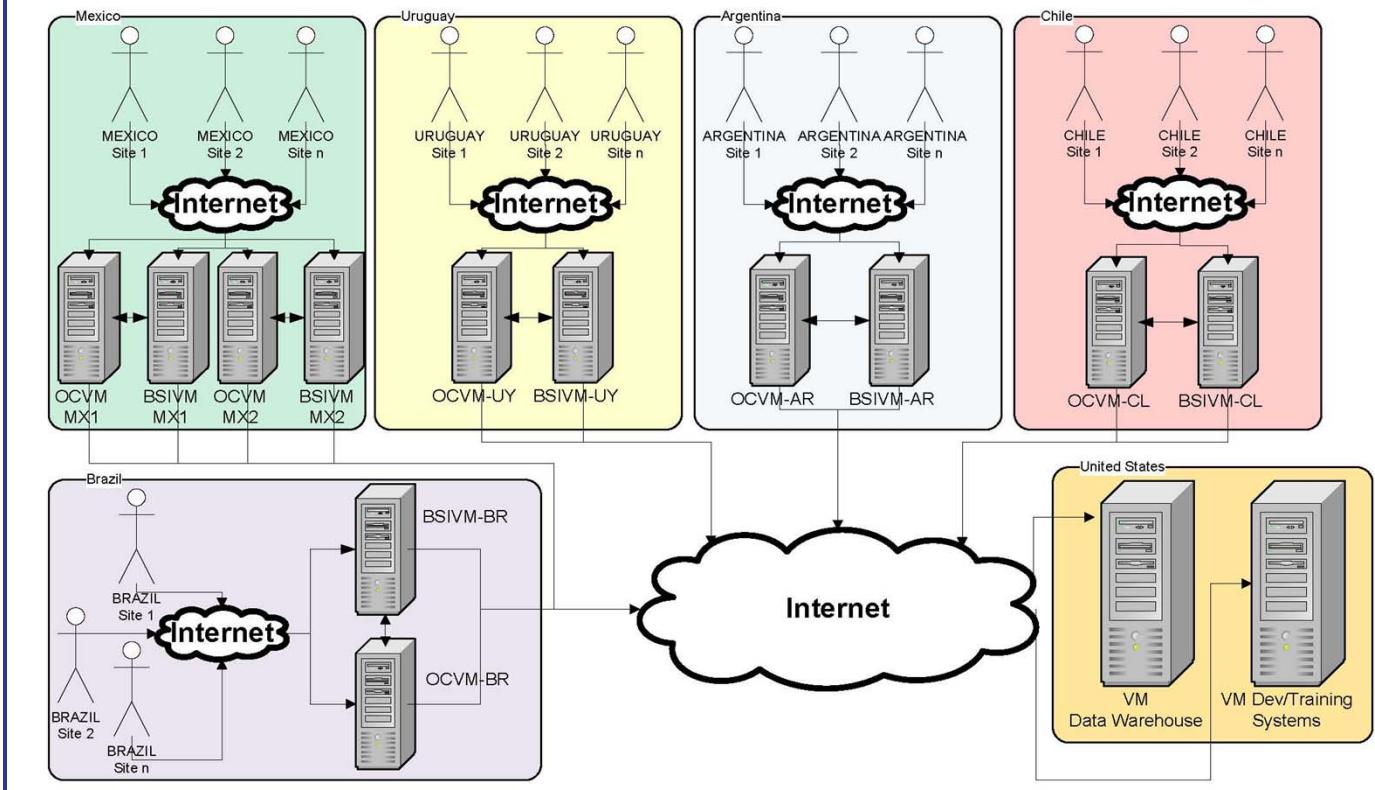
- 14 virtual machines (VM) hosted on a single physical machine located in US – business continuation server will host backup of the VMs.
- One set of servers for each country (Mexico will have 2) and one for training/reporting.
- Each set of VMs is independent of the others thereby maintaining the independent nature of each country's data.
- Per-country reports can be run off each country's VMs. Cross-country data will be aggregated in the VM Warehouse.
- The sites within each country will access the OC and BSI systems located on their country's VMs via the Internet.
- Physical maintenance will be conducted centrally. Each country can have control over maintaining its own VM.
- OpenClinica manages the clinical and sample descriptive data. BSI manages the sample tracking data.



Phase II: OpenClinica™ + BSI™ Distributed to the Lead Sites

Distribution Phase – OpenClinica + BSI Distributed to Each Country's Lead Site

- Cross-country reporting will be upgraded to run against the data warehouse.
- Each country's lead site(s) will prepare their own infrastructure so that they can run their own OC-BSI systems.
- Each country's VMs are placed on that country's physical machines.
- Data will now be sent from each country to the data warehouse for research and reporting.
- Physical and VM maintenance will be conducted by each country on its own servers.





www.openclinica.org

Free, open source clinical trial software for Electronic Data Capture (EDC) and clinical data management in clinical research

- Web-based & designed to support all types of clinical studies in diverse research settings
- caBIG compatible
- Designed to support regulatory guidelines such as US FDA 21 CFR Part 11 (electronic signatures and audit history)
- Reduces duplication of data, data entry errors
- Automates and streamlines discrepancy (data query) management and the clinical trials workflow
- Provides ability to export data into standard formats

OpenClinica™ Features

- Management of many, diverse, clinical studies through a single interface
- Clinical data submission, validation, and annotation
- Data filtering and extraction
- Study oversight, auditing, and reporting
- Protocol configuration, design of Case Report Forms (CRFs)
- Electronic Data Capture (EDC), retrieval, and clinical data management

Functional Areas of the Application

Submit Data

Allows subject enrollment, data submission and validation for use by clinicians and research associates as well as Query Management and Bulk Data Import.

Monitor and Manage Data

Enables ongoing data management and monitoring of clinical trials

Extract Data

Enables data extraction and filtering of datasets for use by investigators

Study Build

Facilitates creation and management of studies (protocols), sites, CRFs, users and study event definitions by investigators and coordinators

Administration

Allows overall system oversight, auditing, configuration, and reporting by administrators

Additional Features

- Organization of clinical research by study, protocol, and site
- User, and role-based security
- Support for sharing resources across studies in a secure and transparent manner
- Dynamic generation of web-based CRFs for electronic data capture via user-defined Excel templates
- Data import/export tools for migration of clinical datasets
- Extensive data query capabilities
- Facilitates compliance with regulatory guidelines (e.g. in US - 21 CFR Part 11)
 - Differentiated user roles and privileges
 - Password and user authentication security
 - Electronic signatures
 - SSL encryption
 - De-identification of Protected Health Information (PHI)
 - Comprehensive auditing to record and monitor access, and data changes

US-LA CRN: Developing Programs in Three Broad Scientific Areas



Basic and Clinical Research

- Supporting Research Studies and Research Networks
- Enhancing Cancer Research Infrastructure in Latin America



Training Programs

- Providing Opportunities for Exchanges in Training
- Developing the Cancer Research Workforce in Latin America



Technology and Capacity Building

- Partnering with Latin American Clinical Cohorts and Biospecimen Networks
- Adapting Best Practices for Advanced Technologies

The Value of Collaborating in Latin America

- Highlights the importance of reaching beyond borders
- Demonstrates the benefit of Latin American cancer research in improving care for the growing Hispanic population in the United States
- Leverages countries' resources and breaks down research silos
- Enhances research capabilities in Latin America and the U.S. for global benefit
- Improves state of the science
- Provides the opportunity for NCI to have significant impact in the United States and abroad

NCI

A Global Leader in Cancer Research,
Diagnosis, Prevention, and Treatment

OLACPD

A Model for International
Research and Collaboration

Global Health as an NIH Priority

"Global health research 'should be a conversation with other countries,' but not one in which the great 'United States tells the world what the answers are without listening to their experiences'."

Remarks of NIH Director Francis Collins
FIC's *Global Health Matters* Newsletter
NIH "Town Meeting"
August 17, 2009



Thank you!
¡Muchas Gracias!
Obrigado!