Fall 2024 Oishi Symposium

Thursday, October 17, 2024

8:00 – 11:00 am

Chicago, IL

SWOG CANCER RESEARCH NETWORK

NCI National Clinical Trials Network
a National Cancer Institute program

NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

WELCOME!

In honor of Dr. Noboru Oishi, who was a great supported of Oncology Research, the Oishi symposium focuses on key issues related to Oncology Research Professionals (ORP).

As always, our gratitude and thanks to the Oishi's for their generous support of the Symposium.

Thank you, Jeri and Noboru Oishi!

Announcement and Updates Oncology Research Professionals (ORP) Committee

Connie Szczepanek, RN, BSN, CCRP
Chair, SWOG ORP Committee

Logistics Details

- Please keep your phone on mute to help with sound quality.
- Questions can be submitted all throughout the meeting via the CHAT icon. We will present them to the speakers during the meeting.
- The presentations will be posted on the SWOG website within a few weeks.

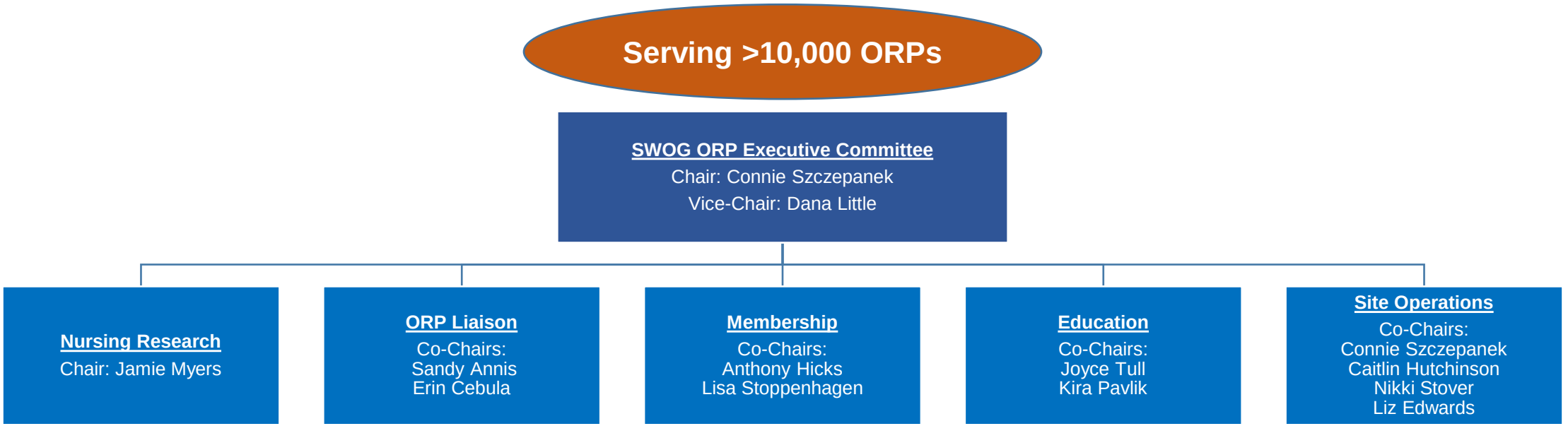
YOU are The ORP Committee!

"SWOG holds a fundamental conviction that the **O**ncology **R**esearch **P**rofessionals (ORP) play a crucial role in the successful development, implementation, and analysis of any SWOG clinical trial."

ORP Executive Committee Members

Deb Bergevin	Erin Cebula	Joyce Nancarrow-Tull
Lisa Stoppenhagen	Sandy Annis	Dana Little
Connie Szczepanek	Liz Edwards	Anthony Hicks
Annette Betley	Caitlin Hutchinson	Jamie Myers
	Kira Pavlik	

The SWOG Oncology Research Professionals (ORP) Committee & Sub-Committees



SWOG Cancer Research Network's Mission

- To significantly improve lives through cancer clinical trials and translational research.

ORP Committee Mission

- To support SWOG activities through promotion of integrity and excellence in clinical research through education, guidance, & collaborative contributions.

Quick Reference

See the ORP page on the SWOG Website:

Member Resources > Oncology Research Professionals

Quick Access to:

- Contact info of Committee Leaders
- Lead ORP (Head CRA) Training Modules
- APP Workshop

Get Involved with ORP

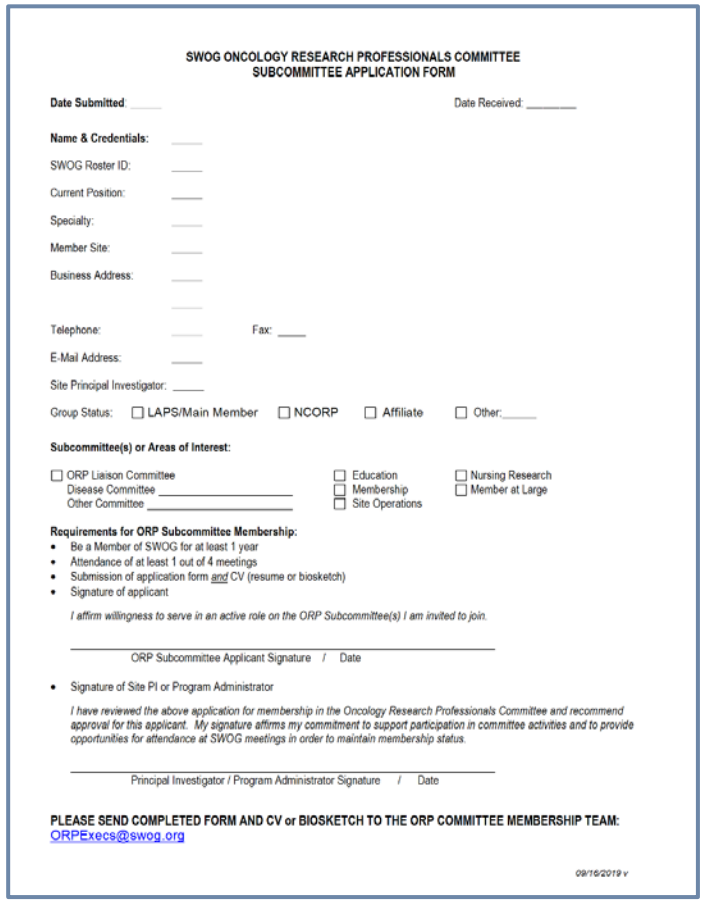
Follow the link to the ORP Membership Application on the ORP Member Resources page:

To get more involved please complete the ORP Membership Application.

Key Involvement Opportunities

- Disease Specific Liaisons
- Liaisons at Large
- Education Team

It only takes 5 minutes to apply!



SWOG ONCOLOGY RESEARCH PROFESSIONALS COMMITTEE
SUBCOMMITTEE APPLICATION FORM

Date Submitted: _____ Date Received: _____

Name & Credentials: _____
SWOG Roster ID: _____
Current Position: _____
Specialty: _____
Member Site: _____
Business Address: _____
_____
Telephone: _____ Fax: _____
E-Mail Address: _____
Site Principal Investigator: _____
Group Status: ☐ LAPS/Main Member ☐ NCORP ☐ Affiliate ☐ Other:_____

Subcommittee(s) or Areas of Interest:

☐ ORP Liaison Committee
Disease Committee _____
Other Committee _____
☐ Education
☐ Membership
☐ Site Operations
☐ Nursing Research
☐ Member at Large

Requirements for ORP Subcommittee Membership:
- Be a Member of SWOG for at least 1 year
- Attendance of at least 1 out of 4 meetings
- Submission of application form *and* CV (resume or biosketch)
- Signature of applicant

I affirm willingness to serve in an active role on the ORP Subcommittee(s) I am invited to join.

_____
ORP Subcommittee Applicant Signature / Date

- Signature of Site PI or Program Administrator

I have reviewed the above application for membership in the Oncology Research Professionals Committee and recommend approval for this applicant. My signature affirms my commitment to support participation in committee activities and to provide opportunities for attendance at SWOG meetings in order to maintain membership status.

_____
Principal Investigator / Program Administrator Signature / Date

PLEASE SEND COMPLETED FORM AND CV or BIOSKETCH TO THE ORP COMMITTEE MEMBERSHIP TEAM:
ORPExecs@swog.org

09/16/2019 v

Upcoming Funding Opportunities

All program information available at:
thehopefoundation.org/funding-opportunities

Apply or nominate by the noted deadlines below.

APP Mentorship Program November 1

Meyskens Lectureship November 1

SEED Fund Grants December 1

Impact Award January 15

CRA/Nurse Travel Support January 15

Vogelzang Scholars January 15

Career Engagement Award March 15

Coltman Fellowship Award March 15

THE HOPE FOUNDATION
FOR CANCER RESEARCH

SWOG CANCER RESEARCH NETWORK

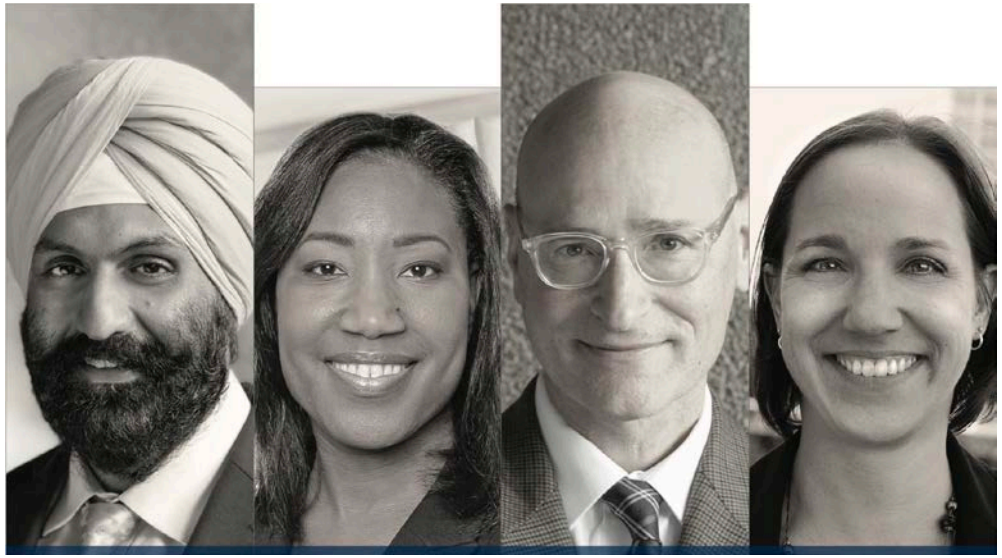
NCI National Clinical Trials Network
a National Cancer Institute program

NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

Complete Your SWOG Member Profile

Help your committee, win a prize! Visit **swogdei.crab.org**

Engage in a bit of friendly competition to help us paint a richer picture of our membership. Check the leaderboard to see how your committee compares!



THE HOPE FOUNDATION
FOR CANCER RESEARCH

Apply by November 1

THE NCTN MAPP PROGRAM

A year-long mentoring program for Advanced Practice Providers including:

- Online APP training workshop
- Focused mentoring sessions
- Travel to professional meetings

APPLY NOW >

GILEAD

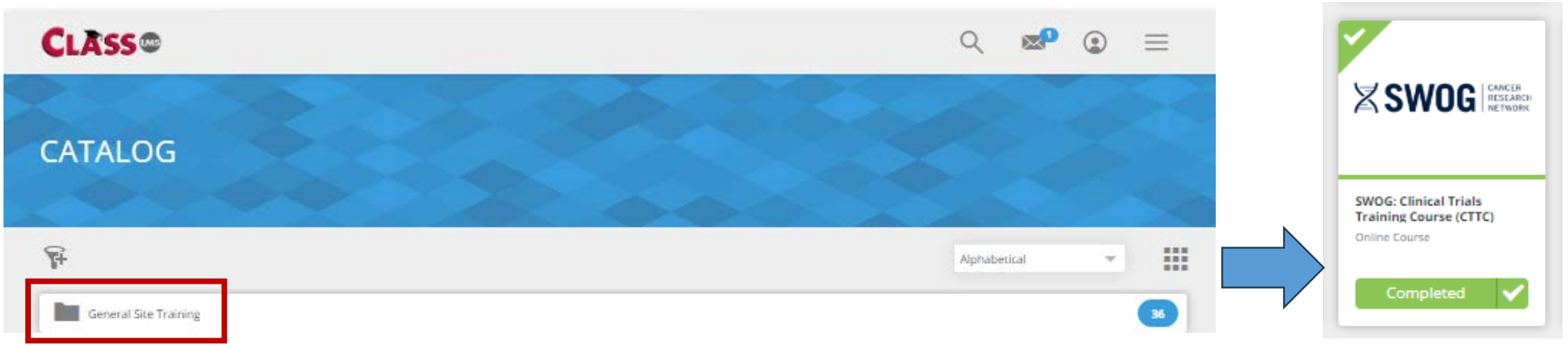
This program is made possible with generous support from Gilead

SWOG Protocol template update – Biospecimen submissions

- SWOG has updated the SWOG protocol template (Section 15) to more clearly communicate biospecimen submission requirements.
- Going forward all newly developed SWOG protocols with biospecimen submission requirements will include a simple summary table at the beginning of the biospecimen submission section of the protocol (Section 15).
    - The table will include the following information: Specimen Type/Amount, Timepoint, whether it is a required submission, and whether a collection kit is being provided.
    - For additional views, sites can refer to sortable tables that will soon be accessible via the SWOG specimen tracking system.

SWOG Clinical Trials Training Course (CTTC) – Now Posted in CTSU (CLASS)

- The online version of the CTTC has been transitioned to the CTSU CLASS learning management system.
  - Anyone with credentials to access NCI systems can access the course in the CLASS Catalog under the "General Site Training" folder or via the direct link to the course: https://www.ctsu.org/Public/class.aspx?courseid=0b0190ea-b489-4505-b4a3-b8c7a368c0bd



  - Please update any local site onboarding materials to reflect the new CTTC link.
  - Effective 10/21/24: Learners will no longer be able to enroll to the CTTC in the SWOG ExpertusOne Learning Management System.
  - Learners who previously enrolled in, but have not yet completed, the CTTC in ExpertusOne will have until April 2025 (at time of next online CTTC course updates) to complete the course in ExpertusOne.

Background/Overview (1)

- Jaccard et al NEJM 2007: Only randomized trial evaluating high dose melphalan v “conventional therapy”
  - Outdated and flawed: 24% 100 Day TRM
  - Medians OS only 22.2m in high dose melphalan arm

PMID: 17855669

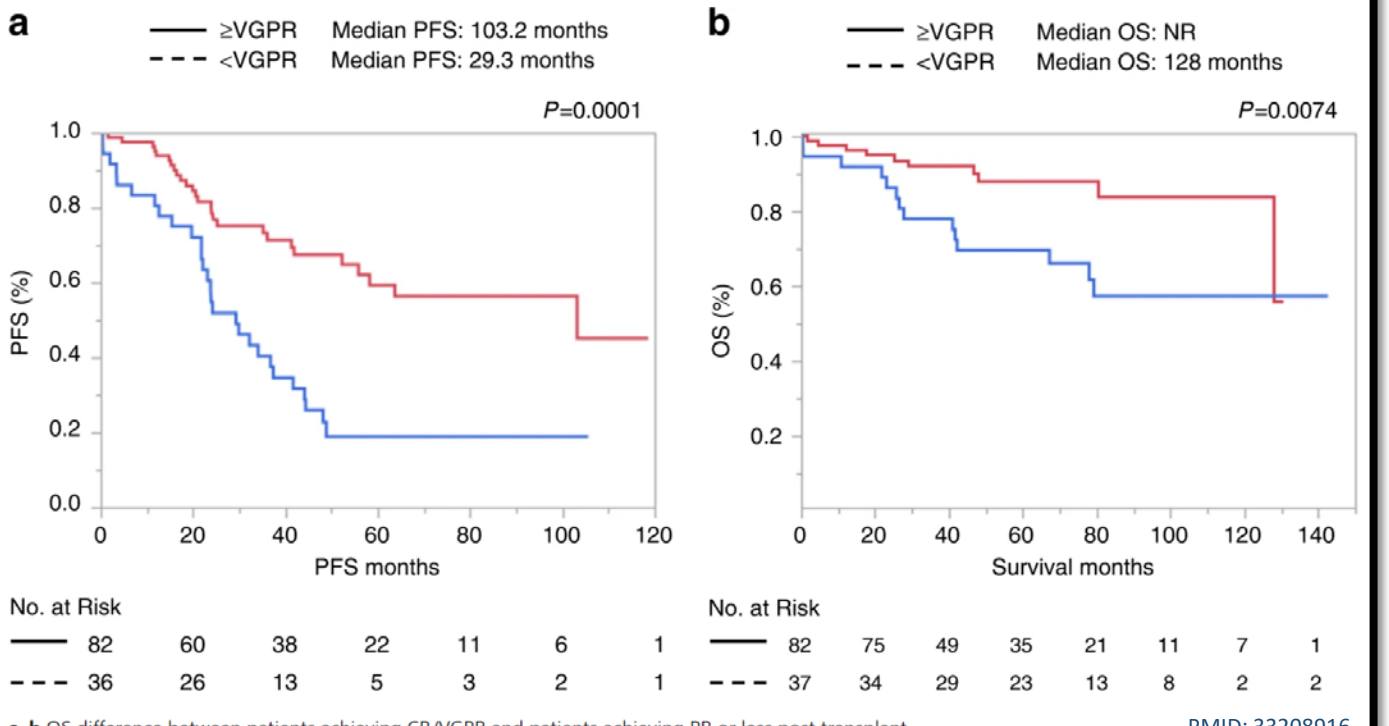
- TRM now consistently in the 2-5% range at “experienced” centers

PMID: 29558277

PMID: 29933072

Fig. 2: PFS difference between patients achieving CR/VGPR and patients achieving PR or less post transplant.

From: Depth of response prior to autologous stem cell transplantation predicts survival in light chain amyloidosis



a, **b** OS difference between patients achieving CR/VGPR and patients achieving PR or less post transplant.

PMID: 33208916

Prior SWOG Quality Assurance Webinars Posted as Enduring Courses

Links to Previous Webinars and Upcoming Webinar Announcements are posted at: **SWOG Quality Assurance Live Webinar Series | SWOG**

CEU Courses in ExpertusOne:

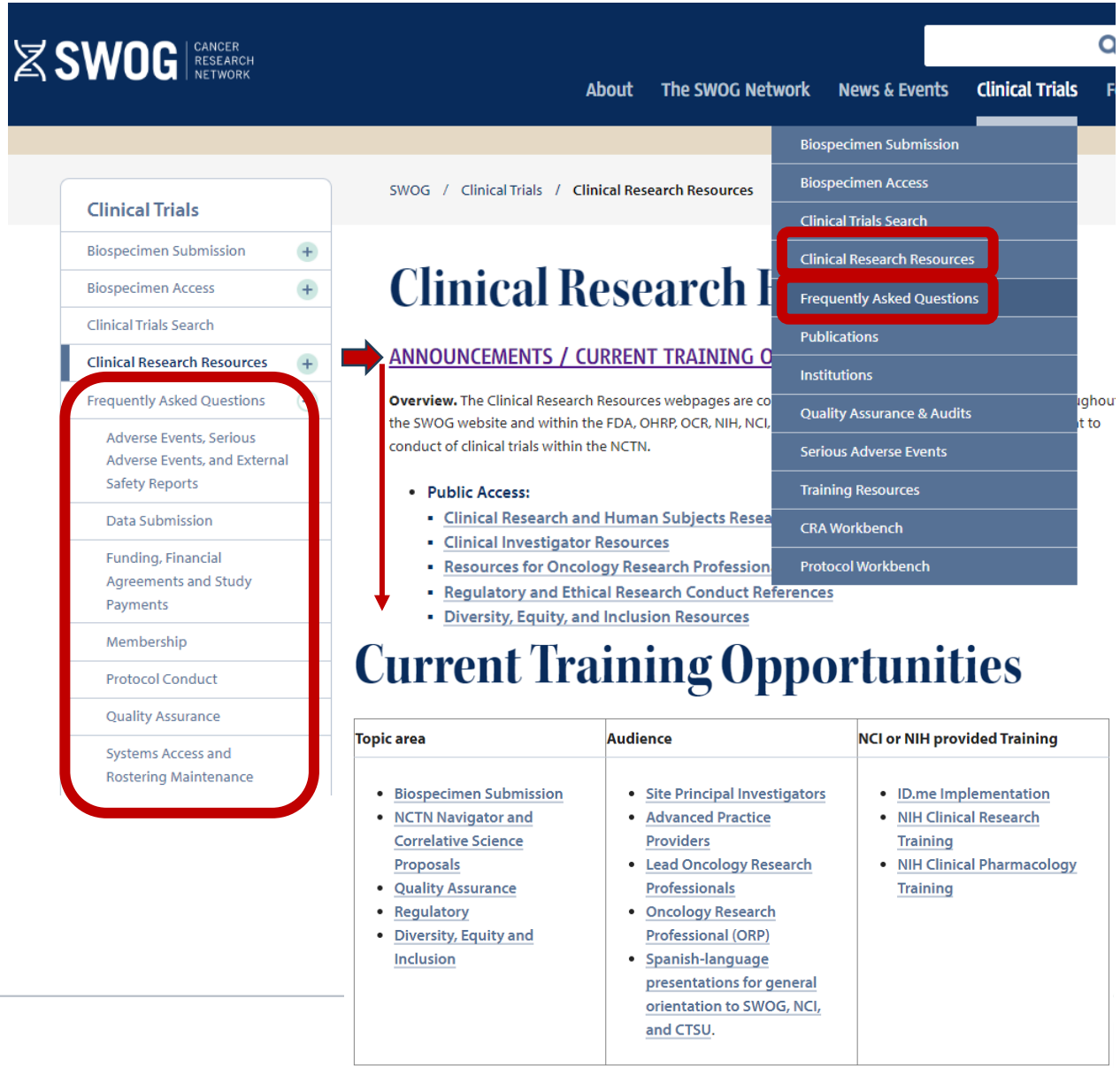
- **Workload Prioritization in Clinical Trials** (1.5 contact hours)
- **Research Protocol Deviations vs Deficiencies** (1 contact hour)
- **Best Practices for Informed Consent** (1 contact hour)

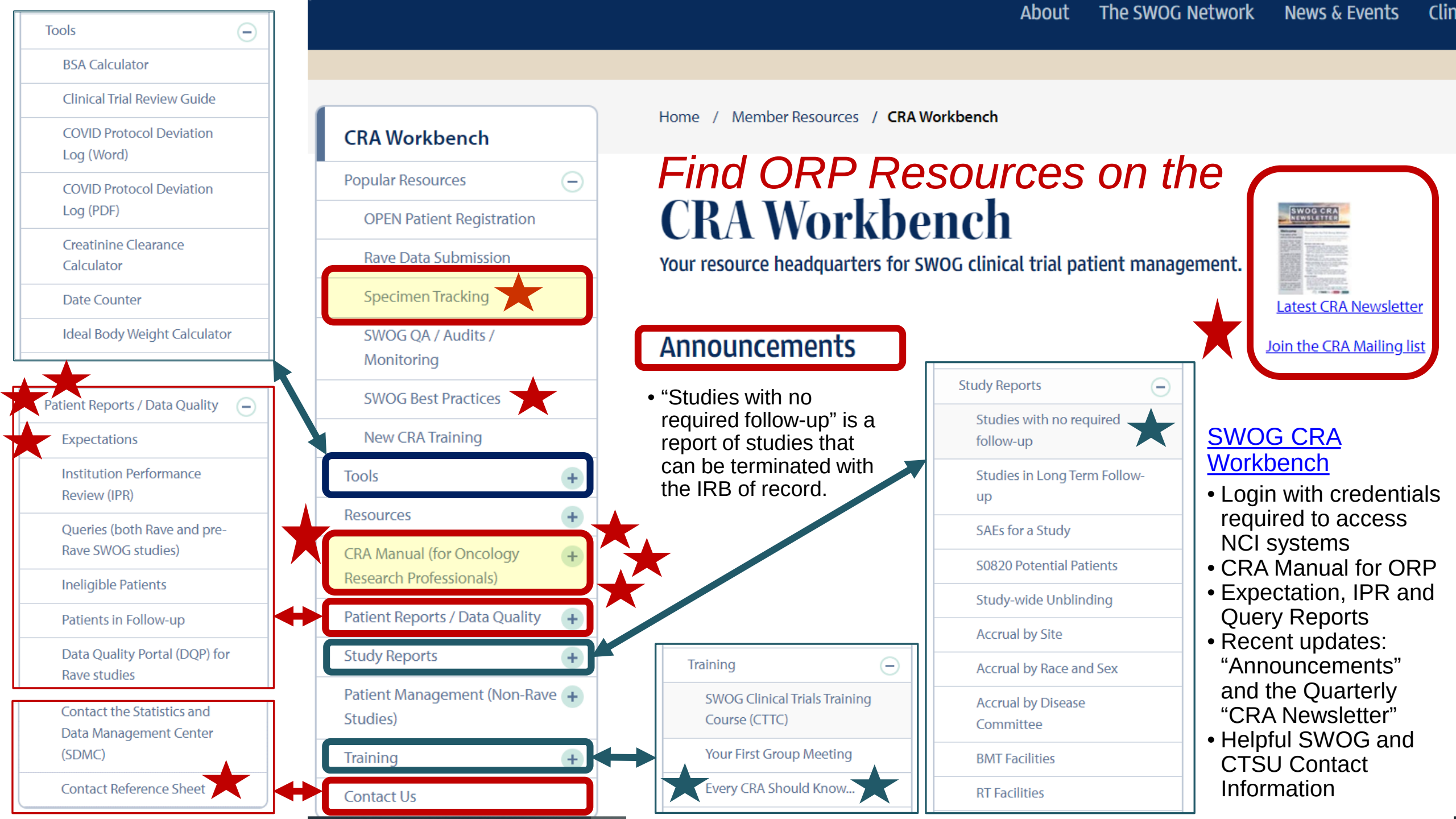
Non-CEU Courses now in CLASS:

- **Adverse Event Reporting**
- **Serious Adverse Event Reporting**
- **SWOG Audits: Preparing for Success and Audit Process**
- **How to Develop a CAPA Plan**

Website Resources – SWOG.org

- Frequently Asked Questions | SWOG Webpages
- Training Resources | SWOG includes direct links to SWOG training workshops.
- The Announcements / Current Training Opportunities | SWOG section of the webpages announces newly published individual training courses that are not part of a complete SWOG training workshop.
  - Includes links to prior Group Meeting presentations (such as SWOG QA Audits - Top 10 Deficiencies, Improving Specimen Submissions to the SWOG Biospecimen Bank, or Biospecimen Quality, Compliance, Tips and Tricks), links to training for SWOG ORPs, such as: the SWOG and NCI Systems Overview Training or NCTN and NCORP Study Funding and Payment Distribution, and links to training materials in Spanish.



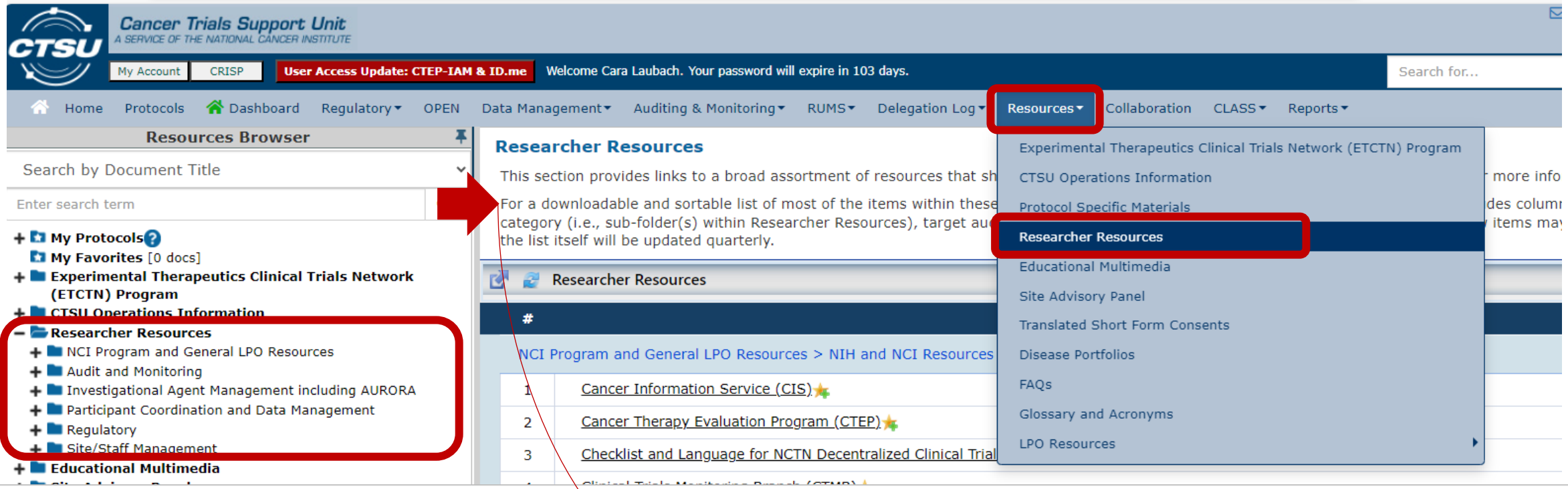

About
The SWOG Network
News & Events
Tools
BSA Calculator
Clinical Trial Review Guide
COVID Protocol Deviation Log (Word)
COVID Protocol Deviation Log (PDF)
Creatinine Clearance Calculator
Date Counter
Ideal Body Weight Calculator
Patient Reports / Data Quality
Expectations
Institution Performance Review (IPR)
Queries (both Rave and pre-Rave SWOG studies)
Ineligible Patients
Patients in Follow-up
Data Quality Portal (DQP) for Rave studies
Contact the Statistics and Data Management Center (SDMC)
Contact Reference Sheet
CRA Workbench
Popular Resources
OPEN Patient Registration
Rave Data Submission
Specimen Tracking
SWOG QA / Audits / Monitoring
SWOG Best Practices
New CRA Training
Tools
Resources
CRA Manual (for Oncology Research Professionals)
Patient Reports / Data Quality
Study Reports
Patient Management (Non-Rave Studies)
Training
Contact Us
Home / Member Resources / CRA Workbench
Find ORP Resources on the
CRA Workbench
Your resource headquarters for SWOG clinical trial patient management.
Latest CRA Newsletter
Join the CRA Mailing list
Announcements
• "Studies with no required follow-up" is a report of studies that can be terminated with the IRB of record.
Training
SWOG Clinical Trials Training Course (CTTC)
Your First Group Meeting
Every CRA Should Know...
Study Reports
Studies with no required follow-up
Studies in Long Term Follow-up
SAEs for a Study
S0820 Potential Patients
Study-wide Unblinding
Accrual by Site
Accrual by Race and Sex
Accrual by Disease Committee
BMT Facilities
RT Facilities
SWOG CRA Workbench
• Login with credentials required to access NCI systems
• CRA Manual for ORP
• Expectation, IPR and Query Reports
• Recent updates: "Announcements" and the Quarterly "CRA Newsletter"
• Helpful SWOG and CTSU Contact Information

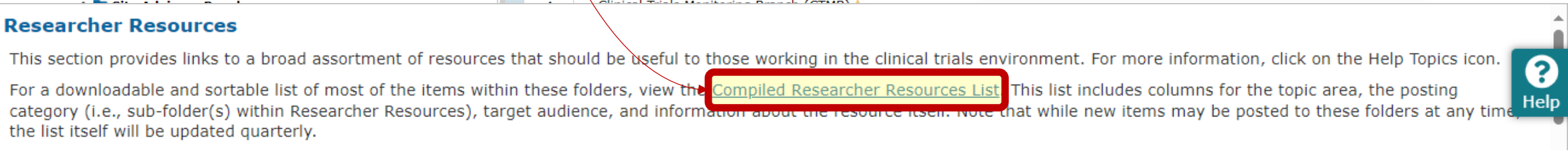
SWOG Training Resources List for Oncology Research Professionals – Transitioned to CTSU.org

- ORP onboarding and training resource list (previously under the Clinical Research Resources section of the SWOG website at: SWOG Training Resources List for Oncology Research Professionals).
    - Includes links to federal and Lead Group training and clinical research resources for oncology research professionals.
- These resources have been transitioned to CTSU.org: Resources >> Researcher Resources.
- Thank you to NCI, CTSU!
  and Lead Group WG members.
    - Please update any local site bookmarks / documents to reflect the NEW compiled researcher resources (downloadable) spreadsheet link (below):
        - https://www.ctsu.org/readfile.aspx?EDocId=1937857&CTSUCreated=Y

CTSU Researcher Resources

- Additional resource links are now accessible on CTSU.org under Resources >> Researcher Resources.





SWOG CANCER RESEARCH NETWORK

NCI National Clinical Trials Network | NCI Community Oncology Research Program

Reminder: SAE Reporting Requirements updates

- Effective August 30, 2024 NCI implemented a global safety update to the notification procedures for serious adverse events (expedited reporting requirements).
- The primary change is to require 24-hour notification to IND/IDE sponsors for ALL SAEs, irrespective of grade/severity, if the AEs meet any of the SAE criterion defined in FDA regulations, followed by a completed expedited report in 5 or 10 calendar days.
- Affected trials include: All CTEP-supported Clinical Trials Networks and Consortia IND/IDE trials (and any trials supported by another organization under CTEP IND) that:
    1. Use the current CTEP expedited reporting tables (effective date of May 5, 2011) and
    2. Still have patients on treatment as of August 30, 2024 (i.e., trials that have a status of “Active”, “Closed to Accrual”, or “Temporarily Closed to Accrual” as of that date).
- For more information, refer to the Memorandum and list of Protocols with Updated Adverse Event (AE) Tables posted on CTSU.org.
- For questions on reporting requirements for SWOG-led studies: Email adr@swog.org.

And Before We Proceed - Feedback is Needed!

A successful Oishi Symposium and Open Forum are only possible with your valued feedback! Please use the link below or QR Code to fill in the simple Qualtrics Survey and tell us what you liked, didn't like, or want to see in future meetings! We value and use your feedback every time! Thanks!

https://yalesurvey.ca1.qualtrics.com/jfe/form/SV_2gbZXcJy2jI2ERM

Cancer Trials Support Unit (CTSU) Updates

Krishna Chothwani

CTSU Protocol Team Manager

Topics

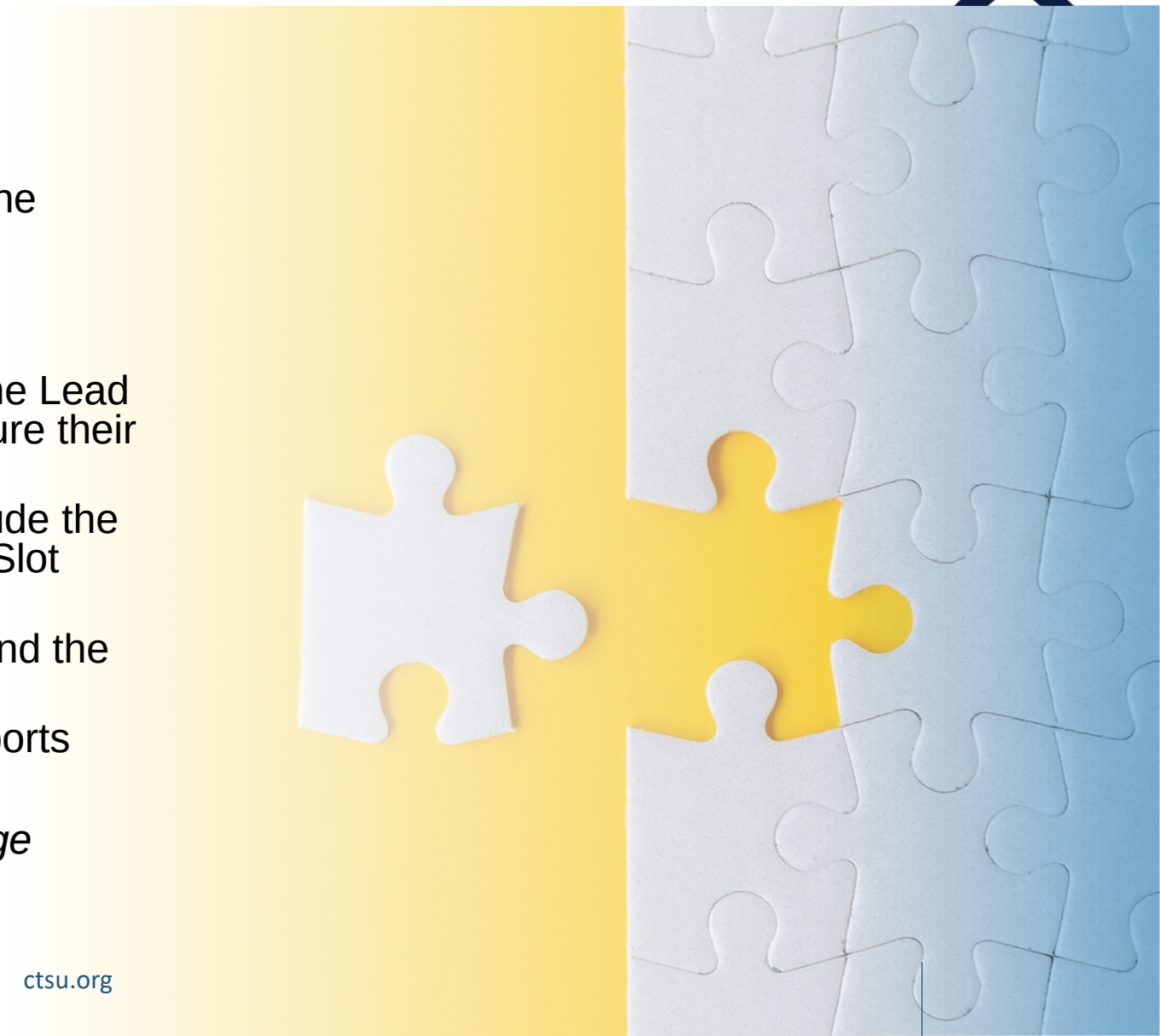
- Oncology Patient Enrollment Network (OPEN) Modernization
- Institutional Review Board (IRB)-Exempt Studies
- Protocol Deviation (PD) Form
- Roster Update Management System (RUMS)
- Source Document Portal (SDP) and Auto-Redaction of Personally Identifiable Information/Protected Health Information (PII/PHI)
- Researcher Resources & Compliance, Learning, and SOP Solutions (CLASS)

OPEN Modernization

CTSU Updates: OPEN Modernization

- In February 2024, the CTSU started work on improving the look, feel, and functionality of the OPEN application
- CTSU is taking a phased approach to the modernization:
  - **Phase 1**: Form setup screens used by the Lead Protocol Organizations (LPOs) to configure their OPEN enrollment forms
  - **Phase 2**: Enrollment screens which include the History and Funding screens as well as Slot Reservation
  - **Phase 3**: Transfer and Update Module and the COG Registry
  - **Phase 4**: Administrative screens and reports

**Phases and timelines are subject to change*

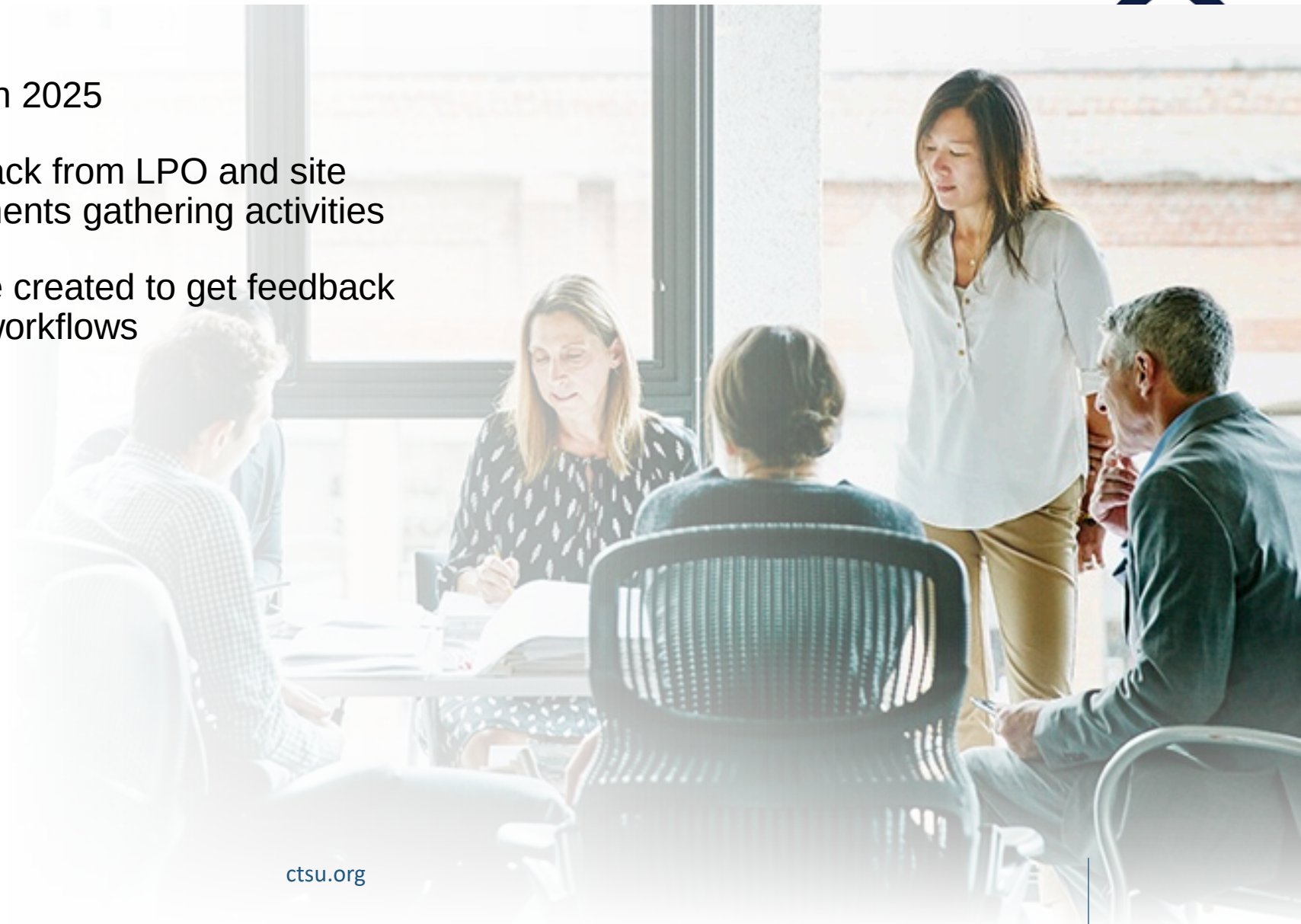


CTSU Updates: OPEN Modernization (Cont.)

- Stakeholder interviews were conducted to get feedback regarding the current OPEN application:
  - Stakeholders consisted of LPO and CTSU staff users
  - Feedback was used to identify areas in need of improvement with OPEN
  - An LPO Working Group was formed to receive feedback on proposed mockups and workflows for Phase 1

OPEN Modernization: Coming Soon

- Phase 2 is targeted to start in 2025
- CTSU will be seeking feedback from LPO and site users as part of the requirements gathering activities
- A Site Advisory Group will be created to get feedback for proposed mockups and workflows



IRB Exempt Studies

IRB Exempt Studies

- CTSU worked with the Division of Cancer Prevention (DCP) to update CTSU Applications to accommodate the management of IRB Exempt studies
  - CTSU Application updates were released to production at the end of July 2024
- An *LPO Approval* requirement will be used to manage site registration statuses for IRB Exempt studies
  - Sites will work with the LPO to obtain approval to participate in the IRB Exempt study
    - Sites will submit the LPO Approval document to the CTSU via the Regulatory Submission Portal on the CTSU members' website
  - Additional requirements may be set up for collection as well, per the LPOs request, but the *LPO Approval* will replace the *IRB Approval* as the mandatory requirement for IRB Exempt studies
- Sites with an *Approved* site registration status after submitting their LPO Approval to the CTSU will be able to complete patient and non-patient (if applicable) enrollments in OPEN

CTSU Members' Website Changes – *Protocol > Protocol Requirements*

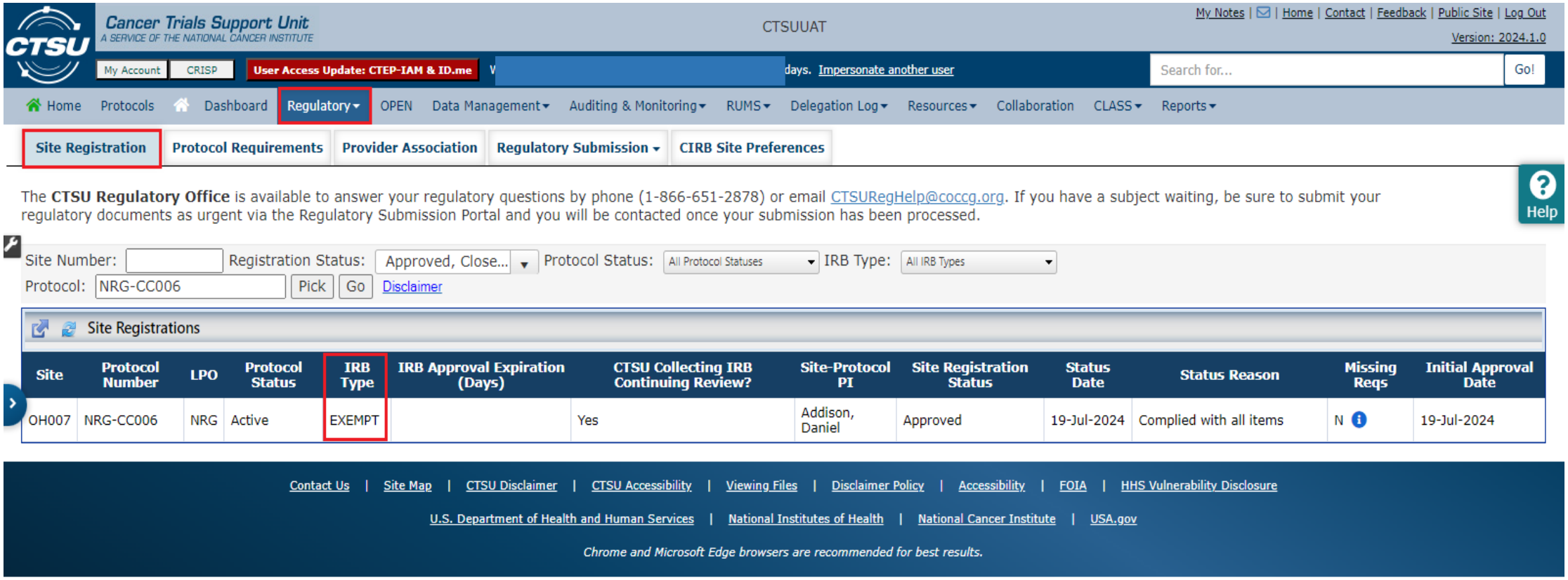
- The Description of the mandatory requirement in the *Protocol Requirements* section of the Protocol page for IRB Exempt studies shows as *LPO Approval* rather than *IRB Approval*

CTSU Members' Website Changes – *Regulatory > Protocol Requirements*

- The Description of the mandatory requirement in the *Protocol Requirements* section of the *Regulatory* page for IRB Exempt studies shows as *LPO Approval* rather than *IRB Approval* as well

CTSU Members' Website Changes – *Regulatory > Site Registration*

- The *IRB Type* field in the *Site Registration* section of the *Regulatory* page shows as *EXEMPT* for IRB Exempt studies



PD Form

PD Form Updates

- The CTSU and NCI are revisiting the PD Form (currently in pilot for SWOG S2012) to streamline the reporting process as much as possible
- Specific changes include, but are not limited to:
  - Reducing required fields for each deviation
  - Consolidating deviation reporting with medication error reporting
  - Expanding available help text
- The CTSU is planning to host online real-time training events to review form updates with site staff
- Additional information about this form update and relevant training sessions will be announced in the CTSU Newsletter and Bi-monthly Broadcast

RUMS

RUMS Update

- Allow bulk addition of person roles during:
  - Add Role Action
  - Add Person Action
- Changes to Summary Page layout
- There are no rule changes for this update

Adding Bulk Roles: Step 1 – Select Sites and Rosters

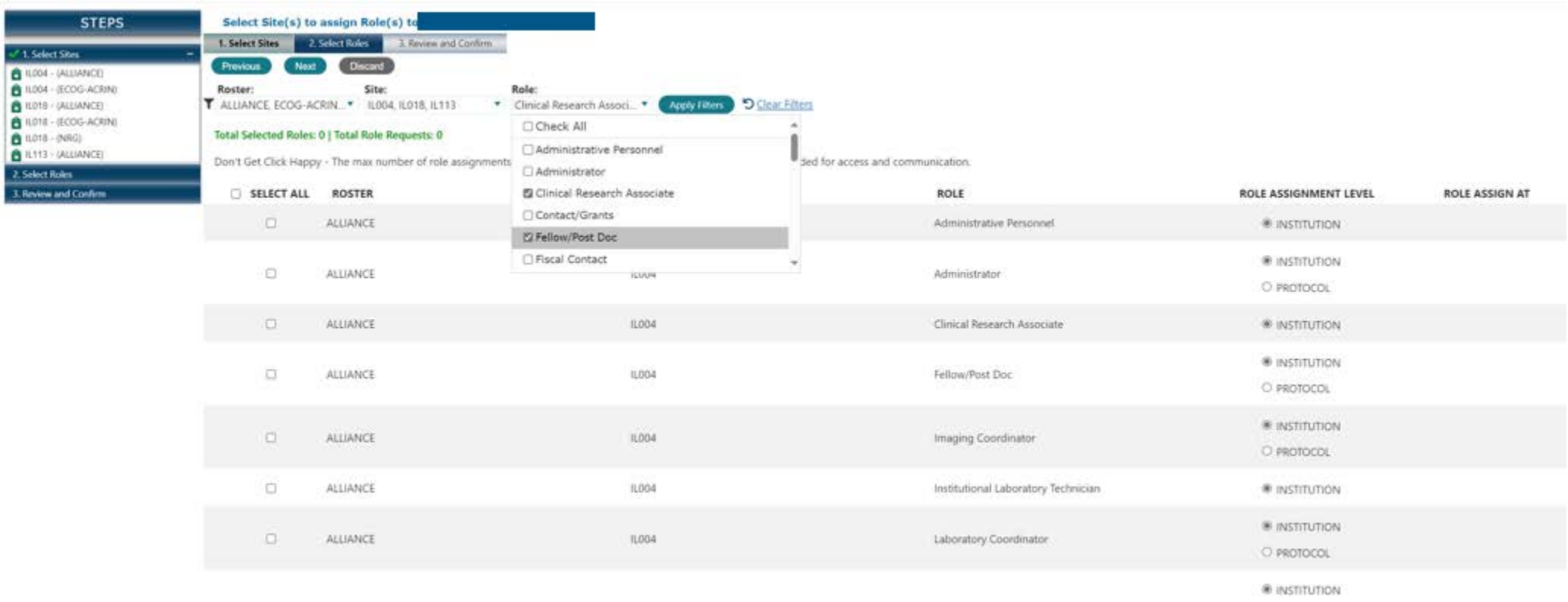
No Change

#	Action	Site CTEP ID		Roster	Role	Member Role Status
1	☐	CIRB-IL018	Northshore University Health System	NCICIRB	CIRB Signatory	Active
2	☑	IL004	NorthShore University HealthSystem-Highland Park Hospital	ALLIANCE	Sub Affiliate	Active
3	☑	IL004	NorthShore University HealthSystem-Highland Park Hospital	ECOG-ACRIN	Affiliate	Active
4	☐	IL004	NorthShore University HealthSystem-Highland Park Hospital	NRG	Affiliate	Active
5	☑	IL018	NorthShore University HealthSystem-Evanston Hospital	ALLIANCE	Main Member	Active
6	☑	IL018	NorthShore University HealthSystem-Evanston Hospital	ECOG-ACRIN	Main Member	Active
7	☑	IL018	NorthShore University HealthSystem-Evanston Hospital	NRG	Main Member	Active
8	☐	IL113	NorthShore University HealthSystem-Glenbrook Hospital	ECOG-ACRIN	Affiliate	Active
9	☑	IL113	NorthShore University HealthSystem-Glenbrook Hospital	ALLIANCE	Sub Affiliate	Active
10	☐	IL113	NorthShore University HealthSystem-Glenbrook Hospital	NRG	Affiliate	Active

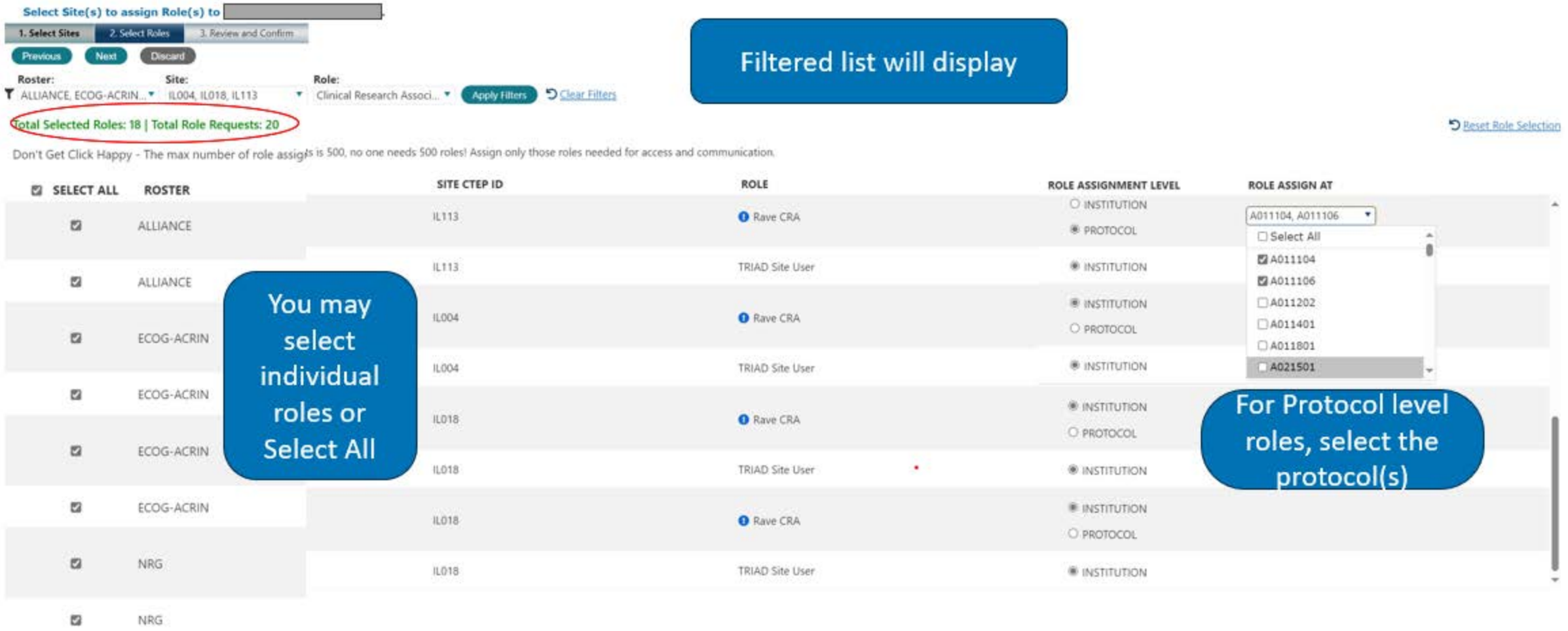
Adding Bulk Roles: Step 2 – Assign Roles

Change - Now allows multiple roles to be selected

Filter for the desired roles - *All available roles will display until the filters are applied*

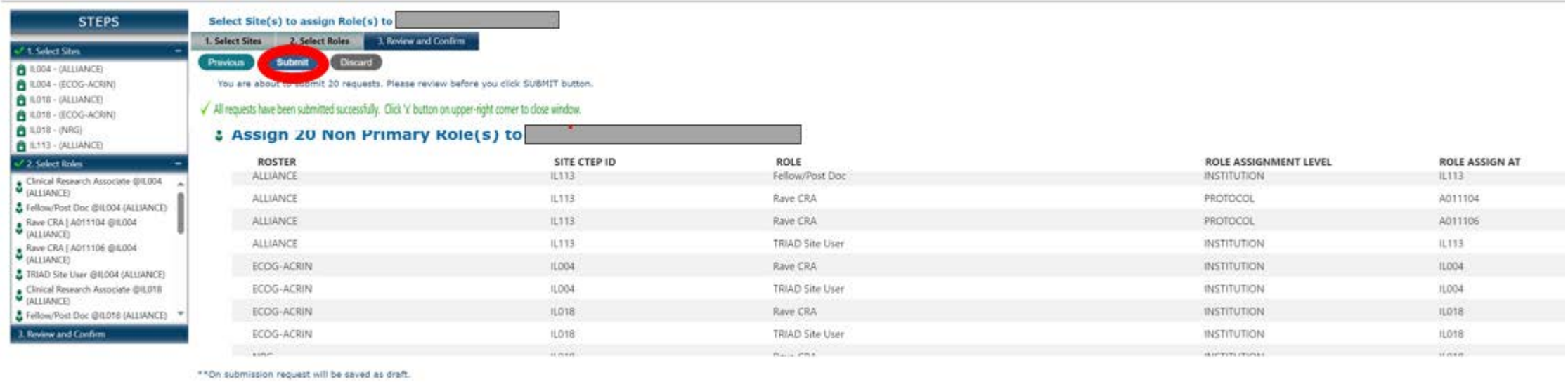


Adding Bulk Roles: Step 2a – Select Roles from Filtered List

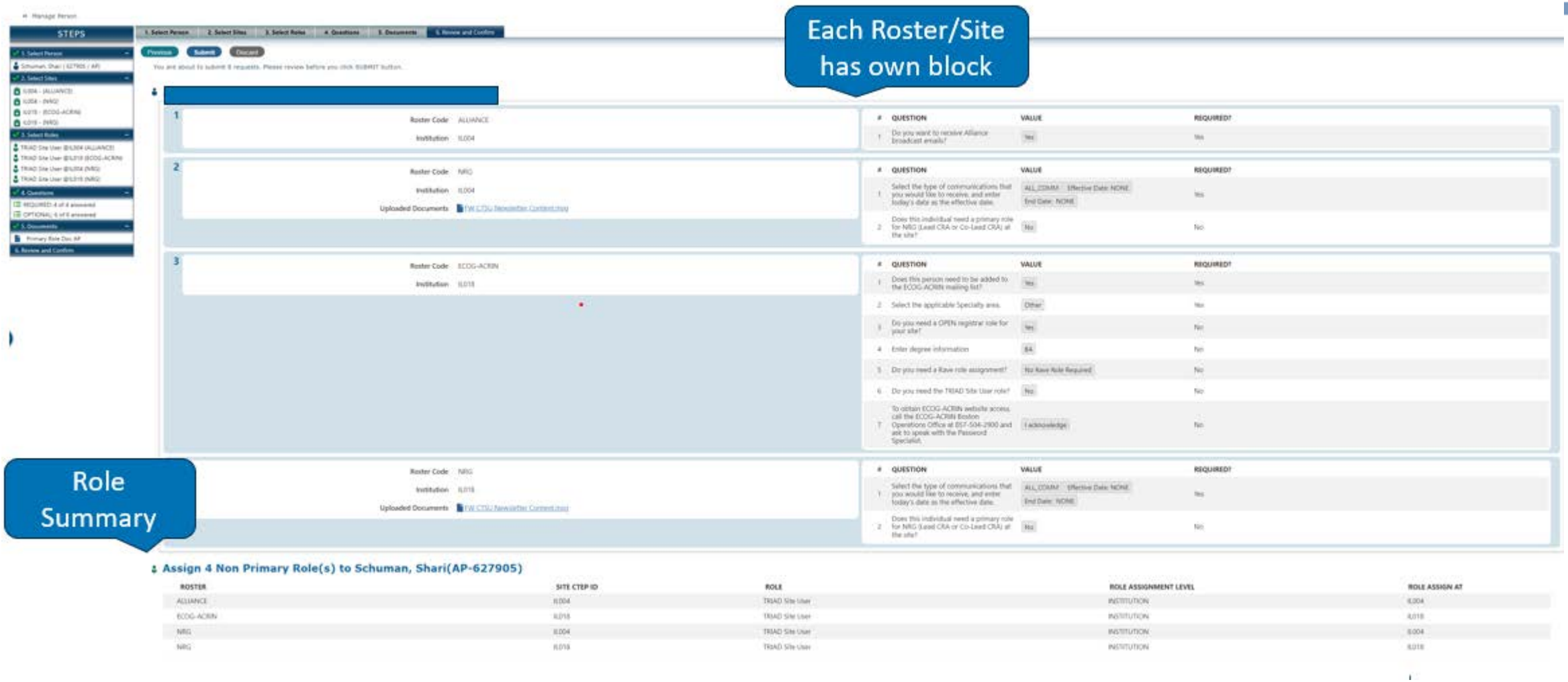


Adding Bulk Roles: Step 3 – Review and Submit

Display Change

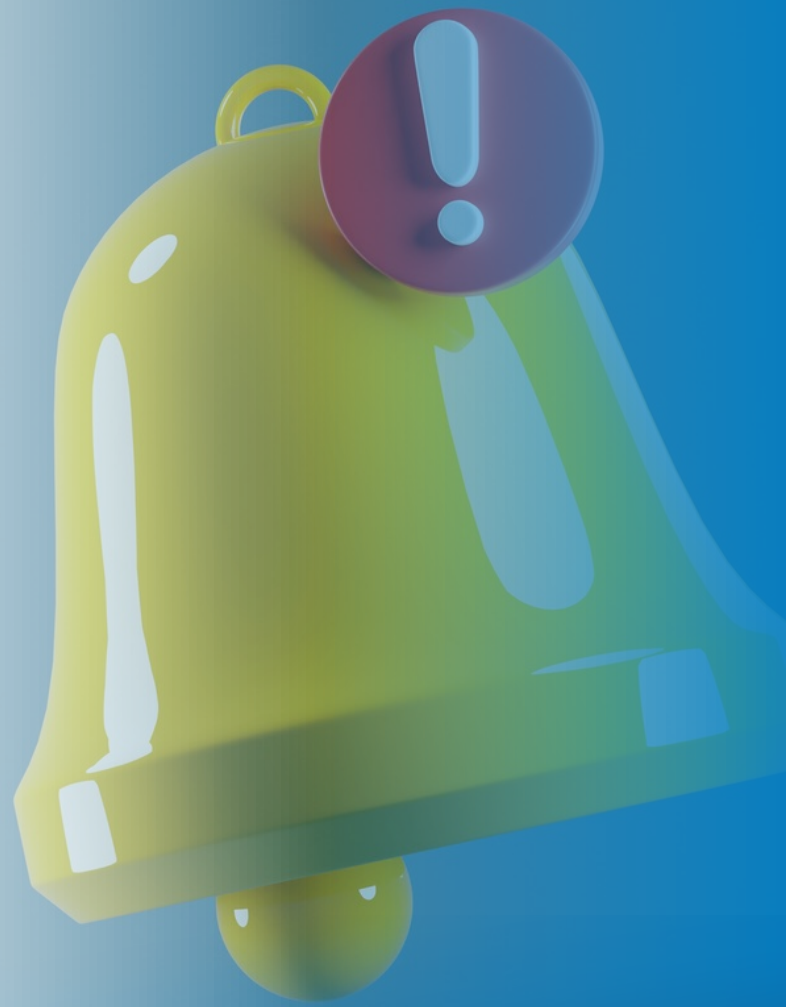


Add Person/Role Summary



Hints

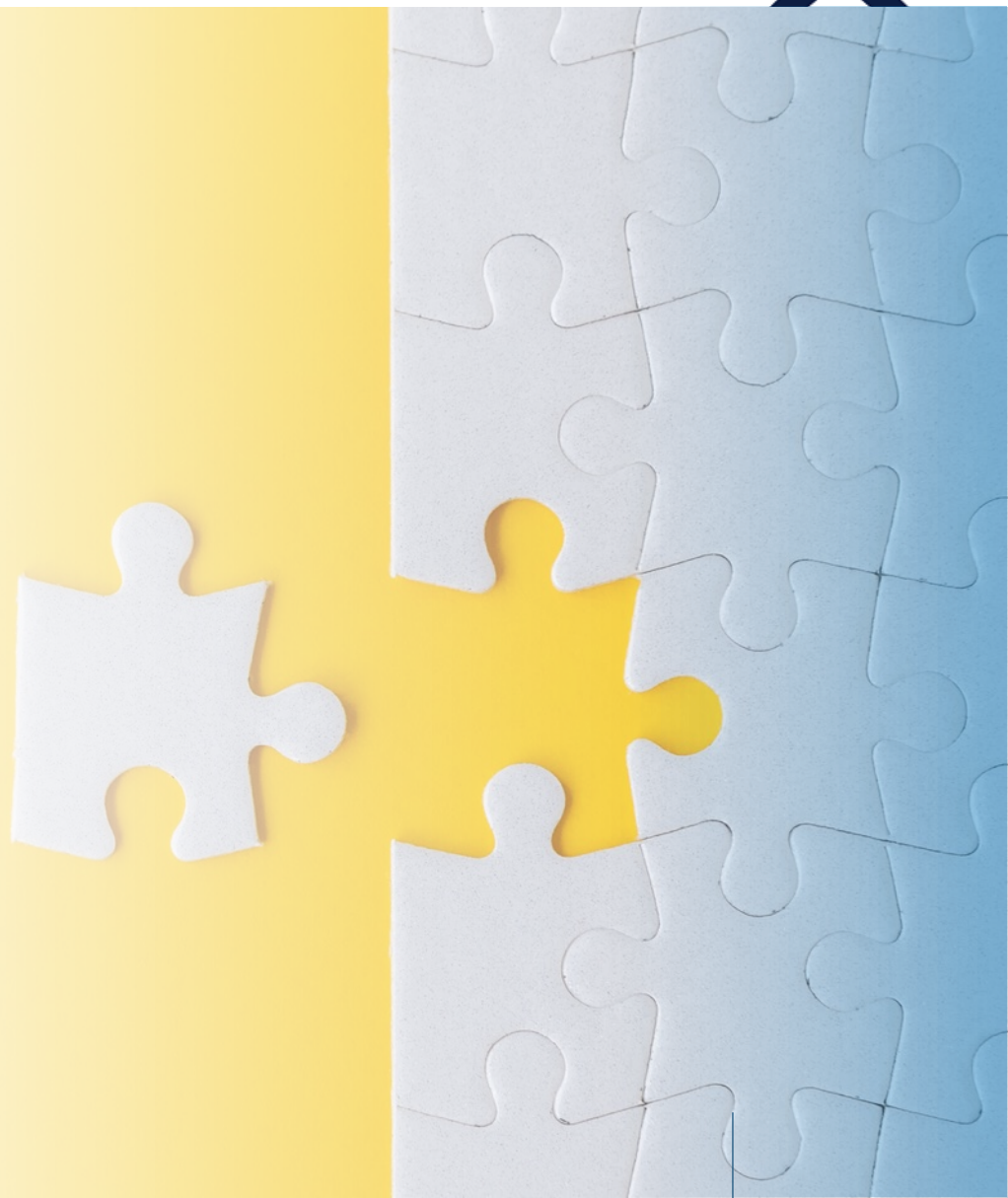
- Contact the Cancer Therapy Evaluation Program (CTEP) Identity Access Management (IAM) Help Desk to remove people:
  - This will set the person to inactive and withdraw/inactivate all their roster affiliations, roles, and task assignments
- Only assign roles that are needed
- The system will allow 500 requests per submission, but do you need that many roles?
- The system functions best when no more than 20 sites are selected – a future update will allow for additional sites to be selected



SDP and Auto-Redaction of PII/PHI

Redaction: Current Method

- CTSU's SDP provides a mechanism for reviewing a patient's chart against data sources such as a clinical database or adverse event report
- When patient documents are uploaded to the SDP, sites are required to remove/redact information that could violate a person's privacy per the Health Insurance Portability and Accountability Act (HIPAA)
- Source documents are manually redacted either:
  - Before uploading documents (use of Sharpie)
  - During upload of documents using a tool within SDP
- Documents which are not fully redacted will be rejected/removed from the SDP



Redaction: Current Pain Points

- The current process can be:
  - Time Consuming:
    - While some source documents are only a few pages, others can be 50+ pages
    - Site staff can spend many hours redacting documents (indicated in 2021 Site Survey & Group Meetings)
    - If LPO Triage staff rejects the document to sites, the process starts over
- Error Prone:
  - Site staff can miss PII/PHI
  - LPO Triage staff can miss PII/PHI
- Distracting:
  - Time spent redacting could be used instead to treat patients

Auto-Redaction: Why should I use this tool?

- The CTSU is planning to launch an auto-redaction tool in the SDP in the next release
- The auto redaction tool uses advances in Artificial Intelligence and Machine Learning (AI/ML) to 'read' and redact PII/PHI when the document is uploaded
- CTSU is planning the next SDP release to be a pilot phase of the auto-redaction tool to determine usefulness for sites
- The goals of the auto-redaction tool are to:
  - Accurately and consistently redact PII/PHI
  - Auto-redact both computer-generated and handwritten text
  - Significantly reduce the time sites are spending manually redacting documents
  - Reduce the time LPOs spend triaging documents after sites upload source documents for review because of more consistent redaction
  - Reduce document rejection by LPO Triage staff for unredacted PII

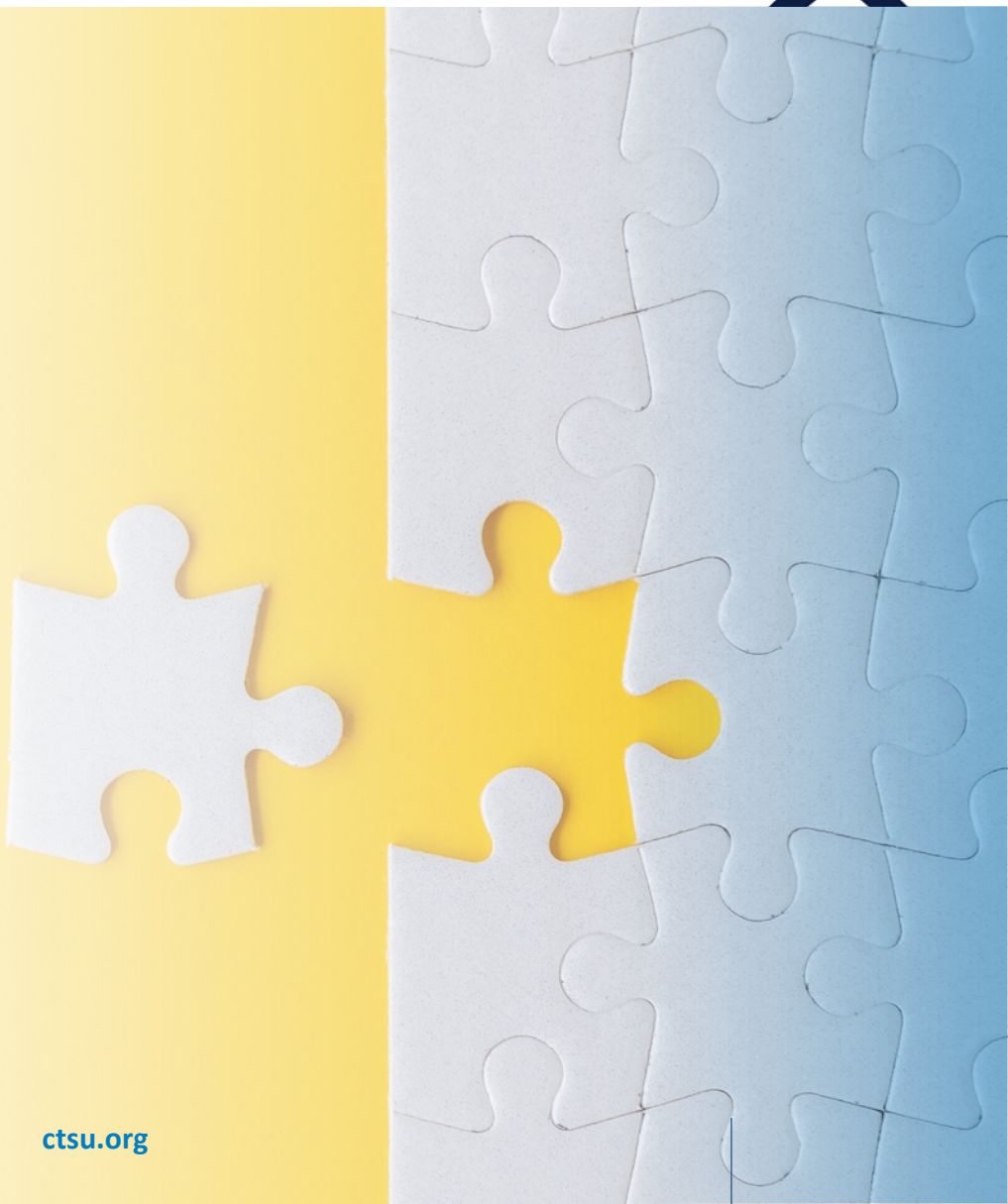
Auto Redaction: Can I make changes?

- The auto-redaction tool will by default be enabled and will immediately run when uploading a document
- The auto-redaction tool can be easily disabled by the site prior to uploading a document
- The auto-redaction tool will display redacted terms prior to saving thus allowing for corrections:
  - Over redaction: terms redacted in error can be unredacted
  - Under redaction: terms which were not redacted can be manually selected for redaction

Researcher Resources & CLASS

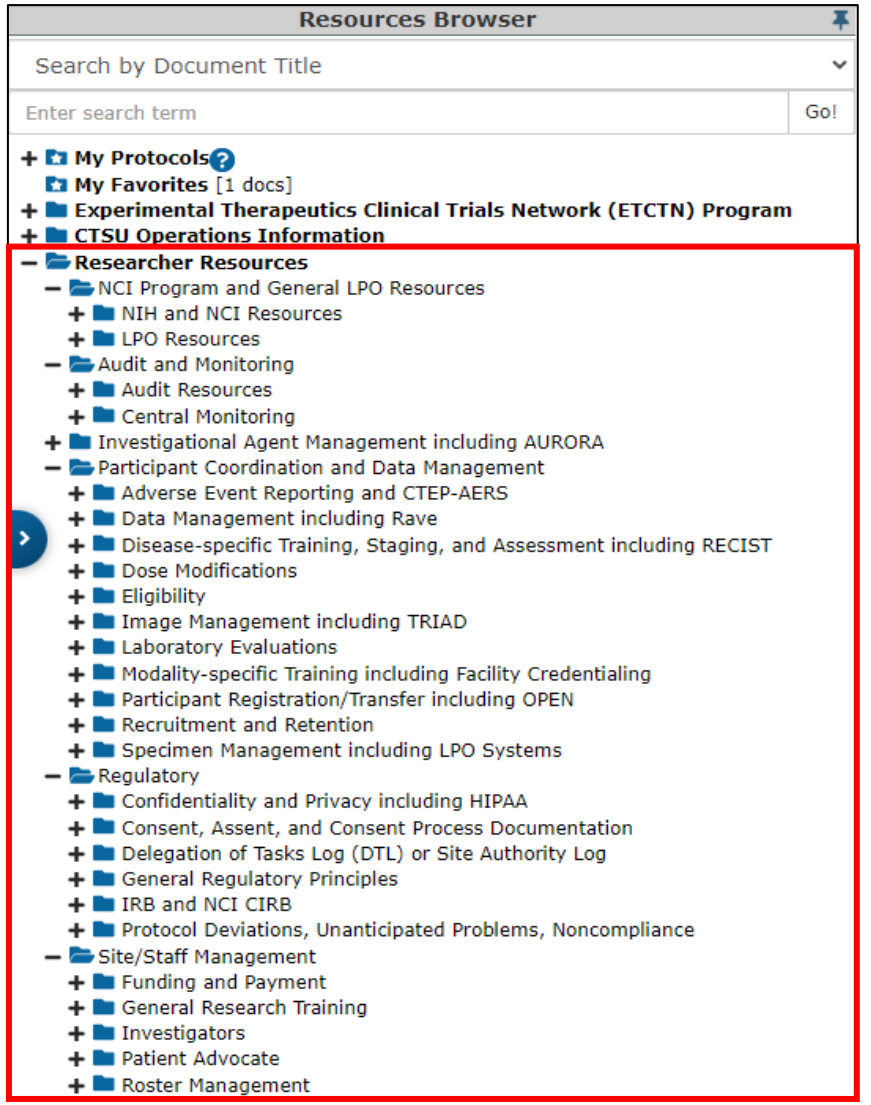
Cross-Network Training Working Group

- The CTSU has been working with the Cross-Network Training Working Group to improve and expand access to staff training resources. Membership includes staff from:
  - CTSU
  - CTEP
  - DCP
  - NCTN Groups
  - NCORP Research Bases
- Intent is not necessarily to always create new resources, but to also collect those that are already out there and make them more easily accessible



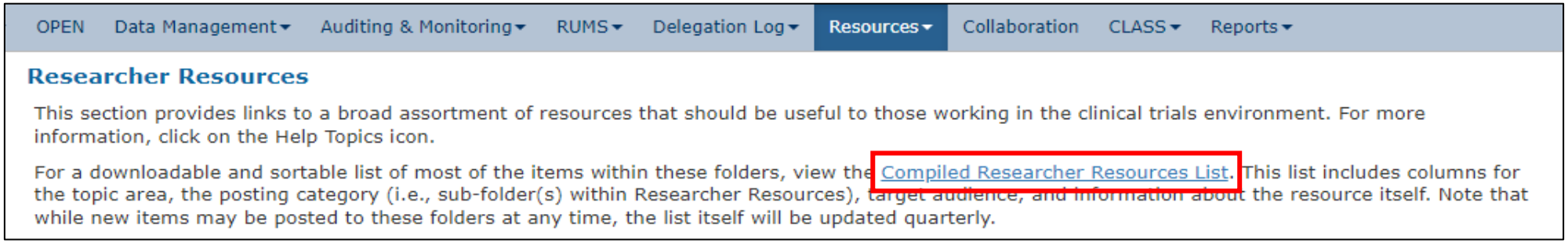
Expanded Researcher Resources

- Reworked and expanded the **Researcher Resources** folders on the CTSU members' website
- Improved categorization
- Links to resources from CLASS, CTSU, NCI, Office for Human Research Protections, etc.



Compiled Researcher Resources List

- Now available: Downloadable, sortable list of the resources

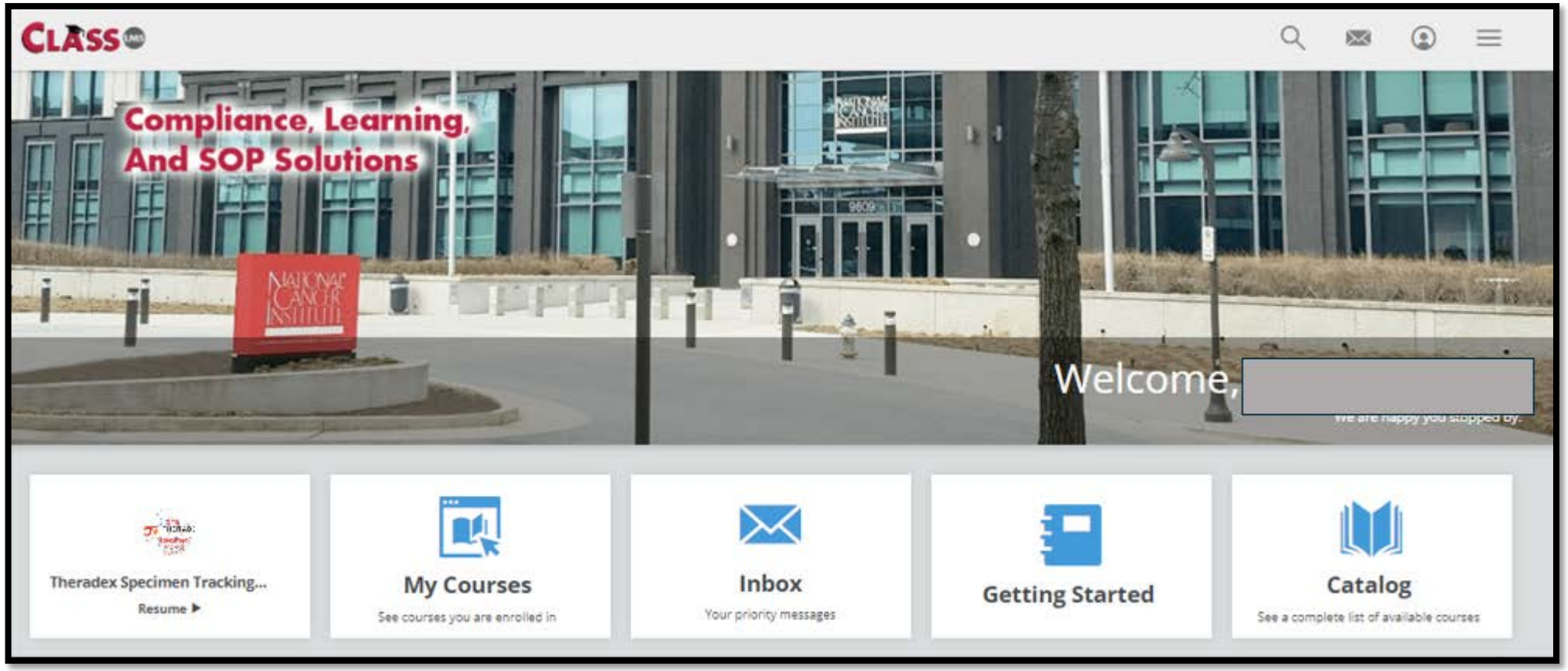


- Currently > 200 items; will be updated quarterly

Topic area	Posting Category	CRC / CRA / Research Associate	Nurse	Institution Administrato	Regulatory Coordinator	Pharmacy	Investigator	Systems Access	Advocate or Patient Resource	Description	Source	Material Type	Lead Group Membership Required to Access	System Access, Training or Resource Link
Accrual	Recruitment and Retention	X	X	X			X			Accrual Quality Improvement Program (AQuIP) - An NCI program	NCI	Webpage	No	http://dcpaquip.com/
Consent	Recruitment and Retention								X	Understanding Informed Consent Forms	NCI	Webpage	No	https://www.cancer.gov/research/participate/articles/understanding-informed-consent-forms
Accrual	Recruitment and Retention								X	NCI's Cancer Information Service	NCI	Webpage	No	https://www.cancer.gov/contact/contact-center
Adverse Event Reporting	Adverse Event Reporting and CTEP-AERS	X	X							Alliance: AE reporting with SAE integration presentation (Spring 2023 Group Meeting) (Login with CTEP credentials required)	Alliance	CLASS Module	No	https://www.ctsu.org/public/class.aspx?courseid=74d40208-7fa5-4dd5-8cb3-0bf9041d22fb
Adverse Event Reporting	Adverse Event Reporting and CTEP-AERS	X	X		X		X	X		Cancer Therapy Evaluation Program Adverse Event Reporting System (CTEP-AERS)	NCI	System	No	https://ctepcore.nci.nih.gov/ctepaers/security/login

CLASS-related Updates

- Expanded course options
- New training report on CTSU website



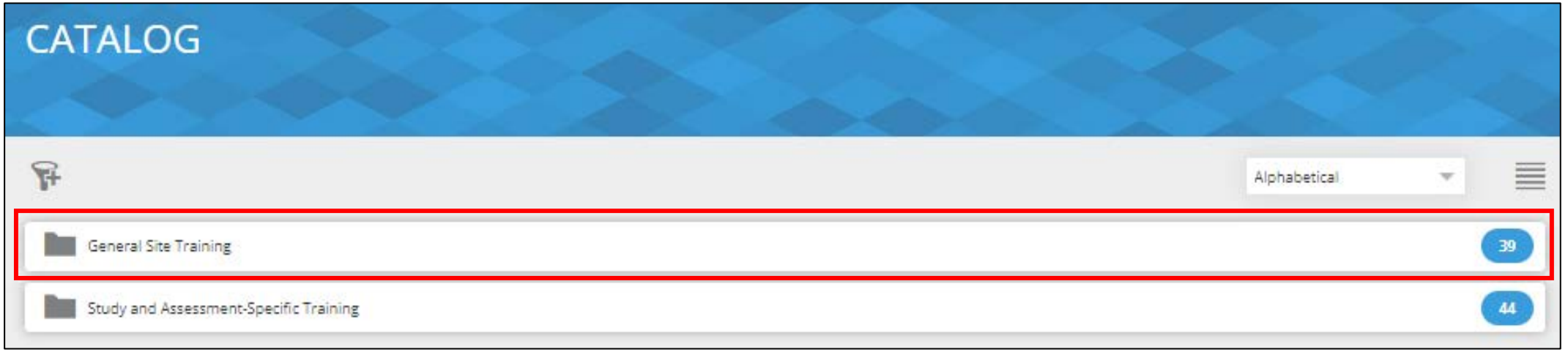
Courses Available in CLASS

Longstanding CLASS trainings:

- Clinical Trials Monitoring Branch (CTMB) auditor training
- Theradex Specimen Tracking System (STS) training for ETCTN, NCICOVID, and Moonshot studies
- Protocol-specific trainings

More recent expansion to include more general research training

- Separate folder in the CLASS catalog



General Site Training

- Wide range of topics
- Generally provided by an NCTN Group (e.g., Alliance, SWOG)
- Most are open to everybody via self-enrollment, although a few are limited to roster members*

NRG: An Overview of NRG*

Alliance: RECIST Basics

Alliance: Data Management Tips & Tricks

Alliance: Regulatory 101 and 102

SWOG Audits: Serious Adverse Event Reporting Training

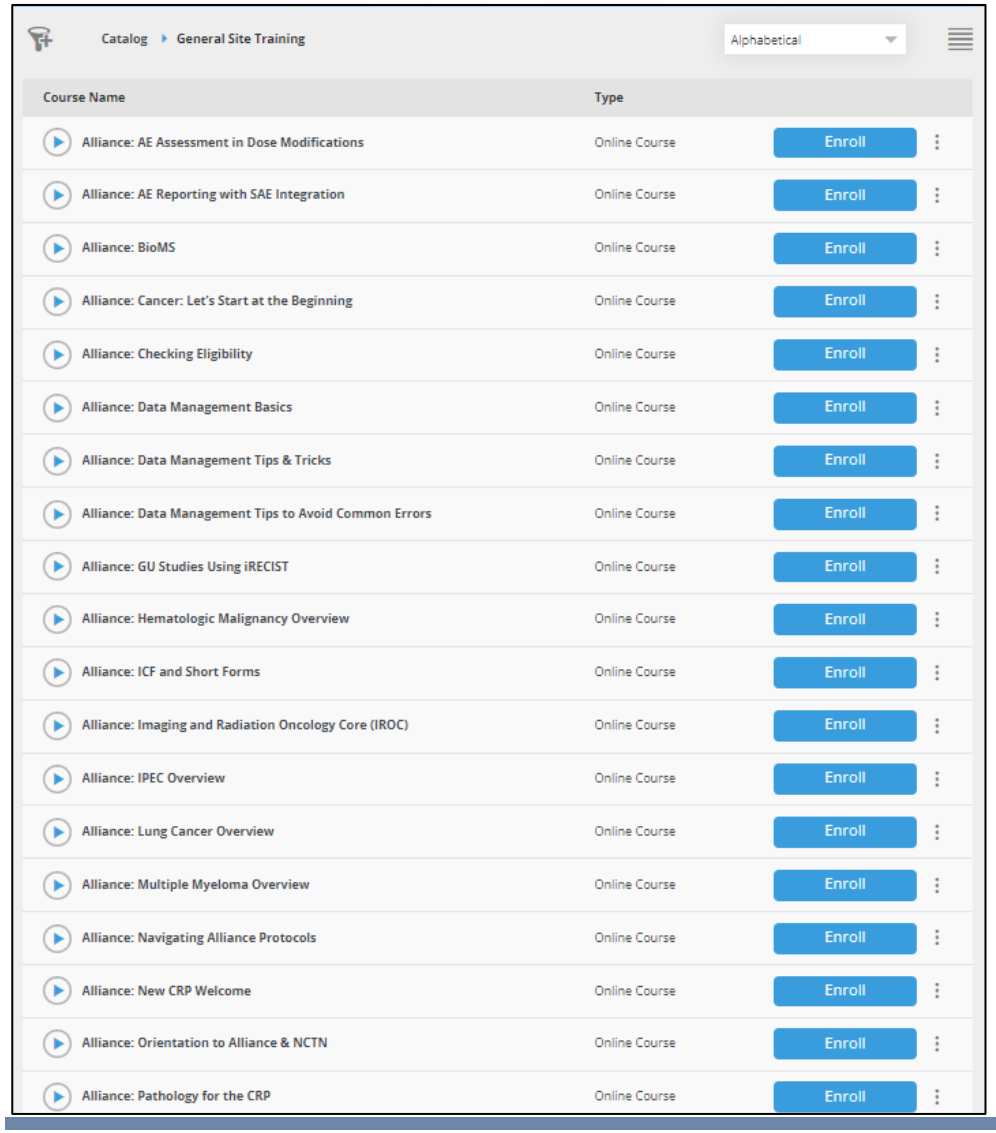
SWOG: Clinical Trials Training Course (CTTC)

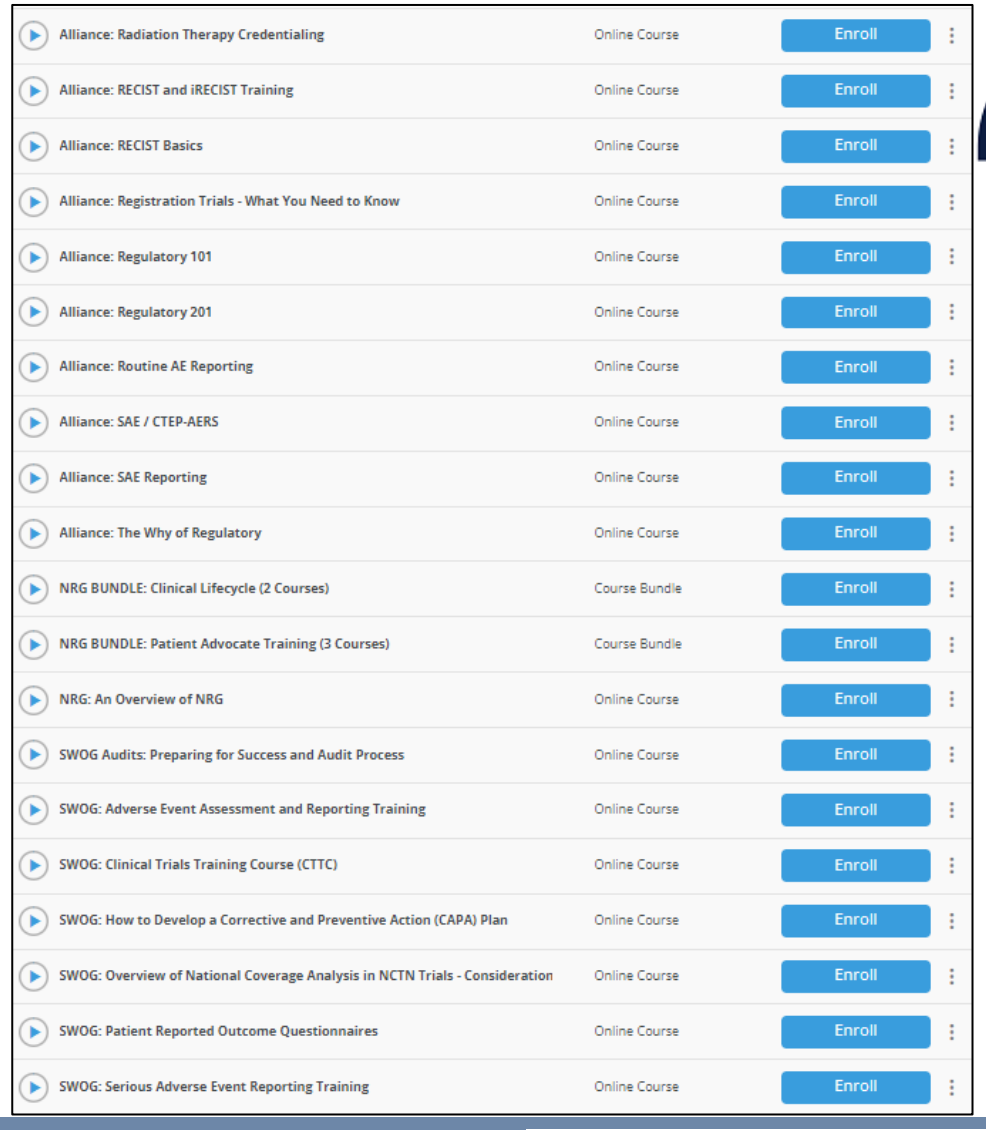
NRG Bundle: Clinical Lifecycle*

Alliance: Hematologic Malignancy Overview

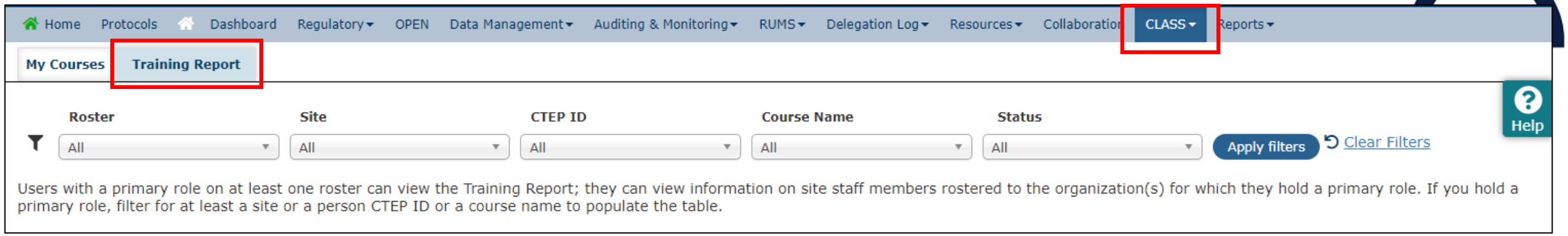
SWOG Audits: Preparing for Success and Audit Process

General Site Training (cont.)





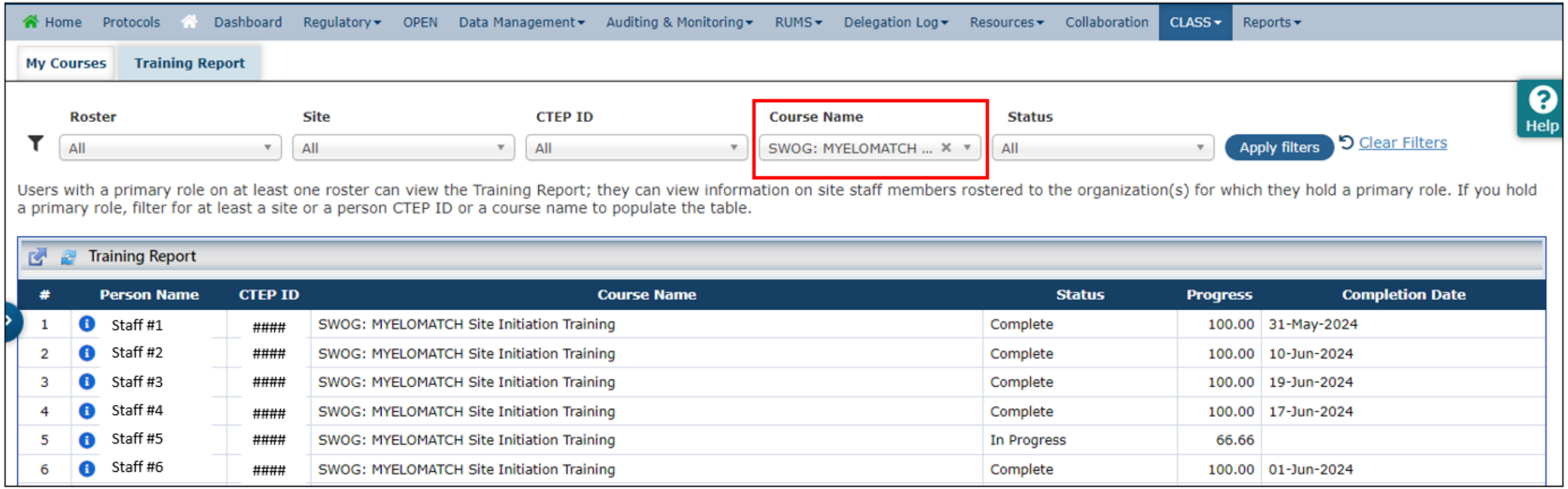
New CLASS Training Report



- Requires primary role on at least one roster/site
- Must set *at least one* of the following filters:
  - Site
  - CTEP ID
  - Course Name
- Export to Excel
- Help Topics available

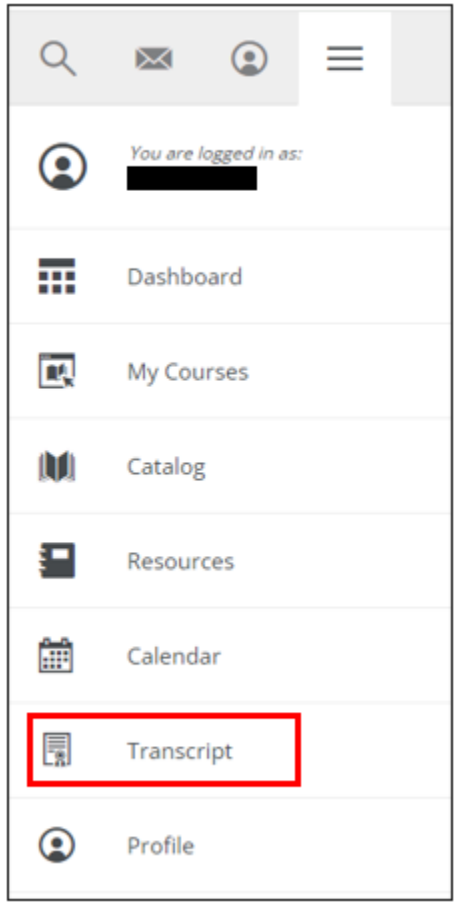
"Who at my site has taken the MyeloMATCH Site Initiation Training course?"

CLASS Training Report - Example



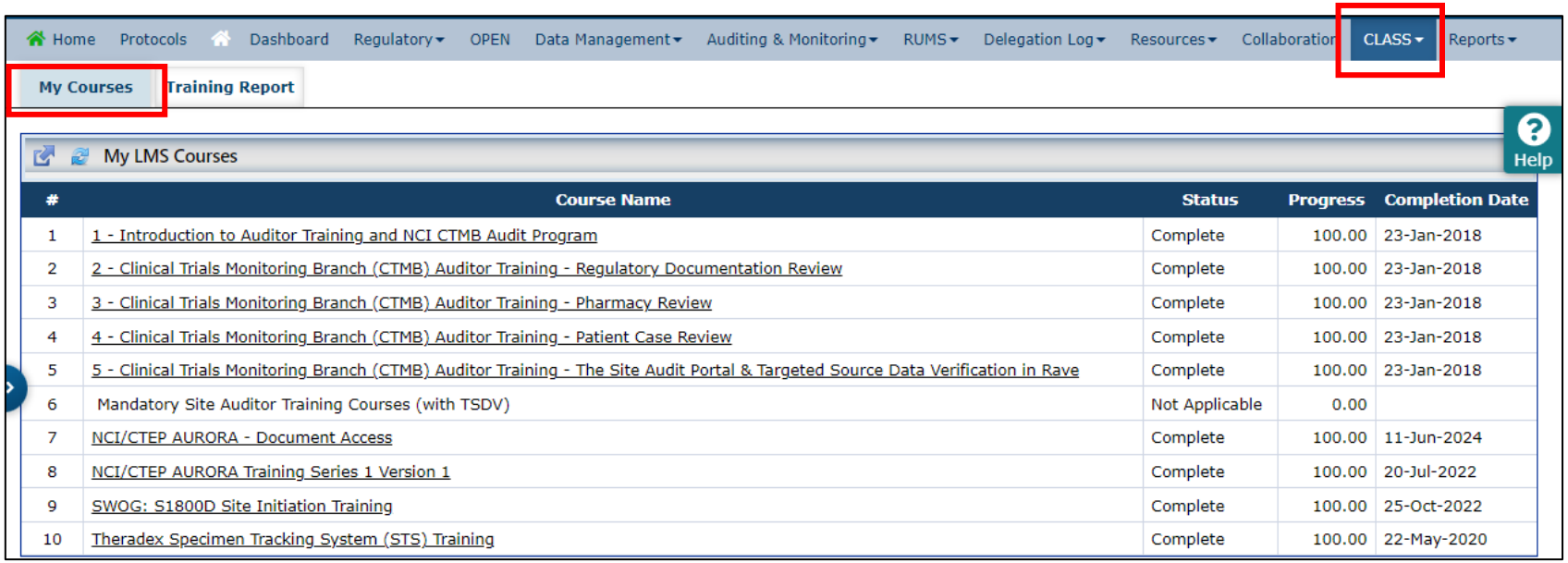
#	Person Name	CTEP ID	Course Name	Status	Progress	Completion Date
1	Staff #1	####	SWOG: MYELOMATCH Site Initiation Training	Complete	100.00	31-May-2024
2	Staff #2	####	SWOG: MYELOMATCH Site Initiation Training	Complete	100.00	10-Jun-2024
3	Staff #3	####	SWOG: MYELOMATCH Site Initiation Training	Complete	100.00	19-Jun-2024
4	Staff #4	####	SWOG: MYELOMATCH Site Initiation Training	Complete	100.00	17-Jun-2024
5	Staff #5	####	SWOG: MYELOMATCH Site Initiation Training	In Progress	66.66	
6	Staff #6	####	SWOG: MYELOMATCH Site Initiation Training	Complete	100.00	01-Jun-2024

Reminder: Checking Your Own Training Status



You can check your training status in CLASS…

…or on the CTSU website.



#	Course Name	Status	Progress	Completion Date
1	1 - Introduction to Auditor Training and NCI CTMB Audit Program	Complete	100.00	23-Jan-2018
2	2 - Clinical Trials Monitoring Branch (CTMB) Auditor Training - Regulatory Documentation Review	Complete	100.00	23-Jan-2018
3	3 - Clinical Trials Monitoring Branch (CTMB) Auditor Training - Pharmacy Review	Complete	100.00	23-Jan-2018
4	4 - Clinical Trials Monitoring Branch (CTMB) Auditor Training - Patient Case Review	Complete	100.00	23-Jan-2018
5	5 - Clinical Trials Monitoring Branch (CTMB) Auditor Training - The Site Audit Portal & Targeted Source Data Verification in Rave	Complete	100.00	23-Jan-2018
6	Mandatory Site Auditor Training Courses (with TSDV)	Not Applicable	0.00	
7	NCI/CTEP AURORA - Document Access	Complete	100.00	11-Jun-2024
8	NCI/CTEP AURORA Training Series 1 Version 1	Complete	100.00	20-Jul-2022
9	SWOG: S1800D Site Initiation Training	Complete	100.00	25-Oct-2022
10	Theradex Specimen Tracking System (STS) Training	Complete	100.00	22-May-2020

Thank You!

- Questions? Contact: krishnachothwani@westat.com
- Please note that the CTSU has a table at the ORP Open Forum session. Stop by with questions about these or other CTSU-related topics!

Oishi Symposium
Welcome to SWOG!
Preparing for an Audit

Thursday, October 17, 2024

Speaker

Laura Gonzales, BSN, MA, RN, OCN

SWOG Quality Assurance Manager

- CRA Workbench
  - Popular Resources
    - OPEN Patient Registration
    - Rave Data Submission
    - Specimen Tracking
    - SWOG QA / Audits / Monitoring
    - SWOG Best Practices
  - Tools
  - Resources
  - CRA Manual (for Oncology Research Professionals)
  - Patient Reports / Data Quality
  - Study Reports
  - Patient Management (Non-Rave Studies)
  - Training
  - Contact Us

Home / Member Resources / **CRA Workbench**

CRA Workbench

Your resource headquarters for SWOG clinical trial patient management.

Home / Member Resources / CRA Workbench / **CRA Manual**

CRA Manual

for Oncology Research Professionals

The CRA Manual for Oncology Research Professionals really is the main resource tool to help CRAs in their day-today tasks working on SWOG trials. The Quality Assurance team and the SDMC (Statistics and Data Management Center) are often asked where certain answers are documented, and most often the information is provided here. Find anything from audits, data submission and expectation reports to long-term follow-up requirements, how to conduct response assessment and forms completion guidelines. We encourage you to share this valuable resource to new and experienced staff at your site!

CRA Manual (for Oncology Research Professionals)

- Introduction
- Chapter 1: Audits
- Chapter 2: Clinical Trials Concept
- Chapter 3: Cooperative Group Concept
- Chapter 4: Data Submission
- Chapter 5: Discipline Review
- Chapter 6: Drug Ordering and Maintenance
- Chapter 7: Ethical and Regulatory Considerations
- Chapter 8: Expectation Report and IPR
- Chapter 9: Intergroup Studies
- Chapter 10: Long Term Follow Up
- Chapter 11: Response Assessment
- Chapter 11a: Response Assessment – Leukemia
- Chapter 11b: Response Assessment – Lymphoma
- Chapter 11c: Response Assessment – Myeloma
- Chapter 12: Registering a Patient
- Chapter 13: Serious Adverse Events
- Chapter 14: Study Protocol
- Chapter 15: Adverse Event Assessments
- Chapter 16: General Forms and Guidelines
- Chapter 16a: General Forms and Guidelines – Leukemia Forms
- Chapter 16b: General Forms and Guidelines – Lung Forms
- Chapter 16c: General Forms and Guidelines – Lymphoma Forms
- Chapter 16d: General Forms and Guidelines – Myeloma Forms
- Chapter 16e: General Forms and Guidelines – Lung-MAP & Sub-studies
- Chapter 16f: General Forms and Guidelines – S1418
- Chapter 16g: General Forms and Guidelines – S1826
- Chapter 16h: General Forms and Guidelines – S1803
- Appendix A: Abbreviations
- Appendix B: ORP Organizations
- Appendix C: ORP Roster
- Appendix D: Clinical Training Sessions
- Appendix E: Technical References and Formulas

SWOG / Clinical Trials / **Training Resources**

- Clinical Trials Training Course (CTTC)

  (The CTTC now resides in the CTSU CLASS learning management system. Site staff who previously enrolled in the CTTC in ExpertusOne may still complete the workshop in ExpertusOne until April 2025.)


Online Course
SWOG: Clinical Trials Training Course (CTTC)
Start
Overview
Lessons
Resources
This training course offers a comprehensive overview of SWOG and reinforces the importance of the CRA's impact in clinical trials research. The CTTC includes presentations on topics such as protocol development, data submission, patient follow-up, the expectation and institutional performance reports, adverse event reporting, audits, and specimen submission. The goals of the CTTC are to introduce the fundamentals of SWOG and National Cancer Institute (NCI) policies and procedures as well as provide the foundation to efficiently perform your responsibilities as a SWOG CRA.

- CRA Workbench
  - Popular Resources
    - OPEN Patient Registration
    - Rave Data Submission
    - Specimen Tracking
    - SWOG QA / Audits / Monitoring
    - SWOG Best Practices
  - Tools
  - Resources
  - CRA Manual (for Oncology Research Professionals)
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  - Study Reports
  - Patient Management (Non-Rave Studies)
  - Training
  - Contact Us

Home / Member Resources / **CRA Workbench**

CRA Workbench

Your resource headquarters for SWOG clinical trial patient management.

Quality Assurance & Audits

The purpose of the Quality Assurance Program is to enhance the reliability and validity of clinical trials data through routine monitoring. Audits are designed to provide assurance that the data reported on research records accurately reflect data in the primary patient record and to verify compliance with protocol and regulatory requirements. The program also surveys data management practices at each institution to provide educational support to clinical trial sites regarding data quality, management, and more.

The following resources can help with clinical trials quality assurance and the audit process.

GUIDELINES | REGULATORY GUIDANCE | FDA INSPECTIONS

INVESTIGATIONAL AGENTS AND PHARMACY | AUDIT RESOURCES

ADDITIONAL RESOURCES | VOLUNTEER AUDITOR PROGRAM

Guidelines

Audits of SWOG Cancer Research Network institutions are conducted in accordance with the guidelines below:

- SWOG Policy 19: Quality Assurance Program
- SWOG Quality Assurance Audit Guidelines

Guidelines

Audits of SWOG Cancer Research Network institutions are conducted in accordance with the guidelines below:

- SWOG Policy 19: Quality Assurance Program
- SWOG Quality Assurance Audit Guidelines
- NCI-CTMB Guidelines for Monitoring of Clinical Trials, effective 2/15/21

Regulatory Guidance

Clinical trials operate under the policies and regulations of the federal Department of Health and Human Services' Office for Human Research Protections (OHRP).

- **Human Subjects Protection**: OHRP provides leadership in the protection of the rights, welfare, and well-being of subjects involved in research conducted or supported by the U.S. Department of Health and Human Services. OHRP helps ensure this by providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight and providing advice on ethical and regulatory issues in biomedical and social-behavioral research.
- **SWOG Regulatory Guidance**: Guidance for a successful regulatory audit including expectations of the audit team for IRB, consent form content, Delegation of Task Log, and patient informed consent.
- **OHRP Guidance on Changes in Informed Consent Documents and Continued Enrollment of New Participants, April 2008**: Changes in informed consent documents in NCI/CTEP-sponsored clinical trials and the continued enrollment of new participants to those trials when new or modified risk information is discovered.
- **OHRP Correspondence, September 2008**: Section E describes information in regard to Communication of New Risk Information to Subjects Already Enrolled in a Clinical Trial Without Obtaining IRB Approval
- **FDA Guidance on AE Reporting, January 2009**: Guidance on reporting of external adverse events to IRBs.
- **OHRP Guidance on AE Reporting, January 15, 2007**: Guidance on reporting of external adverse events to IRBs.

Accountability of Investigational Agents and Pharmacy Operations

Drug accountability and storage procedures described in this section are required under Federal Regulations and CTEP, DCTD, NCI policy.

- ORP Manual: Drug Ordering and Maintenance: Chapter 6 of the ORP Manual provides detailed instructions on completing the NCI Drug Accountability Record Form (DARF).
- NCI Pharmaceutical Management Branch Policies: Pharmaceutical Management Branch (PMB) Guidelines on the management of investigational agents.
- SWOG Investigational Agent Handling Training: Guidance on the proper handling of investigational drugs and is recommended training for new staff involved in ordering, accounting for, and disposing of investigational drugs is accessible to *SWOG members* via the SWOG Investigational Agent Handling Course (or individual modules) maintained in the ExpertusOne learning management system.
- NCI-PMB Investigational Drug Handling Slide Show: A PMB training module that addresses the investigational drug handling process and CTEP's specific policies for maintaining investigational agents.
- Drug Accountability Record Forms (DARFs): The Drug Accountability Record Forms in this section are required under Federal Regulations and CTEP, DCTD, NCI policy.
    - NCI Investigational Agent Record Form (Non-Oral): The NCI DARF must be used to account for all non-oral investigational agents used in NCI sponsored studies.
    - NCI Investigational Agent Record Form for Oral Agents: The NCI DARF must be used to account for all oral investigational agents used in NCI sponsored studies.

Audit Resources

In order to be consistent with standard medical care and to be compliant with Federal regulations, each investigator participating in trials must prepare and maintain adequate and accurate source documentation designed to record all observations and other data pertinent to the investigation of each participant (21 CFR 312.62.b).

- Site Preparation for an Audit: Guidance on how to prepare for a quality assurance audit
- Policy on Auditing Electronic Medical Records: Guidance on providing access and facilitating the audit process if auditors will be expected to review patient records in the EMR.
- SWOG Patient Chart Review Guidance: Tips for a successful patient case review audit including expectations of the audit team for eligibility, treatment administration, toxicity assessment, endpoint assessment, patient informed consent and general data quality

Additional Resources

- **Best Practices for SWOG Studies**: Current information related to expectations for protocol compliance, documentation practices, and consenting issues for those participating on SWOG studies
- **FAQs**: Answers to common questions about record-keeping, data entry and more
- **Record Retention Guidance**: Requirements for record retention of IRB and research records
- **Internal QA Program**: Guidance on implementing an internal QA Program within the research setting
- **Site Authority Log**: This log covers studies that do not that do require a Delegation of Task Log (DTL) available on the CTSU website. All staff who participate in the research process for SWOG and CTSU clinical trials must sign this log which indicates what responsibilities they have authority to perform. The Principal Investigator must sign this form to certify that site staff are trained and qualified to perform the specified duties for NCI Sponsored Protocols. This log must be made available during SWOG audits so that auditors may determine areas of responsibility and verify signatures or initials on data if questions arise during the audit process. Investigators, Advanced Practice Providers, CRAs, Research Nurses and other research personnel should sign it but it is not necessary to include pathologists, surgeons or other medical staff such as residents, infusion nurses and lab personnel whose primary duties are within their scope of practice but not related to research activities. Investigational pharmacy personnel should also be included. During an audit, it is expected that the majority data reviewed would be collected by people who have signed the log. A local version of the log may be used in place of this form provided it includes the required information.

SWOG QUALITY ASSURANCE AUDIT
AUGUSTA UNIVERSITY MEDICAL CENTER
AUGUSTA, GA
SEPTEMBER 23-24, 2024

PATIENT CASE REVIEW **NCI CODE: GA020**

Case #	Study #	Disease Site	Patient #	Registered	Treatment
1.	S1826	LYMPH	291010	15JUL22	**Nivolumab** + AVD
2.	S1912CD	CCD	299367	12FEB24	Financial Navigation
3.	S1918	LYMPH	295643	12MAY23	**CC-486** + R-miniCHOP
4.	S2013	OTHER	294826	14MAR23	Toxicity Assessment

UNANNOUNCED CASE

Case #	Study #	Disease Site	Patient #	Registered	Treatment
5.	S1912CD	CCD	297977	06NOV23	Financial Counseling

IRB REVIEW

A review of regulatory documents will be conducted for ***all*** the protocols listed above. The IRB records required to be available for review include:

- CIRB: Initial *CIRB Approval of the Study-Specific Worksheet About Local Context* giving approval to conduct the study, documentation of date of local activation or implementation of protocol updates/consent versions and reports of serious non-compliance or reportable SAEs
- Informed consent forms: Copies or a comprehensive list of all approved/implemented consent forms

The following information must be submitted to the Network Operations Center for review by September 9, 2024:

CONSENT FORM REVIEW

An unsigned copy of the most current IRB approved version of the consent form for the following protocols:

S1826
S1912CD
S1918
S2013

*Submit a copy of the CIRB approved Annual Signatory Institution Worksheet with local context (boilerplate language).

DRUG ACCOUNTABILITY REVIEW

Copies of the drug accountability records (including shipping receipts, return forms, and transfer forms) for the protocols listed below. This includes records utilized from June 14, 2022 to the present for both the control and satellite pharmacies.

GA020: S1826, S1918

SWOG IRB Review Form - Protocol: MYELOMATCH

Institution: Click or tap here to enter text. | **Inst. Code**: Click or tap here to enter text.

Audit Date: Click or tap to enter a date. | **Previous Audit Date**: Click or tap to enter a date. | **Study Activation Date:** 5/16/24 Version: 5/10/24

Modification	Version	Distributed	Implemented	Modification	Version	Distributed	Implemented
R1	6/12/24	9/22/24					

Initial CIRB Approval:

☐ **DTL**

☒ ~~**TMF**~~

Legend:

£ Patients must be informed
C Consent content updated
✘ Comment below

Comments:

IRB Approved Consent Form Versions

Version / Implementation Date	Coincides with which protocol revision

Update Information:		

Reviewed by: _____ **Date:** _____

SWOG QUALITY ASSURANCE DRUG ACCOUNTABILITY and PHARMACY REVIEW

Institution:	Audit Date:

Protocol #:						
Corresponding Case#:						
NCI Code:						
NCI Drug Accountability Forms						
• Completely & correctly filled out						
• Satellite records accounted for						
• Patient treatment records cross-checked						
Tracking and Disposition						
• Drug shipping receipts kept						
• Return & transfer forms kept						
• Drugs ret'd/transferred in timely manner						
• Expired drugs returned or destroyed						

Storage Conditions

- Identified by protocol number _____
- Secure/limited access area _____
- Temperature monitoring _____

Destruction Policy _____

Verification of current CTEP registration of prescribing provider at time IND is ordered _____

Physical Inventory

Protocol #	Drug/Dose/Lot #	DARF Balance/Date	Actual Balance/Expired

Comments:

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Institution:	**Audit Date:**

SWOG QUALITY ASSURANCE CASE REVIEW FORM

Case #:	Protocol #:	Disease Site:
SWOG Patient #:	Registration Date:	Investigator:

ELIGIBILITY	**OK**	**Major**	**Lesser**	**NA**
Review of documentation available confirms patient did not meet all eligibility criteria.				
Documentation missing; unable to confirm eligibility.				
Eligibility affirmation signed by investigator (lesser in data quality if not signed/dated)				

TREATMENT:				
Incorrect agent/treatment/intervention used.				
Additional agent/treatment/intervention used which is not permitted by protocol.				
Dose deviations or incorrect calculations (> ± 10% is a major).				
Dose modification/treatment interventions not per protocol; incorrectly calculated.				
Treatment incorrect, not administered correctly, or not adequately documented.				
Timing and sequencing of treatment/intervention not per protocol.				
Unjustified delays in treatment.				

DISEASE OUTCOME/RESPONSE				
Inaccurate documentation of initial sites of involvement.				
Tumor measurements/evaluation of disease not performed/reported per protocol.				
Protocol-directed response criteria not followed.				
Claimed response (PR, CR, stable) cannot be verified.				
Failure to detect cancer (prevention study) or failure to identify cancer progression.				

ADVERSE EVENTS				
Failure to report or delayed reporting of a Serious Adverse Event (SAE).				
Adverse events not assessed by the investigator in a timely manner per protocol.				
Grades, types, or dates/duration of serious adverse events inaccurately recorded.				
Adverse events cannot be substantiated.				
Follow-up studies necessary to assess adverse events not performed.				
Recurrent under- or over-reporting of adverse events.				

DATA QUALITY **Last contact reported:** _____ **Off treatment:** _____				
Recurrent missing documentation in the patient/study participant records.				
Protocol-specified laboratory tests or other parameters not done/reported/documented.				
Protocol-specified diagnostic studies including baseline assessments not done/reported.				
Protocol-specified research (QOL/PRO, specimens) or advanced imaging not done.				
Frequent data inaccuracies (to include use of white out/poor clinical documentation).				
Errors in submitted data; data cannot be verified.				
Delinquent data submission.				

Auditor Signature: _____

CONSENT FORM **Version** _____ **Date Signed:** _____	**OK**	**Major**	**Lesser**	**NA**
Consent form not signed and dated by patient or LAR.				
Patient signature cannot be corroborated.				
Consent form not protocol specific.				
Failure to document the informed consent process with the patient.				
Patient signed consent form containing changes not approved by CIRB/LIRB.				
Consent form document missing.				
Translated consent not available or signed/dated by non-English speaking patient				
Consent form not signed by patient prior to study registration/enrollment.				
Consent form does not contain all required signatures.				
Consent form used was not the most current IRB-approved version at patient registration.				
Consent form does not include updates or information required by IRB.				
Reconsent not obtained as required.				
Consent for ancillary/advanced imaging studies not executed properly.				
HIPAA authorization signed (Consent Form – other)				

Notification required: No_____ Yes_____

MYELOMATCH Revision #1 Audit Worksheet (PVD 06/12/24) Patient # _____ Case # _____

1.0 OBJECTIVES

- **Screening and Reassessment (MSRP)**
- **Tier Advancement Pathway (TAP)**
- **Specimens for translational medicine and banking**

4.1 Diagnostic Criteria
Acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) as defined by the WHO (Section 18.4) or the international consensus classification (ICC) (Section 18.3)

5.0 ELIGIBILITY CRITERIA
5.1 Disease Related Criteria

_____a. Participants must be suspected to have previously untreated acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). Participants with AML cannot have a history of previously treated myeloproliferative neoplasms (MPN) or MDS.

_____b. Participants must be ≥ 18 years of age.

5.2 Prior/Concurrent Therapy Criteria

_____a. Participants must not have received prior anti-cancer therapy for AML or MDS.
NOTE: Hydroxyurea to control the white blood cell count (WBC) is allowed.
NOTE: Prior erythroid stimulating agent (ESA) is not considered prior therapy for the purposes of eligibility. Participants must not be currently receiving any cytarabine-containing therapy other than up to 1 g/m2 of cytarabine, which is allowed for urgent cytoreduction.

_____b. Participants are allowed prior use of hydroxyurea, all-trans retinoic acid (ATRA), BCR-ABL directed tyrosine kinase inhibitor, erythropoiesis-stimulating agent, thrombopoietin receptor agonist and lenalidomide, with a maximum limit of 1 month of exposure.
NOTE: Participants receiving hydroxyurea prior to treatment substudy or TAP assignment must agree to discontinue hydroxyurea within 24 hours before beginning substudy or TAP treatment.

5.3 Clinical/Laboratory Criteria

_____a. Participants must not have a prior or concurrent malignancy that requires concurrent anti-cancer therapy.
NOTE: active hormonal therapy is allowed.

_____b. Participants must have a Zubrod Performance Status evaluation within 28 days prior to registration

7.0 General Considerations
Participants must register to MYELOMATCH prior to submitting specimens to the MDNet. It is recommended that participants register to MYELOMATCH no more than 14 calendar days prior to submitting specimens to the MDNet.

7.1 Central laboratory assessment through MDNet for Treatment Assignment to a myeloMATCH Treatment Substudy or TAP – Initial Screening
Molecular and clinical data will be used to assign participants to myeloMATCH treatment substudies or TAP.
No investigational treatment plan is included in the MSRP and TAP. The goal is to assign participants to myeloMATCH treatment substudies based on clinical, genomic, and/or measurements of remaining disease burden.
Successful biomarker profiling results through MDNet are required to register a participant to a myeloMATCH treatment substudy (see Sections 5.4. 14.4, and 15.0).
Sites will be notified of MDNet testing failures and have the option to submit additional specimens for repeat testing (see Section 18.1).

7.2 Tier Advancement Pathway (TAP)
Participants who do not have an available myeloMATCH treatment substudy will be assigned to standard of care (SOC) treatment per treating investigator and institutional preference. Note: participants cannot receive investigational drugs or enroll on local clinical trials. Participants may receive Tier 1 through Tier 3 TAP therapy at a non-NCTN site.
TAP specimen collections should be done at treating investigator discretion at the suggested reassessment timepoints indicated in Table 7.4 below.

7.3 Reassessment through MDNet for Treatment Assignment to a myeloMATCH Treatment Substudy or TAP – Rescreening for Participants Assigned to a Treatment Substudy
Within 30 days after the participant reaches a reassessment event (as defined in the respective myeloMATCH treatment substudy protocol, reassessment specimens must be submitted to MDNet (See Section 18.1).
If the site wants to have the participant evaluated for reassignment to a subsequent tier of treatment, the MYELOMATCH Re-Screening Registration Worksheet may be completed in OPEN. This will register the participant to the next step of the MSRP to determine eligibility and trigger assignment for additional myeloMATCH therapy (see Section 14.4).

A new myeloMATCH assignment will be provided within 10 days of MDNet receipt of all required specimens. If there is a new myeloMATCH treatment substudy assignment, participants must register to the assigned myeloMATCH treatment substudy to receive their treatment assignment on the treatment substudy.
NOTE: The myeloMATCH treatment substudy assignment will expire in OPEN after 10 days, and the site will be unable to register the participant to the assigned myeloMATCH treatment substudy. If this occurs, contact the myeloMATCH Helpdesk for assistance (myelo-match-support@nih.gov).

7.4 Reassessment through MDNet for Treatment Assignment to a myeloMATCH Treatment Substudy or TAP – Rescreening for Participants Assigned to TAP
TAP participants will be evaluated at suggested reassessment timepoints (indicated in Table 7.4 below). Within 30 days after the participant reaches a reassessment event, specimens may be submitted to MDNet at the discretion of the treating investigator (see Section 18.1). Specimens for MDNet submission must be collected by the participating NCTN site.
If the site wants to have the participant evaluated for reassignment to a subsequent tier of treatment, the MYELOMATCH Re-Screening Registration Worksheet may be completed in OPEN. This will register the participant to the next step of the MSRP to determine eligibility and trigger assignment for additional myeloMATCH therapy (see Section 14.5).
NOTE: The myeloMATCH treatment substudy assignment will expire in OPEN after 10 days, and the site will be unable to register the participant to the assigned myeloMATCH treatment substudy. If this occurs, contact the myeloMATCH Helpdesk for assistance (myelo-match-support@nih.gov).

Table 7.4: Suggested Specimen Collection for Participants Receiving SOC Therapy Through the TAP (See Section 15.1 for specimen collection information)

Tier	Treatment Type	Specimen Collection Time for Reassessment	
		Less-Intensive Therapy	Intensive Therapy
Tier 1	Induction	After 2-6 cycles	Response Assessment
Tier 2	Consolidations/Post-Remission	End of post-remission therapy	End of post-remission therapy
Tier 3	Hematopoietic Stem Cell Transplant (HCT)	Day 30 & Day 100 post-HCT	Day 30 & Day 100 post-HCT
Tier 4	Maintenance/Observation	As clinically indicated	As clinically indicated

For questions regarding specimen collection timing, please contact the Treatment Advisement Group (TAG)

7.5 Criteria for removal from MSRP
1. Progressive or refractory disease.
2. Upon morphologic relapse from morphologic CR/CRh/CRi, a first attempt in TAP to regain complete response fails.
3. Participation in a non-myeloMATCH clinical trial.
4. Receipt of non-myeloMATCH investigational treatment.

7.6 Follow-Up Period
All participants will be followed until death or 10 years after registration, whichever occurs first.

8.0 ADVERSE EVENT REPORTING AND DOSAGE MODIFICATIONS
Because TAP treatments associated with registration to the MSRP are standard of care (SOC), no toxicity data will be collected on the MSRP. Toxicity data will be collected as per the specific myeloMATCH treatment substudies.

9.0 Study Calendar

9.1 Study Calendar-For all TAP-Tier Equivalents

REQUIRED STUDIES	Before TAP Treatment Starts	At Time Of Response Assessment	At Time Of TAP Treatment Failure Or To Receive Non-MyeloMATCH Therapy
PHYSICAL			
H&P	X	X	X
Wt & PS	X	X	X
LABORATORY			
CBC (only when marrow submitted)	X	X	X
MSRP SPECIMEN SUBMISSION			
BM Aspirate/Blood for MSRP Reassessment **(REQUIRED)**		X	X
BM Aspirate/Blood for MSRP Reassessment **(REQUIRED IF PT CONSENTS)**		X	X

See Sections 15.2-15.4 for details regarding specimen submission timepoints and procedures.

10.0 Criteria for Evaluation and Endpoint Definitions

10.1 Time to Treatment Substudy or TAP Assignment

Measured from latest date of MDNet receipt of all required specimens (if specimens not received on the same day) to date treatment substudy or TAP assignment is returned via email to participant's site. Reliant upon receipt of local pathology report to release participant assignment.

10.2 Remission and Treatment Failure Definitions

a. Morphologic complete remission (CR): Bone marrow blasts <5%; absence of circulating blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count (ANC) ≥ 1.0 x 109/L (1000/mcL); platelet count ≥ 100 x 109/L (100,000/µL)

b. Morphologic complete remission with partial hematological recovery (CRh): All CR criteria except count recovery for CR are not met AND ANC > 0.5 x 109/L (500/mcL) AND platelets > 50 x 109/L (50,000/mcL).

c. Morphologic complete remission with incomplete blood count recovery (CRi): All CR criteria except for residual neutropenia (<1.0 x 109/L [1000/mcL]) OR thrombocytopenia (< 100 x 109/L [100,000/mcL])

d. Partial remission (PR): All hematologic criteria of CR; decrease of bone marrow blast percentage to 5% to 25%; and decrease of pretreatment bone marrow blast percentage by at least 50%

e. Morphologic leukemia-free state (MLFS): Bone marrow blasts < 5%; absence of blasts with Auer rods; absence of extramedullary disease; no hematologic recovery required (Note: for myeloMATCH this will not be reported as part of a composite overall response, but may be reported alone as an observed non-response)

f. Stable disease (SD): Failure to achieve at least a PR, but with no evidence of progression as defined below for at least 8 weeks

Disease Progression:

1. Evidence for an increase in bone marrow blast percentage and/or increase of absolute blast counts in the blood:
   a. 50% increase in marrow blasts over baseline (a minimum 15% increase is required in cases with <30% blasts at baseline; or persistent marrow blast percentage of >70% over at least 3 months; without at least a 100% improvement in absolute neutrophil count (ANC) to an absolute level [> 0.5 x 109/L (500/mcL), and/or platelet count to >50 x 109/L (50,000/mcL) non-transfused]; or b. 50% increase in peripheral blasts (WBC x % blasts) to >25 x 109/L (>25,000/mcL) (in the absence of differentiation syndrome)
2. New extramedullary disease

Note: Transient cytopenias during chemotherapy courses should not be considered disease progression, as long as they recover to the previous levels

g. Refractory disease: failure to achieve CR, CRh, CRi, PR, or SD, excluding patients with death in aplasia or death due to indeterminate cause

h. Death in aplasia: Deaths occurring ≥ 7 days following completion of initial treatment while cytopenic; with an aplastic or hypoplastic bone marrow obtained within 7 days of death, without evidence of persistent leukemia

i. Death from indeterminate cause: Deaths occurring before completion of therapy, or < 7 days following its completion; or deaths occurring ≥ 7 days following completion of initial therapy with no blasts in the blood, but no bone marrow examination available

10.3 Minimal residual disease (MRD) response

MRD response is based on flow cytometry studies performed by the MDNet.

a. MRD negative complete remission (MRD neg CR): all criteria for morphologic CR are met and there is no evidence of AML based on flow cytometry from central MDNet lab; MRD will be considered undetectable if <10-3.

14.4 Data Submission Overview and Timepoints	**FORMS**
AFTER REGISTRATION TO THE MSRP SUBMIT	• Specimens as outlined in section 15.0 • Upload the participant's local pathology report(s) in OPEN NOTE: It is recommended that the participant submit specimens to the MDNet no more than 14 days after registering to the MSRP.
WITHIN 15 DAYS AFTER REGISTRATION TO THE MSRP SUBMIT	• MYELOMATCH Vistal Status Form • MYELOMATCH Onstudy form • MYELOMATCH Eligibility Criteria Form
WITHIN 30 DAYS AFTER THE PARTICIPANT HAS A REASSESSMENT EVENT ON THEIR MYELOMATCH TREATMENT SUBSTUDY (defined in each treatment protocol) SUBMIT	• MYELOMATCH Vital Status Form • Specimens as outlined in Section 15.0.
AT ANY TIME WHEN THE PARTICIPANT SHOULD BE EVALUATED FOR RE-ASSIGNMENT TO A SUBSEQUENT TIER OF TREATMENT SUBMIT	• MYELOMATCH Re-screening Registration Worksheet (completed in OPEN) • Upload the participant's local pathology report(s) in OPEN (recommended)
WITHIN 30 DAYS AFTER THE PARTICIPANT DISCONTINUES PARTICIPATION ON THE MYELOMATCH PROTOCOL SUBMIT	• MYELOMATCH Vital Status Form • PMI Off Study Standard Form
WITHIN 30 DAYS AFTER PARTICIPANT REFUSES ALL FURTHER FOLLOW-UP AND CONTACT FOR THE MYELOMATCH PROTOCOL SUBMIT	• MYELOMATCH Vital Status Form • PMI Off Study Standard Form
WITHIN 30 DAYS AFTER PARTICIPANT REFUSES ALL FURTHER FOLLOW-	• MYELOMATCH Vital Status Form • PMI Consent Withdrawal Standard Form

UP AND CONTACT FOR THE MYELOMATCH PROTOCOL SUBMIT	
IF NOT SUBMITTED OTHERWISE, AT LEAST EVERY 6 MONTHS UNTIL 10 YEARS AFTER REGISTRATION SUBMIT	• MYELOMATCH Vital Status Form
WITHIN 30 DAYS (IF ON MYELMATCH PROTOCOL) OR 60 DAYS (IF OFF MYELOMATCH PROTOCOL) AFTER KNOWLEDGE OF DEATH, SUBMIT	• MYELOMATCH Vital Status Form • MYELOMATCH Notice of Death Form • If not previously submitted, PMI Off Study Standard Form
14.5 Tier Advancement Pathway (TAP) Data Submission Overview and Timepoints	**FORMS**
WITHIN 15 DAYS AFTER PARTICIPANT IS ASSIGNED TO A TAP TIER EQUIVALENT TREATMENT SUBMIT	• MYELOMATCH Vital Status Form • MYELOMATCH TAP Tier-equivalent Onstudy Form (this form is tier-specific)
WITHIN 30 DAYS AFTER EACH DISEASE ASSESSMENT SUBMIT	• MYELOMATCH Vital Status Form • MYELOMATCH TAP Disease Assessment Form
AT ANY TIME WHEN THE PARTICIPANT HAS A REASSESSMENT EVENT (defined in Section 7.2) SUBMIT	• MYELOMATCH Vital Status form • Specimens as outlined in Section 15.0
AT ANY TIME WHEN THE PARTICIPANT SHOULD BE EVALUATED FOR RE-ASSIGNMENT TO A SUBSEQUENT TIER OF TREATMENT SUBMIT	• MYELOMATCH Re-screening Registration Worksheet (completed in OPEN) • Upload the participant's local pathology report(s) in OPEN (recommended)
WITHIN 30 DAYS AFTER DISCONTINUING TAP TIER EQUIVALENT THERAPY SUBMIT	• MYELOMATCH Vital Status Form • MYELOMATCH TAP Treatment Summary Form

15.2 Translational Medicine (REQUIRED)

a. Timepoint: Pre-Enrollment/Diagnosis and Progression

Table 15.2.a

Assay	Specimens	Ship To
Flow Cytometry1 (Required)	1 EDTA tube bone marrow aspirate (3-5 mL)	Children's Hospital Los Angeles (CHLA)
Cytogenetics 2 (Required)	1 Sodium Heparin tube bone marrow aspirate (3-5 mL)	Fred Hutchinson Cancer Center (FHCC) Specialty Labs – Clinical Cancer Genomics Laboratory
NCI Myeloid Assay 1 (Required)	1 EDTA tube bone marrow aspirate (3-5 mL)	If shipping on Sunday-Wednesday for overnight delivery: Molecular Characterization Laboratory (MoCha) If shipping on Thursday-Saturday for overnight delivery: Molecular Oncology Fred Hutchinson Cancer Center

1 If marrow is dry tap, 10 mL of whole blood collected into institutionally supplied EDTA tubes may be substituted for bone marrow aspirate.
2 When total specimen acquisition is limited, please allocate volumes to help ensure at least 3mL are put into the Sodium Heparin (green top) tube. Assay failure is high for cytogenetics when there is less than 3mL. If marrow is dry tap, 10 mL of whole blood collected into institutionally supplied Sodium Heparin (green top) tubes may be substituted for bone marrow aspirate.

b. Timepoint: Reassessment Event

Table 15.2.b

Assay	Specimens	Ship To
Flow Cytometry1 (Required)	1 EDTA tube bone marrow aspirate (3-5 mL)	Children's Hospital Los Angeles (CHLA)
Cytogenetics 2 (Required)	1 Sodium Heparin tube bone marrow aspirate (3-5 mL)	Fred Hutchinson Cancer Center (FHCC) Specialty Labs – Clinical Cancer Genomics Laboratory
NCI Myeloid Assay 1 (Required)	1 EDTA tube bone marrow aspirate (3-5 mL)	If shipping on Sunday-Wednesday for overnight delivery: Molecular Characterization Laboratory (MoCha)

		If shipping on Thursday-Saturday for overnight delivery: Molecular Oncology Fred Hutchinson Cancer Center
Add rows for any treatment-protocol-specific collections.	*[Specimens]* **This row is to be added to treatment protocols.**	*[Destination]*

1 If marrow is dry tap, 10 mL of whole blood collected into institutionally supplied EDTA tubes may be substituted for bone marrow aspirate.
2 When total specimen acquisition is limited, please allocate volumes to help ensure at least 3mL are put into the Sodium Heparin tube. Assay failure is high for cytogenetics when there is less than 3mL. If marrow is dry tap, 10 mL of whole blood collected into institutionally supplied Sodium Heparin (green top) tubes may be substituted for bone marrow aspirate.

15.3 SPECIMEN BANKING (REQUIRED IF PARTICIPANT CONSENTS)

a. Timepoint: Pre-Enrollment/Diagnosis and Progression

Table 15.3.a

Assay	Specimens	Ship To
Biobanking (Required if participant consents)	- 2 Streck cfDNA tubes peripheral blood (20 mL total or 10 mL each) - 2 EDTA tubes peripheral blood (20 mL total or 10 mL each) - 1 Buccal Swab[1]	SWOG Biospecimen Bank

1 Buccal swab is to be collected only once, preferably at Pre-Enrollment/Diagnosis timepoint. If not collected initially, buccal swab should be collected at a subsequent timepoint.

b. Timepoint: Reassessment Event

Table 15.3.b

Assay	Specimens	Ship To
Biobanking (Required if participant consents)	- 1 EDTA tube bone marrow aspirate[1] (3-5 mL) - 1 Sodium Heparin tube bone marrow aspirate (3-5 mL) [1] - 2 Streck tubes peripheral blood (20 mL total or 10 mL each) [1] - 2 EDTA tubes peripheral blood (20 mL total or 10 mL each) - Buccal Swab (only if not previously obtained) [2]	SWOG Biospecimen Bank

1 If marrow is dry tap, 10 mL of whole blood collected into institutionally supplied EDTA tubes may be substituted for bone marrow aspirate.
2 Buccal swab is to be collected only once, preferably at Pre-Enrollment/Diagnosis timepoint. If not collected initially, buccal swab should be collected at a subsequent timepoint

15.4 SHIPPING SAMPLES

Table 15.4

Initial Activation *Note: At initial activation, paper forms will be used to collect required study data.* For initial activation, fax (or securely email) Generic Specimen Submission Forms, CLIA Submission Form, and Local Pathology Group Information Form to each receiving laboratory.	Post-Activation Transition to Rave *Notes:* *These documents are required after MyeloMATCH transitions to electronic data entry in Rave. Paper forms will no longer be accepted after this transition. Rave forms do not need to be faxed.*
- myeloMATCH Specimen Submission Form - Local Pathology Group Information Form - CLIA Submission Form	- Rave-generated Samples Tracking and Manifest Form - Rave-generated Local Pathology Group Information Form - Rave-generated CLIA Submission Form

A copy of all pathology reports must be uploaded via the MYELOMATCH OPEN Registration for initial registration.

Questions?

qamail@swog.org

Fall 2024 Oishi Symposium

Thursday, October 17, 2024

Chicago, IL

Jerry Radich, MD

PI: SWOG myeloMATCH

myeloMATCH

Myeloid Malignancies Molecular Analysis for Therapy Choice
NCI National Clinical Trials Network

October 17, 2024
Jeri and Noboru Oishi Symposium Presentation

Presenter:

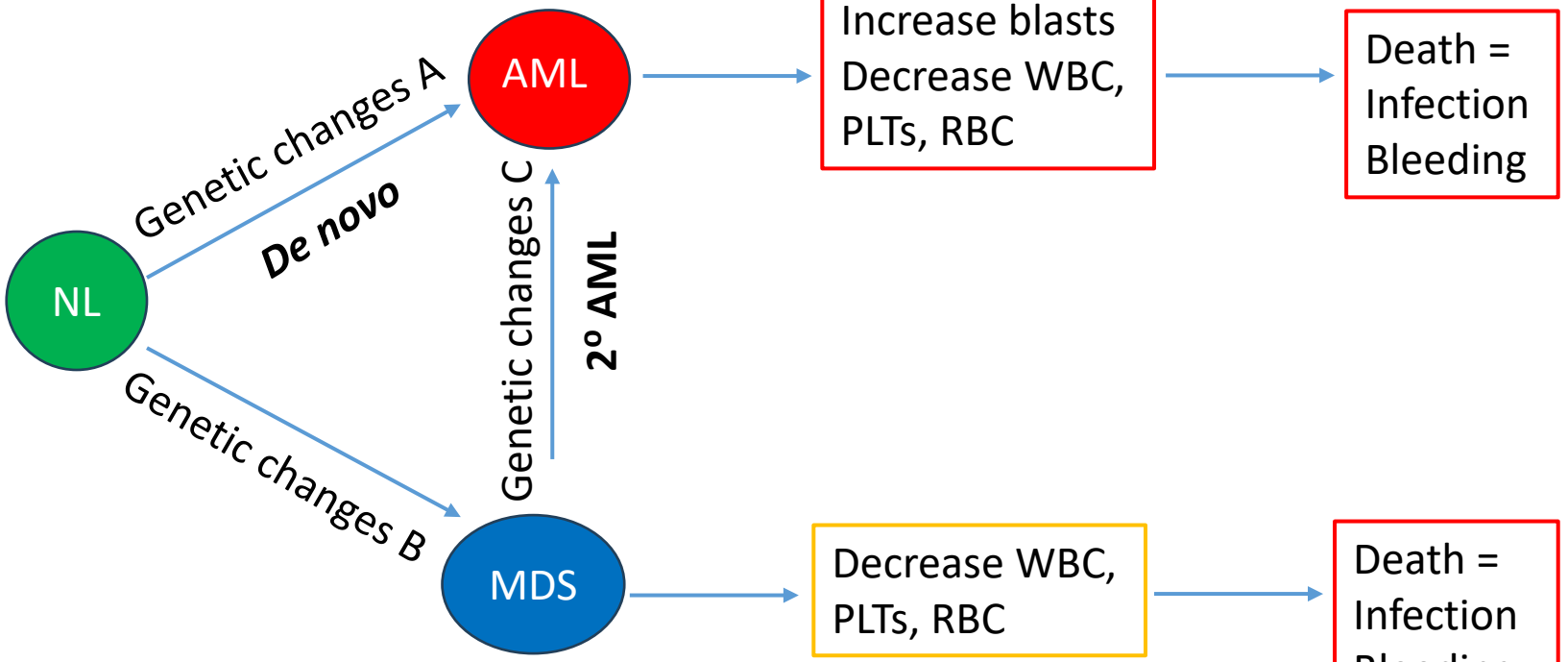
Jerald Radich, MD

myeloMATCH Chair, Professor, Translational Science and Therapeutics Division, Fred Hutch, and Kurt Enslein Endowed Chair, Fred Hutch Cancer Center

AML 2024: “Precision” medicine, MRD, and beyond

Jerry Radich, MD

Pathophysiology of MDS and AML for poets



Treatment options

Supportive care
- Low risk MDS
- Elder AML

Chemotherapy
- Intense v. less

"Targeted" agents
- e.g., FLT3 inhibitors, IDH

Transplant
- More or less intense

Diagnosis defining gene mutations in AML

AML-DEFINING GENETIC ABNORMALITIES: WHO 2022 AND ICC[2,3,32]

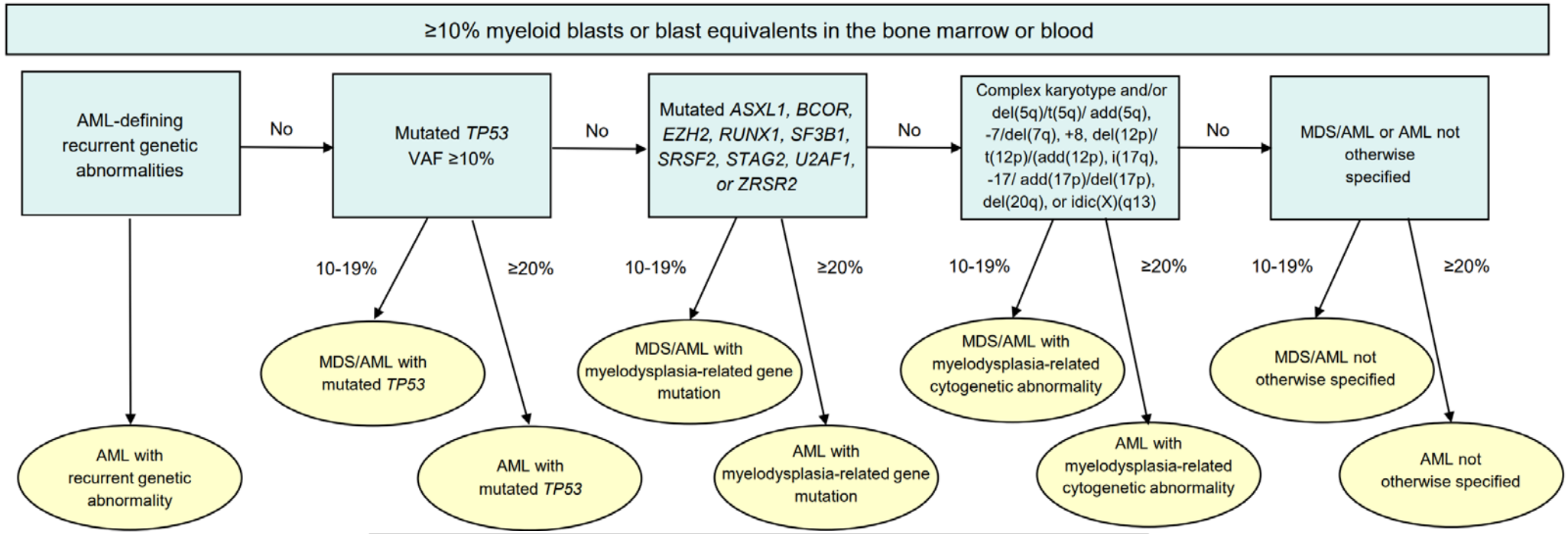
AML	Acute promyelocytic leukemia (APL)
• t(8;21)(q22;q22.1)/*RUNX1::RUNX1T1* • inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB::MYH11* • t(9;11)(p21.3;q23.3)/*MLLT3::KMT2A* • Other *KMT2A* rearrangements • t(6;9)(p22.3;q34.1)/*DEK::NUP214* • inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2; MECOM(EVI1)* • Other *MECOM* rearrangements • Mutated *NPM1* • *CEBPA* (WHO only), in-frame bZIP *CEBPA* mutations (ICC only) • *RBM15::MRTFA* fusion (WHO only) • *NUP98* rearrangement (WHO only)	• t(15;17)(q24.1;q21.2)/*PML::RARA* • Other *RARA* rearrangements

ELN 2024 risk stratification by cyto and mutations

ELN RISK STRATIFICATION BY BIOLOGICAL DISEASE FACTORS FOR PATIENTS WITH NON-APL AML TREATED WITH INTENSIVE INDUCTION CHEMOTHERAPY[1]

Risk Category[a,b]	Genetic Abnormality
Favorable	t(8;21)(q22;q22.1)/*RUNX1*::*RUNX1T1*[b,c] inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB*::*MYH11*[b,c] Mutated *NPM1*[b,d] without *FLT3*-ITD bZIP in-frame mutated *CEBPA*[e]
Intermediate	Mutated *NPM1*[b,d] with *FLT3*-ITD Wild-type *NPM1* with *FLT3*-ITD (without adverse-risk genetic lesions) t(9;11)(p21.3;q23.3)/*MLLT3*::*KMT2A*[b,f] Cytogenetic and/or molecular abnormalities not classified as favorable or adverse
Poor/Adverse	t(6;9)(p23.3;q34.1)/*DEK*::*NUP214* t(v;11q23.3)/*KMT2A*-rearranged[g] t(9;22)(q34.1;q11.2)/*BCR*::*ABL1* t(8;16)(p11.2;p13.3)/*KAT6A*::*CREBBP* inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*, *MECOM(EVI1)* t(3q26.2;v)/*MECOM(EVI1)*-rearranged -5 or del(5q); -7; -17/abn(17p) Complex karyotype,[h] monosomal karyotype[i] Mutated *ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1*, and/or *ZRSR2*[j] Mutated *TP53*[k,l]

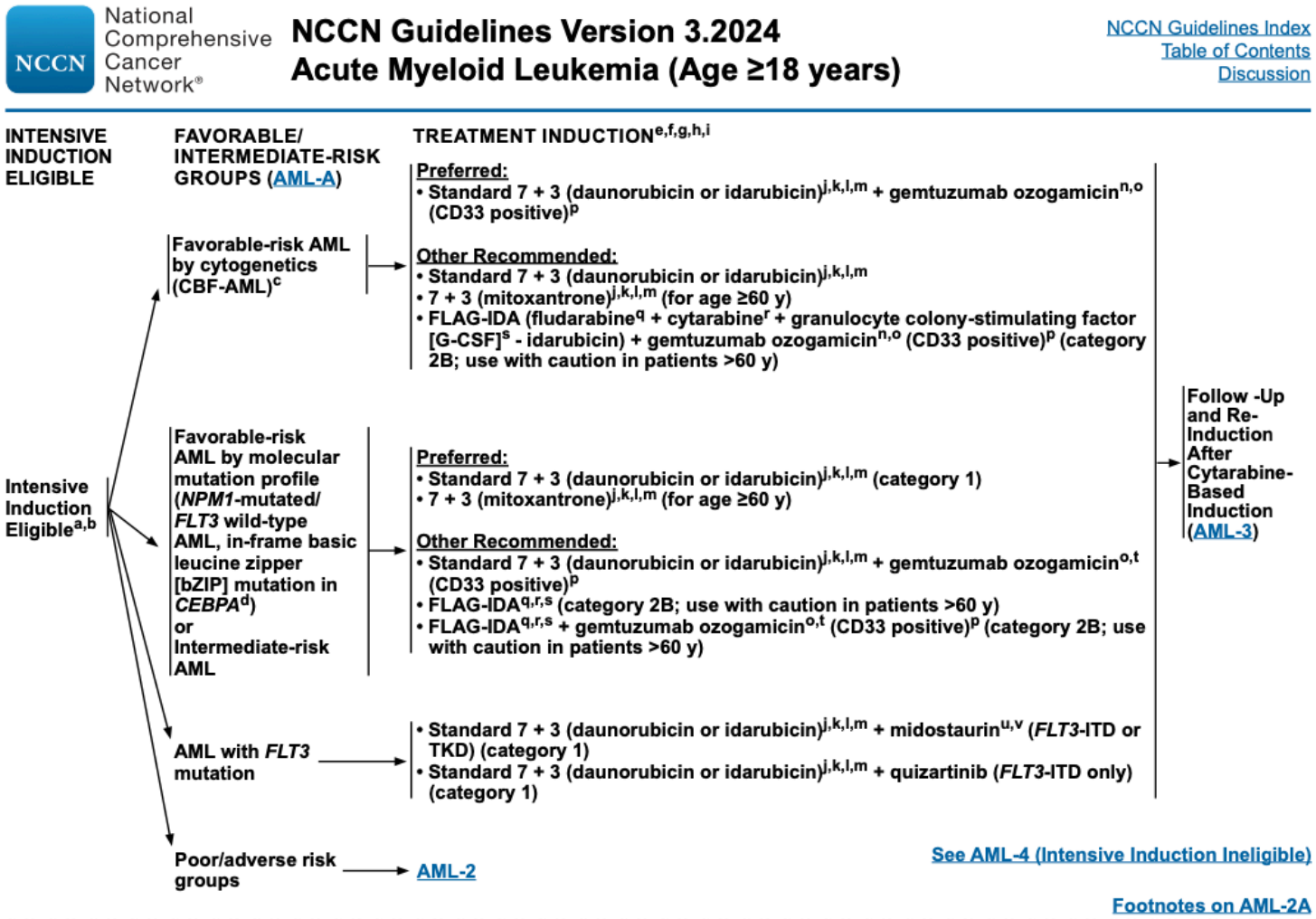
2022 International Consensus Classification of MDS/AML and AML



AML with recurrent genetic abnormalities (requiring ≥10% blasts in BM or PB)[a]
• APL with t(15;17)(q24.1;q21.2)/*PML*::*RARA*
• AML with t(8;21)(q22;q22.1)/*RUNX1*::*RUNX1T1*
• AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB*::*MYH11*
• AML with t(9;11)(p21.3;q23.3)/*MLLT3*::*KMT2A*
• AML with t(6;9)(p22.3;q34.1)/*DEK*::*NUP214*
• AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*::*MECOM*(*EVI1*)
• AML with other rare recurring translocations
• AML with mutated *NPM1*
• AML with in-frame bZIP mutated *CEBPA*
• AML with t(9;22)(q34.1;q11.2)/*BCR*::*ABL1*[a]

Arber DA, et al. *Blood* 2022; 140: 1200-1228.

ELN


National Comprehensive Cancer Network®
NCCN Guidelines Version 3.2024
Acute Myeloid Leukemia (Age ≥18 years)
NCCN Guidelines Index
Table of Contents
Discussion
INTENSIVE INDUCTION ELIGIBLE
FAVORABLE/ INTERMEDIATE-RISK GROUPS (AML-A)
TREATMENT INDUCTION[e,f,g,h,i]
Intensive Induction Eligible[a,b]
Favorable-risk AML by cytogenetics (CBF-AML)[c]
Preferred:
• Standard 7 + 3 (daunorubicin or idarubicin)[j,k,l,m] + gemtuzumab ozogamicin[n,o] (CD33 positive)[p]
Other Recommended:
• Standard 7 + 3 (daunorubicin or idarubicin)[j,k,l,m]
• 7 + 3 (mitoxantrone)[j,k,l,m] (for age ≥60 y)
• FLAG-IDA (fludarabine[q] + cytarabine[r] + granulocyte colony-stimulating factor [G-CSF][s] - idarubicin) + gemtuzumab ozogamicin[n,o] (CD33 positive)[p] (category 2B; use with caution in patients >60 y)
Favorable-risk AML by molecular mutation profile (NPM1-mutated/ FLT3 wild-type AML, in-frame basic leucine zipper [bZIP] mutation in CEBPA[d]) or Intermediate-risk AML
Preferred:
• Standard 7 + 3 (daunorubicin or idarubicin)[j,k,l,m] (category 1)
• 7 + 3 (mitoxantrone)[j,k,l,m] (for age ≥60 y)
Other Recommended:
• Standard 7 + 3 (daunorubicin or idarubicin)[j,k,l,m] + gemtuzumab ozogamicin[o,t] (CD33 positive)[p]
• FLAG-IDA[q,r,s] (category 2B; use with caution in patients >60 y)
• FLAG-IDA[q,r,s] + gemtuzumab ozogamicin[o,t] (CD33 positive)[p] (category 2B; use with caution in patients >60 y)
AML with FLT3 mutation
• Standard 7 + 3 (daunorubicin or idarubicin)[j,k,l,m] + midostaurin[u,v] (FLT3-ITD or TKD) (category 1)
• Standard 7 + 3 (daunorubicin or idarubicin)[j,k,l,m] + quizartinib (FLT3-ITD only) (category 1)
Follow -Up and Re-Induction After Cytarabine-Based Induction (AML-3)
Poor/adverse risk groups
AML-2
See AML-4 (Intensive Induction Ineligible)
Footnotes on AML-2A

Common “intensive” chemotherapy for AML

PRINCIPLES OF SYSTEMIC THERAPY
INTENSIVE INDUCTION ELIGIBLE (AML-1, AML-2)

Therapy	Regimen
Standard 7 + 3 (daunorubicin or idarubicin) + gemtuzumab ozogamicin (CD33 positive)[a,1,2,3,4,5]	Cytarabine 200 mg/m^2 continuous infusion x 7 days with daunorubicin 60 mg/m^2 or idarubicin 12 mg/m^2 x 3 days and a single dose of gemtuzumab ozogamicin 3 mg/m^2 (up to one 4.5-mg vial) given on day 1, or day 2, or day 3, or day 4; alternatively, three total doses may be given on days 1, 4, and 7
Standard 7 + 3 (daunorubicin or idarubicin)[6,7,8,9,10]	Cytarabine 100–200 mg/m^2 continuous infusion x 7 days with idarubicin 12 mg/m^2 or daunorubicin 60 or 90 mg/m^2 x 3 days
Standard 7 + 3 (mitoxantrone)[b,11]	Cytarabine 100-200 mg/m^2 continuous infusion x 7 days with mitoxantrone 12 mg/m^2 x 3 days
FLAG-IDA + gemtuzumab ozogamicin (CD33 positive)[a,c,d,12,13]	Fludarabine 30 mg/m^2 days 2–6, cytarabine 2 g/m^2 over 4 hours starting 4 hours after fludarabine infusion on days 2–6, idarubicin 8 mg/m^2 IV on days 4–6, and G-CSF subcutaneously (SC) daily days 1–7 plus a single dose of gemtuzumab ozogamicin 3 mg/m^2 in first course
FLAG-IDA[c,d,1,12]	Fludarabine 30 mg/m^2 days 2–6, cytarabine 2 g/m^2 over 4 hours starting 4 hours after fludarabine infusion on days 2–6, idarubicin 8 mg/m^2 IV on days 4–6, and G-CSF SC daily days 1–7
Standard 7 + 3 (daunorubicin[14] or idarubicin[15]) + midostaurin (*FLT3*-ITD or TKD)	Cytarabine 100–200 mg/m^2 continuous infusion x 7 days with daunorubicin 60 mg/m^2 or idarubicin 12 mg/m^2 x 3 days and oral midostaurin 50 mg every 12 hours, days 8–21
Standard 7 + 3 (daunorubicin or idarubicin) + quizartinib[16] (*FLT3*-ITD only)	Cytarabine 100–200 mg/m^2 continuous infusion x 7 days with daunorubicin 60 mg/m^2 or idarubicin 12 mg/m^2 x 3 days and quizartinib 35.4 mg PO daily, days 8–21

Newer intensive regimens for AML

PRINCIPLES OF SYSTEMIC THERAPY
INTENSIVE INDUCTION ELIGIBLE (AML-1, AML-2)

Therapy	Regimen
CPX-351/dual-drug liposomal cytarabine and daunorubicin[17]	CPX-351/dual-drug liposomal cytarabine 100 mg/m^2 and daunorubicin 44 mg/m^2 on days 1, 3, and 5 x 1 cycle
Decitabine (days 1–5) + venetoclax	Decitabine 20 mg/m^2 IV (days 1–5 of each 28-day cycle) and venetoclax PO once daily (100 mg day 1, 200 mg day 2, and 400 mg day 3 and beyond)
Azacitidine + venetoclax	Azacitidine 75 mg/m^2 SC or IV days 1–7 of each 28-day cycle and venetoclax PO once daily (100 mg day 1, 200 mg day 2, and 400 mg days 3 and beyond)
LDAC + venetoclax[18]	LDAC 20 mg/m^2/day SC days 1–10 of each 28-day cycle and venetoclax PO once daily (100 mg day 1, 200 mg day 2, 400 mg day 3, and 600 mg days 4 and beyond)
Low-intensity therapy (azacitidine or decitabine)	Azacitidine 75 mg/m^2 SC or IV days 1–7 of each 28-day cycle Decitabine 20 mg/m^2/day IV (days 1–5 or days 1–10 of each 28-day cycle)
Cytarabine (HiDAC) + (daunorubicin or idarubicin) + etoposide[d,19-21]	Cytarabine 2 g/m^2 every 12 hours x 6 days or 3 g/m^2 every 12 hours x 4 days with daunorubicin 50 mg/m^2 or idarubicin 12 mg/m^2 x 3 days, and etoposide 50 mg/m^2 days 1–5 (1 cycle)

Regimens for patients “unfit” for intensive regimens

PRINCIPLES OF SYSTEMIC THERAPY
LOWER INTENSITY THERAPY (INTENSIVE INDUCTION INELIGIBLE OR DECLINES)
(AML-4)

Therapy	Regimen
Azacitidine + venetoclax[24]	Azacitidine 75 mg/m^2 SC or IV days 1–7 of each 28-day cycle and venetoclax PO once daily (100 mg day 1, 200 mg day 2, and 400 mg days 3 and beyond)
Azacitidine + ivosidenib (*IDH1* mutation)[25]	Azacitidine 75 mg/m^2 SC or IV (days 1–7 or days 1–5, 8, and 9 of each 28-day cycle) and ivosidenib 500 mg PO once daily on days 1–28
Decitabine + venetoclax[26]	Decitabine 20 mg/m^2 IV (days 1–5 or days 1–10) and venetoclax PO once daily (100 mg day 1, 200 mg day 2, and 400 mg day 3 and beyond)
Ivosidenib[27,28,29] (*IDH1* mutation)	500 mg PO once daily on days 1–28 of a 28-day cycle
LDAC + venetoclax[30]	LDAC 20 mg/m^2/day SC days 1–10 of each 28-day cycle and venetoclax PO once daily (100 mg day 1, 200 mg day 2, 400 mg day 3 and 600 mg days 4 and beyond)
Azacitidine	75 mg/m^2 SC or IV days 1–7 of each 28-day cycle
Decitabine	20 mg/m^2/day IV (days 1–5 of each 28-day cycle)
Gemtuzumab ozogamicin (CD33 positive)[a,1,31]	6 mg/m^2 IV on day 1 and 3 mg/m^2 IV on day 8

The many subgroups of MDS

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Myelodysplastic Syndromes

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PATHOLOGIC-MORPHOLOGIC CLASSIFICATIONS OF MYELODYSPLASTIC NEOPLASMS 2023[a,b]

Transition from Clinically Based Classifications to New Systems Including Genomic Features in 2022

WHO 2016[1]	WHO 2022[2]	ICC 2022[3]	Bone Marrow Blasts
	MDS, genetically defined		
MDS-del(5q)	MDS-5q[d]	MDS-del(5q)[d]	<5%
MDS-RS	MDS-*SF3B1*[e]	MDS-*SF3B1*[e,h]	<5%
—	MDS-bi*TP53*[f]	Myeloid neoplasms with m*TP53*[i]	<20%
	MDS, morphologically defined		
MDS-SLD, MDS-MLD	MDS-LB	MDS-NOS[j]	<5%
—	MDS-hypoplastic[g]	—	<5%
MDS-EB1	MDS-IB1	MDS-EB	5%–9%
MDS-EB2	MDS-IB2[c]	MDS/AML[c]	10%–19%
—	MDS with fibrosis	—	5%–19%
AML[c]	AML[c]	AML[c]	≥20%[c]

The cottage industry of MDS classification

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Myelodysplastic Syndromes

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PROGNOSTIC SCORING SYSTEMS

INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS)[a,1]

Survival and AML Evolution					
	Score Value				
Prognostic variable	0	0.5	1.0	1.5	2.0
Marrow blasts (%)[b]	<5	5–10	—	11–20	21–30
Karyotype[c]	Good	Intermediate	Poor	—	—
Cytopenia[d]	0/1	2/3	—	—	—

PROGNOSIS ACCORDING TO IPSS RISK SCORE[1]

IPSS Risk Category (% IPSS pop.)	Overall Score	Median Survival (y) in the Absence of Therapy	25% AML Progression (y) in the Absence of Therapy
LOW (33)	0	5.7	9.4
INT-1 (38)	0.5–1.0	3.5	3.3
INT-2 (22)	1.5–2.0	1.1	1.1
HIGH (7)	≥2.5	0.4	0.2

For IPSS: Low/Intermediate-1, see MDS-4 through MDS-6
For IPSS: Intermediate-2/High, see MDS-7

[a] IPSS should be used for initial prognostic and planning purposes. WPSS permits dynamic estimation of prognosis at multiple time points during the course of MDS.
[b] Patients with 20%–29% blasts may be considered to have MDS (FAB) or AML (WHO).
[c] Cytogenetics: Good = normal, -Y alone, del(5q) alone, del(20q) alone; Poor = complex (≥3 abnormalities) or chromosome 7 anomalies; Intermediate = other abnormalities. [This excludes karyotypes t(8;21), inv16, and t(15;17), which are considered to be AML and not MDS.]
[d] Cytopenias: neutrophil count <1,800/mcL, platelets <100,000/mcL, Hb <10 g/dL.
[e] Cytogenetic risks: Very good = -Y, del(11q); Good = normal, del(5q), del(12p), del(20q), double including del(5q); Intermediate = del(7q), +8, +19, i(17q), any other single or double independent clones; Poor = -7, inv(3)/t(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities; Very poor = complex: >3 abnormalities.

REVISED INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS-R)[2]

	Score Value						
Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetic[e]	Very good	—	Good	—	Intermediate	Poor	Very poor
Marrow blasts (%)	≤2	—	>2–<5	—	5–10	>10	—
Hemoglobin	≥10	—	8–<10	<8	—	—	—
Platelets	≥100	50–<100	<50	—	—	—	—
ANC	≥0.8	<0.8	—	—	—	—	—

PROGNOSIS ACCORDING TO IPSS-R RISK SCORE[2]

IPSS-R Risk Category (% IPSS-R pop.)	Overall Score	Median Survival (y) in the Absence of Therapy	25% AML Progression (y) in the Absence of Therapy
VERY LOW (19)	≤1.5	8.8	Not reached
LOW (38)	>1.5–≤3.0	5.3	10.8
INT[3] (20)	>3.0–≤4.5	3	3.2
HIGH (13)	>4.5–≤6.0	1.6	1.4
VERY HIGH (10)	>6.0	0.8	0.7

For IPSS-R: Very Low/Low/Intermediate, see MDS-4 through MDS-6
For IPSS-R: Intermediate/High/Very High, see MDS-7

[1] Adapted with permission from: Greenberg PL, Cox C, LeBeau M, et al. International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 1997;89:2079-2088; Erratum. Blood 1998;91:1100.
[2] Adapted with permission from: Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood 2012;120:2454-2465. Websites for accessing the IPSS-R calculator tool: http://www.ipss-r.com or http://mds-foundation.org/calculator/index.php. A mobile app for the calculator tool is also available.

Continued

IPSS-M: adding mutations to the scorecard

PROGNOSTIC SCORING SYSTEMS

GENE MUTATIONS FOR THE IPSS-M PROGNOSTIC RISK SCHEMA[5]

Main Effect Genes (n=16)[h]	Residual Genes (Nres) (n=15)
TP53^{multi}	*BCOR*
MLL^{PTD}	*BCORL1*
FLT3	*CEBPA*
SF3B1^{5q}	*ETNK1*
NPM1	*GATA2*
RUNX1	*GNB1*
NRAS	*IDH1*
ETV6	*NF1*
IDH2	*PHF6*
CBL	*PPM1D*
EZH2	*PRPF8*
U2AF1	*PTPN11*
SRSF2	*SETBP1*
DNMT3A	*STAG2*
ASXL1	*WT1*
KRAS	
SF3B1[a]	

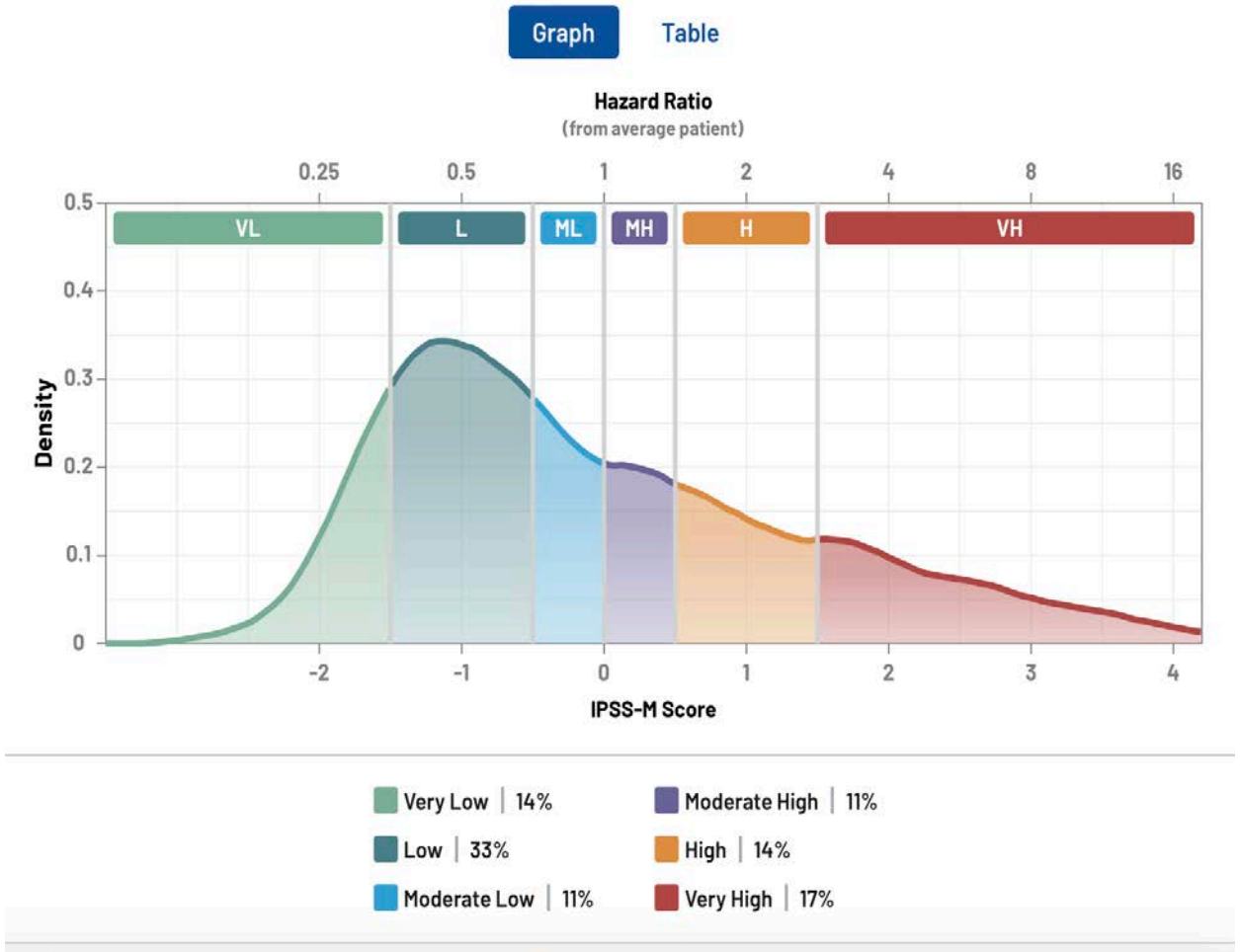
PROGNOSTIC SCORING SYSTEMS

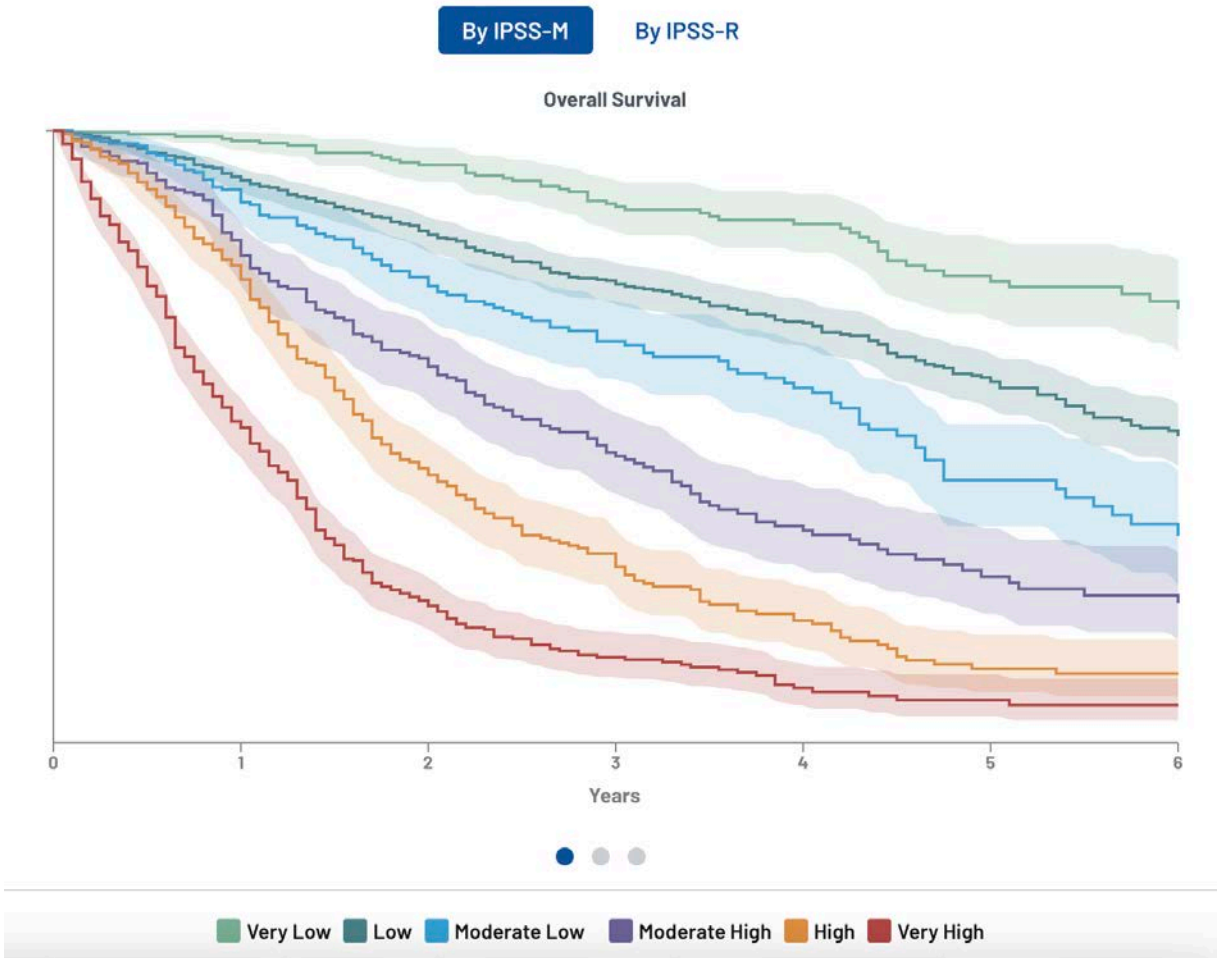
INTERNATIONAL PROGNOSTIC SCORING SYSTEM MOLECULAR (IPSS-M)[f,5]

IPSS-M	Very Low VL	Low L	Moderate Low ML	Moderate High MH	High H	Very High VH
Patients, % (n = 2701)	14% (381)	33% (889)	11% (302)	11% (281)	14% (379)	17% (469)
Risk score	≤ –1.5	> –1.5 to –0.5	> –0.5 to 0	> 0 to 0.5	> 0.5 to 1.5	> 1.5
Hazard ratio[g] (95% CI)	0.51 (0.39–0.67)	1.0 reference	1.5 (1.2–1.8)	2.5 (2.1–3.1)	3.7 (3.1–4.4)	7.1 (6.0–8.3)
Median LFS, y 25%–75% LFS range, y	9.7 5.0–17.4	5.9 2.6–12.0	4.5 1.6–6.9	2.3 0.91–4.7	1.5 0.80–2.8	0.76 0.33–1.5
Median OS, y 25%–75% OS range, y	10.6 5.1– 7.4	6.0 3.0–12.8	4.6 2.0–7.4	2.8 1.2–5.5	1.7 1.0–3.4	1.0 (0.5–1.8)
AML-t by 1 y, % 2 y 4 y	0.0 1.2 2.8	1.7 3.4 5.1	4.9 8.8 11.4	9.5 14.0 18.9	14.3 21.2 29.2	28.2 38.6 42.8
Death w/o AML, by 1 y, % 2 y 4 y	2.2 7.0 15.9	8.5 16.2 29.5	12.0 19.8 33.6	18.0 31.1 51.1	19.3 39.8 54.2	30.6 45.6 51.3

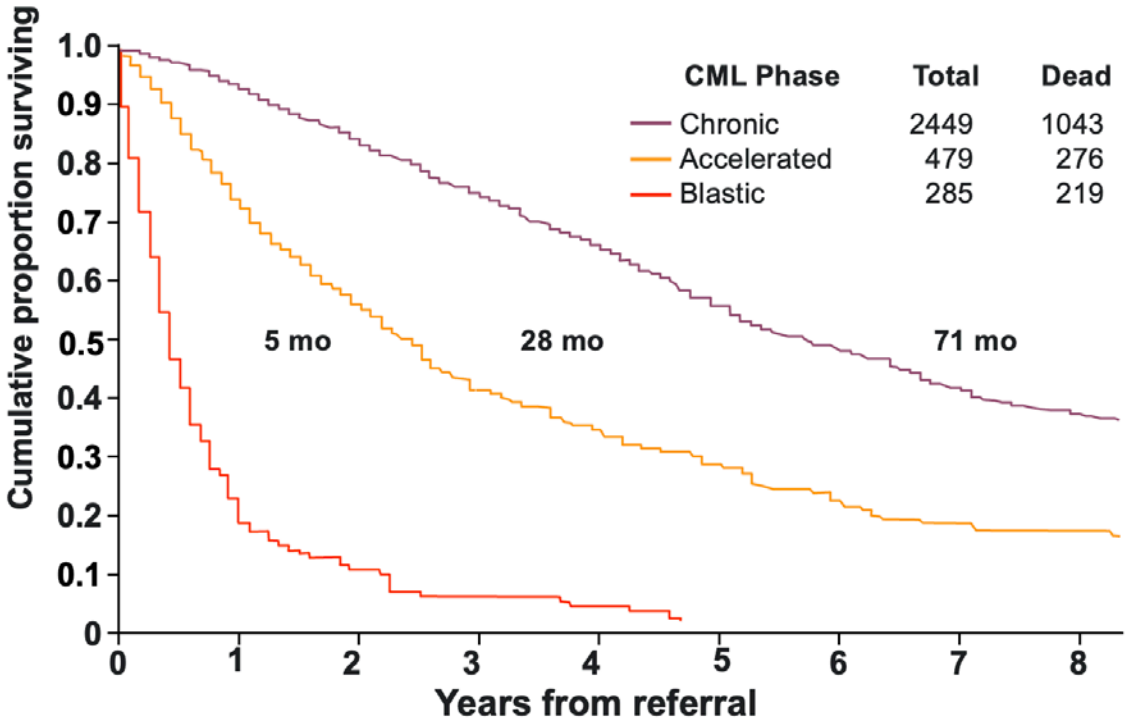
Abbreviations: LFS, leukemia-free survival; OS, overall survival; AML-t, AML transformation

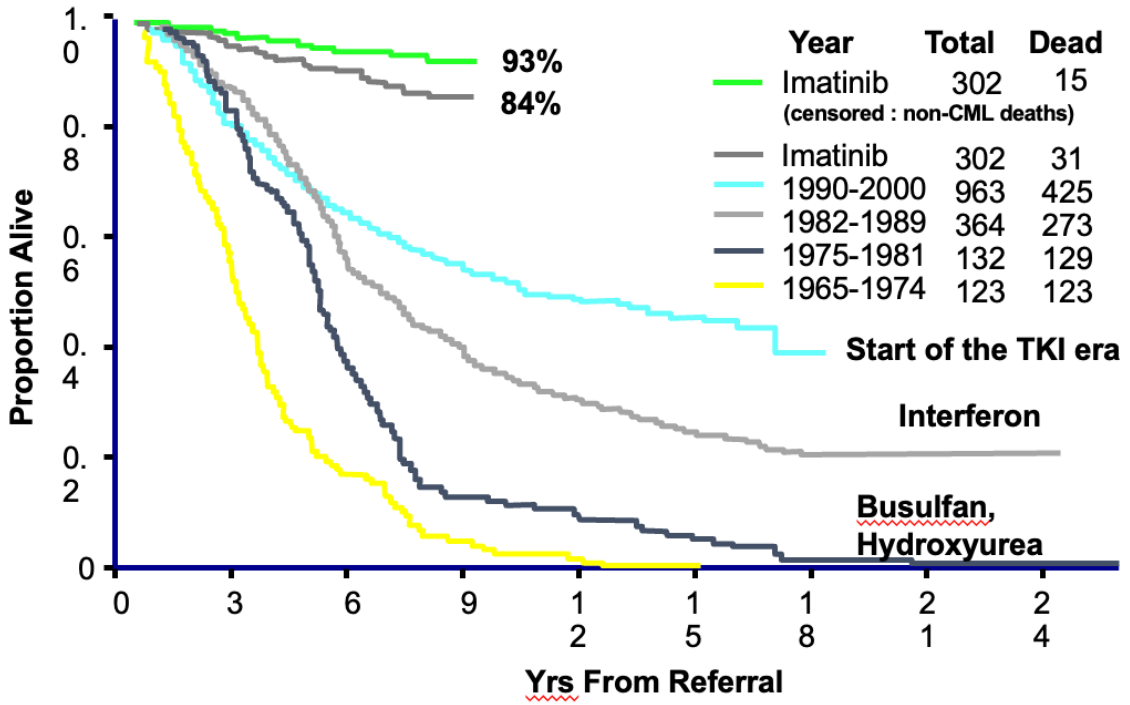
Distribution of risk groups and outcomes





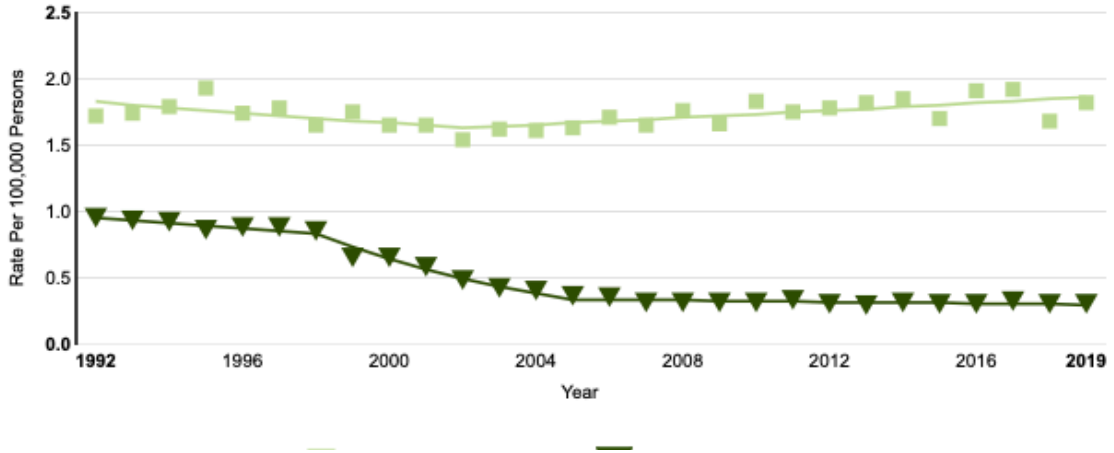
Chronic myeloid leukemia is the poster child of "precision medicine"



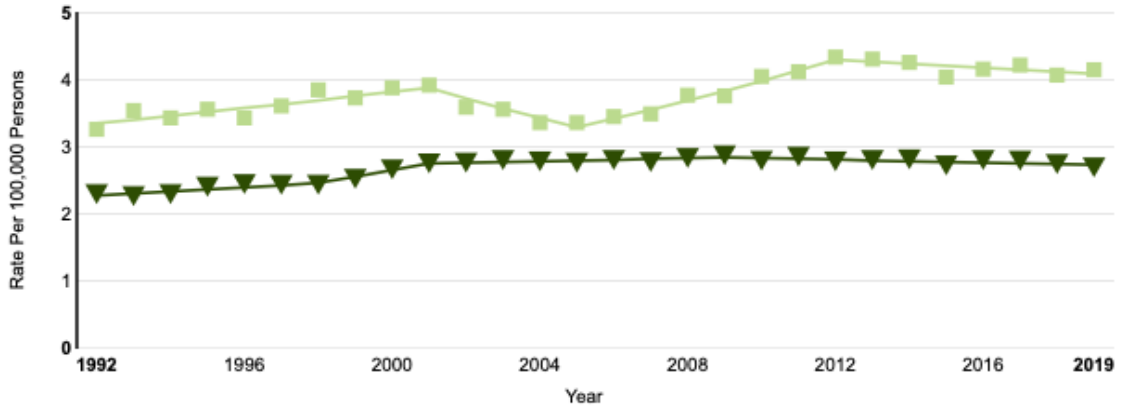


A tale of two (myeloid) leukemias

CML



AML

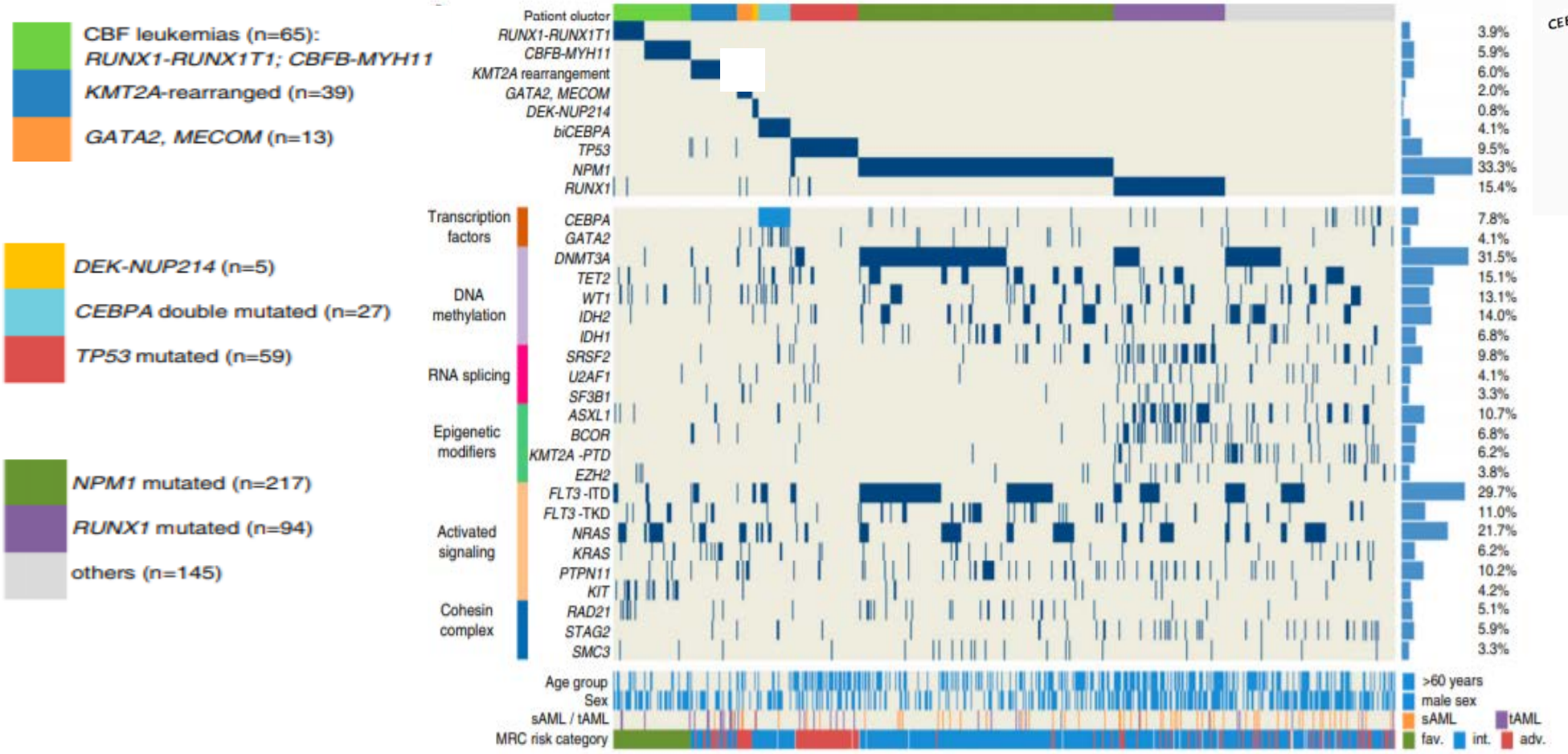


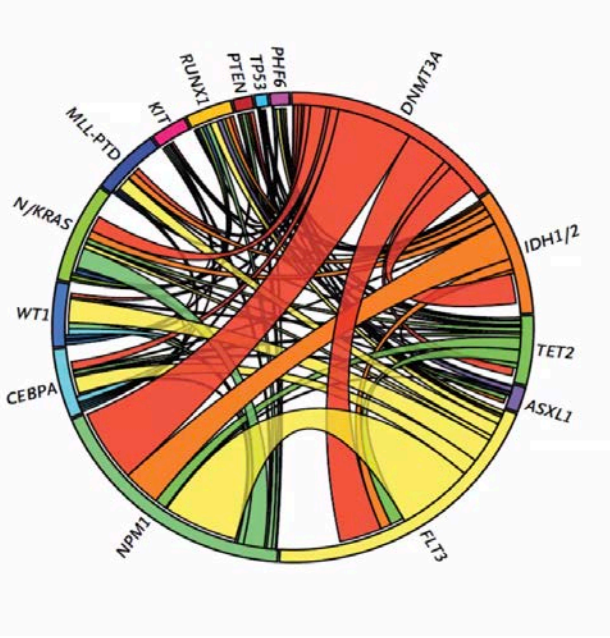
Rate of New Cases Death Rate

Background: The Mutational Heterogeneity of AML

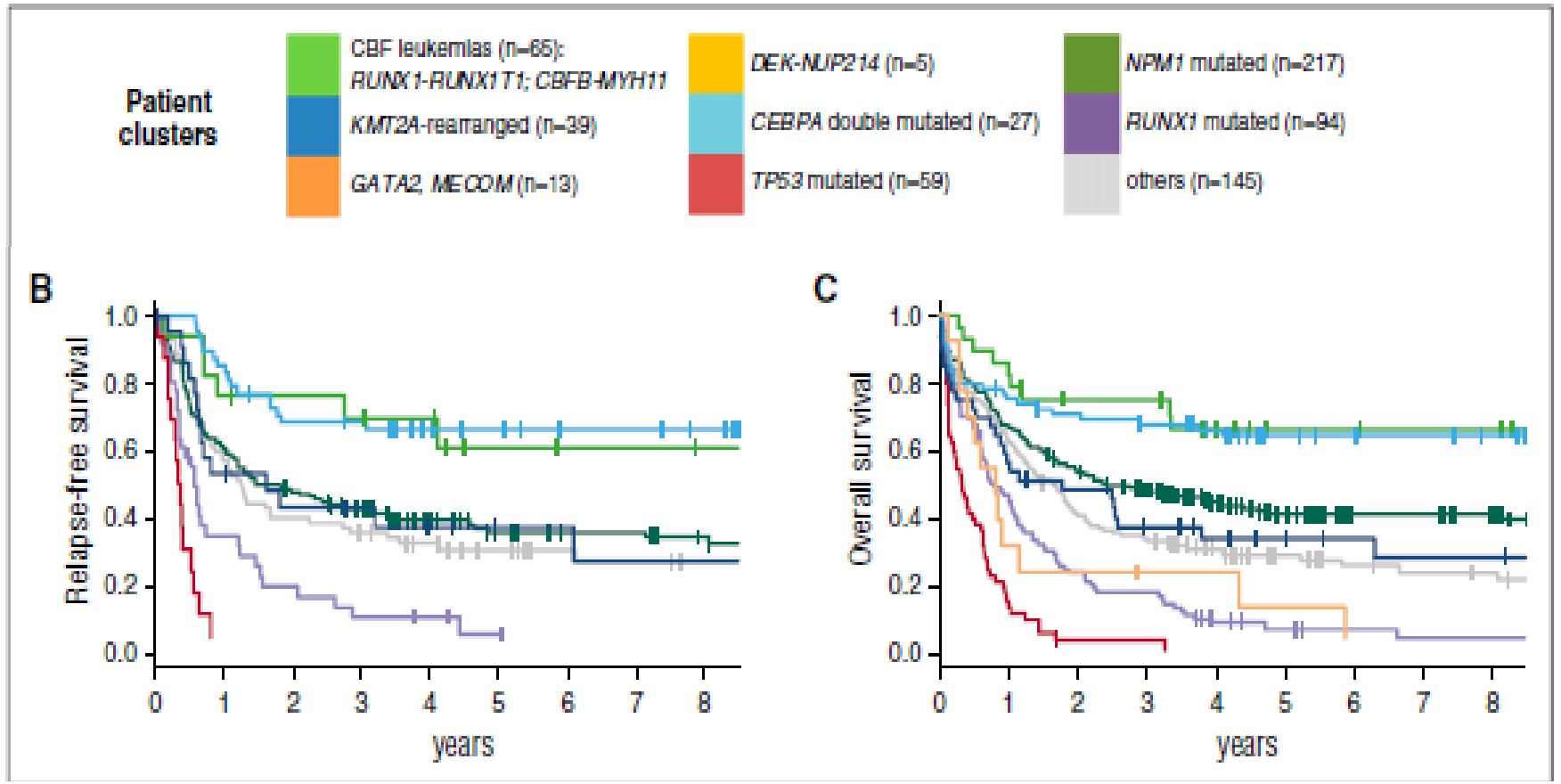
Patient Clusters

Metzeler KH, et al. *Blood.* 2016; 128: 686-696.



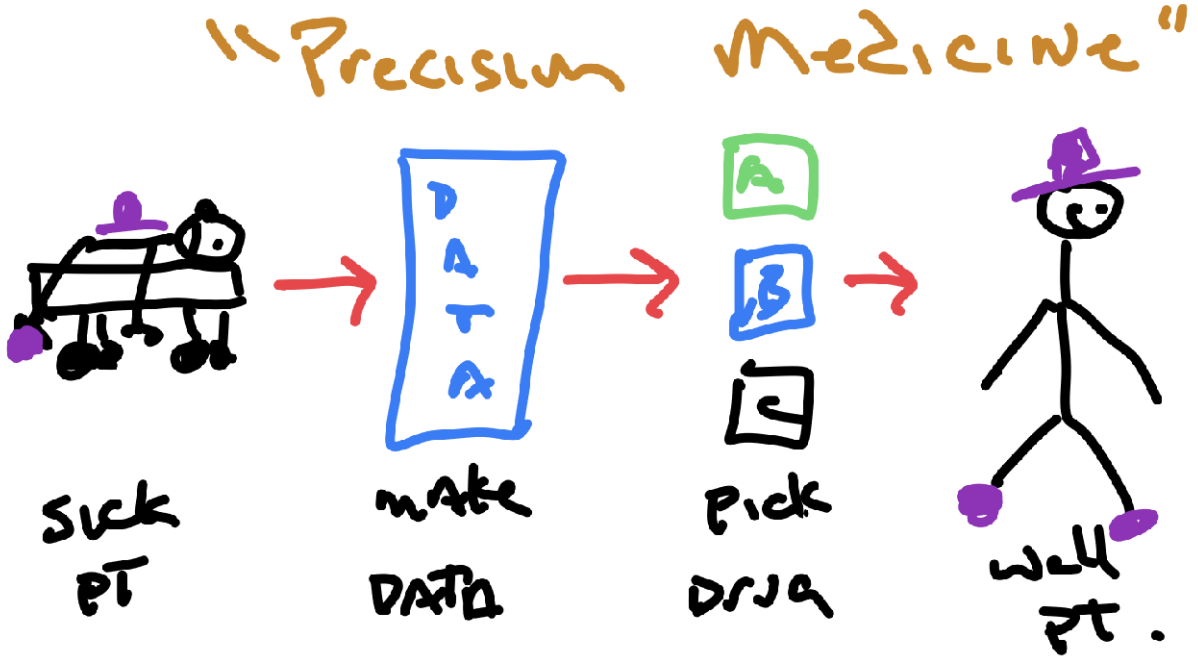


AML outcomes by cytogenetic and molecular clusters



Metzeler KH et al. *Blood.* 2016; 128 (5): 686-696

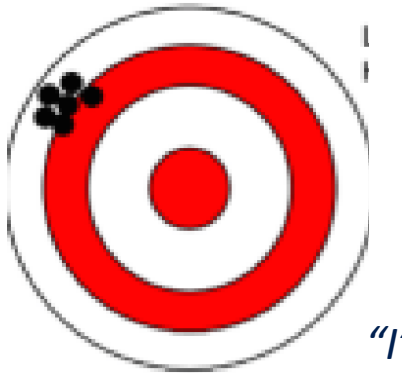
What I used to think of “Precision Medicine”



NIH/NCI/FDA MRD in AML

AML Precision Medicine

- Rapid diagnostics (3d)
- Trials based on targets
- MRD as endpoint
- MRD eraser trials



fNIH MRD in AML

- Reagents for testing
- "Sandbox" for testing new analyses
- Winner of bake off goes into next trials
- NIH and partners fund (pharma and biotech)

"I'd rather be vaguely right than precisely wrong."
(John Maynard Keyes)

NCI Myeloid Malignancies Molecular Analysis for Therapy Choice "myeloMATCH"

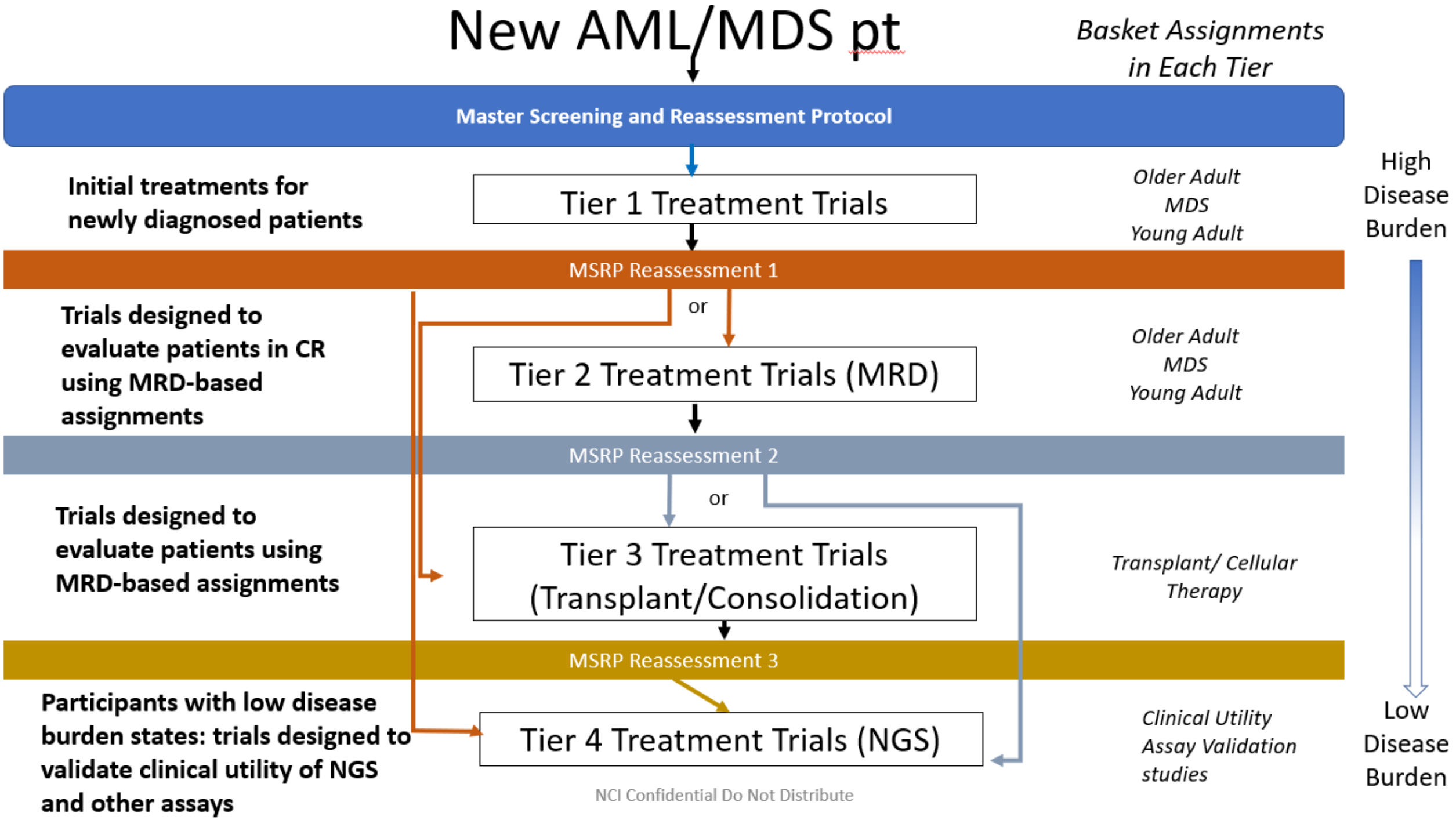
1. **Genetic driven** protocol assignment (cyto, mutations)
2. Predominately **phase 2** trials
3. Predominately **MRD driven** endpoints (flow cytometry)

myeloMATCH Aims

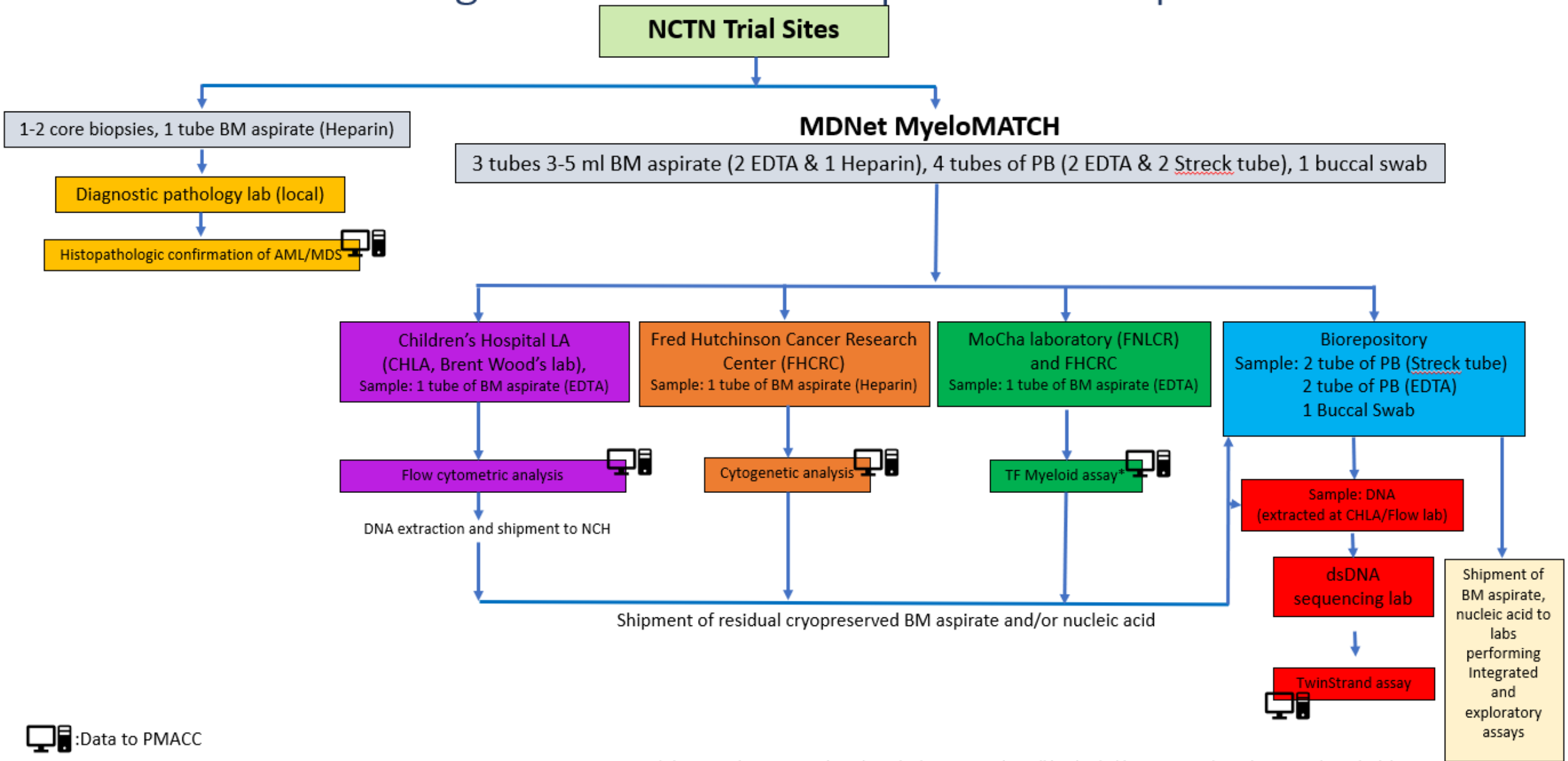
- To create a portfolio of rationally designed treatment substudies onto which patients sequentially enroll over their entire treatment journey. As increasingly lower remaining tumor burden is achieved, the focus will be to target residual disease more effectively.

- Create an efficient operational model attractive to industry partners and NCTN sites to accelerate therapeutic advances for myeloid malignancies.

- Develop the careers of young investigators by promoting leadership throughout the clinical trial portfolio and laboratory program.


New AML/MDS pt
Basket Assignments in Each Tier
Master Screening and Reassessment Protocol
Initial treatments for newly diagnosed patients
Tier 1 Treatment Trials
Older Adult
MDS
Young Adult
High Disease Burden
MSRP Reassessment 1
or
Trials designed to evaluate patients in CR using MRD-based assignments
Tier 2 Treatment Trials (MRD)
Older Adult
MDS
Young Adult
MSRP Reassessment 2
or
Trials designed to evaluate patients using MRD-based assignments
Tier 3 Treatment Trials (Transplant/Consolidation)
Transplant/ Cellular Therapy
MSRP Reassessment 3
Participants with low disease burden states: trials designed to validate clinical utility of NGS and other assays
Tier 4 Treatment Trials (NGS)
Clinical Utility
Assay Validation studies
Low Disease Burden
NCI Confidential Do Not Distribute

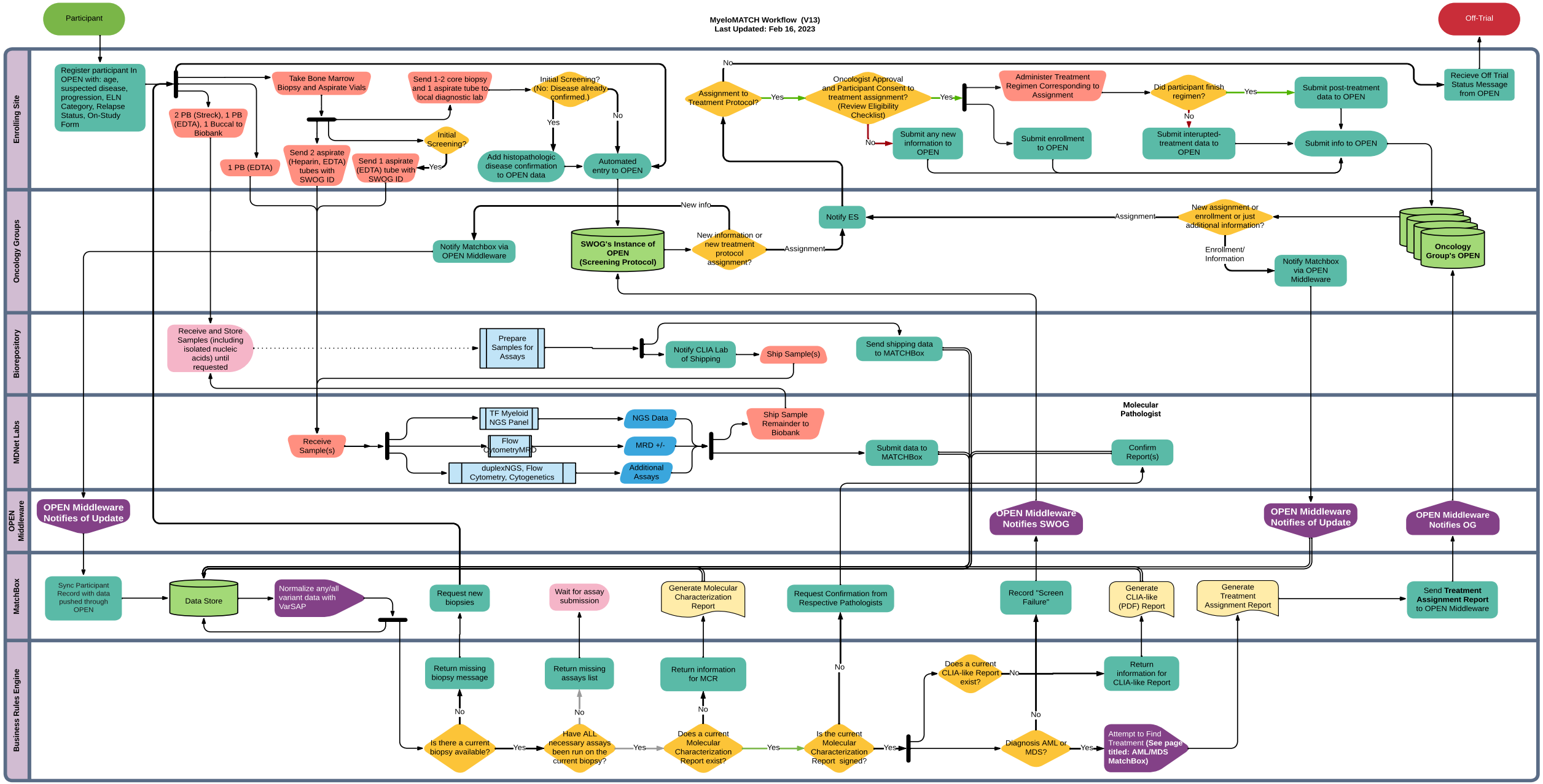
myeloMATCH:
Master screening and reassessment protocol sample work flow



*Thermo Fisher Genexus-based Myeloid assay samples will be divided between Fred Hutchinson and MoCha labs

Essential components

- **Informational technology-*touches everything***
  - Enrollment from local sites, follows patients throughout trials
  - Tracks samples to labs and from labs
  - Integrates clinical info and lab data
  - Oversees treatment assignment algorithms and trial assignment
- **Agents**
  - Links new targets with new agents
  - Finds pharma partners
  - Develops contracts
- **Testing**
  - Cyto, FISH, flow, NGS-have validated, CLIA assays
  - Work with FDA for IDE
- **Trials**
  - Integrate agents and testing
  - Work with pharma for acceptable design


MyeloMATCH Workflow (V13)
Last Updated: Feb 16, 2023
Participant
Off-Trial
Enrolling Site
Oncology Groups
Biorepository
MDNet Labs
OPEN Middleware
MatchBox
Business Rules Engine
Register participant In OPEN with: age, suspected disease, progression, ELN Category, Relapse Status, On-Study Form
2 PB (Streck), 1 PB (EDTA), 1 Buccal to Biobank
1 PB (EDTA)
Take Bone Marrow Biopsy and Aspirate Vials
Send 2 aspirate (Heparin, EDTA) tubes with SWOG ID
Send 1 aspirate (EDTA) tube with SWOG ID
Send 1-2 core biopsy and 1 aspirate tube to local diagnostic lab
Initial Screening?
Initial Screening? (No: Disease already confirmed.)
Yes
No
Add histopathologic disease confirmation to OPEN data
Automated entry to OPEN
Assignment to Treatment Protocol?
No
Yes
Oncologist Approval and Participant Consent to treatment assignment? (Review Eligibility Checklist)
Yes
No
Submit any new information to OPEN
Administer Treatment Regimen Corresponding to Assignment
Submit enrollment to OPEN
Did participant finish regimen?
Yes
No
Submit interupted-treatment data to OPEN
Submit post-treatment data to OPEN
Submit info to OPEN
Recieve Off Trial Status Message from OPEN
Notify Matchbox via OPEN Middleware
New info
SWOG's Instance of OPEN (Screening Protocol)
New information or new treatment protocol assignment?
Assignment
Notify ES
Assignment
New assignment or enrollment or just additional information?
Enrollment/ Information
Notify Matchbox via OPEN Middleware
Oncology Group's OPEN
Receive and Store Samples (including isolated nucleic acids) until requested
Prepare Samples for Assays
Notify CLIA Lab of Shipping
Ship Sample(s)
Send shipping data to MATCHBox
Receive Sample(s)
TF Myeloid NGS Panel
Flow CytometryMRD
duplexNGS, Flow Cytometry, Cytogenetics
NGS Data
MRD +/-
Additional Assays
Ship Sample Remainder to Biobank
Submit data to MATCHBox
Molecular Pathologist
Confirm Report(s)
OPEN Middleware Notifies of Update
OPEN Middleware Notifies SWOG
OPEN Middleware Notifies of Update
OPEN Middleware Notifies OG
Sync Participant Record with data pushed through OPEN
Data Store
Normalize any/all variant data with VarSAP
Request new biopsies
Wait for assay submission
Generate Molecular Characterization Report
Request Confirmation from Respective Pathologists
Record "Screen Failure"
Generate CLIA-like (PDF) Report
Generate Treatment Assignment Report
Send Treatment Assignment Report to OPEN Middleware
Return missing biopsy message
Return missing assays list
Return information for MCR
Does a current CLIA-like Report exist?
No
Return information for CLIA-like Report
Is there a current biopsy available?
Yes
No
Have ALL necessary assays been run on the current biopsy?
Yes
No
Does a current Molecular Characterization Report exist?
Yes
No
Is the current Molecular Characterization Report signed?
Yes
No
Diagnosis AML or MDS?
Yes
No
Attempt to Find Treatment (See page titled: AML/MDS MatchBox)

Overview of myeloMATCH **Agents and Genes** Working Group

- Meeting timeline
  - Internal NCI meeting vetting company and agent
  - myeloMATCH Agents and Genes Working Group meeting
  - Typically, several follow-up meetings with regulatory affairs or myeloMATCH leadership
    - CRADA negotiation process can take up to 6 months
- NCI and the myeloMATCH Agents and Genes Working Group have reviewed **over 30 agents.**

208-228 hours required for each agent brought into program
35-60 hours for agents not brought into program

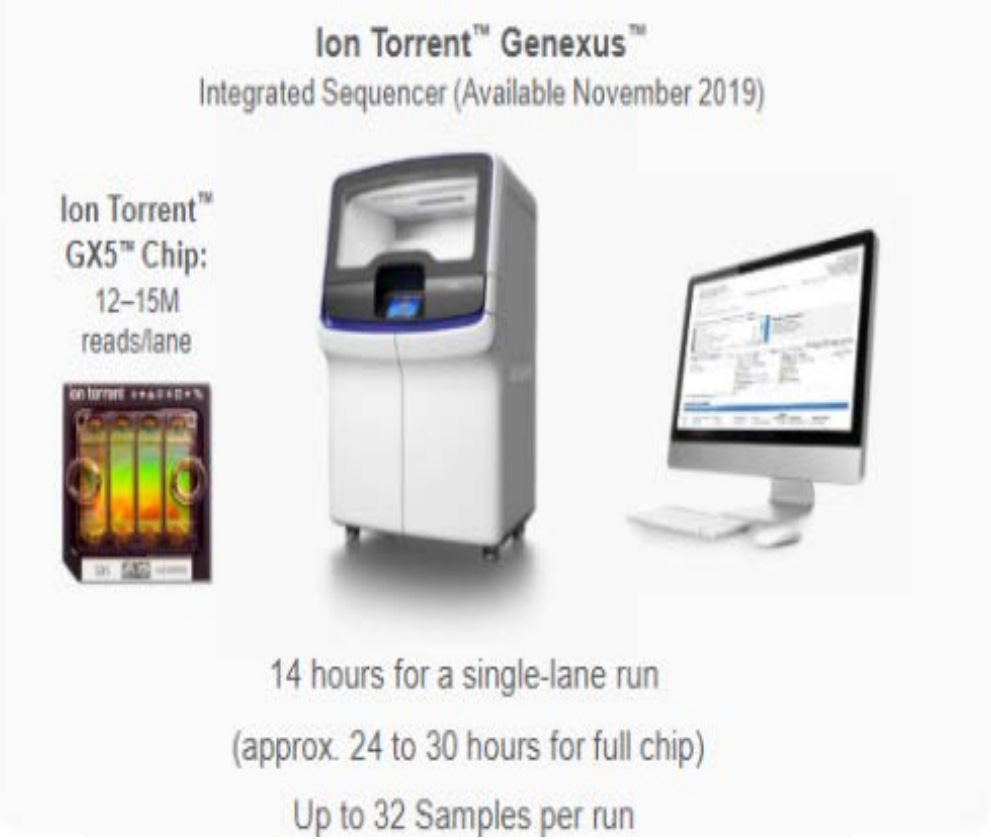
Molecular Diagnostics Laboratory Network (MDNet)
Integral Assays Under NCI IDE
72 Hours for Initial Patient Assignment

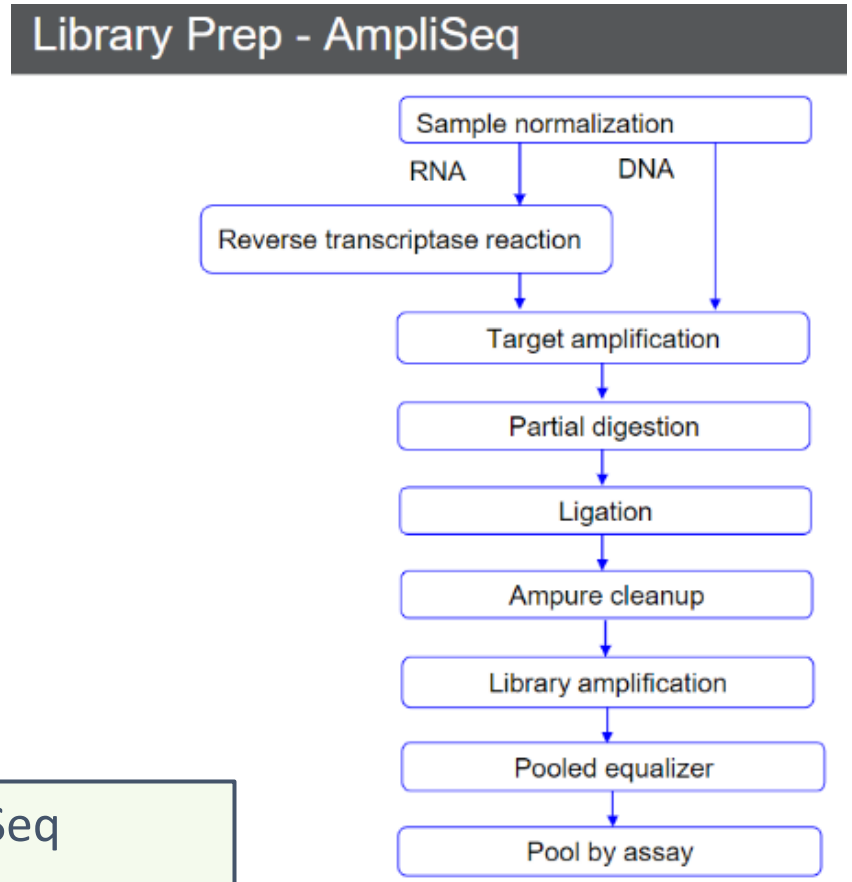
- Cytogenetics and FISH
- NCI Myeloid Assay version 2 (Genexus platform)
- Error-corrected Sequencing (Duplex Sequencing)
- Flow Cytometric Analysis

Methodologies

	What?	Who and where?
Integral	• Cytogenetics	• Min Fang (Fred Hutch)
	• Flow cytometry	• Brent Wood (Children's LA)
	• Rapid NGS	• MOCHA (NIH), JR (Fred Hutch)
Integrated	• Duplex Seq	• TS (Seattle) (JR backup?)
	• Single cell "omics	• JR (Fred Hutch)
	• RNA seq	• JR (Fred Hutch)

NCI Myeloid Assay = Genexus Ion Torrent NGS





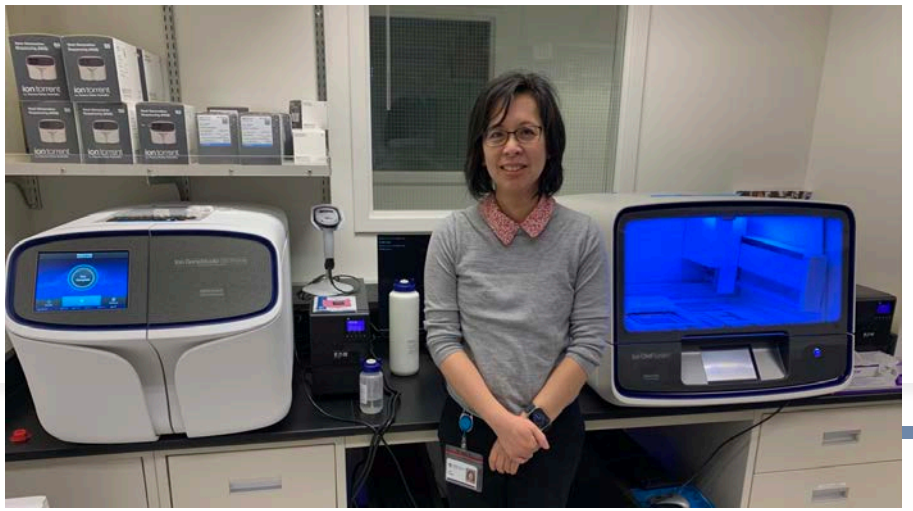
- Automated library preparation using Ion AmpliSeq technology
- Template preparation via isothermal amplification
- Rapid semiconductor pH sensor-based sequencing

Ion Torrent GeneStudio and Genexus

Complementary Systems for Infectious Disease and Oncology

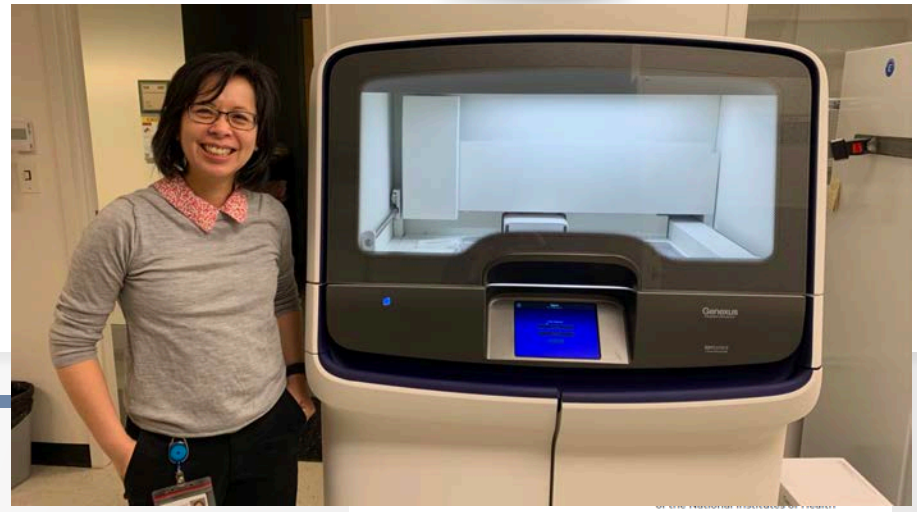
Ion GeneStudio S5 Series

Scalable, targeted NGS to support small and large projects



Genexus System

Specimen to report in a single day with a hands off, automated workflow*



NCI Myeloid Assay targets in V2: RNA and DNA

AML: 93.3% of variants at >=3% frequency and 72% of variants at >1% frequency in AML

- ~1600 DNA hotspots
- ~800 RNA fusion isoforms and exon splice variants
- RNA input of 14.25ng and DNA of 27.75ng per sample
- Avg 1.5 -2 mil DNA reads and 300-500k RNA reads/sample
- Targets: AML, MDS, MPN, and other myeloid neoplasms

Hotspot genes (28)	
ANKRD26	KRAS
ABL1	MPL
BRAF	MYD88
CBL	NPM1
CSF3R	NRAS
DDX41	PPM1D
DNMT3A	PTPN11
FLT3 (ITD + TKD)	SMC1A
GATA2	SMC3
HRAS	SETBP1
IDH1	SF3B1
IDH2	SRSF2
JAK2	U2AF1
KIT	WT1

Full genes (17)	
ASXL1	PRPF8
BCOR	RB1
CALR	RUNX1
CEBPA	SH2B3
ETV6	STAG2
EZH2	TET2
IKZF1	TP53
NF1	ZRSR2
PHF6	

Fusion Driver genes (35)		
ABL1	JAK2	NTRK3
ABL2	KAT6A (MOZ)	NUP214
BCL2	KAT6B	NUP98
BRAF	KMT2A	PAX5
CCND1	KMT2A-PTDs	PDGFRA
CREBBP	MECOM	PDGFRB
EGFR	MET	RARA
ETV6	MLLT10	RUNX1
FGFR1	MRTFA (MKL1)	TCF3
FGFR2	MYBL1	TFE3
FUS	MYH11	ZNF384
HMGA2	NTRK2	

Expression genes (5)
BAALC
MECOM
MYC
SMC1A
WT1

Expression control genes (5)
EIF2B1
FBXW2
PSMB2
PUM1
TRIM27

OCAv3
DNA & RNA
4 samples (16 barcodes)
2 lanes

Validation summary (FHCC/MoCha NCI Frederick's)

- 163 unique samples
  - Patient samples (PB/BM)
  - Healthy donor (PB/BM)
  - Cells lines (Cancer and normal), and contrived materials
  - DNA = covered 45 genes, 1661 hotspots, 1052 SNP, 609 indel
  - RNA = 35 driver genes, 779 fusions
- Sensitivity of 98.62% /98.97%
- Specificity of 100%/100%
- Accuracy of >99.99%/>99.99%
- Reproducibility
  - positive percent agreement (PPA) = 100%/99%
  - negative percent agreement (NPA) =100%/100%

NCI Myeloid assay Specificity (%)	SNVs	Indels	Fusions	Overall
MO (FHCC)	100	100	100	100
MoCha (FNLCR)	100	100	100	100
Acceptance criteria	≥99	≥99	≥99	≥99

NCI Myeloid assay Sensitivity (%)	SNVs	Indels	Fusions	Overall
MO (FHCC)	97.78 (132/135)	99.22 (128/129)	100 (27/27)	98.62 (287/291)
MoCha (FNLCR)	97.78 (132/135)	100 (129/129)	100 (27/27)	98.97 (288/291)
Combined	97.78 (264/270)	99.61 (257/258)	100 (54/54)	98.80 (575/582)
Acceptance criteria	≥95	≥90	≥90	≥90

NCI Myeloid assay Accuracy (%)	SNVs	Indels	Fusions	Overall
MO (FHCC)	>99.99	>99.99	100	>99.99
MoCha (FNLCR)	>99.99	100	100	>99.99
Acceptance criteria	≥99	≥99	≥99	≥99

JAMA Oncology | Original Investigation

Association of Measurable Residual Disease With Survival Outcomes in Patients With Acute Myeloid Leukemia

A Systematic Review and Meta-analysis

Nicholas J. Short, MD; Shouhao Zhou, PhD; Chenqi Fu, MS; Donald A. Berry, PhD; Roland B. Walter, MD, PhD, MS; Sylvie D. Freeman, DPhil, MBChB; Christopher S. Hourigan, DM, DPhil; Xuelin Huang, PhD; Graciela Nogueras Gonzalez, MPH; Hyunsoo Hwang, PhD; Xinyue Qi, PhD; Hagop Kantarjian, MD; Farhad Ravandi, MD

61 studies, >9,000 patients

Figure 2. Estimated Survival Curves, Stratified by Measurable Residual Disease

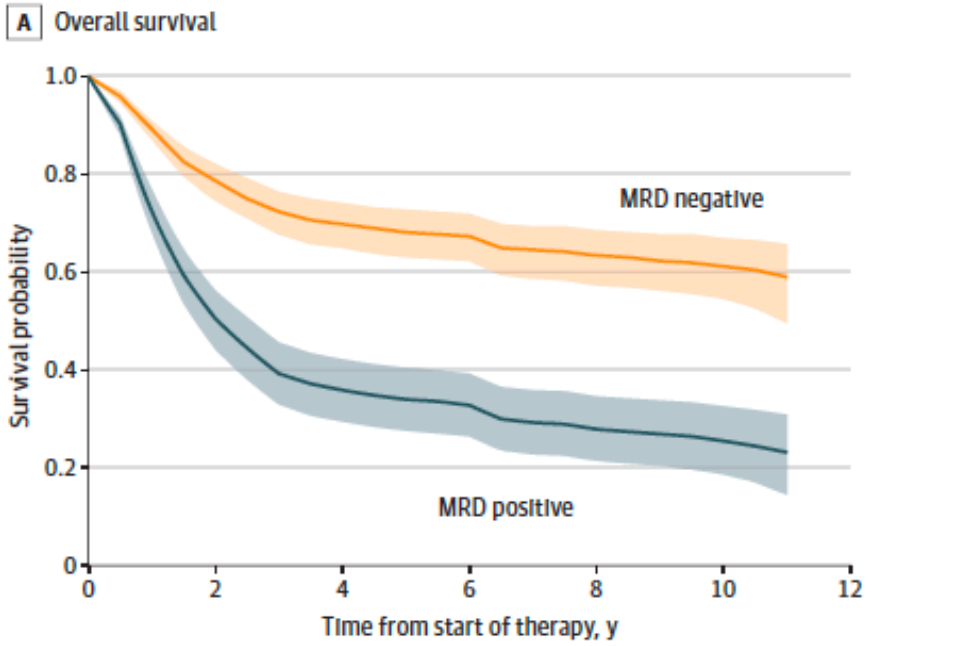
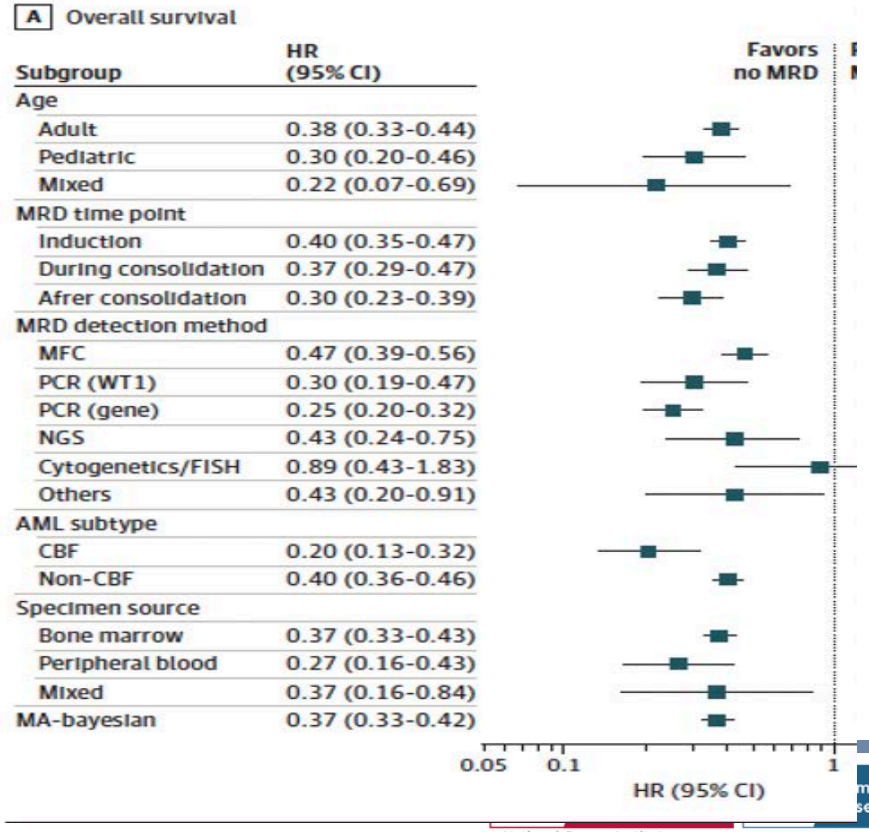
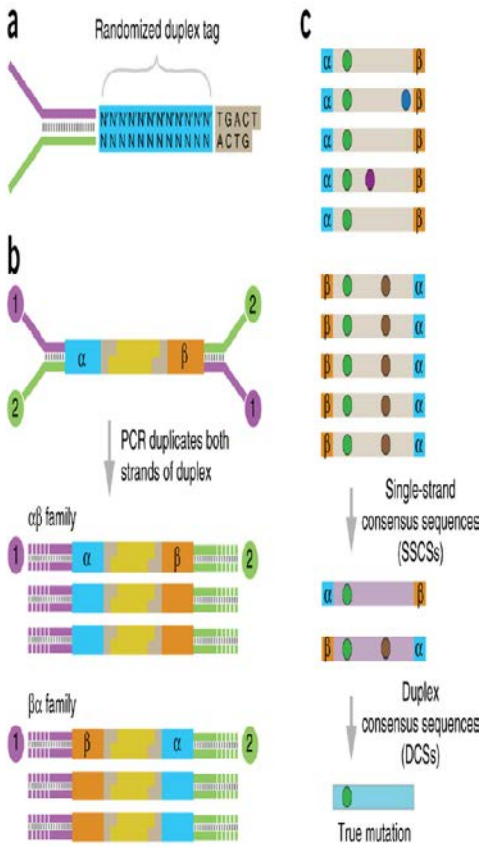
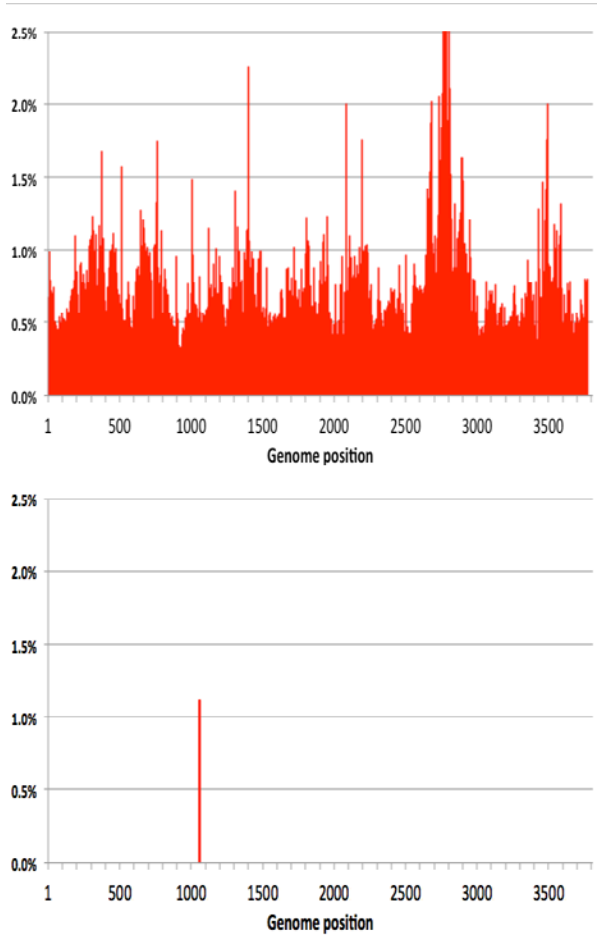


Figure 3. Hazard Ratios (HRs) for Subgroups



Duplex seq and ABL TKD mutation detection

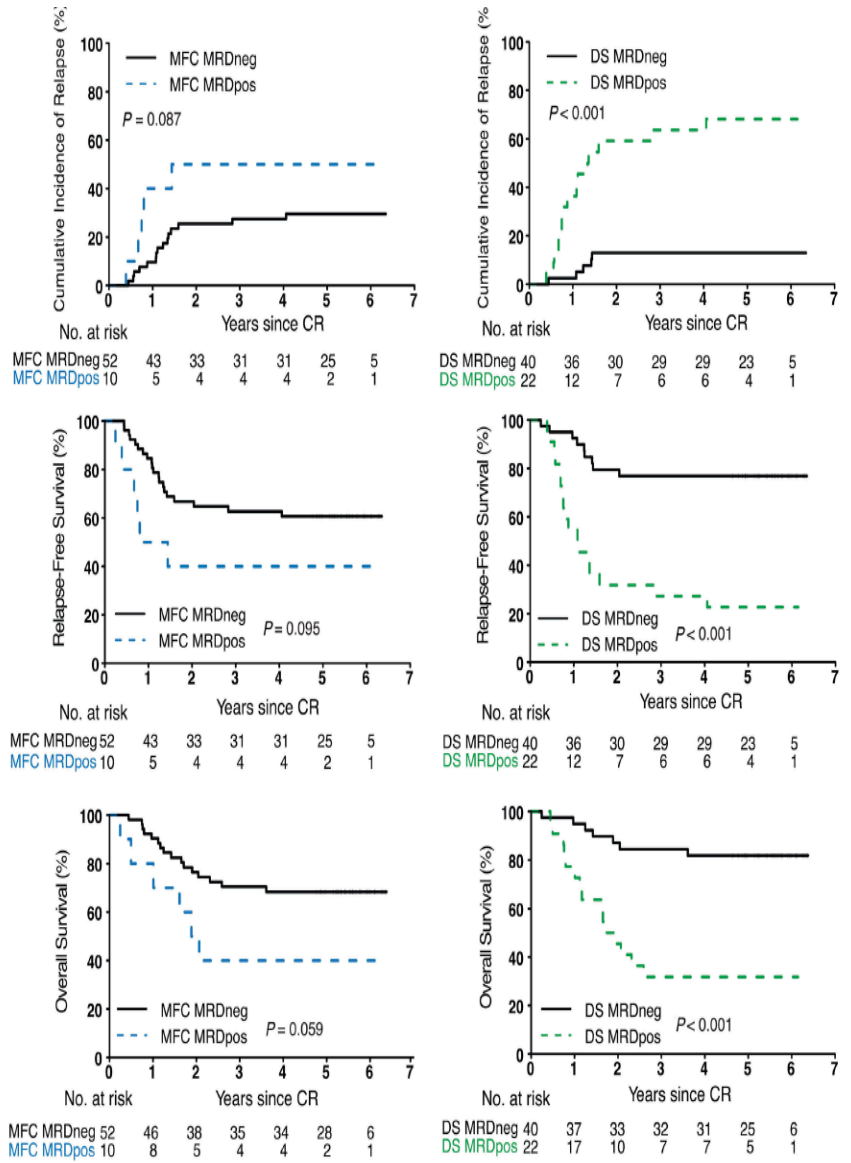




- Compare Sanger seq of mRNA to Duplex Seq of DNA
- 1/26 cDNA molecules have artifact error
- Most errors are transition mutations (e.g. C->T)
- Most mutations are artifact
- Most true mutations that happen during therapy were pre-existent
- Pre-existent mutations CML cp< CML bc < Ph+ ALL

Outcomes of residual disease

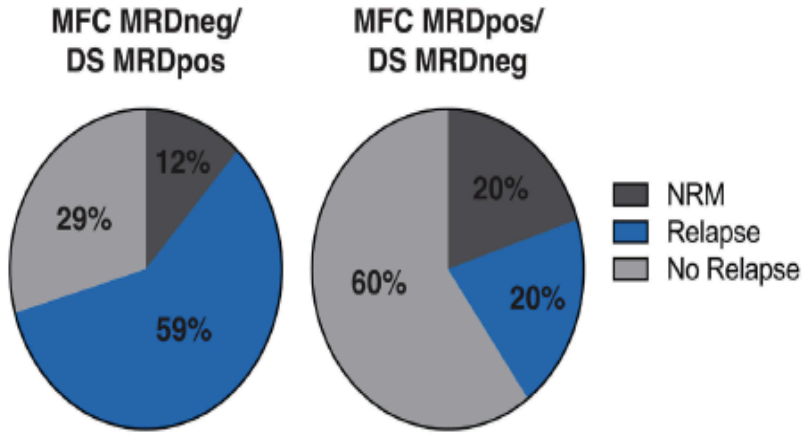
Residual disease definition	Time to relapse	Relapse-free survival	Overall survival
DS1: Non-DTA VAF > 0.1% with NPM1 > 0.01%	7.1 (2.7, 18.9) <0.001	4.9 (2.2, 10.9) <0.001	5.1 (2.1, 12.3) <0.001
DS2: Non-DTA VAF > 0.1%	4.8 (1.9, 11.8) <0.001	4.1 (1.8, 9.1) <0.001	4.8 (2.1, 11.1) < 0.001
DS3: Any mutation with VAF > 0.1%	4.3 (1.6, 11.3) 0.003	3.5 (1.5, 7.9) 0.003	3.2 (1.3, 7.7) 0.009
DS4: Fold change < 2	3.0 (1.2, ,7.5) 0.018	2.4 (1.1, 5.2) 0.032	2.1 (0.9, 4.8) 0.089
DS5: Non-DTA fold change < 2	3.9 (1.6, 9.7) 0.004	2.4 (1.1, 5.2) 0.032	4.3 (1.9, 10.0) <0.001
DS6: Non-DTA VAF > 1% with NPM1 > 0.01%, agnostic to diagnostic variants	5.5 (2.0, 15.2) 0.001	3.4 (1.5, 7.8) 0.003	4.0 (1.6, 9.7) 0.003
Flow	2.5 (0.9-6.7) 0.08	2.2 (0.9-5.4) 0.09	2.4 (0.97-6.1) 0.06

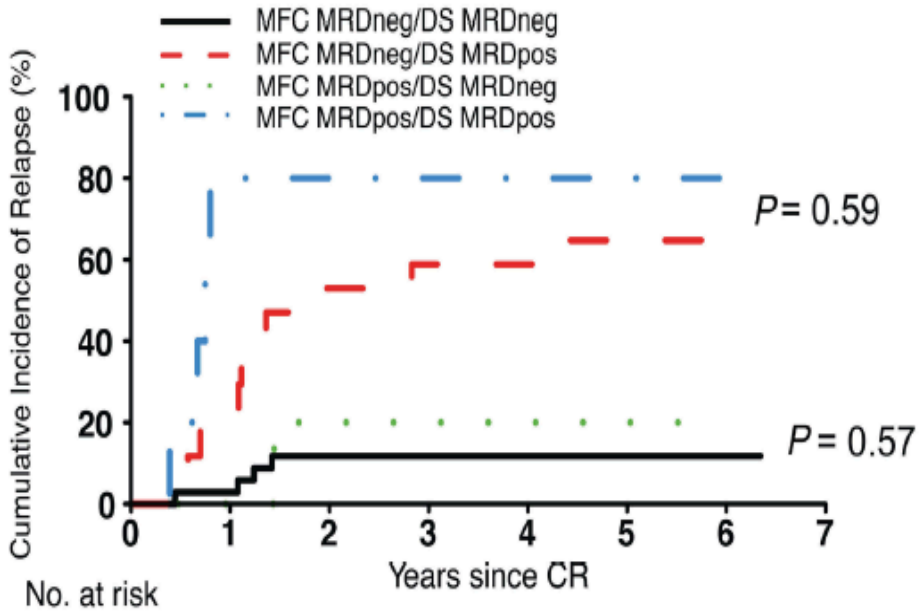


Dillon et al, Haematologica 2024

- SWOG S0106 (Randomized 7&3 v. 7&3 + GO)
- N=62 with paired dx and CR samples with flow
- 29 gene panel
- At diagnosis
  - 172 potential deleterious variants detected
  - Most common *FLT3*
  - Average VAF 31%
  - 90% had at least one variant (med. 2, range 0-9)
- At remission
  - Average VAF 0.2% (41-0.0036%)
  - Most common *DMNT3A, TET2, ASXL1*
  - All patients had at least one variant detected
  - 68% had a diagnostic variant found in remission sample

	MFC MRDneg (N=52)	MFC MRDpos (N=10)	Total
DS MRDneg	35 (67%)	5 (50%)	40 (64.5%)
DS MRDpos	17 (33%)	5 (50%)	22 (35.5%)





myeloMATCH protocol development

Updates on myeloMATCH prospective trials

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1	Basket	Study Population	Tier	Lead PI	Consult with combined chairs (ppt)	Formal combined chairs review	Group Ops submits Concept to PIO	LKSC reviews Concept	Concept CTEP AOH	Concept final CTEP approval	Group Ops submits protocol to PIO	Group Ops submits revised protocol to PIO	Protocol CTEP AOH	Protocol to CIRB	Protocol to FDA	Protocol final CTEP approval
2	MSRP	"MSRP" MYELOMATCH	All	Radich	NA	NA	3/11/21	(PRC)		4/5/21	12/2/21	4/11/2023 - Revision 7 submitted	Done	Next step	Next step	Next step
3	Younger	ERASE (MM2YA-EA01)	2	Atallah	8/9/19	Done	Done	4/27/21	10/8/21	11/1/21	Submitted - 1/21/2022; Review - 2/10/2022	5/2/2022 Remaining reviews on hold for FDA approval	Done	Submitted on 9/13/2022	Next step	Next step
4	Younger	High Risk (MM1YA-S01)	1	Shami	8/9/19	Done	12/24/20	2/23/21	8/3/21	8/27/21	12/2/21	9th revision deemed 'acceptable' on 10/04/2023	9th revision deemed 'acceptable' on 10/04/2023	Submitted on 9/2/2022; Approved on 4/26/2023	Next step	Next step
5	Younger	Intermediate Risk (MMY01-CTG01) new (MM1YA-CTG01)	1	Assouline	8/9/19	Done	1/13/21	2/23/21	8/3/21	8/26/21	11/30/21	7th revision deemed 'acceptable' on 7/13/2023	7th revision deemed 'acceptable' on 7/13/2023	Submitted on 9/2/2022	Next step	Next step
6	Younger	NPM1	1	Mims	4/16/2021, 7/2/2021	9/24/21	Next Step									
7	Younger	FLT3 Mutant (MM1YA-EA04)	1	Pratz	4/2/2021, 1/21/2022	10/7/22	Next step									
8	Younger	CBF	1	Ustun	1/5/24	Done - 1/5/2024										
9	Older	Newly dx, IDH2 mut (MM1OA-S03)	1	Huselton/Borate	8/14/2020, 1/22/2021, 3/12/2021	8/20/21	Submitted 1/30/2023	Reviewed on 2/28/2023	Done	Approved: 06/08/2023	Next Step PIO review 12/28/23					
10	Older	TP53 mut (MM1OA-S02)	1	Shallis (Zeidan/Sallman)	8/14/2020, 12/11/2020, 3/12/2021, 4/7/2021	6/25/21	10/31/21	1/4/22	5/13/22	5/13/22	10/17/22	3rd revision in review				
11	Older	FLT3 Mutant (MM1OA-EA02)	1	Altman/Perl	3/5/2021, 6/18/2021	11/19/21	5/31/22	6/28/22	Done	8/29/22	11/29/22	3rd revision submitted 12/08/2023	Next Step			
12	Older	Marker-negative	1	~~Menghrajani~~	4/16/2021, 2/4/2022, 8/26/2022, 10/6/2023	Next step										
13	Older	NPM1 (MM1OA-A02)	1	Im/ Wang	7/9/2021 8/27/2021 4/1/2022	7/15/22	Submitted on 10/27/2023	Next step - Review on 11/28/2023								
14	Older	Newly dx, IDH1 mut	1	Regan/Lachowiez	6/16/2023, 11/17/2023	11/17/23										
15	Older	HMA-Refractory	1	Reagan	Next step											

1) IND, IDE approved; 2) MSRP approved; 3) three protocols approved; 4) >100 sites

Life history of a myeloMATCH sample

- **Wednesday 9/25 11am**: Sample collection/shipment by site AND Pathology report uploaded in MatchBox
- **Thursday 9/26 10am-12:30 pm**: Sample receipt by MDNet labs
- **Saturday 9/28 8:30pm:** Cyto/FISH report uploaded into MatchBox
- **Sunday 9/29 12:20am:** Flow report uploaded into MatchBox.
- **Sunday 9/29 1:20am**: NGS official report signed out
- **Sunday 9/29 6:00am:** NGS official report uploaded into MatchBox
- **Sunday 9/29 8:00 am**: ELN risk assigned in MatchBox
- **Sunday 9/29 8:27am:** Bioinformatics team reviewed results and emailed Assignment Report

< 72 hrs!!!, including assignment!

MyeloMATCH Registration for Participant [redacted]

M

matchbox@nih.gov <matchbox@nih.gov> Today at 10:35 AM

To: NCI-FrederickMoCha-CLIA@nih.gov; Cytogenetics Laboratory; +10 more

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

myeloMATCH

New Registration to myeloMATCH

Participant [redacted] has been enrolled on myeloMATCH. You should expect samples for this participant soon.

Participant ID [redacted]

Need help?

Send us an email at myelo-match-support@mail.nih.gov

National Cancer Institute at the National Institutes of Health

MyeloMATCH Myeloid Sample Received

M

matchbox@nih.gov <matchbox@nih.gov> Today at 12:29 PM

To: [redacted] +6 more

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

myeloMATCH

MyeloMATCH Myeloid Sample Received

A Myeloid sample for participant [redacted] has been received and requires assay to be uploaded.

Please log into the myeloMATCH UI to upload the assay.

Participant ID [redacted]

Need help?

Send us an email at myelo-match-support@mail.nih.gov

National Cancer Institute at the National Institutes of Health

MyeloMATCH Flow Cytometry Has Been Confirmed for Participant [redacted]

M

matchbox@nih.gov <matchbox@nih.gov>

Today at 12:00 PM

To: NCI-FrederickMoCha-CLIA@nih.gov; Cytogenetics Laboratory; +9 more

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

myeloMATCH

Flow Cytometry Assay has been confirmed

The Flow Cytometry assay has been confirmed. Participant ID [redacted]

Participant ID [redacted]

Need help?

Send us an email at myelo-match-support@mail.nih.gov

National Cancer Institute at the National Institutes of Health

MyeloMATCH Assignment Report Ready for Review for Participant [redacted]

M

matchbox@nih.gov <matchbox@nih.gov>

Today at 10:20 A

To: [redacted] +27 more

UTION: This email originated from outside of the organization. Do not click links or open achments unless you recognize the sender and know the content is safe.

myeloMATCH

Assignment Report Ready for Review

An assignment report for participant [redacted] has been generated and is ready for review.

Please log into the myeloMATCH UI to review and confirm the report.

Participant ID [redacted]

Assignment Result MM1YA-S01

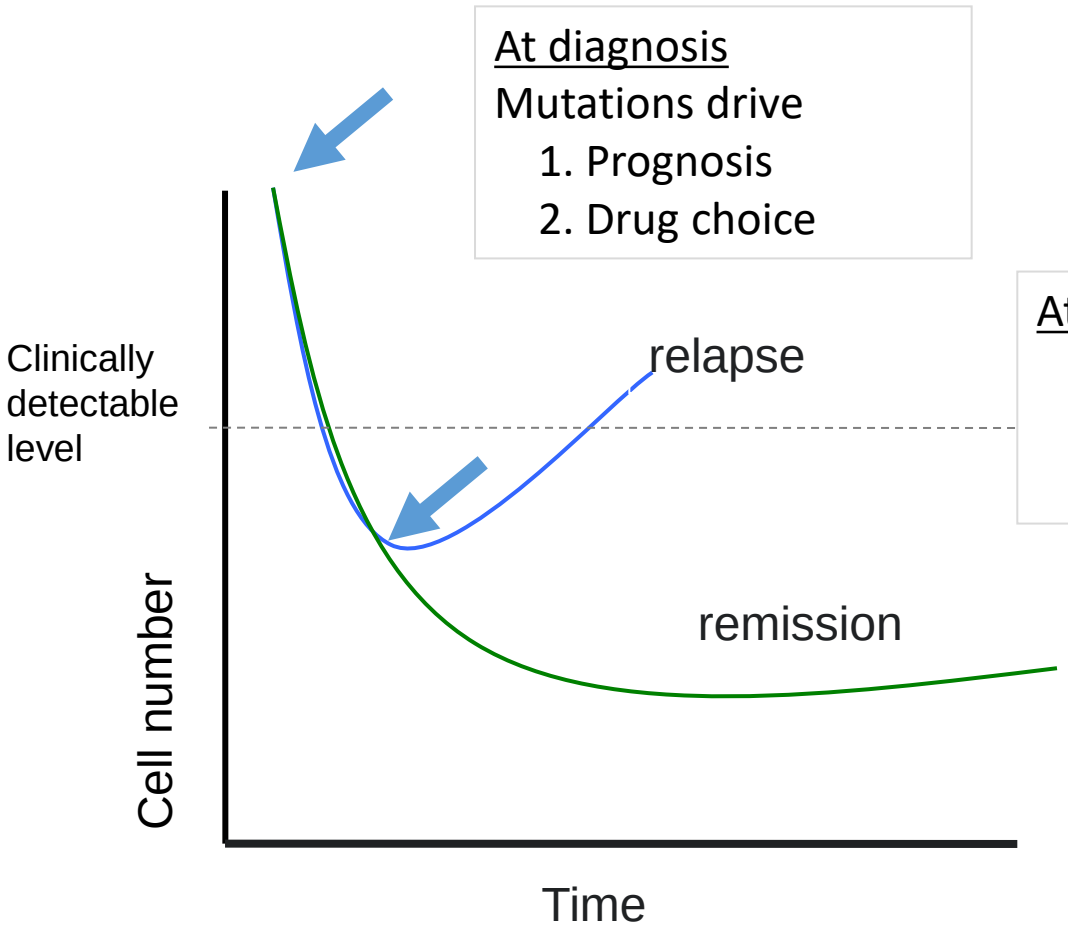
Review Assignment Report

Need help?

Send us an email at myelo-match-support@mail.nih.gov

National Cancer Institute at the National Institutes of Health

Molecular diagnostics, clinical care, and trials



At diagnosis
Mutations drive
1. Prognosis
2. Drug choice

At "CR": MRD
1. Change therapy?
2. Drug development
3. MRD eraser trials

Wish list for assays
1. Fast
2. Reliable
3. Sensitive
4. Flexible
5. Cheap

Fast, cheap, and good… pick two. If it's fast and cheap it won't be good. If it's cheap and good it won't be fast. If it's fast and good it won't be cheap. Fast, cheap and good… pick two words to live by. (Jim Jarmucsh, as told to Tom Waits)


JER'S GENETICS
GARAGE

We welcome our panelists to the myeloMATCH Discussion:

- Jerald Radich, M.D.; Fred Hutchinson CCC
- Jazelle Sugay, MSN, RN, OCN; Robert H. Lurie CCC
- Patrick McNamara; Robert H. Lurie CCC
- Tricia Drews, BSN, OCN; Michigan Cancer Research Consortium
- Sewan Gurung; Fred Hutchinson CCC
- Margaret Corkrin, RN, BSN, VCU Massey CCC
- Jessie Lamphier; University of Kansas CCC
- Alexis M. Cruz-Chacon, MD, FACP; Puerto Rico NCORP

Panel Discussion: myeloMATCH

Jazel Sugay, *MSN, RN, OCN*

- Senior Clinical Research Nurse
- Leukemia Disease team lead overseeing patient and trial coordination

Northwestern Medicine | Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Panel Discussion: myeloMATCH

Patrick McNamara

- Clinical Operations Manager
- Manages staff and caseload administration for Leukemia Disease Team

Northwestern Medicine | Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Study Timeline by Site: Robert H. Lurie CCC

myeloMATCH Timeline	
myeloMATCH Activation	7/22/2024
My Site's IRB Approval	7/15/2024
My Site's Internal SIV	7/31/2024
My Site's Open to Enrollment Date	7/31/2024
My Site's First Enrollment	8/23/2024

Panel Discussion: myeloMATCH

Tricia Drews, RN, BSN, OCN

- Oncology Research Nurse
- Screen and recruit eligible patients for the 100+ trials available at our site
- Collaborate with oncology providers to coordinate patient's care throughout treatment and follow up on study

Study Timeline by Site: Michigan Cancer Research Consortium

myeloMATCH Timeline	
myeloMATCH Activation	6/10/2024
My Site's IRB Approval	6/5/2024
My Site's Internal SIV	NA; CLASS Site Initiation Training Completed 5/29/2024
My Site's Open to Enrollment Date	6/10/2024
My Site's First Enrollment	8/8/2024

Panel Discussion: myeloMATCH

Sewan Gurung

- Clinical Research Coordinator
- For all things MyeloMATCH

Study Timeline by Site: Fred Hutchinson Cancer Center, Clinical Cancer Genomics Lab

myeloMATCH Timeline	
myeloMATCH Activation	16 May 2024
My Site's IRB Approval	NA
My Site's Internal SIV	21 March 2024
My Site's Open to Enrollment Date	16 May 2024
My Site's First Enrollment	**18 June 2024**

Panel Discussion: myeloMATCH

Margaret Corkrin RN, BSN

- Clinical Research Nurse
- Provide direct care to candidates for and participants in VCU Massey Comprehensive cancer center clinical trial research protocols in collaboration with treating, principal and sub investigators. Coordinate research study needs through recognizing and responding appropriately to deviations from normal, identifying, interpreting, analyzing and evaluating patient's condition and making alterations in treatment and diagnostic regiments in collaboration with treating principal and sub investigators.

Study Timeline: VCU Massey Comprehensive Cancer Center

myeloMATCH Timeline	
myeloMATCH Activation	06/26/2024
My Site's IRB Approval	06/25/2024
My Site's Internal SIV	06/25/2024
My Site's Open to Enrollment Date	06/26/2024
My Site's First Enrollment	06/26/2024

Panel Discussion: MYELOMATCH

Jessie Lamphier, BS, CCRP

- Clinical Operations Manager BMT and Cellular Therapeutics
- Responsible for overseeing clinical trial operations from start to finish, ensuring project deliverables are met and leading cross-functional teams to support the Cancer Center's mission. Responsible for monitoring compliance with departmental policies, serving as the primary contact for disease working groups, performing functional management duties, mentoring team members, and training staff. Additionally, I carry a 25% patient workload and am involved in resource planning and addressing any barriers that arise.

Study Timeline by Site: University of Kansas CCC

MyeloMATCH Timeline	
MyeloMATCH Activation	8/5/2024
My Site's IRB Approval	7/29/2024
My Site's Internal SIV	8/2/2024
My Site's Open to Enrollment Date	8/5/2024
My Site's First Enrollment	9/5/2024

Panel Discussion: MYELOMATCH

Alexis M. Cruz Chacon, MD FACP

- PI Puerto Rico NCORP
- Malignant Hematology Studies

PRNCORP
NCI COMMUNITY ONCOLOGY RESEARCH PROGRAM

CENTRO COMPRENSIVO DE CÁNCER
UNIVERSIDAD DE PUERTO RICO
HOSPITAL

YOUR PICTURE(s) HERE

Study Timeline by Site: Puerto Rico NCORP

MyeloMATCH Timeline	
MyeloMATCH Activation	5-16-2024
My Site's IRB Approval	5-23-2024
My Site's Internal SIV	6-02-2024
My Site's Open to Enrollment Date	6-11-2024
My Site's First Enrollment	6-18-2024

Challenges and Opportunities

Would each panelist please discuss the following challenges and opportunities with Myelomatch:

1. What do you and your site PI appreciate about this protocol?
2. Could you please remark on the time-to-activation process at your site noted in the previous slide?
3. What considerations in feasibility, logistics, and operations are important to know and address?
4. Have you experienced any enrollment or registration challenges?
5. What challenges or opportunities have you experienced in collaborating with ancillary departments to make the protocol successful?
6. Could you share any operational tips and tricks for Myelomatch?
7. If you were in charge of this study, what changes you would make to the protocol?

Myeloid Malignancies Molecular Analysis for Therapy Choice
NCI National Clinical Trials Network
October 17, 2024 Post-Activation
Jeri and Noboru Oishi Symposium Presentation

Presenter:

Jerald Radich, MD	*myeloMATCH Chair, Professor, Translational Science and Therapeutics Division, Fred Hutch, and Kurt Enslein Endowed Chair, Fred Hutch Cancer Center*

Discussion Panel:

Jazel Sugay, MSN, RN, OCN	*Clinical Research Nurse and Team Lead, Robert H Lurie Comprehensive Cancer Center*
Patrick McNamara	*Clinical Operations Manager, Robert H Lurie Comprehensive Cancer Center*
Tricia Drews, RN, BSN, OCN	*Oncology Research Nurse, Michigan Cancer Research Consortium*
Sewan Gurung	*Clinical Research Coordinator, Fred Hutchinson CCC*
Margaret Corkrin RN, BSN	*Clinical Research Nurse, VCU Massey CCC*
Jessie Lamphier	*Clinical Operations Manager BMT and Cellular Therapeutics, University of Kansas CCC*
Alexis M. Cruz-Chacon, MD, FACP	*PI, Puerto Rico NCORP*

Questions for Panel Exploration/Discussion

Are there any questions either from the panel or the virtual and in-person audience they would like to address with the SWOG PI, Dr. Jerald Radich, for this study?

Thank you, Panelists, for your participation!

Building Patient Partnerships: A Roadmap for Meaningful Collaboration

Anne Marie Mercurio

Oishi Symposium

October 17, 2024

SWOG CANCER RESEARCH NETWORK

NCI National Clinical Trials Network
a National Cancer Institute program

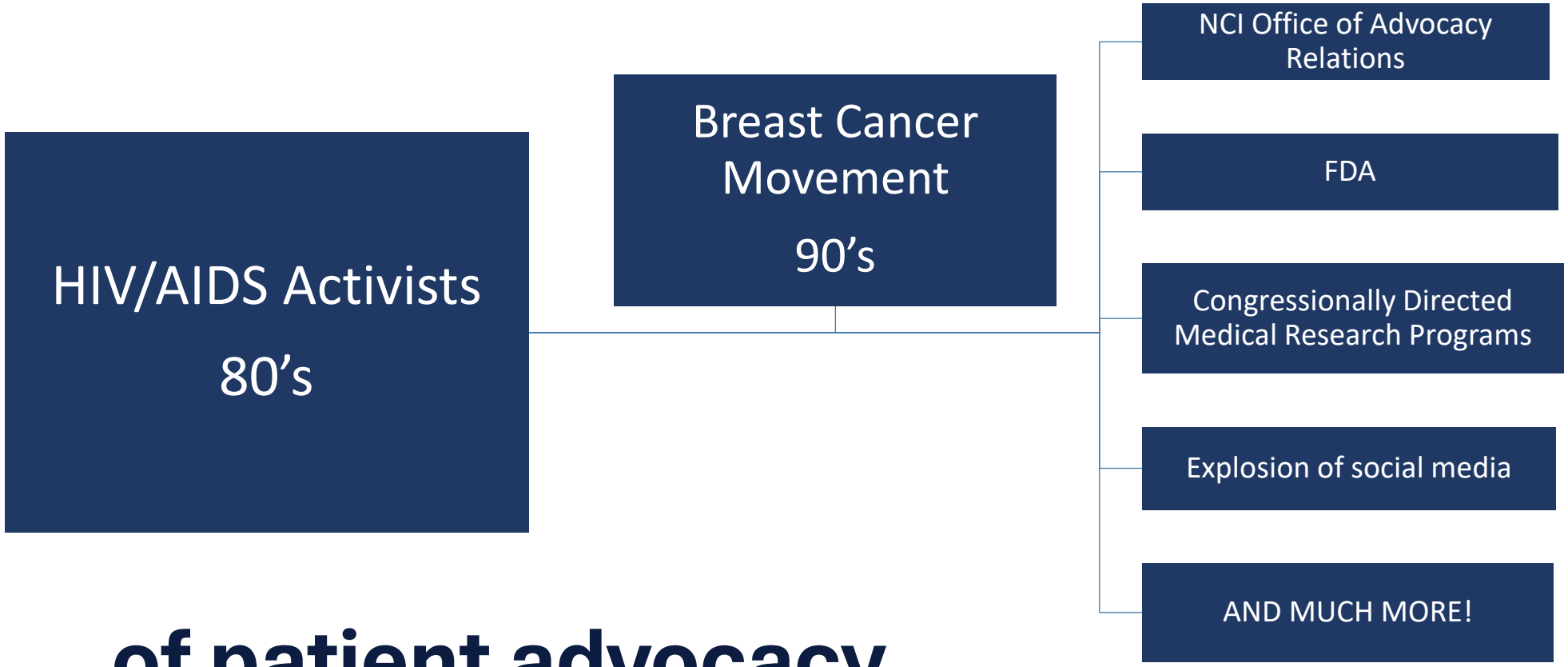
NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

"When you've seen one cancer center, you've seen one cancer center"

Dr. Joseph Simone
(via Skip Trump; via Eric Rosenthal)

(Spoiler alert – also applies to advocate interactions)

a (very) brief background …



… of patient advocacy

Patient Advocacy – One Term, Many Hats!

Awareness

RESEARCH!

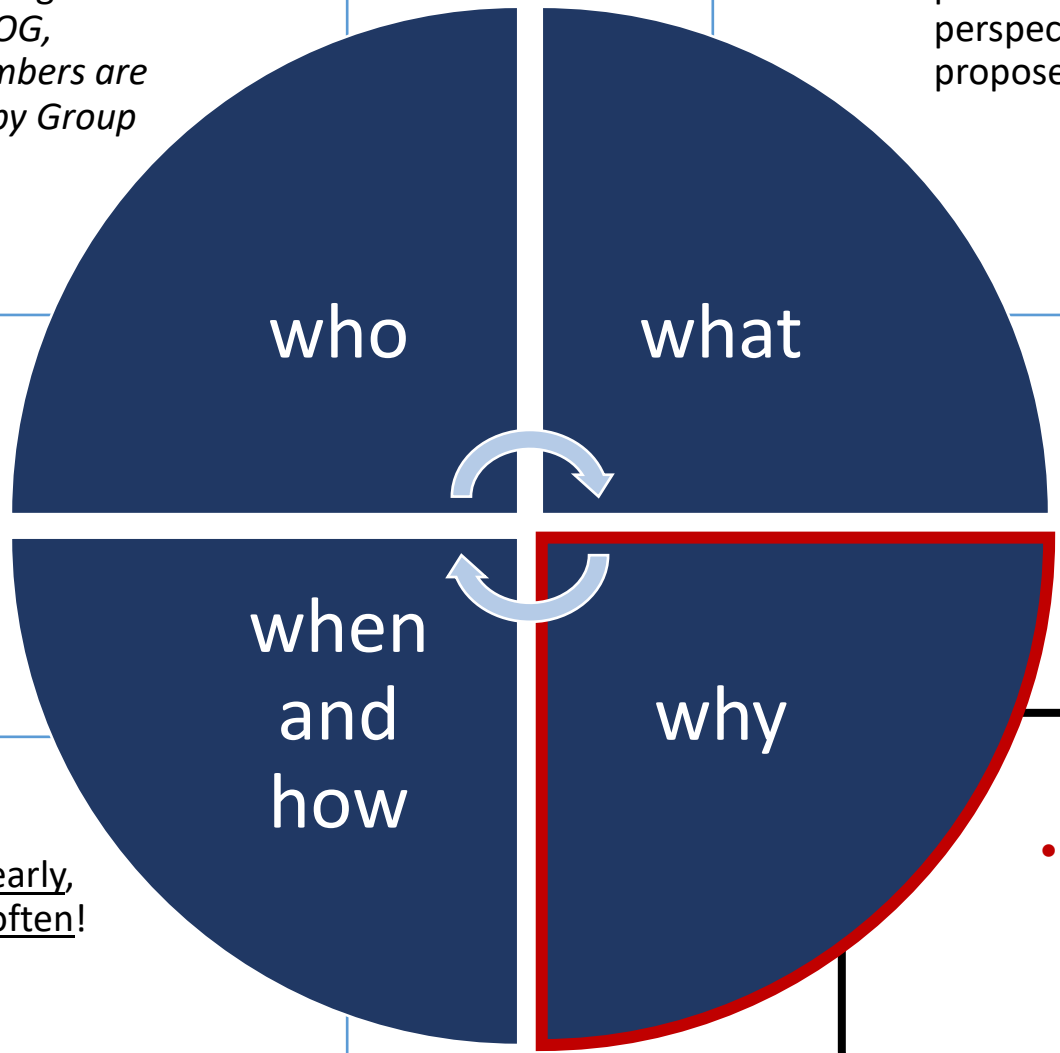
Support

Policy

Education

- patients, caregivers *(within SWOG, official members are appointed by Group Chair)*

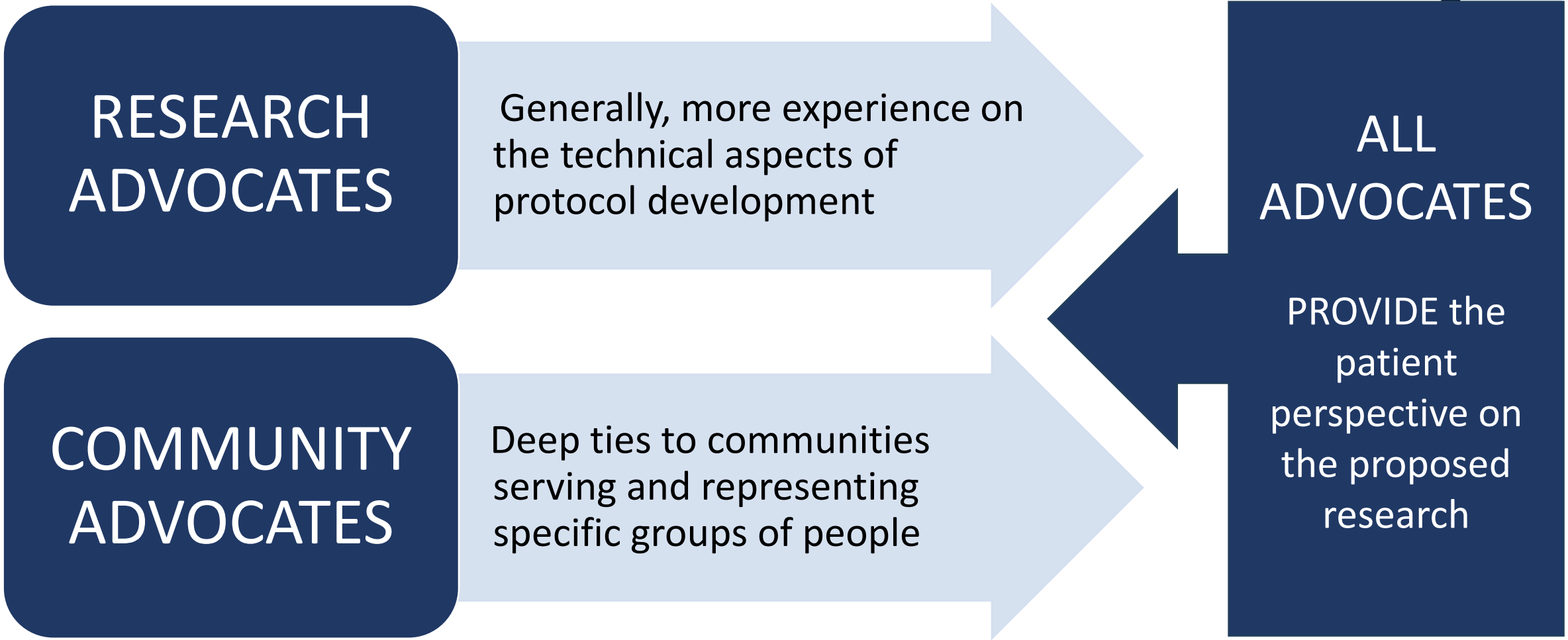
- provide a patient perspective on the proposed ideas



- engage us <u>early</u>, engage us <u>often</u>!

- **to make sure your studies and ideas are strong and are important for patient impact**

SWOG Advocates: In A Nutshell



SWOG Patient Advocates

Lived experience across many cancer types

Diverse backgrounds

Ties to many communities

27 members

NCTN Committees

Primary Committee Member (Top/Bold*)

Personal History/Expertise

Breast	GI	GU	Leukemia	Lung	Lymphoma	Melanoma	Myeloma	Rare	Other
Ginny*	**Carole* (pancreas)**	**Darrell* (bladder)**	**Gail***	**Judy***	**Tricia***	**Sam***	**Paul***	**Marcia***	Brain (Amy)
Roberta*	**Marielle* (CRC)**	**Laura* (kidney)**	Bruce (CLL)	Plus 2 in caregiving roles	**Lauren**	Plus 2 in caregiving roles	Plus 2 in caregiving roles	Plus 1 in caregiving role	Endometrial (Ginny)
Plus 7 (Barbara, AM, Cheryl, Desiree, Valerie, Judy, Eileen)	Allison (CRC)	**Lee* (prostate)**			Plus 1 in caregiving role				Testicular (Jonathan)
AND 2 in caregiving role	Lee (CRC)	Bruce (prostate)							Cervical
	JJ (CRC)	Joël (prostate)							HPV Tonsil
	Plus 4 in caregiving roles	Plus 2 in caregiving roles							Fallopian
									Uterine

SWOG CANCER RESEARCH NETWORK

NCI National Clinical Trials Network
a National Cancer Institute program

NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

NCORP COMMITTEES

Primary Committee Member

Cancer Care Delivery	Palliative Care (Advanced Cancer)	Prevention, Screening and Surveillance	Symptom Management and Survivorship
Barbara	Valerie	Cheryl	Lee J
			Amy (term concludes after this meeting)

Merged from 5 committees into 4 as of August 2024

SUPPORT AND ADMINISTRATIVE COMMITTEES

Primary Committee Member (Top/Bold*)

AYA	Digital Engagement	Recruitment and Retention	VA Committee	Conflict Mgt	DEI Leadership	Publications	DSMB
Allison*	**Jonathan***	**Desiree***	**Bruce**	**Cheryl***	**Joël***	**Amy***	**Elda (former PAC member)**
Lauren	**Anne Marie***			**Lee J***	**Barbara***		
Jonathan	Ginny				**Jonathan (ChEER)**		
Laura	Allison						

AT NCI:
CIRB, Steering Committees, Accrual Core Team

PAC COMMUNITY FOCUS

NAMED COMMUNITY ADVOCATE * IN TOP BOX

BLANK TOP BOX INDICATES NO "ASSIGNED" ADVOCATE

AAPI	AYA	Advanced Cancer	Black & African American	Caregiver	Latino and Hispanic	Older >70	Rural	SGM (LGBTQ+)	VA
	Lauren*	**JJ***			**Eileen***			**Joël***	**Bruce***
Darrell	Allison	Lee J	Desiree	Carole	Barbara	Lee J	JJ	Darrell	Lee M
	Jonathan	Laura	Roberta	Cheryl	Tricia	Bruce	Cheryl	Tricia	
	Laura	Cheryl	Lee M	AM	Desiree	Judy	Ginny	Cheryl	
	Tricia	Joël	Eileen	Laura	Marielle	Cheryl			
	Desiree	Amy		Desiree		Joël			
	Eileen	Ginny		Eileen		Carole			
	Marielle	AM		Roberta		Ginny			
	JJ			Amy		Amy			
				Ginny		AM			

SWOG CANCER RESEARCH NETWORK

NCI National Clinical Trials Network
a National Cancer Institute program

NCI Community Oncology Research Program
A program of the National Cancer Institute of the National Institutes of Health

PAC ANALYSIS: Where are the gaps?

Gender

- 8 Male
- 19 Female

Cancer Type

- Breast
  - •9 survivors
  - •2 caregivers
- CRC
  - • 4
- Prostate
  - • 3
- Lung
  - •Very busy and just one active advocate

Age

- AYA
  - • 9
- Older adults
  - • 9

Race or Ethnic Group

- Black/AA
  - • 4
- Latino/ Hispanic
  - • 5
- Asian American
  - • 1

SGM

- 4

Rural

- 3

VA

- 2

Currently: 27 Advocates Total (soon to be 26)
Goal is 30 – Fill Black/AA, Asian, Rural, ?? (where needed)
Funded through February 28, 2026: 30 (20 RA's/10 CA's)

Gender
- 29.6% Male underrepresented
- Population 50/50

Breast Cancer
- 33.3% (overrepresented)
- Survivors (not incl. Caregivers)

Age
- 33.3% AYA
- 33.3% Older Adults

	Black/AA	Hispanic/Latino	Asian American *UNDERREPRESENTED*	SGM	Rural Populations *UNDERREPRESENTED*	Veterans
US Population ESTIMATES	15.4%	19.1%	7%	7%	17.9%	6%
PAC Percentage	14.8%	18.5%	3.7%	14.8%	11.1%	7.4%

Additional Steps Toward Collaboration

We encourage you to engage with your "assigned" advocate.

- Don't hesitate to contact PAC co-chairs
- Ask your assigned advocate if other PAC members might be able to help, too

Consider a "Pitch the PAC" session.

PITCH THE PAC

Your ideas, our insights

PAC chairs set it up at your request

One-hour informal meeting

Study team presents the concept

Open discussion with PAC

It's never too soon.
Indeed, earlier is better.
And earliest is best!

Email: barbarasegarra@swog.org or mercurio.annemarie@gmail.com

BY THE NUMBERS

10 to 20+	• Number of PAC members per session
7	• Number of sessions held to date
10+	• PAC is represented in many communities and across many cancer types

NEW INITIATIVE AFTER FALL 2023 GROUP MEETING

11/23	• Cancer Care Delivery • Changed study aims, expanded eligibility criteria
2/24	• Symptom Management/Quality of Life • Feedback on PRO collection, how will you measure success (reduce fatigue after radiation)
3/24	• GU Committee (Bladder Cancer Study) • Recommended by “triage” to discuss with PAC/bladder preservation is a big motivator for this study
4/24	• Lung Committee • How to present study to patient as an alternative to standard of care, study schema was clarified
5/24	• Cancer Care Delivery • Metastatic breast cancer study, how to approach patients, appropriate compensation amounts
7/24	• Lung Committee • Need for patient friendly study materials, support of use of PRO to accurately assess tolerability
8/24	• Early Therapeutic/Rare Cancer • Protocol coordinators joined, asked to be invited to all future sessions because of the depth of the insights!