Appendix H: MDS/MPN Subtypes

The following MDS / MPN subtypes are used on the Pre-TED Disease Classification (2402) Form, AML Pre-Infusion (2010), the MDS Pre-Infusion (2014) Form, and the MPN Pre-Infusion (2057) Form.[1]

Myelodysplastic Syndrome (MDS) Subtypes

Myelodysplastic Syndrome with Single Lineage Dysplasia (MDS-SLD)

- Includes Refractory Anemia (RA), Refractory Neutropenia (RN), and Refractory Thrombocytopenia (RT)
- Unilineage dysplasia in ≥ 10% affected lineage
- Of erythroid precursors, < 15% are ringed sideroblasts
- Myeloblasts are not increased (< 5%)
- Unicytopenia or bicytopenia of peripheral blood with < 1% blasts

Myelodysplastic Syndrome with Multilineage Dysplasia (MDS-MLD)

- One or more blood cytopenias with dysplasia in two or more lines
- Multilineage dysplasia in ≥ 10% precursors
- Absence of auer rods
- Blasts are not increased (< 5% marrow, < 1% peripheral blood)
- Multiple peripheral blood cytopenias
- Peripheral blood with $< 1 \times 10^9$/L monocytes

Myelodysplastic Syndrome with Ringed Sideroblasts with Single Lineage Dysplasia (MDS-RS-SLD)

- Unilineage, erythroid dysplasia in ≥ 10% of red blood cell precursors
- Ringed sideroblasts comprise ≥ 15% nucleated erythroid precursors
- Myeloblasts are not increased (< 5%)
- Peripheral blood anemia with no blasts

Myelodysplastic Syndrome with Ringed Sideroblasts with Multilineage Dysplasia (MDS-RS-MLD)

- Multilineage dysplasia in ≥ 10% of precursors
- Ringed sideroblasts comprise ≥ 15% nucleated erythroid precursors
- Myeloblasts are not increased (< 5%)
- Peripheral blood anemia with no blasts

Refractory Anemia with Excess Blasts-1 (MDS-EB-1)

- 5-9% blasts in the bone marrow and < 5% blasts in the peripheral blood
- If < 5% blasts in the bone marrow, then 2-4% blasts in the peripheral blood
- Unilineage or multilineage dysplasia
- Absence of auer rods
- Multiple peripheral blood cytopenias

- Peripheral blood with < 1 × 10^9/L monocytes

Refractory Anemia with Excess Blasts-2 (MDS-EB-2)

- 10-19% blasts in the bone marrow or 5-19% blasts in the peripheral blood
- Unilineage or multilineage dysplasia
- Auer rods may be present
- Multiple peripheral blood cytopenias
- Peripheral blood with < 1 × 10^9/L monocytes

Refractory Cytopenia of Childhood

- Multilineage dysplasia in ≥ 10% of precursors
- Blasts are not increased (< 5% marrow, < 2% peripheral blood)
- Dysplastic changes in ≥ 10% of neutrophils on peripheral blood smear

Myelodysplastic syndrome with isolated del(5q), aka 5q-syndrome

- Peripheral blood anemia
- Frequently hypolobated small megakaryocytes
- Blasts are not increased (< 5% blasts in marrow, < 1% blasts in peripheral blood)
- Deletion of part of the long arm of chromosome 5, del(5q)
- Must not meet criteria of any other specific category

Myelodysplastic Syndrome, Unclassifiable (MDS-U)

MDS that cannot be classified into any other defined category due to one or more atypical features Examples include:

- Hypocellular MDS
- MDS with myelofibrosis
- < 5% blasts in the marrow with Auer rods present
- MDS with unilineage dysplasia with associated pancytopenia

Myelodysplastic / Myeloproliferative Neoplasm,Unclassifiable (MDS / MPN, U)

- Clinical, laboratory, and morphological features that overlap MPN and MDS; this includes blasts < 20% in peripheral blood and bone marrow, platelet count ≥ 450 × 10^9/L, and WBC ≥ 13 × 10^9/L
- No Ph+ or BCR-ABL fusion and no abnormalities of PDGFRA, PDGFRB, or FGFR1
- MDS / MPN, U should not be used for patients with a previous, well-defined MPN who develop dysplastic features consistent with transformation to a more aggressive histology

Chronic Myelomonocytic Leukemia (CMMoL)

- Blasts and promonocytes < 20% in peripheral blodd and bone marrow
- Peripheral blood monocytosis > 1 × 10^9/L
- Dysplasia in one more lines, typically seen, but not an absolute requirement for diagnosis

- No Ph+ or BCR-ABL fusion and no abnormalities of PDGFRA or PDGFRB

Juvenile Myelomonocytic Leukemia (JMML)

- Blasts < 20% in bone marrow
- Peripheral blood monocytosis > 1 × 10^9/L
- No Ph+ or BCR-ABL fusion
- Splenomegaly
- May exhibit clonal chromosomal abnormality (may include monosomy 7)
- May have GM-CSF hypersensitivity
- May h ave peripheral blood leukocytosis, > 10 × 10^9/L
- May have increased fetal hemoglobin (Hb F)

Atypical chronic myeloid leukemia, BCR-ABL1-negative

- Peripheral blood leukocytosis, ≥ 13 × 10^9/L
- Blasts < 20% in peripheral blood and bone marrow
- Dysgranulopoiesis is present in the bone marrow
- Myelodysplastic and myeloproliferative features
- No evidence of PDGFRA, PDGFRB or FGFR1 rearrangement
- No Ph+ or BCR-ABL fusion

Myeloproliferative Neoplasm (MPN) Subtypes

Chronic neutrophilic leukemia

- Peripheral blood leukocytosis, ≥ 25 × 10^9/L with segmented neutrophil > 80% and immature granulocytes < 10%
- Blasts are not increased (< 5% marrow, < 1% peripheral blood)
- Normal granulocytic maturation
- No Ph+ or BCR-ABL fusion and no abnormalities of PDGFRA, PDGFRB, or FGFR1
- Reactive neutrophilia, PV, PMF, ET, MDS, and MDS/MPN must be ruled out

Chronic eosinophilic leukemia, NOS

- Peripheral blood eosinophilia ≥ 1.5 × 10^9/L
- Evidence of clonal abnormality but must not be Ph+ or BCR-ABL fusion, rearrangement of PDGFRA, PDGFRB, or FGFR1, or inversion or translocation of (16)(p13.1,q22)

or

- 3-19% blasts in the peripheral blood or 6-19% blasts in the bone marrow.
- Reactive and secondary Eosinophilia must be ruled out

Essential thrombocythemia

- Includes primary thrombocytosis, idiopathic thrombocytosis, and hemorrhagic thrombocythemia

- Bone marrow with megakaryocytic hyperplasia; may have minimal fibrosis. Typically no erythroid or granulocytic hyperplasia. No ringed sideroblasts or increased blasts.
- JAK2 mutation or other clonal marker
- Peripheral blood thrombocytosis, ≥ 450 × 10^9/L
- CML, PMF, PV, MDS, and other myeloid neoplasms must be ruled out

Polycythemia Vera (PCV)

Presence of two major and one minor criterion, or presence of one major and two minor criterion

Major

- Increased hemoglobin (> 18.5 g/dL in men, > 16.5 g/dL in women)
- JAK2 mutation

Minor

- Low serum erythropoietin (EPO)
- Hypercellular bone marrow with panmyelosis
- In vitro endogenous erythroid colony formation

Primary myelofibrosis

- Includes chronic idiopathic myelofibrosis (CIMF), agnogenic[2] myeloid metaplasia (AMM), myelofibrosis/sclerosis with myeloid metaplasia (MMM), and idiopathic myelofibrosis
- Megakaryocytic hyperplasia with fibrosis (MF 2-3) or hypercellular marrow with granulocytic hyperplasia
- JAK2 mutation or other clonal marker
- PV, CML, MDS, and other myeloid neoplasms must be ruled out
- At least two of the following: splenomegaly, anemia, increased serum LDH, and leukoerythroblastosis

Myeloproliferative Neoplasm, Unclassifiable (MPN, U)

- Definite clinical, laboratory, and morphological features that fail to meet criteria for specific MPN classification, or overlap two or more MPN categories
- No Ph+ or BCR-ABL fusion and no abnormalities of PDGFRA, PDGFRB, or FGFR1
- MPN,U should not be used when clinical data is insufficient or not available for proper classification of disease

[1] World Health Organization. (2008). *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues* (4th ed.). Lyon, France.

[2] There is a typo on the form; the form should read “agnogenic” rather than angiogenic.

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual

can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for any of the appendices, please reference the retired appendix on the Retired Forms Manuals webpage.

Date	Manual Section	Add/ Remove/ Modify	Description
10/6/2020	Appendix H: MDS/MPN Subtypes	Modify	Updated the criteria of the different variations of atypical CML to only "atypical CML, BCR-ABL1-negative" as the variations were all of the same thing: ***Atypical chronic myeloid leukemia, ~~Ph – / BCR – (CML, NOS)~~ BCR-ABL1-negative*** • *Peripheral blood leukocytosis, ≥ 13 × 109/L* • *Blasts < 20% in peripheral blood and bone marrow* • *Dysgranulopoiesis is present in the bone marrow* • *Myelodysplastic and myeloproliferative features* • *No evidence of PDGFRA, PDGFRB, or FGFR1 rearrangement* • *~~No abnormalities of PDGFRA or PDGFRB~~* • *No Ph+ or BCR-ABL fusion* ***~~Atypical chronic myeloid leukemia Ph – / BCR unknown (CML, NOS)~~*** • *~~Peripheral blood leukocytosis, ≥ 13 × 109/L~~* • *~~Blasts < 20% in peripheral blood and bone marrow~~* • *~~Dysgranulopoiesis is present in the bone marrow~~* • *~~Myelodysplastic and myeloproliferative features~~* • *~~No abnormalities of PDGFRA or PDGFRB~~* • *~~No Ph+ and BCR-ABL fusion unknown~~* ***~~Atypical chronic myeloid leukemia Ph unknown / BCR – (CML, NOS)~~*** • *~~Peripheral blood leukocytosis, ≥ 13 × 109/L~~* • *~~Blasts < 20% in peripheral blood and bone marrow~~* • *~~Dysgranulopoiesis is present in the bone marrow~~* • *~~Myelodysplastic and myeloproliferative features~~* • *~~No abnormalities of PDGFRA or PDGFRB~~* • *~~Ph chromosome unknown and no BCR-ABL fusion~~* ***~~Atypical chronic myeloid leukemia Ph unknown / BCR unknown (CML, NOS)~~*** • *~~Peripheral blood leukocytosis, ≥ 13 × 109/L~~* • *~~Blasts < 20% in peripheral blood and bone marrow~~* • *~~Dysgranulopoiesis is present in the bone marrow~~* • *~~Myelodysplastic and myeloproliferative features~~* • *~~No abnormalities of PDGFRA or PDGFRB~~* • *~~Ph chromosome and BCR-ABL fusion unknown~~*
7/7/	Appendix	Modify	Updated subtypes listed in Appendix H to coincide with the Spring (May) 2020

20	H: MDS/MPN Subtypes		Form Revision.
6/30/17	Appendix H: MDS/MPN Subtypes	Modify	Appendix X: MDS/MPN Subtypes has been renamed as Appendix H: MDS/MPN Subtypes.

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