Cancer Research Consortium of West Michigan
P: 616.391.1230 | 800.336.6299 | www.crcwm.org

FAST FACTS

Study Title for Study Participants: Protocol for the collection of information and samples to be used in the study of MDS

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: The National Myelodysplastic Syndromes Natural History Study

Eligibility Requirements

1. Suspected (e.g., persistent unexplained cytopenia, circulating peripheral blasts etc.) MDS or MDS/MPN overlap disorders and undergoing diagnostic work-up with planned bone marrow assessments
   OR
   Diagnosed with de novo or therapy-related MDS within 12-months of enrollment per the World Health Organization (WHO) criteria1 and undergoing clinical evaluation and planned bone marrow assessments to confirm MDS or to evaluate disease status

2. Bone marrow aspirate expected to be performed within 1 week of registration, and in all cases must be performed no later than 4 weeks after enrollment

3. Age 18 or older

4. No prior treatment for MDS at entry and through the time of the entry bone marrow aspirate

5. No treatment with hematopoietic growth factors in prior 6 months

6. If anemic without prior MDS diagnosis, the following tests within the prior 6 months. Values that are significantly outside of normal range do not exclude participation but should prompt investigation of alternative etiologies for anemia.

   a. B12 level
   b. serum folate
   c. Mean Corpuscular volume (MCV)
   d. Red Cell distribution width (RDW)
   e. Ferritin
   f. Iron studies (Iron, Total Iron-binding Capacity (TIBC) Test, percent saturation)

7. No diagnosis of a solid tumor or hematologic malignancy within two years prior to enrollment except for in situ cancer of the skin (basal or squamous cell), cervix, bladder, breast, or prostate

8. No treatment with radiation therapy in the two years prior to registration

9. No non-hormonal treatment for malignancy within the two years prior to registration

10. No established hereditary bone marrow failure syndrome

11. No known primary diagnosis of aplastic anemia, classical paroxysmal nocturnal hemoglobinuria, amegakaryocytic thrombocytopenic purpura, or large granular lymphocyte leukemia

12. Not enrolled in the Connect® MDS/AML Disease Registry

1See Appendix III for WHO peripheral blood and bone marrow findings in MDS.

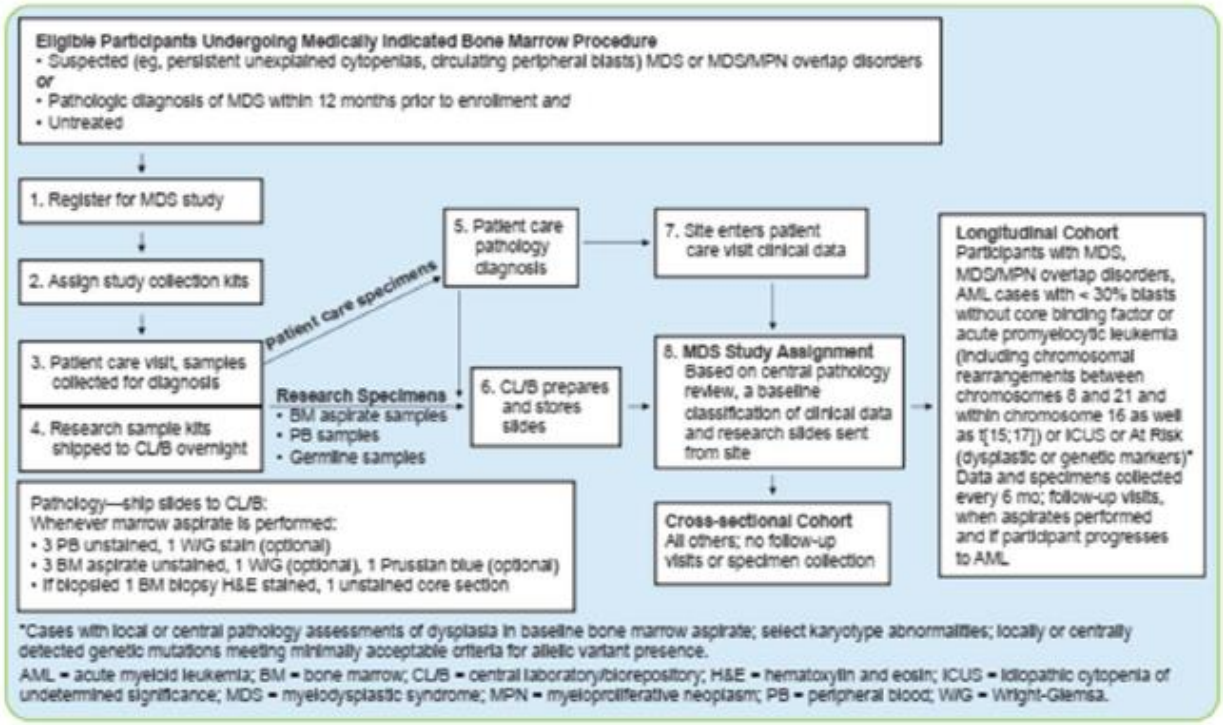
In participants with suspected MDS and prior to registration with subsequent bone marrow evaluation, alternative causes for the cytopenias should be considered (e.g., internal bleeding, autoimmune cytopenias, thyroid disorders, other causes of anemia etc.). In select individuals, the following tests could be performed to assist in the diagnostic work-up. These evaluations are not required by the protocol; however, abnormal results in advance of enrollment may reduce the number of non-MDS cases.

a. Copper, serum level
b. Direct Antiglobulin Test
c. Antinuclear Antibody (ANA) Test
d. Creatine
e. Calculated Glomerular filtration rate (GFR)
f. Thyroid – stimulating Hormone (TSH) test performed in prior 6 months

Based on centralized pathology review, participants will be classified into the longitudinal cohort of cases (MDS; MDS/MPN overlap disorders; AML with < 30% blasts without core binding factor or acute promyelocytic leukemia [AML < 30% blasts including chromosomal rearrangements between chromosomes 8 and 21 and within chromosome 16 as well as t(15;17)]; ICUS, or at risk based on selected genetic markers (described in Section 5.1) of the protocol) and the cross-sectional cohort (all others). It is not known in advance what percentages of individuals will fall into each cohort. In addition to baseline biological samples, longitudinal samples and data will be collected for approximately 1000 participants assigned to the longitudinal cohort. Sample and data collection will cease at baseline for all cases assigned to the cross-sectional cohort. Submitted samples will be reviewed by a central pathologist to determine eligibility for the longitudinal cohort (i.e., an MDS, MDS/MPN, AML with < 30% blasts without core binding factor or acute promyelocytic leukemia, or ICUS diagnosis). Should a discrepancy in diagnosis occur between the central review and study site, the study site will be notified to allow for additional information to be submitted to clarify the diagnosis. Such notifications will not occur in real time, and are not intended to assist in patient care. Additional central sequencing of selected genetic targets will be performed.

Re-screening Subjects

Subjects that are not entered in the longitudinal study are eligible to be re-screened for participation in this study if progression of signs or symptoms provides evidence to support a probable diagnosis of MDS, MDS/MPN overlap disorders or ICUS.


Eligible Participants Undergoing Medically Indicated Bone Marrow Procedure
• Suspected (eg, persistent unexplained cytopenias, circulating peripheral blasts) MDS or MDS/MPN overlap disorders
or
• Pathologic diagnosis of MDS within 12 months 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 sample kits shipped to CL/B overnight
patient care specimens
5. Patient care pathology diagnosis
Research Specimens
• BM aspirate samples
• PB samples
• Germline samples
6. CL/B prepares and stores slides
7. Site enters patient care visit clinical data
8. MDS Study Assignment
Based on central pathology review, a baseline classification of clinical data and research slides sent from site
Longitudinal Cohort
Participants with MDS, MDS/MPN overlap disorders, AML cases with < 30% blasts without core binding factor or acute promyelocytic leukemia (including chromosomal rearrangements between chromosomes 8 and 21 and within chromosome 16 as well as t[15;17]) or ICUS or At Risk (dysplastic or genetic markers)* Data and specimens collected every 6 mo; follow-up visits, when aspirates performed and if participant progresses to AML
Cross-sectional Cohort
All others; no follow-up visits or specimen collection
Pathology—ship slides to CL/B:
Whenever marrow aspirate is performed:
• 3 PB 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
*Cases with local or central pathology assessments of dysplasia in baseline bone marrow aspirate; select karyotype abnormalities; locally or centrally detected genetic mutations meeting minimally acceptable criteria for allelic variant presence.
AML = acute myeloid leukemia; BM = bone marrow; CL/B = central laboratory/biorepository; H&E = hematoxylin and eosin; ICUS = idiopathic cytopenia of undetermined significance; MDS = myelodysplastic syndrome; MPN = myeloproliferative neoplasm; PB = peripheral blood; W/G = Wright-Giemsa.