NHLBI-MDS
STUDY UPDATE

ECOG-ACRIN GROUP MEETING
PHARMACIST, ONCOLOGY NURSE, CRA/DATA MANAGER EDUCATION SYMPOSIUM
OCTOBER 27, 2017
Study Overview

- Protocol # NHLBI-MDS
- Open to NCORP and NCTN sites
- Study Objectives
  - Create a multi-institutional, longitudinal biorepository with samples from participants with Myelodysplastic Syndromes (MDS) or Idiopathic Cytopenias of Undetermined Significance (ICUS)
  - Consistently process specimens
  - Collect clinical data linked to the specimens
  - Support future studies that will have high-impact for MDS patients
Eligible Participants Undergoing Medically Indicated Bone Marrow Procedure
- Suspected (e.g., persistent unexplained cytopenias, circulating peripheral blasts etc.) MDS or MDS/MPN overlap disorders
- OR
  - Pathological diagnosis of MDS in 6 mos. Prior to enrollment, and
  - Untreated

1. Register for MDS Study
2. Assign Study Collection Kits
3. Patient Care Visit Samples Collected for Diagnosis
4. Research Samples Kits Shipped to CL/B Overnight
5. Patient Care Pathology Diagnosis
6. CL/B Prepares & Stores Slides
7. Site Enters Patient Care Visit Clinical Data
8. MDS Study Assignment

Pathology – Ship slides to CL/B:
Whenever a marrow aspirate is performed:
- 3PB unstained. 1 W/G stain (optional)
- 3 BM aspirate unstained.
  1 W/G (optional).
  1 Prussian blue (optional)
- If biopsied 1 BM biopsy H&E stained.
  1 unstained core section

Data and Specimens for participants with MDS, MDS/MPN overlap disorders, AML cases with < 30% blasts without core binding factor or acute promyelocytic leukemia, or ICUS (subject to accrual cap) q 6 months, when aspirates performed and progression to AML
Others – No Follow-up (Sites notified prior to Month 6)
Study Overview

- Study classification is determined by a centralized pathology review
  - Longitudinal Cohort
    - MDS, MDS/MPN Overlap Disorders, ICUS, AML with <30% blasts without core binding factor or APL
    - Follow-up visits every 6-months
  - Cross-Sectional Cohort
    - Other classifications
    - Baseline visit only
• Highlights from Protocol Addendum 3
  o Eligibility criteria updates
    □ In anemic patients without prior MDS diagnosis, test results are required in the prior 6 months:
      ▪ B12, serum folate, MCV, RDW, ferritin, iron studies (iron TIBC, percent saturation)
  o Updates to optional lab tests
    □ TSH (no longer required), GFR, creatinine
  o AML with <30% blasts without core binding factor or APL added to the longitudinal cohort
  o Optional skin biopsy removed
Rescreening

- Cross-sectional may be rescreened if progression of signs or symptoms provides evidence to support a probable diagnosis of MDS, MDS/MPN overlap disorders, or ICUS
- Indicate in Rave
- Samples and data must be submitted for central review (same requirements as baseline visit)

- **0.25 credits for rescreening visit**
  - 0.5 credits for baseline visit
  - 0.5 credits for longitudinal assignment (after baseline or rescreening!)
Study Status

• 294 participants enrolled as of October 22, 2017
  o Over 170 open sites
  o Planned enrollment:
    • 2000 with MDS, MDS/MPN, or eligible AML
    • 500 with ICUS
    • Up to 1000 who do not have MDS or ICUS
National Myelodysplastic Syndromes Natural History Study

Projected Accrual Report

Monday, October 23, 2017

Total enrolled to date: 294

Number Enrolled

Date

Actual Enrollment
100% Enrollment Projection
75% Enrollment Projection
25-50% Enrollment Projection
• Challenges
  o Central Pathology Review
    □ Scale up issues
    □ New review processes are starting to increase throughput
    □ 2 levels of review may be required, which can increase the time to return cohort assignment
    □ Study Team is discussing other potential steps to ensure sites receive feedback before the 6-month time point
Study Status

• Challenges
  o Central Pathology Review continued
    □ Incomplete data, outstanding queries, and missing specimens or slides will delay readiness for review
    □ Ensure all required slides are submitted
    □ Use correct kit type (*Histopathology Kit* for PB and BM aspirate, and *Core Biopsy Kit* for BM core biopsy slides)

<table>
<thead>
<tr>
<th>Pathology Material Required for Central Review</th>
<th>Unstained</th>
<th>Wright Giemsa*</th>
<th>Prussian Blue (iron)*</th>
<th>H&amp;E*</th>
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</thead>
<tbody>
<tr>
<td>Peripheral Blood</td>
<td>required</td>
<td>3 slides</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>optional</td>
<td>1 slide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Marrow Aspirate</td>
<td>required</td>
<td>3 slides</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>optional</td>
<td>1 slide</td>
<td>1 slide</td>
<td></td>
</tr>
<tr>
<td>Bone Marrow Core Biopsy</td>
<td>required if biopsied</td>
<td>1 slide</td>
<td></td>
<td>1 slide</td>
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</tbody>
</table>
• Challenges
  o Accrual
    □ Goal of 30 participants/month
    □ Need enrollment of MDS and ICUS participants
      ▪ Consider alternate etiologies for cytopenias to rule out non-MDS participants
    ▪ Optional tests in protocol
Study Procedures

• Data Reminders for Rave
  o Marrow Assessment Forms
    □ Form must be complete for patient to be reviewed
    □ Pathology and additional cytogenetic and/or molecular diagnostics reports must be redacted and uploaded
    □ Review 2008 and 2016 classifications for discrepancies
    □ Do not report decimals in the blast % and cellularity % section

  o Hematology/Chemistry Forms
    □ Ensure lab values are entered with the units designated on the form (may require conversion)
    □ If lab is not performed, indicate ‘Not Done’
Source documents

- Upload PDF reports if molecular diagnostics, FISH, or cytogenetic karyotyping were performed
- Ensure subject ID is on document before uploading

Remove PHI

- [https://www.hhs.gov/hipaa/for-professionals/privacy/special-topics/de-identification/#safeharborguidance](https://www.hhs.gov/hipaa/for-professionals/privacy/special-topics/de-identification/#safeharborguidance)
Study Procedures

• Follow-Up
  o Reminder: Schedule follow-up visits every 6 months for longitudinal participants
    □ Blood submission
    □ CBC with differential
    □ QOL (6-months and 1-year, and then annually)
    □ Follow-up data
    □ Visit window is +/- 2 months from target visit date
Study Procedures

- Occasionally, this very important step is missed -

Please click ‘Send Shipment’!

<table>
<thead>
<tr>
<th>Shipment ID: 0000000049</th>
<th>Date Created: 09/08/2016</th>
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<tbody>
<tr>
<td>Destination: Moffitt Cancer Center/M2Gen Central Lab (MCCLB)</td>
<td>Created By: Brianna Johnson - Clinic</td>
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<tr>
<td>Carrier: Federal Express</td>
<td>Tracking #: 123</td>
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<tr>
<td>Comment:</td>
<td>Check Status</td>
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Update Shipment  Delete Shipment  Send Shipment  View Shipment Manifest

Add Kits to Shipment

<table>
<thead>
<tr>
<th>#</th>
<th>Kit</th>
<th>Patient</th>
<th>Visit Number</th>
<th>Kit Type</th>
<th>Shipment Item Status</th>
<th>Remove</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>BAT-2111096</td>
<td>15005</td>
<td>08</td>
<td>Bone Marrow Kit</td>
<td>In prep/transit</td>
<td>X</td>
</tr>
</tbody>
</table>

The above grid contains 1 records.

Download displayed results to Excel
Study Procedures

• Expired Kit Tracking
  o Per coordinator request - No longer required!
  o Memo to be distributed, and study materials to be updated
  o Expired kits should be disposed at your site
Study Contacts

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