Schema

### Eligible Participants Undergoing Medically Indicated Bone Marrow Procedure
- **Suspected** (e.g., persistent unexplained cytopenias, circulating peripheral blasts etc.) MDS or MDS/MPN overlap disorders
- **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

Based on a Pathology Review of the Clinical Data & Research slides sent from the Site

Pathology – Ship slides to CL/B:
- 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, 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)
3. **Selection of Patients**

3.1 **Eligibility**

- 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 6-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
- 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
- Age 18 or older
- No prior treatment for MDS at entry and through the time of the entry bone marrow aspirate
- No treatment with hematopoietic growth factors in prior 6 months
- B12 level, serum folate, ferritin, and Thyroid-Stimulating Hormone (TSH) tests performed in prior 6 months
- 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
- No treatment with radiation therapy in the two years prior to registration
- No non-hormonal treatment for malignancy within the two years prior to registration
- No established hereditary bone marrow failure syndrome
- No known primary diagnosis of aplastic anemia, classical paroxysmal nocturnal hemoglobinuria, amegakaryocytic thrombocytopenic purpura, or large granular lymphocyte leukemia
- Not enrolled in the Connect® MDS/AML Disease Registry

¹See [Appendix II](#) 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.

- Copper, serum level
- Iron studies (Iron, Total Iron-Binding Capacity (TIBC) Test, Percent Saturation)
- Direct Antiglobulin Test
- Antinuclear Antibody (ANA) Test

Based on centralized pathology review, participants will be classified into Cases (MDS, MDS/MPN overlap disorders, or ICUS) and Others. It is not known in
advance what percentages of individuals will fall into each class. In addition to baseline biological samples, longitudinal samples and data will be collected for approximately 2000 Cases of MDS or MDS/MPN overlap disorders and 500 Cases of ICUS. Submitted samples will be reviewed by a central pathologist to determine eligibility for the longitudinal cohort (i.e., an MDS, MDS/MPN, 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.