



20 Ways to Improve Pathology Submissions

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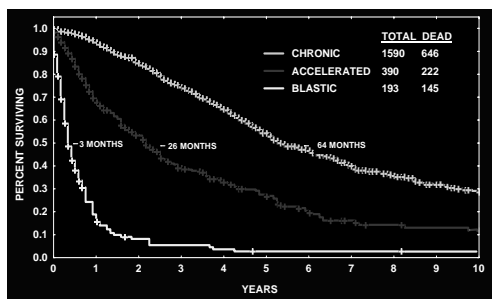
Importance of Correlative Sciences

- In 2006, The University of Chicago CALGB CRA group submitted over 650 separate shipments of samples to the various repositories.
- The new paradigm of cancer research and treatment: "targeted therapy," "protocols driven by molecular testing," "personalized cancer care."
- We will examine strategies to improve the sample submission process.

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CML Survival by Phase of Disease (1965-2000)

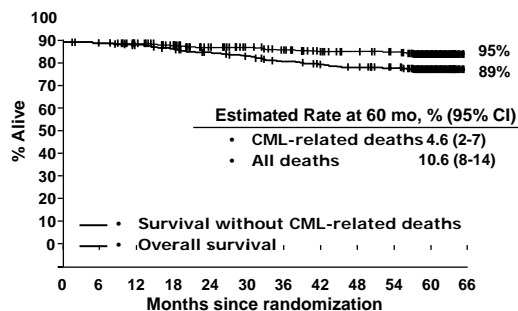


Data from J Cortes M.D. Anderson

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IRIS Study: Overall Survival of First-Line Imatinib Mesylate

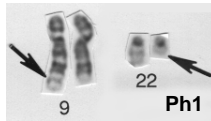
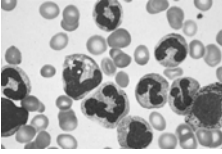


Druker et al. ASCO, 2006. Abstract 6506.

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1973: A chromosome translocation in CML

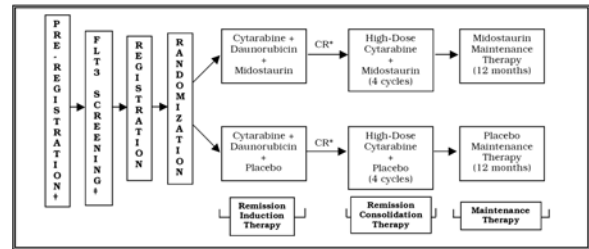


Janet Rowley M.D.
U. Chicago
Lasker Award 1998

Rowley, J.D. (1973) A new consistent chromosomal abnormality in chronic myelogenous leukaemia identified by quinacrine fluorescence and Giemsa staining. *Nature*, 243, 290–293.

Cytogenetic testing for molecular diagnosis, monitoring

CALGB 10603 FLT3 Screening: Protocol Driven by Molecular Testing



[†] Screening for FLT3 mutation and ITD allelic ratio for stratification will be performed with a 48-hour turn around. North American patients will be screened at The Ohio State University Medical Center. Screening for European sites will be performed by centralized laboratories in each cooperative group. Pending results of FLT3 mutation status, patients may receive hydroxyurea for as long as 5 days prior to registration/randomization. Only patients with FLT3 TKD and ITD mutations will be registered and randomized to treatment on CALGB 10603. FLT3^{WT} patients will not be eligible for enrollment on this study.

[‡] Results of FLT3 screening analysis will be available in 48 hours. While awaiting results of FLT3 analysis, patients may be treated with hydroxyurea for as many as 5 days.

Commit to the Process

- Goal of 100% compliance with sample submission requirements
- Become an advocate for the correlative sciences
- Narrative vs. systemic approach
- Organize, Organize, Organize!!!

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Sample Submissions for CALGB 10105

- Central morphology review
 - Pretreatment
 - Aspirate and peripheral blood smears
 - Stained and unstained biopsy sections

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Sample Submissions for CALGB 10105

- Mandatory microvessel density and tenascin expression sample submission
 - Pretreatment, time of maximum response, and relapse or removal from protocol therapy
 - Serum, plasma, and biopsy sections
 - Shipped on dry ice

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Sample Submissions for CALGB 10105

- Mandatory pharmacokinetic sample
 - 4 time points on day 1, 2 time points between day 7 and 14, prior to 2nd cycle...
 - Plasma
 - Shipped on dry ice

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Sample Submissions for CALGB 10105

- Pharmacogenetic sample submission
 - Pretreatment
 - Peripheral blood

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Sample Submissions for CALGB 10105

- Cytogenetic submission (CALGB 8461)
 - Pretreatment, complete remission, and relapse or transformation to AML
 - Karyotype

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Sample Submissions for CALGB 10105

- Leukemia Tissue Bank (CALGB 9665)
 - Pretreatment, complete remission, and relapse or transformation to AML
 - Bone marrow aspirate, peripheral blood, and buccal swab (pretreatment only)

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Specimen Tracking Database for CALGB 10105

Central Morphology Review	C-022 Diagnostic PB/BM Evaluation Form	8461 Submission	C-030 Cytogenetics Referral Form	9665 Submission	C-428 LTB Specimen Routing Form	MVD & Tenascin Expression Sample	MVD & Tenascin Expression Slides	C-1195 MVD & Tenascin Expression Sample Form
X ²	X	X	X	X	X	X ¹	Note 6	X
X ¹	X	6/3/2004	X	X ¹	X	X ¹	X ¹	X
7/15/04 ¹	X	6/21/2004	X	6/21/2004	X	X ¹	X ⁰	X

Sample Submission Overview for CALGB 10002

	Pre-treatment	After Course III	Follow-up At Relapse
Burkitt Leukemia			
Buccal Swab	1 Buccal Swab (9665)		
Peripheral Blood	1 Purple Top (10002) 1 Red Top	1 Purple Top (10002) 1 Red Top	
	1 Green Top (9665)	1 Green Top (9665)	1 Green Top (9665)
Bone Marrow Aspirate	2-3cc Green Top (8461)		
Bone Marrow Biopsy*	1 Green Top (9665)	1 Green Top (9665)	1 Green Top (9665)
	1 H&E or PAS with 1 Wright-Giesema smear (10002) Paraffin block of marrow or 15-5µ thick slides	1 H&E or PAS with 1 Wright-Giesema smear (10002) Paraffin block of marrow or 15-5µ thick slides	
Burkitt Lymphoma			
Peripheral Blood	1 Purple Top (10002) 1 Red Top	1 Purple Top (10002) 1 Red Top	
Bone Marrow Aspirate*	2-3cc Green Top (8461)		
Bone Marrow Biopsy	Wright-Giesema smear (10002)** Paraffin block of marrow or 15-5µ thick slides**	Wright-Giesema smear (10002)** Paraffin block of marrow or 15-5µ thick slides**	
	Paraffin block (9764-Optional)	Paraffin block (9764-Optional)	Paraffin block (if pt refractory) (9764-Optional)

* For Burkitt lymphoma patients with bone marrow involvement only.
** Pre-treatment samples required. If bone marrow examination is performed as part of a patient's clinical care, please submit bone marrow biopsy section as per Section 5.3.1.2.

Acquiring Samples Building a Support Network

- Clinic coordinators
- Phlebotomists
- Lab technicians
- Hem/Path
- Surg/Path
- Radiation oncology
- Radiology
- CRAs/Nurses/Nurse practitioners/PAs/Fellows
- Cytogenetics
- Physicians

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Pathology Specimen Database

Program	CALGB Protocol	Pathology Report No.	Surg/Path Date Requested	CALGB Date Received	CALGB Date Shipped	Notes
Lymphoma	50103	S03-8369	2/9/2004	2/10/2004		Sent 3 H & E slides. Did not acquire 9 unstained. PCO said it was ok, would cut own slides.
Lymphoma	9764	S03-8369	2/9/2004	2/10/2004		Sent 1 paraffin block
Lymphoma	50103		11/4/2003	11/19/2003	11/20/2003	
Lymphoma	9764		12/17/2003	1/29/2004	1/29/2004	Sent 2 H & E (top, middle), 2 20u eppendorf, 2 5u eppendorf
Lymphoma	59905		11/4/2003	11/19/2003	11/24/2003	
Leukemia	10102		11/4/2003	11/19/2003	11/20/2003	Sent 3 unstained BM & PB smears, 1 H & E biopsy slide, 4 unstained biopsy sections. Complete.

CALGB 50502 TRACKING FORM (LYMPHOMA TISSUE BLOCKS)

Send a copy of this form to CALGB Statistical Center, Data Operations

2001 Francis Johnson
Columbus, OH 43240
Tel: 614-293-7973
Fax: 614-293-7967
Path_Calgb@osumc.edu

LabTrak shipment ID (CALGB users only)

Received by: _____ Date sample received: _____

Form: G-1476 v2 10/05/2006 Page 1 of 1

Difficult Cases

5.6.3 Paraffin-Embedded Tissue Block Submission

The CALGB Lymphoma Committee is committed to conducting correlative science studies utilizing tissue from consenting patients enrolled on treatment trials, and has chosen tissue microarrays (TMAs) as the method of archiving tissue. TMAs are constructed by removing two 1 mm diameter tissue cores from the lymphoma tissue block using a specially designed instrument (Beecher Instruments, Sun Prairie, WI). The resulting tissue array can contain 100 cases in a single tissue block, and allows rapid, high throughput analysis of markers by immunohistochemistry or in situ hybridization. The original tissue block remains intact with only a small amount of tissue removed with no significant distortion. The original block may then be returned to the submitting institution.

If a patient has consented and agreed to allow their tissue to be kept for future unknown use in research to learn about, prevent, treat, or cure cancer (model consent question #3), send a formalin-fixed, paraffin-embedded block of well-fixed lymphoma tissue to:

CALGB Pathology Coordinating Office (PCO)
Innovation Centre
2001 Polaris Parkway
Columbus, OH 43240
Tel: 614-293-7973 Fax: 614-293-7967
path.calgb@osumc.edu

Samples should be logged and shipped via the LabTrak application.

If patient has consented to allow their tissue to be kept for future unknown use, only one tissue block need be submitted to accommodate both histologic confirmation of diagnosis and future correlative science studies (see Section 5.5).

Challenge #1: CALGB 50502 Tumor Block Submission

- **Problem:**
 - Institution does not release blocks although this is mandated by the protocol.
- **Action:**
 - CRA contacted study chair and institutional PI and requested that they contact the chairmen of the department of surgical pathology.
 - Hematopathologist also contacted the chair to advocate our cause.
- **Resolution:**
 - Chairmen agreed to release block to the PCO for this particular case.

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Challenge #2:

- **Problem:**
 - Patients pathology was from an outside institution who refused to submit slides because the clinical slides they had sent to the U of C had never been returned.

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Challenge #2 continued

- **Action:**
 - CRA offered to retrieve the institution's slides if they would agree to cut and send research slides.
 - CRA went to The U of C department of cytology and personally found the slides.
 - CRA convinced the cytology department to release the slides and ship them to the outside institution.
- **Resolution:**
 - The outside institution sent the required research slides.

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Summary

- Development of mechanisms of specimen procurement.
- Build a support network.
- Encourage a narrative, "case by case" approach to sample submission.
- Close working relationship between all the elements of the CALGB network.
- Become an advocate for the correlative sciences.

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