Classificatie van MDS en AML

Myelodysplastisch syndroom (MDS) en acute myeloïde leukemie (AML) kunnen geclassificeerd worden volgens de International Consensus Classification (ICC) en de World Health Organization (WHO) criteria.

Classificatie volgens ICC 2022

Tabellen

Bron: International consensus classification of myeloid neoplasms and acute leukemias: integrating morphologic, clinical and genomic data – Arber et al. – Blood 2022 – 140 (11): 1200-1228.

Table 20. Myelodysplastic syndromes (MDS) and myelodysplastic syndrome/acute myeloid leukemia (MDS/AML)

	Dysplastic lineages	Cytopenias	Cytoses*	BM and PB Blasts	Cytogenetics†	Mutations
MDS with mutated *SF3B1* (MDS-*SF3B1*)	Typically ≥1‡	≥1	0	<5% BM <2% PB	Any, except isolated del(5q), −7/del(7q), abn3q26.2, or complex	*SF3B1* (≥ 10% VAF), without multi-hit *TP53*, or *RUNX1*
MDS with del(5q) [MDS-del(5q)]	Typically ≥1‡	≥1	Thrombocytosis allowed	<5% BM <2% PB§	del(5q), with up to 1 additional, except −7/del(7q)	Any, except multi-hit *TP53*
MDS, NOS without dysplasia	0	≥1	0	<5% BM <2% PB§	−7/del(7q) or complex	Any, except multi-hit *TP53* or *SF3B1* (≥ 10% VAF)
MDS, NOS with single lineage dysplasia	1	≥1	0	<5% BM <2% PB§	Any, except not meeting criteria for MDS-del(5q)	Any, except multi-hit *TP53*;not meeting criteria for MDS-*SF3B1*
MDS, NOS with multilineage dysplasia	≥2	≥1	0	<5% BM <2% PB§	Any, except not meeting criteria for MDS-del(5q)	Any, except multi-hit *TP53*,; not meeting criteria for MDS-*SF3B1*
MDS with excess blasts (MDS-EB)	Typically ≥1‡	≥1	0	5-9% BM, 2-9% PB§	Any	Any, except multi-hit *TP53*
MDS/AML	Typically ≥1‡	≥1	0	10-19% BM or PB‖	Any, except AML-defining¶	Any, except *NPM1*, bZIP *CEBPA* or *TP53*

*Cytoses: Sustained white blood count ≥ 13 × 10^9/L, monocytosis (≥0.5 × 10^9/L and ≥10% of leukocytes) or platelets ≥450 × 10^9/L; thrombocytosis is allowed in MDS-del(5q) or in any MDS case with inv(3) or t(3;3) cytogenetic abnormality.

†*BCR::ABL1* rearrangement or any of the rearrangements associated with myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions exclude a diagnosis of MDS, even in the context of cytopenia.

‡Although dysplasia is typically present in these entities, it is not required.

§Although 2% PB blasts mandates classification of an MDS case as MDS-EB, the presence of 1% PB blasts confirmed on 2 separate occasions also qualifies for MDS-EB.

‖For pediatric patients (<18 y), the blast thresholds for MDS-EB are 5% to 19% in BM and 2% to 19% in PB, and the entity MDS/AML does not apply.

¶AML-defining cytogenetics are listed in the AML section.

Table 21. Myeloid neoplasms with mutated *TP53*

Type	Cytopenia	Blasts	Genetics
MDS with mutated *TP53*	Any	0-9% bone marrow and blood blasts	Multi-hit TP53 mutation* or *TP53* mutation (VAF > 10%) and complex karyotype often with loss of 17p†
MDS/AML with mutated *TP53*	Any	10-19% bone marrow or blood blasts	Any somatic *TP53* mutation (VAF > 10%)
AML with mutated *TP53*	Not required	≥20% bone marrow or blood blasts or meets criteria for pure erythroid leukemia	Any somatic *TP53* mutation (VAF > 10%)

*Defined as 2 distinct *TP53* mutations (each VAF > 10%) OR a single *TP53* mutation with (1) 17p deletion on cytogenetics; (2) VAF of >50%; or (3) Copy-neutral LOH at the 17p *TP53* locus.

†If *TP53* locus LOH information is not available.

Table 25. Classification of AML with percentage of blasts required for diagnosis

Acute promyelocytic leukemia (APL) with t(15;17)(q24.1;q21.2)/*PML*::*RARA* ≥ 10%
APL with other *RARA* rearrangements* ≥ 10%
AML with t(8;21)(q22;q22.1)/*RUNX1*::*RUNX1T1* ≥ 10%
AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB*::*MYH11* ≥ 10%
AML with t(9;11)(p21.3;q23.3)/*MLLT3*::*KMT2A* ≥ 10%
AML with other *KMT2A* rearrangements† ≥ 10%
AML with t(6;9)(p22.3;q34.1)/*DEK*::*NUP214* ≥ 10%
AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*; *MECOM*(*EVI1*) ≥ 10%
AML with other *MECOM* rearrangements‡ ≥ 10%
AML with other rare recurring translocations (see supplemental Table 5) ≥ 10%
AML with t(9;22)(q34.1;q11.2)/*BCR*::*ABL1*§ ≥ 20%
AML with mutated *NPM1* ≥ 10%
AML with in-frame bZIP *CEBPA* mutations ≥ 10%
AML and MDS/AML with mutated *TP53*† 10-19% (MDS/AML) and ≥ 20% (AML)
AML and MDS/AML with myelodysplasia-related gene mutations 10-19% (MDS/AML) and ≥ 20% (AML) Defined by mutations in *ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1*, or *ZRSR2*
AML with myelodysplasia-related cytogenetic abnormalities 10-19% (MDS/AML) and ≥ 20% (AML) Defined by detecting a complex karyotype (≥ 3 unrelated clonal chromosomal abnormalities in the absence of other class-defining recurring genetic abnormalities), del(5q)/t(5q)/add(5q), −7/del(7q), +8, del(12p)/t(12p)/add(12p), i(17q), −17/add(17p) or del(17p), del(20q), and/or idic(X)(q13) clonal abnormalities
AML not otherwise specified (NOS) 10-19% (MDS/AML) and ≥ 20% (AML)
Myeloid sarcoma

*Includes AMLs with t(1;17)(q42.3;q21.2)/*IRF2BP2*::*RARA*; t(5;17)(q35.1;q21.2)/*NPM1*::*RARA*; t(11;17)(q23.2;q21.2)/*ZBTB16*::*RARA*; cryptic inv(17q) or del(17) (q21.2q21.2)/*STAT5B*::*RARA*, *STAT3*::*RARA*; Other genes rarely rearranged with *RARA*:*TBL1XR1* (3q26.3), *FIP1L1* (4q12), *BCOR* (Xp11.4).

†Includes AMLs with t(4;11)(q21.3;q23.3)/*AFF1*::*KMT2A*[#]; t(6;11)(q27;q23.3)/*AFDN*::*KMT2A*; t(10;11)(p12.3;q23.3)/*MLLT10*::*KMT2A*; t(10;11)(q21.3;q23.3)/*TET1*::*KMT2A*; t(11;19)(q23.3;p13.1)/*KMT2A*::*ELL*; t(11;19)(q23.3;p13.3)/*KMT2A*::*MLLT1* (occurs predominantly in infants and children).

‡Includes AMLs with t(2;3)(p11∼23;q26.2)/*MECOM*::?; t(3;8)(q26.2;q24.2)/*MYC*, *MECOM*; t(3;12)(q26.2;p13.2)/*ETV6*::*MECOM*; t(3;21)(q26.2;q22.1)/*MECOM*::*RUNX1*.

§The category of MDS/AML will not be used for AML with *BCR*::*ABL1* due to its overlap with progression of CML, *BCR*::*ABL1*-positive.

Table 26. Diagnostic qualifiers that should be used following a specific MDS, AML (or MDS/AML) diagnosis

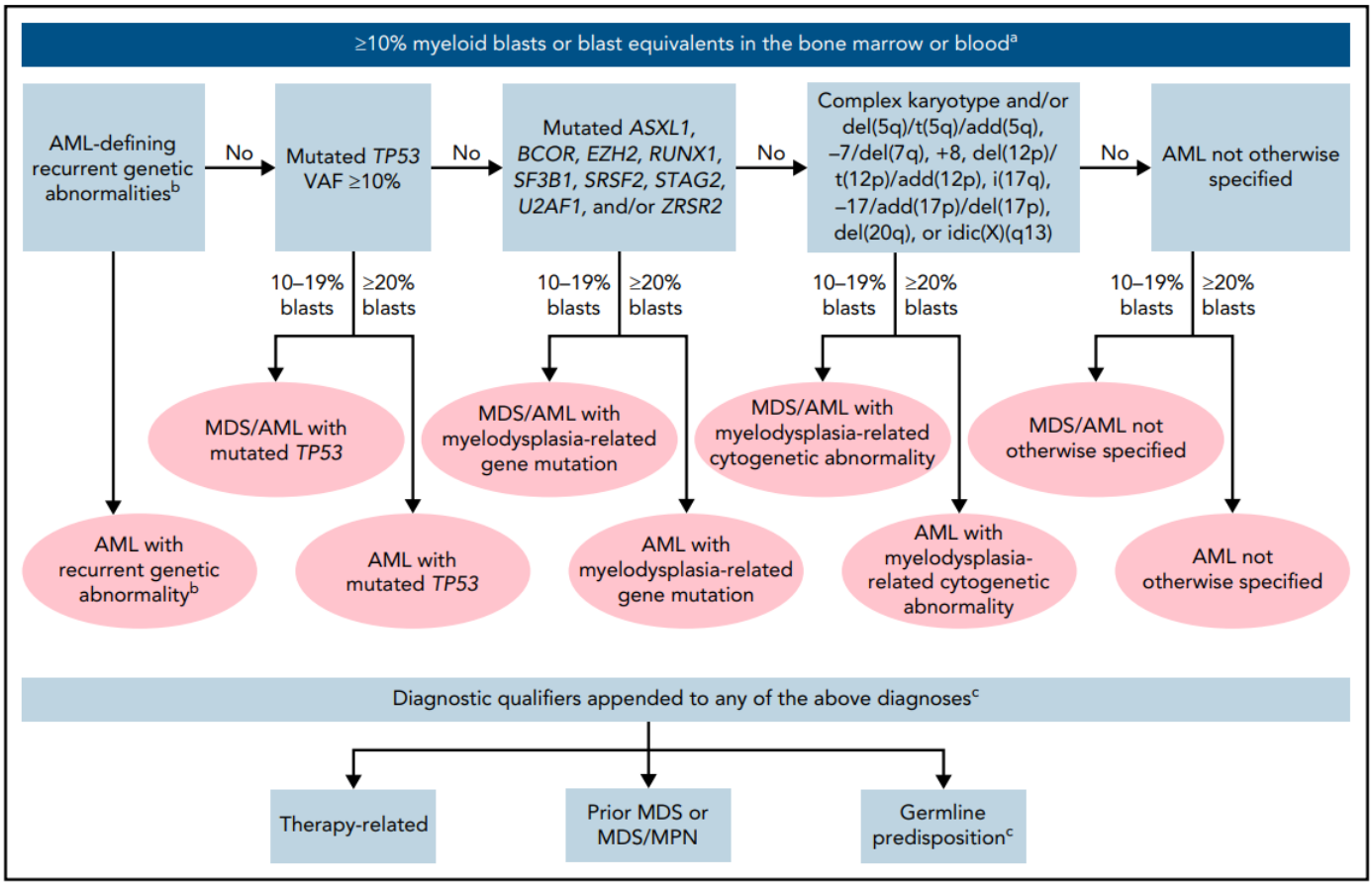
Therapy-related* • prior chemotherapy, radiotherapy, immune interventions
Progressing from MDS • MDS should be confirmed by standard diagnostics
Progressing from MDS/MPN (specify) • MDS/MPN should be confirmed by standard diagnostics
Germline predisposition

Examples: AML with myelodysplasia-related cytogenetic abnormality, therapy-related; AML with myelodysplasia-related gene mutation, progressed from MDS; AML with myelodysplasia-related gene mutation, germline *RUNX1* mutation.

*Lymphoblastic leukemia/lymphoma may also be therapy-related, and that association should also be noted in the diagnosis.

Flowschema

Bron: Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN – Blood 2022 – 140 (12): 1345-1377.



Classificatie volgens WHO 2022

Bron: The 5th edition of the world health organization classification of haematolymphoid tumours: myeloid and histiocytic dendritic neoplasms – Khoury et al. – Leukemia 2022 – 36: 1703-1719.

Table 3. Classification and defining features of myelodysplastic neoplasms (MDS).

	Blasts	Cytogenetics	Mutations
MDS with defining genetic abnormalities			
MDS with low blasts and isolated 5q deletion (MDS-5q)	<5% BM and <2% PB	5q deletion alone, or with 1 other abnormality other than monosomy 7 or 7q deletion	
MDS with low blasts and *SF3B1* mutation[a] (MDS-*SF3B1*)		Absence of 5q deletion, monosomy 7, or complex karyotype	*SF3B1*
MDS with biallelic *TP53* inactivation (MDS-bi*TP53*)	<20% BM and PB	Usually complex	Two or more *TP53* mutations, or 1 mutation with evidence of *TP53* copy number loss or cnLOH
MDS, morphologically defined			
MDS with low blasts (MDS-LB)	<5% BM and <2% PB		
MDS, hypoplastic[b] (MDS-h)			
MDS with increased blasts (MDS-IB)			
MDS-IB1	5–9% BM or 2–4% PB		
MDS-IB2	10-19% BM or 5–19% PB or Auer rods		
MDS with fibrosis (MDS-f)	5–19% BM; 2–19% PB		

[a]Detection of ≥15% ring sideroblasts may substitute for *SF3B1* mutation. Acceptable related terminology: MDS with low blasts and ring sideroblasts.
[b]By definition, ≤25% bone marrow cellularity, age adjusted.
BM bone marrow, *PB* peripheral blood, *cnLOH* copy neutral loss of heterozygosity.

Table 7. Acute myeloid leukaemia.

Acute myeloid leukaemia with defining genetic abnormalities
Acute promyelocytic leukaemia with *PML*::*RARA* fusion
Acute myeloid leukaemia with *RUNX1*::*RUNX1T1* fusion
Acute myeloid leukaemia with *CBFB*::*MYH11* fusion
Acute myeloid leukaemia with *DEK*::*NUP214* fusion
Acute myeloid leukaemia with *RBM15*::*MRTFA* fusion
Acute myeloid leukaemia with *BCR*::*ABL1* fusion
Acute myeloid leukaemia with *KMT2A* rearrangement
Acute myeloid leukaemia with *MECOM* rearrangement
Acute myeloid leukaemia with *NUP98* rearrangement
Acute myeloid leukaemia with *NPM1* mutation
Acute myeloid leukaemia with *CEBPA* mutation
Acute myeloid leukaemia, myelodysplasia-related
Acute myeloid leukaemia with other defined genetic alterations
Acute myeloid leukaemia, defined by differentiation
Acute myeloid leukaemia with minimal differentiation
Acute myeloid leukaemia without maturation
Acute myeloid leukaemia with maturation
Acute basophilic leukaemia
Acute myelomonocytic leukaemia
Acute monocytic leukaemia
Acute erythroid leukaemia
Acute megakaryoblastic leukaemia

Table 8. Cytogenetic and molecular abnormalities defining acute myeloid leukaemia, myelodysplasia-related.

Defining cytogenetic abnormalities
Complex karyotype (≥3 abnormalities)
5q deletion or loss of 5q due to unbalanced translocation
Monosomy 7, 7q deletion, or loss of 7q due to unbalanced translocation
11q deletion
12p deletion or loss of 12p due to unbalanced translocation
Monosomy 13 or 13q deletion
17p deletion or loss of 17p due to unbalanced translocation
Isochromosome 17q
idic(X)(q13)
Defining somatic mutations
ASXL1
BCOR
EZH2
SF3B1
SRSF2
STAG2
U2AF1
ZRSR2

Summary Box:

- AML is arranged into two families: AML with *defining genetic abnormalities* and AML *defined by differentiation*. AML, NOS is no longer applicable.
- Most AML with defining genetic abnormalities may be diagnosed with <20% blasts.
- AML-MR replaces the former term AML "with myelodysplasia-related changes", and its diagnostic criteria are updated. AML transformation of MDS and MDS/MPN continues to be defined under AML-MR in view of the broader unifying biologic features.
- AML with rare fusions are incorporated as subtypes under AML with *other defined genetic alterations*.
- AML with somatic *RUNX1* mutation is not recognized as a distinct disease type due to lack of sufficient unifying characteristics.