



## The Importance of Correlative Science in CALGB

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Science Operations*

*CALGB CRA Committee Meeting, June 2007*

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## Today's Talk

- The purpose of today's talk is to bring the CRA Committee up-to-date with some of the specimen banking and correlative science initiatives within CALGB and to discuss the importance of the correlative research we conduct as part of our CALGB trials.

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Slide 2

## Objectives

- The Importance of Correlative Research
- - 1) *To better understand the importance of the CS studies that we design as part of our trials*
  - 2) *To better understand the role that specimen processing plays in CS research*
  - 3) *To be able to give examples of the next generation of clinical trials that will be driven by the correlative research we have done in previous trials*

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Slide 3

## Types of CS Studies

- Marker discovery - expression profiling, aCGH, whole genome sequencing, etc. These types of studies are designed to discover new prognostic or predictive markers
- Marker assessment/validation - after small studies have been completed it is important to confirm the utility of the marker in larger studies like those done in a clinical trial setting.
- Marker driven - already established marker is used to select patients for a study and/or make therapeutic decisions

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Slide 4

## Specimens and CS Research

- Specimen collection and processing is key to good CS studies. This is critical to the success of CALGB!
- Many specimens need to be processed at the site. This adds variability but it may be critical for the sample to be processed within 24 hours for the marker analysis. If it is not critical for a sample to be processed quickly then we prefer to have the specimen processed at the repository.
- It is critical that the instructions in the protocol are clear. If the specimen collection/processing is not clear then the specimen(s) may not be useful.

*– Example: CALGB 150205 (80101) calls for analysis of IGF-1, IGF-2 and IGFBP-3 in serum. The protocol does not indicate clearly that a serum sample needs to be collected. We happen to have banked plasma from the PET study blood tube and some markers can be analyzed on plasma but not all of them.*

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## We Need to Improve the Process

- Protocols need to include all the appropriate details related to the CS project (new template)
- Summary tables need to be in the protocols to make it clear which samples need to be collected and when.
- SOPs are in development for sample collection (New Biospecimen & CS Advisory Committee)
- Standardization of consent questions is needed (GBC)
- "Real-time" monitoring of sample submission (New Specimen Tracking System)

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## The Next Generation of Clinical Trials

- In the very near future, the drug you receive will reflect your genetic makeup.
- Here are some examples of such new trials.
  - CALGB 40601 and 40603 (HER-2)
  - CALGB 10501 (IgV<sub>H</sub>) and 10603 (FLT3)
  - ECOG 4203 (TS) and 2000 (MSI and 18q LOH)
  - TAILORx (21-gene signature) - "A Cancer Research Trial Assigning Individualized Options For Treatment (Rx)"

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## TAILORx

- Patients will be stratified to a treatment arm using the OncotypeDX assay.
- The assay analyzes the expression of certain genes in the breast tumor and estimates a person's risk of cancer recurrence.
- The Genomic Health laboratory that performs the test is certified to perform it according to Clinical Laboratory Improvement Amendments (CLIA) by federal and state agencies in the United States.

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## TAILORx

- The test result is expressed as a Recurrence Score, which is a number from 0 to 100.
- This number correlates to a specific likelihood of breast cancer recurrence within ten years of initial diagnosis.
- The higher the score, the greater the chance of having a recurrence when treated with hormonal therapy alone.
- The treatment that patients will receive on this trial will depend upon the results of the Recurrence Score.

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## TAILORx

| Recurrence Score | Risk of Recurrence                   | Patients (%) | Treatment Assignment                                    |
|------------------|--------------------------------------|--------------|---|
| 10 or lower      | 5% or less with hormonal alone       | 30           | Hormonal therapy  |
| 11 - 25          | 10-15% with hormonal alone           | 45           | Randomization to hormonal plus chemo vs. hormonal alone |
| 26 or higher     | 30% hormonal alone<br>10% plus chemo | 25           | Hormonal plus chemotherapy                              |

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## Objectives

- Development of a New Specimen Tracking System
  - 1) *To understand the rationale behind the development of the new system*
  - 2) *To understand the process we have put in place to develop the new system*
  - 3) *To become familiar with the functional requirements of the new system*

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## Development of a New Specimen Tracking System

- Specimen tracking is critical to our success for CS studies. We need to be able to:
  - *Monitor specimen submissions in real-time*
  - *Send reminders to sites when they have not submitted required samples*
  - *Assist in the audit process*
  - *Move to the "pay on receipt" model*
  - *Decrease the burden on the sites and the repositories*

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## The Reality

|  |     |
|--|-----|
| Patients accrued to the clinical trial   | 601 |
| Patients that consented to the companion and have a high quality sample banked       | 362 |
| Patients that consented to the companion and have a poor quality sample banked       | 13  |
| Patients that consented to the companion and have no sample banked                   | 85  |
| Patients that did not consent to the companion and have a high quality sample banked | 17  |
| Patients that did not consent to the companion and have no sample banked             | 124 |

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Slide 13

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## Specimen Tracking Project

- Gathered initial input from CRAs, repositories and CO staff to understand what the issues were.
- LabTrak is clearly not meeting the needs of the group.
- Discussed the issue with the Ops Committee and decided to move forward with a proposal to fund the development or purchase of a new system that would meet our needs.
- We got approval for the funding for a new system at the CALGB Foundation Board of Directors meeting at the 2006 Fall Core meeting. The project began in January and is scheduled to be complete in 18 months.

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## Specimen Tracking Team

- Assembled a team to develop the Functional Requirements for the new system
  - Central Office: P. Friedman, M. Kelly
  - IS: D. Ens, B. Martin, A. Shah, K. Johnson
  - Stats/DCs: G. Broadwater, E. Leung
  - Repositories: D. Bucci, S. Jewell, B. Richards, J. Ramaradjou, C. Vetanovetz, D. Rohrer
  - CRAs: H. Weiner, J. Cuevo, M. Dierker
  - We can always use more help from CRAs!!

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## First Steps

- User Interviews
- Review systems already developed
  - ECOG, SWOG
  - Commercial systems
- Develop Functional Requirement for the system. Use these to develop the Technical Requirements
- Build vs. Buy decision

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## Functional Requirements Summary

- System will be web-based and accessible to all clinical trial sites
- System will be user-friendly.
- System will be pre-loaded with the information about the specimen collection events
- Users will be able to search and retrieve data about specimens logged
- System will exchange data with both the registration system and the inventory management systems at the repositories.

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## Specimen Banking & CS Initiatives

- Make protocols clearer and include tables of specimen collection events.
- SOPs for sample collection.
- Standardized consent questions.
- New Specimen Tracking system.
- Patient brochures on the importance of sample donation.
- New committee - Biospecimen & CS Advisory
- PCO - new facility and capabilities

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## The PCO

- The PCO has moved to a new facility which is located off campus. The facility is state-of-the-art and includes better lab and storage facilities.
- Please do not send specimens to the old address!!
- PCO's main issues with specimen submissions are:
  - Incomplete submissions
    - *Missing forms*
    - *Full accession numbers for blocks submitted (often the block number isn't included on the paperwork)*
    - *Protocol requirements not followed (e.g. normal and tumor block in 80101)*
  - Please include your contact information on the form regardless if there is a space provided or not (E-mail and phone number)

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## The PCO

- The new coordinator of the CALGB PCO is Dan Rohrer.  
Email: [dan.rohrer@osumc.edu](mailto:dan.rohrer@osumc.edu)
- New address:
  - CALGB Pathology Coordinating Office
  - Innovation Centre
  - 2001 Polaris Parkway
  - Columbus, OH 43240
  - Tel: 614-293-7073
  - Fax: 614-293-7967
  - [path.calgb@osumc.edu](mailto:path.calgb@osumc.edu)
- <http://www.pathology.osu.edu/htrn/calgb/default.asp>

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## Summary

- We are doing lots of things to improve the process.
- We need your input as to what are the most important areas to focus on.
- Our goal is to make your life easier!!

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## Contact Information

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Slide 23

