DIAK KLINIKUM
Landkreis Schwäbisch Hall

Indikation zur allogenen SZT bei AML und MDS

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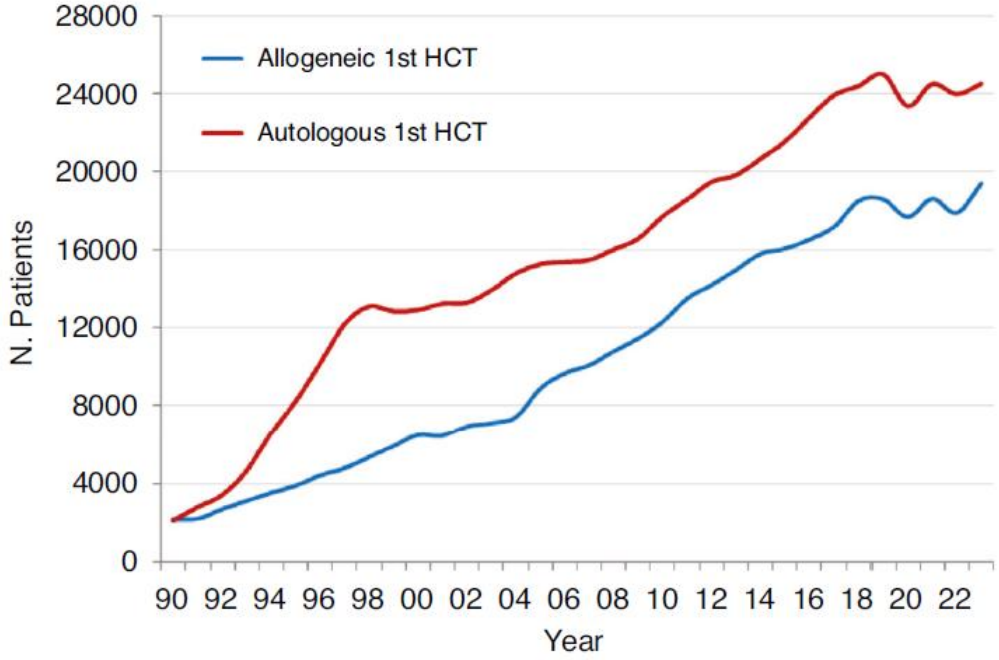
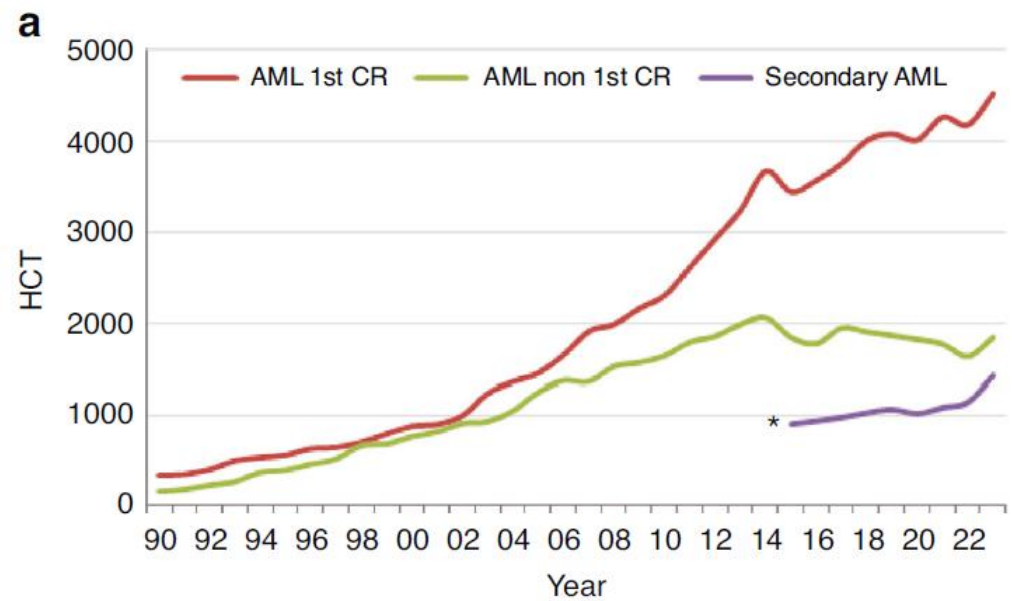
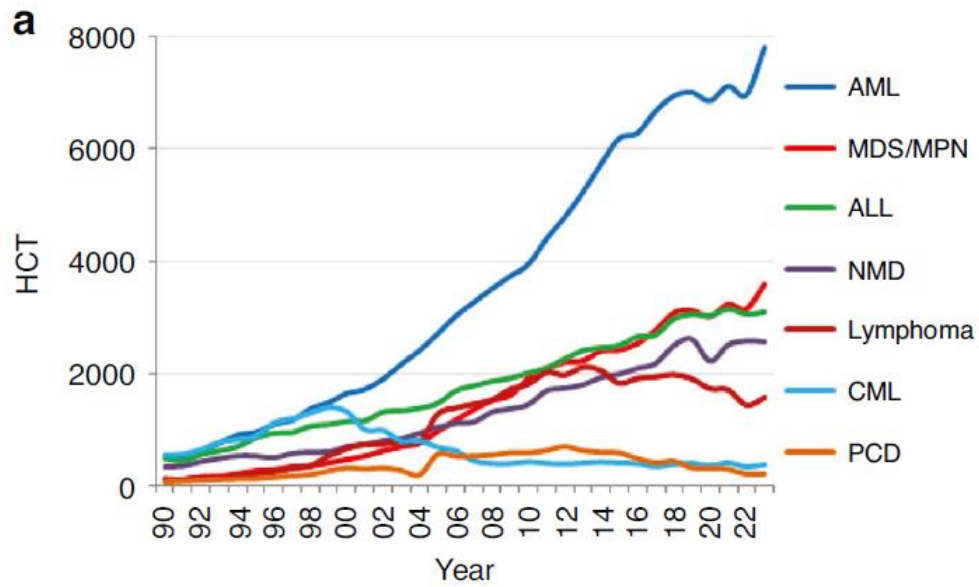
Offenlegung potentieller Interessenkonflikte

- Vortragshonorare: AbbVie, Servier, Novartis
- Kongresskosten: Sanofi-Aventis, Sobi





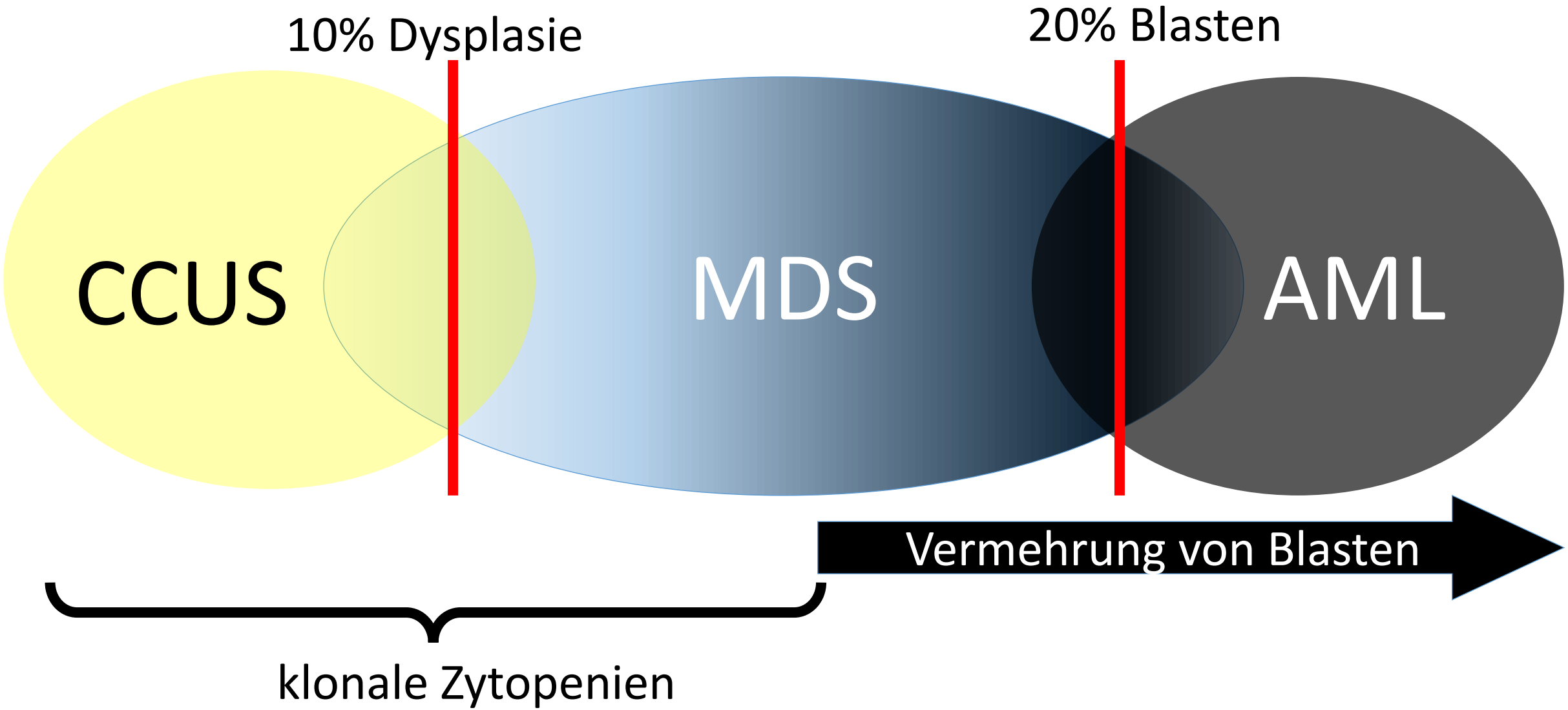


The 2023 EBMT report on hematopoietic cell transplantation and cellular therapies. Increased use of allogeneic HCT for myeloid malignancies and of CAR-T at the expense of autologous HCT

Jakob R. Passweg[1], Helen Baldomero[1✉], Marina Atlija[2], Iliana Kleovoulou[2], Aleksandra Witaszek[2], Tobias Alexander[3], Emanuele Angelucci[4], Dina Averbuch[5], Ali Bazarbachi[6], Fabio Ciceri[7], Raffaella Greco[7], Mette D. Hazenberg[8,9], Krzysztof Kalwak[10], Donal P. McLornan[11], Bénédicte Neven[12], Zinaida Perić[13], Antonio M. Risitano[14], Annalisa Ruggeri[7], Isabel Sánchez-Ortega[15], John A. Snowden[16] and Anna Sureda[17]

Diagnosis

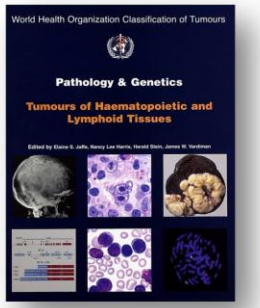
Die Grenzen MDS-AML



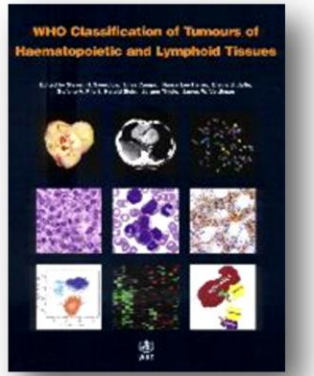
WHO – ICC: nur 28 Jahre nach REAL

1832	Hodgkin beschreibt die nach ihm benannte Krankheit				
1925/27	Brill and Symmers beschreiben das follikuläre Lymphoma				
1958	Burkitt beschreibt das nach ihm benannte Lymphom				
1962–1966	Entdeckung der blastischen Transformation von Lymphozyten und Existenz von B-Zellen und T-Zellen				
1966	Rappaports Klassifikation				
1974	Kiel (Lennert, Stein Kaiserling)	Lukes & Collins	B.N.L.I.*1	Dorfmann	
1976					W.H.O.
1982	Working Formulation NCI-Study*2				
1985		ALCL*3 Stein et al.			
1986			MALT-L*4 (Isaacson & Wright)		
1988	Kiel aktualisiert				
1994	R.E.A.L.-Klassifikation*5 Internationaler Konsensus				
1998	WHO-Konsensus-Klassifikation				

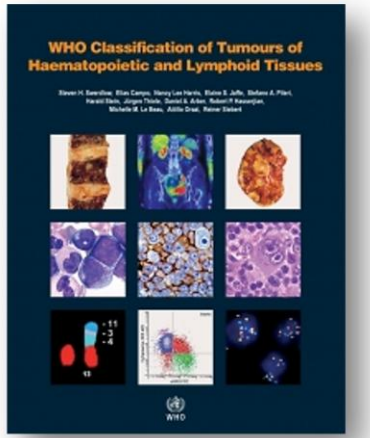
Stein et al. 1999



2001



2008



2017

blood Special Report

International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data

Leukemia www.nature.com/leu

REVIEW ARTICLE OPEN

The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms

AML Classification - ICC

ICC AML

AML with recurrent genetic abnormalities (requiring ≥10% blasts in BM or PB)[a]
• APL with t(15;17)(q24.1;q21.2)/*PML*::*RARA*[b]
• AML with t(8;21)(q22;q22.1)/*RUNX1*::*RUNX1T1*
• AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB*::*MYH11*
• AML with t(9;11)(p21.3;q23.3)/*MLLT3*::*KMT2A*[b]
• AML with t(6;9)(p22.3;q34.1)/*DEK*::*NUP214*
• AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*, *MECOM(EVI1)*[b]
• AML with other rare recurring translocations
• AML with mutated *NPM1*
• AML with in-frame bZIP mutated *CEBPA*[c]
• AML with t(9;22)(q34.1;q11.2)/*BCR*::*ABL1*[a]

Categories designated AML (if ≥20% blasts in BM or PB) or MDS/AML (if 10-19% blasts in BM or PB)
• AML with mutated *TP53*[d]
• AML with myelodysplasia-related gene mutations Defined by mutations in *ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1*, or *ZRSR2*
• AML with myelodysplasia-related cytogenetic abnormalities[e]
• AML not otherwise specified (NOS)

[a] Bone marrow or peripheral blood blast count of ≥10% required, except for AML with t(9;22)(q34.1;q11.2); *BCR*::*ABL1*.
[b] Variant rearrangements involving *RARA*, *KMT2A*, or *MECOM* should be recorded accordingly.
[c] AML with in-frame mutation in the bZIP domain of the CEBPA gene, either monoallelic or biallelic.
[d] The presence of a pathogenic somatic *TP53* mutation (at a variant allele fraction of at least 10%, with or without loss of the wild-type TP53 allele) defines the entity AML with mutated *TP53*.
[e] Cytogenetic abnormalities sufficient for the diagnosis of AML with MDS-related cytogenetic abnormalities and the absence of other AML-defining disease categories.
- Complex karyotype: ≥3 unrelated chromosome abnormalities in the absence of other class-defining recurring genetic abnormalities.
- Unbalanced clonal 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)

Major changes

- Changes concerning **blast thresholds** defining AML
  - **≥10% blasts** → AML with recurrent genetic abnormalities
  - **10-19% blasts** → other categories → MDS/AML (genetic and clinical continuum
  - **≥20% blasts** → AML
- Introduction of new **genetically defined entities**
  - AML with mutated TP53
  - AML with myelodysplasia-related gene mutations (high association with sAML after prior hematologic neoplasms)
  - AML with myelodysplasia-related cytogenetic abnormalities
- **Pre-existing AML** in medical history
  - MDS or MDS/MPN no seperate categories but rather classified as „qualifiers“

AML, acute myeloid leukaemia; ICC, International Consensus Classification. IDH, isocitrate dehydrogenase.
Weinberg OK, et al. Virchows Arch. 2023;482(1):27-37. doi:10.1007/s00428-022-03430-4.

AML Risk Classification - ELN

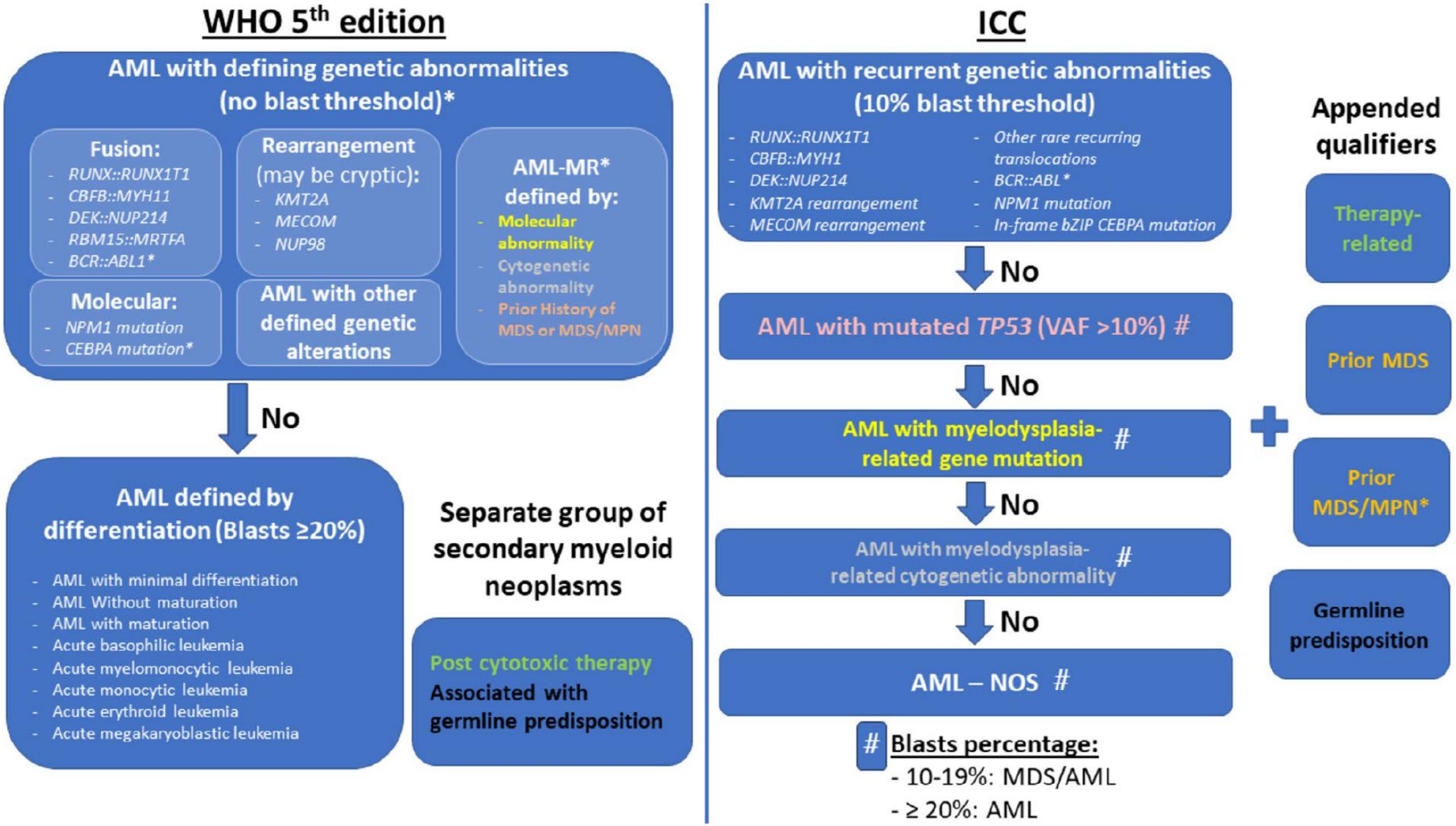
ELN risk classification 2022

Risk Category	Genetic Abnormality
Favorable	• t(8;21)(q22;q22.1)/*RUNX1*::*RUNX1T1* • inv(16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB*::*MYH11* • Mutated *NPM1*[a] without *FLT3*-ITD • bZIP in-frame mutated *CEBPA*
Intermediate	• Mutated *NPM1*[a] with *FLT3*-ITD • Wild-type *NPM1* with *FLT3*-ITD • t(9;11)(p21.3;q23.3)/*MLLT3*::*KMT2A* • Cytogenetic and/or molecular abnormalities not classified as favorable or adverse
Adverse	• t(6;9)(p23;q34.1)/*DEK*::*NUP214* • t(v;11q23.3)/*KMT2A*-rearranged • t(9;22)(q34.1;q11.2)/*BCR*::*ABL1* • t(8;16)(p11;p13)/*KAT6A*::*CREBBP* • inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*,*MECOM(EVI1)* • t(3q26.2;v)/*MECOM*(*EVI1*)-rearranged • -5 or del(5q); -7; -17/abn(17p) • Complex karyotype, monosomal karyotype • Mutated *ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1*, or *ZRSR2* • Mutated *TP53*

Major changes

- **AML with FLT3-ITD now categorized as intermediate risk**
  - irrespective of allelic ratio and NPM1 status
  - Impacxt of midostaurin-based therapy
- **Prognostic impact of myelodysplasia-related gene mutations or s-AML → adverse**
  - ASXL1, BCOR, EZH2, RUNX1,SF3B1, SRSF2, STAG2, U2AF1, ZRSR2
- **Prognostic impact of CEBPA mutation, now → favorable**
  - $CEBPA^{bZIP\text{-}inf}$ shows significantly superior outcome

AML, acute myeloid leukaemia; ELN, European LeukemiaNet. IDH, isocitrate dehydrogenase.
Döhner H, et al. Blood. 2022; doi: 10.1182/blood.2022016867 [ePub ahead of print]..


WHO 5th edition
AML with defining genetic abnormalities (no blast threshold)*
Fusion:
- RUNX::RUNX1T1
- CBFB::MYH11
- DEK::NUP214
- RBM15::MRTFA
- BCR::ABL1*
Rearrangement (may be cryptic):
- KMT2A
- MECOM
- NUP98
AML-MR* defined by:
- Molecular abnormality
- Cytogenetic abnormality
- Prior History of MDS or MDS/MPN
Molecular:
- NPM1 mutation
- CEBPA mutation*
AML with other defined genetic alterations
No
AML defined by differentiation (Blasts ≥20%)
- AML with minimal differentiation
- AML Without maturation
- AML with maturation
- Acute basophilic leukemia
- Acute myelomonocytic leukemia
- Acute monocytic leukemia
- Acute erythroid leukemia
- Acute megakaryoblastic leukemia
Separate group of secondary myeloid neoplasms
Post cytotoxic therapy
Associated with germline predisposition
ICC
AML with recurrent genetic abnormalities (10% blast threshold)
- RUNX::RUNX1T1
- CBFB::MYH1
- DEK::NUP214
- KMT2A rearrangement
- MECOM rearrangement
- Other rare recurring translocations
- BCR::ABL*
- NPM1 mutation
- In-frame bZIP CEBPA mutation
No
AML with mutated TP53 (VAF >10%) #
No
AML with myelodysplasia-related gene mutation #
No
AML with myelodysplasia-related cytogenetic abnormality #
No
AML – NOS #
Blasts percentage:
- 10-19%: MDS/AML
- ≥ 20%: AML
Appended qualifiers
Therapy-related
Prior MDS
Prior MDS/MPN*
Germline predisposition

MRD

Approaches for the detection of MRD in patients with AL.

Technique	MFC	RQ-PCR and ddPCR	NGS	sDNAseq
Target	Aberrant immunophenotype	Ig/TCR; fusion genes; gene mutation	Ig/TCR; gene mutation	Gene mutation
Specimen	Fresh viable cells obtained from PB, BM, or tissues	DNA or RNA	DNA	DNA
Applicability	AML: >90% ALL: >95%	AML: Fusion genes and mutation: 40%–50% ALL: Ig/TCR >90%; fusion genes: 35%–45%	AML: nearly for all patients ALL: >90%	AML: nearly for all patients
Sensitivity	AML: 10^{-4} (LAIP and DfN based); 10^{-5} (LSC-based) ALL: 10^{-5}	AML: 10^{-4}–10^{-5} ALL: 10^{-4}–10^{-5}	AML: 10^{-2}–10^{-6} ALL: 10^{-6}	AML: 10^{-2}–10^{-3} ALL: NA
Routine use	Yes	Yes	No (clinical trial)	No (in research)
Standardization	Limited	Good, such as Ig/TCR and BCR/ABL	Good	No
Advantages	• High sensitivity (for NGF) • No access to diagnostic sample • Relatively inexpensive • Requires no individual optimization • Fast (within 24 h)	• High sensitivity and specificity • Patient-specific methods • Easy-to-use • Broad applicability	• Very high sensitivity • Potential to track small subclones and clone evolution • Relatively fast • Broad applicability	Broad applicability Accurately resolve clonal architectures and identify clonal origins of drug resistance Determine specific alterations in immunphenotype depending on clonality
Disadvantages	• Fresh samples are needed • Confounders, such as phenotype shift and hematogone during marrow recovery • Skilled experts are required	• Expensive • Might miss small subclones or clonal evolution • Time-consuming • Skilled experts are required • Slow • Need diagnostic sample	• Expensive • Highly specialized bioinformatics approaches and expertise are needed • Need diagnostic sample • Few experienced laboratory • Confounders, such as CHIP	Expensive and low throughout Highly specialized bioinformatics approaches and experts are needed Low sensitivity and need diagnostic sample Few experienced laboratory Small mutation panels and allelic dropout

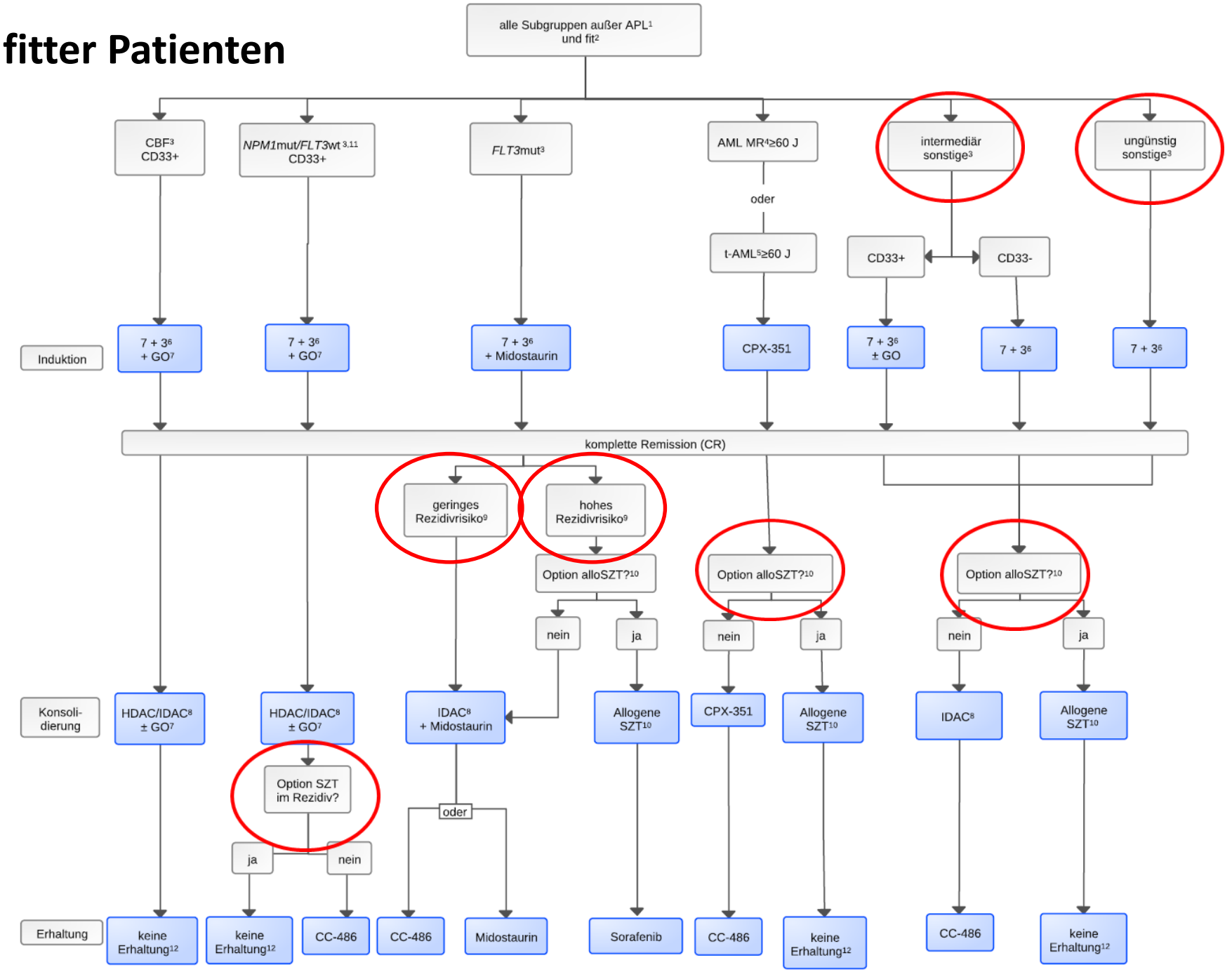
REVIEW ARTICLE
Blood Science
OPEN

Stem cell transplantation indications for patients with acute leukemia determined by measurable residual disease: what we know and what we do not know

Xiao-Su Zhao[a], Xiao-Tong Chen[a], Ying-Jun Chang[a,*]

Indication allo-HSCT

Therapie fitter Patienten



Onkopedia 2023

Indications for haematopoietic cell transplantation for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2022

John A. Snowden[1✉], Isabel Sánchez-Ortega[2], Selim Corbacioglu[3], Grzegorz W. Basak[4], Christian Chabannon[5], Rafael de la Camara[6], Harry Dolstra[7], Rafael F. Duarte[8], Bertram Glass[9], Raffaella Greco[10], Arjan C. Lankester[11], Mohamad Mohty[12], Bénédicte Neven[13], Régis Peffault de Latour[14], Paolo Pedrazzoli[15], Zinaida Peric[16], Ibrahim Yakoub-Agha[17], Anna Sureda[18], Nicolaus Kröger[19] for the European Society for Blood and Marrow Transplantation (EBMT)

Table 2. Proposed classification of transplant indications for adults—2022.

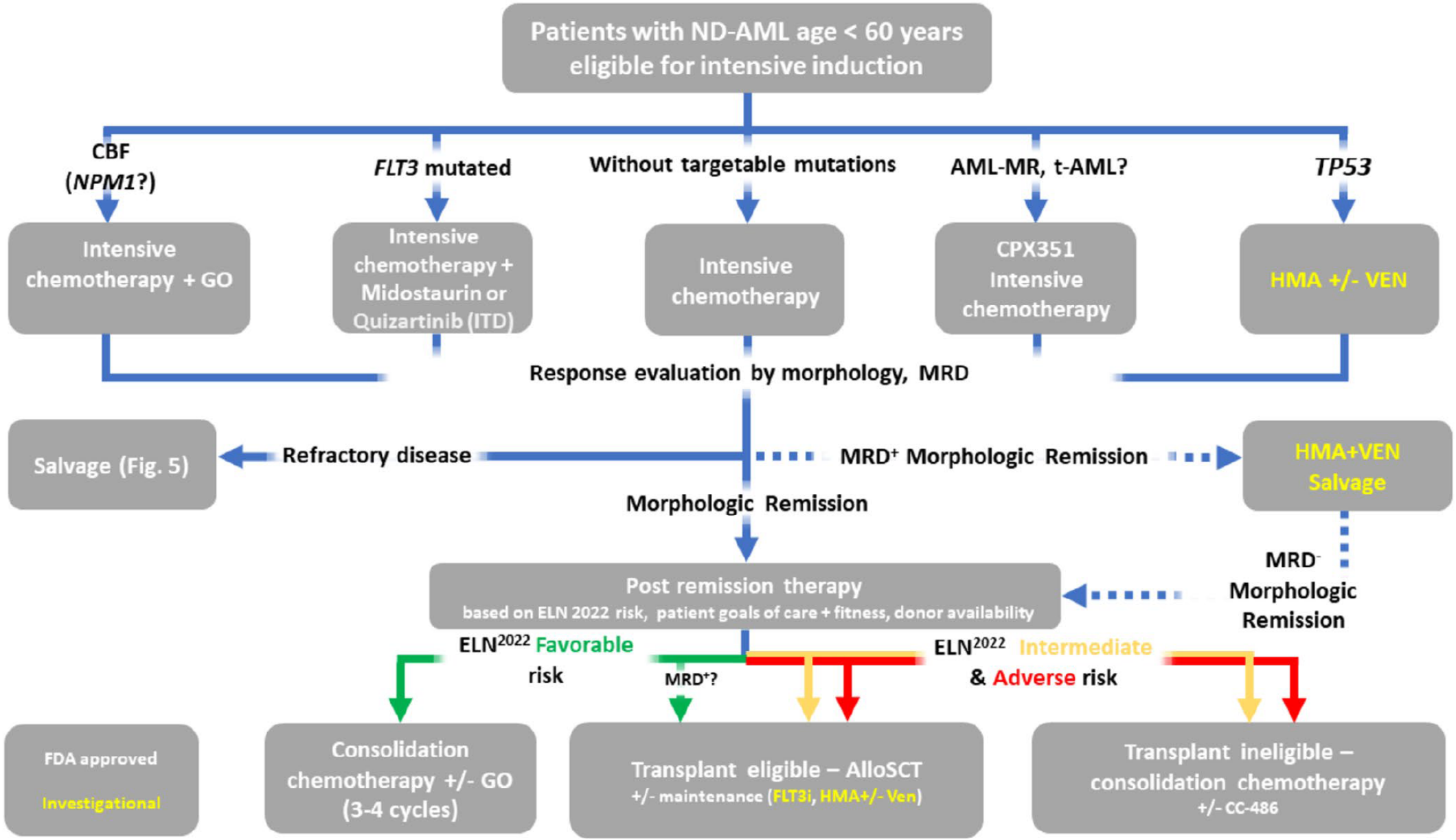
Disease	Disease status	MSD allo	MUD allo	MMAD allo	Auto	CAR-T
Haematological malignancies						
AML[a]	CR1 (favourable risk and MRD–)[b]	GNR/II	GNR/II	GNR/II	CO/I	
	CR1 (favourable risk and MRD+)[b]	S/II	CO/II	CO/II	GNR/II	
	CR1 (intermediate risk)[b]	S/II	CO/II	CO/II	CO/I	
	CR1 (adverse risk)[b]	S/II	S/II	S/II	GNR/I	
	CR2	S/II	S/II	S/II	CO/II	
	APL Molecular CR2	S/II	CO/II	GNR/III	S/II	
	Relapse or refractory	CO/II	CO/II	CO/II	GNR/III	

ELN 2022 risk score

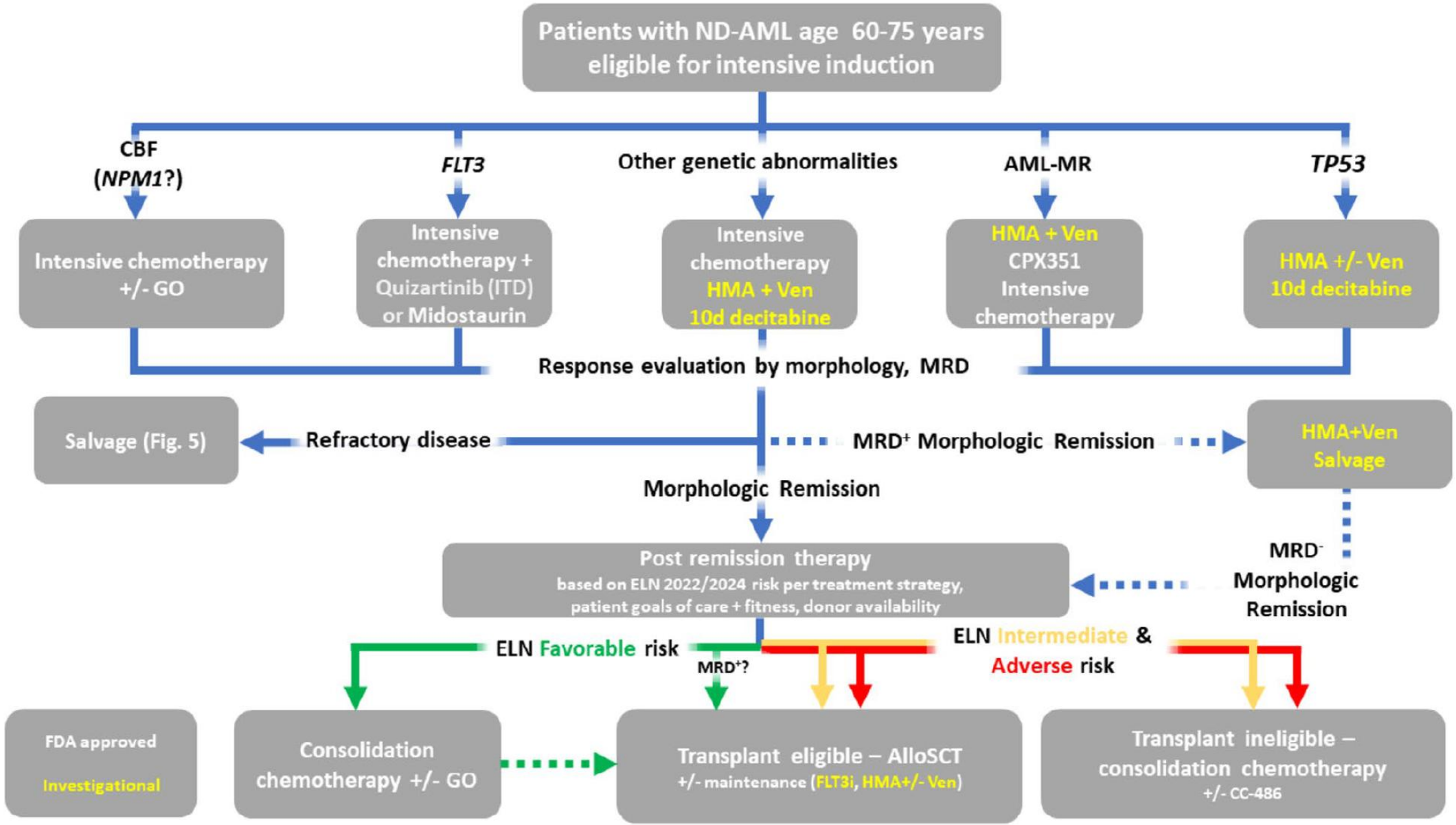
Risk category	Genetic abnormality
Favorable	t(8;21)(q22;q22.1)/*RUNX1*::*RUNX1T1*[a]
	inv (16)(p13.1q22) or t(16;16)(p13.1;q22)/*CBFB*::*MYH11*[a]
	Mutated *NPM1* without *FLT3*-ITD[b]
	bZIP in-frame mutated *CEBPA*[c]
Intermediate	*FLT3*-ITD (irrespective of allelic ratio or *NPM1* mutation)
	t(9;11)(p21.3;q23.3)/*MLLT3*::*KMT2A*[d]
	Cytogenetic and/or molecular abnormalities not classified as favorable or adverse
Adverse	t(6;9)(p23;q34.1)/*DEK*::*NUP214*
	t(v;11q23.3)/*KMT2A* rearranged (excluding *KMT2A-PTD*)
	t(9;22)(q34.1;q11.2)/*BCR*::*ABL1*
	(8;16)(p11;p13)/*KAT6A*::*CREBBP*
	inv (3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)/*GATA2*, *MECOM*(*EVI1*)
	t(3q26.2;v)/*MECOM*(*EVI1*)-rearranged
	−5 or del(5q); −7; −17/abn(17p)
	Complex karyotype (change in definition)[e]; Monosomal Karyotype[f]
	Mutated *ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1, or ZRSR2*[g]
	Mutated *TP53* (variant allele frequency ≥ 10%)

ELN 2024 less-intensive chemotherapy

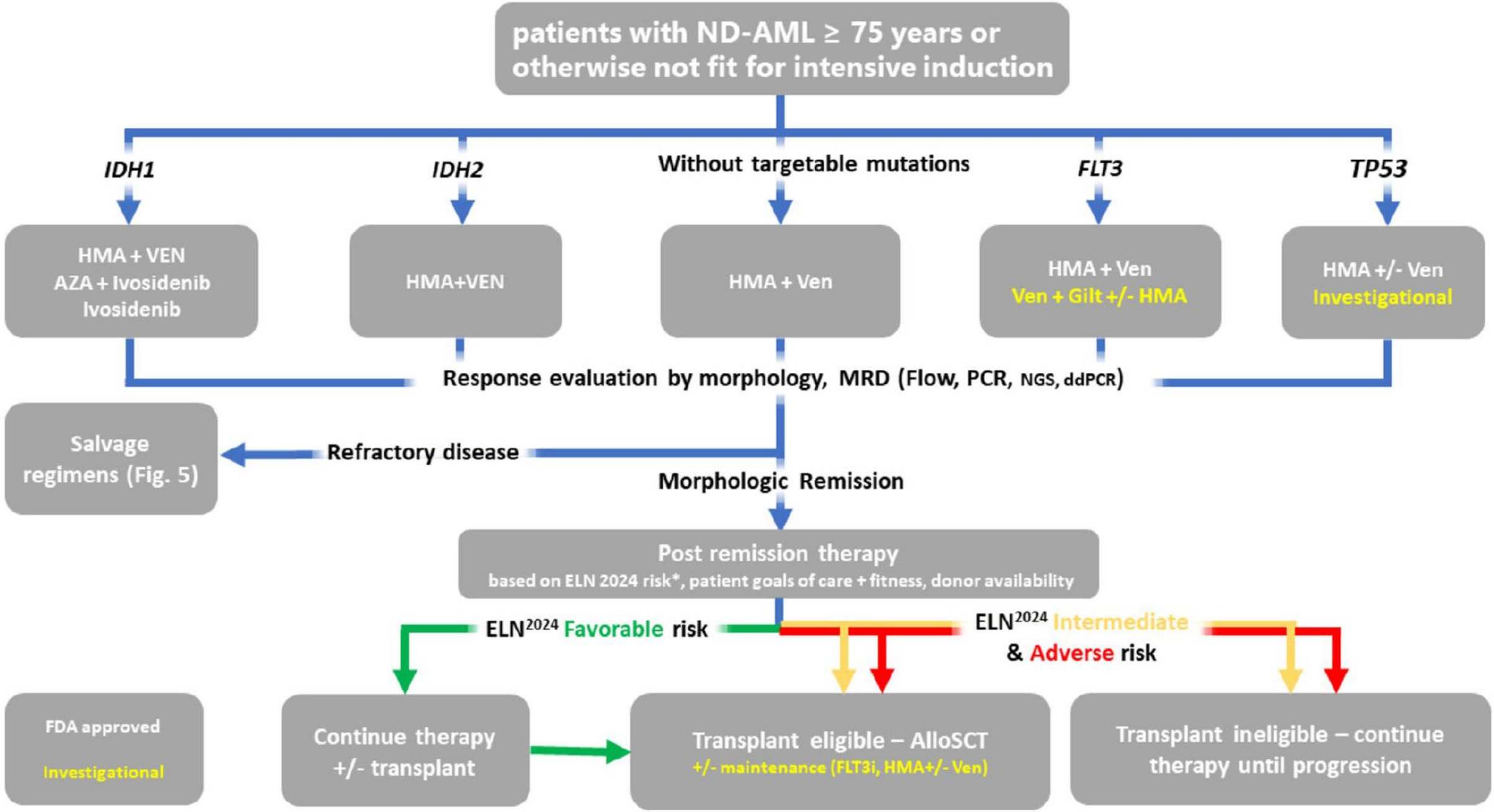
Risk category	Genetic abnormality
Favorable	Mutated *NPM1* (*FLT3*-ITD^{wt}, *NRAS*^{wt}, *KRAS*^{wt}, *TP53*^{wt})
	Mutated *IDH2* (*FLT3*-ITD^{wt}, *NRAS*^{wt}, *KRAS*^{wt}, *TP53*^{wt})
	Mutated *IDH1*[a] (*TP53*^{wt})
	Mutated *DDX41*[b]
	Other cytogenetic and/or molecular abnormalities[c] (*FLT3*-ITD^{wt}, *NRAS*^{wt}, *KRAS*^{wt}, *TP53*^{wt})
Intermediate	Other cytogenetic and/or molecular abnormalities[c] (*FLT3*-ITD^{pos} *and/or* *NRAS*^{mut}, and/or *KRAS*^{mut}, *TP53*^{wt})
Adverse	Mutated *TP53*



Shimony et al AJH 2025



Shimony et al AJH 2025



Shimony et al AJH 2025

MDS

Indications for haematopoietic cell transplantation for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2022

John A. Snowden[1✉], Isabel Sánchez-Ortega[2], Selim Corbacioglu[3], Grzegorz W. Basak[4], Christian Chabannon[5], Rafael de la Camara[6], Harry Dolstra[7], Rafael F. Duarte[8], Bertram Glass[9], Raffaella Greco[10], Arjan C. Lankester[11], Mohamad Mohty[12], Bénédicte Neven[13], Régis Peffault de Latour[14], Paolo Pedrazzoli[15], Zinaida Peric[16], Ibrahim Yakoub-Agha[17], Anna Sureda[18], Nicolaus Kröger[19] for the European Society for Blood and Marrow Transplantation (EBMT)

MDS	Very low and low-risk (IPSS-R)	CO/II	CO/II	CO/II	GNR/III
	Intermediate-risk without additional factors[c] (IPSS-R)	CO/II	CO/II	CO/II	CO/II
	Intermediate-risk with additional factors[c] (IPSS-R)	S/II	S/II	S/II	GNR/III
	High-, very high-risk (IPSS-R)	S/II	S/II	S/II	
	sAML in CR1 or CR2	S/II	S/II		

Clinical-genomic profiling of MDS to inform allo-HCT: recommendations from an international panel on behalf of the EBMT

Carmelo Gurnari,[1,2] Marie Robin,[3] Lionel Adès,[3] Mahmoud Aljurf,[4] Antonio Almeida,[5] Fernando Barroso Duarte,[6] Elsa Bernard,[7] Corey Cutler,[8] Matteo Giovanni Della Porta,[9] Theo De Witte,[10] Amy DeZern,[11] Joanna Drozd-Sokolowska,[12] Eric Duncavage,[13] Pierre Fenaux,[3] Nico Gagelmann,[14] Guillermo Garcia-Manero,[15] Claudia Haferlach,[16] Torsten Haferlach,[16] Robert Hasserjian,[17] Eva Hellström-Lindberg,[18] Meagan Jacoby,[19] Austin Kulasekararaj,[20] R. Coleman Lindsley,[8] Jaroslaw P. Maciejewski,[2] Hideki Makishima,[21] Luca Malcovati,[22] Moshe Mittelman,[23] Anders E. Myhre,[24] Seishi Ogawa,[25] Francesco Onida,[26] Elli Papaemmanuil,[27] Jakob Passweg,[28] Uwe Platzbecker,[29,30] Lisa Pleyer,[31] Kavita Raj,[32] Valeria Santini,[33] Anna Sureda,[34] Magnus Tobiasson,[18] Maria Teresa Voso,[1] Ibrahim Yakoub-Agha,[35] Amer Zeidan,[36] Matthew Walter,[19] Nicolaus Kröger,[14] Donal P. McLornan,[32,*] and Mario Cazzola[22,*]

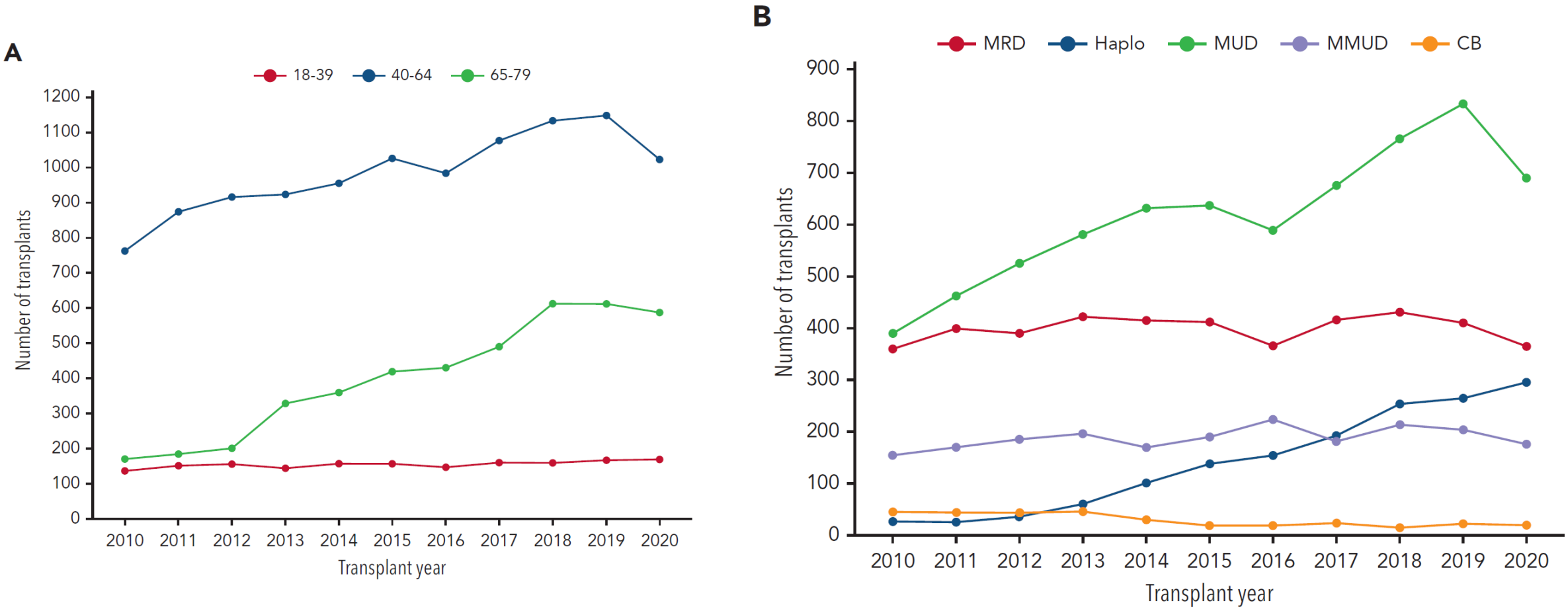


Table 1. MDS entities according to WHO-HAEM5 2022 and ICC 2022 classifications

WHO-HAEM5 2022	ICC 2022
MDS with defining genetic abnormalities	
MDS with low blasts and isolated 5q deletion	MDS with del(5q)
MDS with low blasts and *SF3B1* mutation*	MDS with mutated *SF3B1*
MDS with biallelic *TP53* inactivation	MDS with mutated *TP53*
MDS, morphologically defined	
MDS with low blasts (<5% blasts; dysplasia is a prerequisite)	
MDS with low blasts and single-lineage dysplasia (MDS-LB-SLD)	MDS, NOS without dysplasia
MDS with low blasts and multilineage dysplasia (MDS-LB-MLD)	MDS, NOS with single lineage
MDS with ring sideroblasts (MDS-RS)	MDS, NOS with multilineage dysplasia
MDS, hypoplastic (<5% blasts)	
MDS with increased blasts (5% to <20% blasts)	
MDS-IB1 (5% to <10% blasts)	MDS with excess blasts (5% to <10% blasts)
MDS-IB2 (10% to <20% blasts)	MDS/AML (10% to <20% blasts)
MDS with fibrosis (5% to <20% blasts)	

Table 2. MDS entities defined by genetic abnormalities in the ICC and WHO-HAEM5

WHO-HAEM5	ICC	Implications of genomic profiling
MDS with low blasts and isolated 5q deletion BM blasts of <5% del(5q) alone or with 1 additional abnormality, except −7/del(7q) Any somatic mutation, except biallelic *TP53* inactivation	**MDS with del(5q)** BM blasts of <5% del(5q) alone or with 1 additional abnormality, except −7/del(7q) Any somatic mutation, except biallelic *TP53*	Genomic profiling is fundamental to diagnosis. Patients with biallelic inactivation of *TP53* have poor outcomes and are therefore classified as TP53-mutant MDS.
MDS with low blasts and *SF3B1* mutation BM blasts of <5% Absence of del(5q), −7, or complex karyotype *SF3B1* mutation, no biallelic *TP53*	**MDS with mutated *SF3B1*** BM blasts of <5% Absence of del(5q), −7/del(7q), abn3q26.2, or complex karyotype *SF3B1* mutation (VAF ≥10%), no biallelic *TP53* inactivation, no *RUNX1* mutation	Genomic profiling is fundamental to diagnosis (exclusion of biallelic inactivation of *TP53*) and important for prognosis. Patients with comutation patterns in other genes such as *BCOR*, *BCORL1*, *NRAS*, *RUNX1*, or *STAG2* have worse clinical outcomes.
MDS with biallelic *TP53* inactivation BM blasts of <20% Two or more *TP53* mutations, or one mutation with evidence of *TP53* copy number loss or cnLOH Usually complex karyotype	**MDS with mutated *TP53*** BM blasts of 0%-9% Biallelic *TP53* inactivation* or *TP53* mutation (VAF >10%) and complex karyotype often with loss of 17p† **MDS/AML with mutated *TP53*** BM blasts of 10%-19% Any somatic *TP53* mutation (VAF >10%)	This condition is associated with exceptionally poor clinical outcomes. The identification of a biallelic *TP53* inactivation requires the implementation of ad hoc copy number and LOH analysis.

Table 3. IPSS-M risk score, risk categories, and clinical outcomes

Risk category	IPSS-M score	Median leukemia-free survival (y)	Median OS (y)	AML transformation by 1 y (%)
Six-category risk schema				
Very low (14% of all patients)	Less than or equal to −1.5	9.7	10.6	0
Low (33%)	More than −1.5 to −0.5	5.9	6.0	1.7
Moderate low (11%)	More than −0.5 to 0	4.5	4.6	4.9
Moderate high (11%)	>0 to 0.5	2.3	2.8	9.5
High (14%)	>0.5 to 1.5	1.5	1.7	14.3
Very high (17%)	>1.5	0.7	1.0	28.2
Lower-risk vs higher-risk MDS				
Lower-risk MDS (58%)	≤0 (negative value)	6.0 (95% CI, 5.7-6.7)	6.3 (95% CI, 5.8-7.2)	2.0
Higher-risk MDS (42%)	>0 (positive value)	1.2 (95% CI, 1.1-1.3)	1.5 (95% CI, 1.4-1.6)	18.9

Table 4. Genetically derived subgroups of MDS that have been defined in the ad hoc study of the International Working Group for Prognosis in MDS

Molecular subgroup	Clinical features, outcomes, and disease-related eligibility for allogeneic transplantation
Morphological MDS with the absence of recurrent genetic events in myeloid genes	Good OS with low risk of leukemic transformation. Most patients are not transplant candidates. Patients with VEXAS and severe rheumatic disease may be considered.
SF3B1-mutant MDS	Indolent clinical course with low risk of leukemic transformation. Most of these patients are not transplant candidates.
ZRSR2-mutant MDS	Male patients with refractory macrocytic anemia, no excess blasts, and indolent clinical course. These patients are not transplant candidates.
MDS NOS	Mild phenotype and favorable outcomes in most patients. Most of these patients are not transplant candidates.
CCUS-like MDS	Mild phenotype and favorable outcomes in most patients. Most of these patients are not transplant candidates.
MDS del(5q)	Well-established MDS subtype whose outcomes are determined by comutation patterns. Patients with comutation in *SF3B1*, *RUNX1*, or *TP53* should be considered for allogeneic transplantation.
MDS with biallelic *TET2* mutation	Older patients, monocytosis overlapping with CMML. Indolent clinical course in most patients. Most of these patients are not transplant candidates.
DDX41-mutant MDS	Cytopenia with hypoplastic bone marrow with excess blasts. Disorder with high risk of leukemic evolution, but favorable prognosis compared with other MDS with excess blasts. Genomic diagnosis is crucial in the transplantation setting for donor selection and prevention of acute GVHD with PTCy. All patients are potential transplant candidates.
U2AF1-mutant MDS *SRSF2*-mutant MDS *BCOR/L1*-mutant MDS *IDH-STAG2*-mutant MDS MDS with der(1;7) *–7/SETBP1*-mutant MDS *EZH2-ASXL1*-mutant MDS	Aggressive diseases with poor survival and high risk of leukemic transformation. Although specific agents targeting the driver mutation are being developed (such as spliceosome inhibitors, ivosidenib, or enasidenib). These patients are potential transplant candidates.
AML-like MDS	Biologically this condition resembles AML, except for <20% bone marrow blasts. All patients are potential transplant candidates.
TP53-complex MDS	Extremely aggressive disease with a median survival <1 year. Poorly responsive to any currently available treatment. High relapse rate after transplantation. All patients are potential transplant candidates, preferably within a clinical trial.

BOX 1

Key recommendations

- The patient's eligibility for allogeneic transplantation should be assessed at the time of diagnosis of MDS.
- Disease- and patient-related risk factors, as well as donor availability, and the patient's values and wishes, should be considered when assessing eligibility for transplantation.
- Evaluation of the MDS risk, requires the calculation of the IPSS-M score, based on conventional cytogenetics, genomic profiling, and *TP53* allelic state. Additionally, germ line testing is needed for identifying genetic predisposition to MDS.
- All patients with higher-risk MDS (according to IPSS-M) are potential candidates for immediate transplantation. A subset of patients with lower risk MDS may also benefit from this procedure at an earlier stage of the disease.
- Assessment of patient-related risk factors should consider performance status, comorbidities, and frailty.
- Although accurate assessment of biological age has made allogeneic transplantation a feasible option for patients with MDS up to the eighth decade of life, this procedure should generally be avoided in patients aged >80 years.
- HLA-matched relatives, MUDs, and haploidentical donors can be used for patients with MDS undergoing allogeneic transplantation, with a preference for younger donors in the selection algorithm.
- The choice of intensity of the conditioning regimen must consider not only chronological age but also a comprehensive assessment of organ/system function and disease characteristics.
- Patients with MDS with blast excess (≥10%) may benefit from cytoreductive therapy before allogeneic transplantation, but results of ongoing clinical trials are needed for more definitive conclusions.
- Measurable residual disease assessment is recommended after allo-HCT regardless of MDS risk, but there is insufficient evidence to recommend prophylaxis or maintenance.
- Posttransplant therapeutic strategies for patients with measurable residual disease or relapsed patients include treatment with HMAs and DLI.

Timepoint

Single or Double Induction With 7 + 3 Containing Standard or High-Dose Daunorubicin for Newly Diagnosed AML: The Randomized DaunoDouble Trial by the Study Alliance Leukemia

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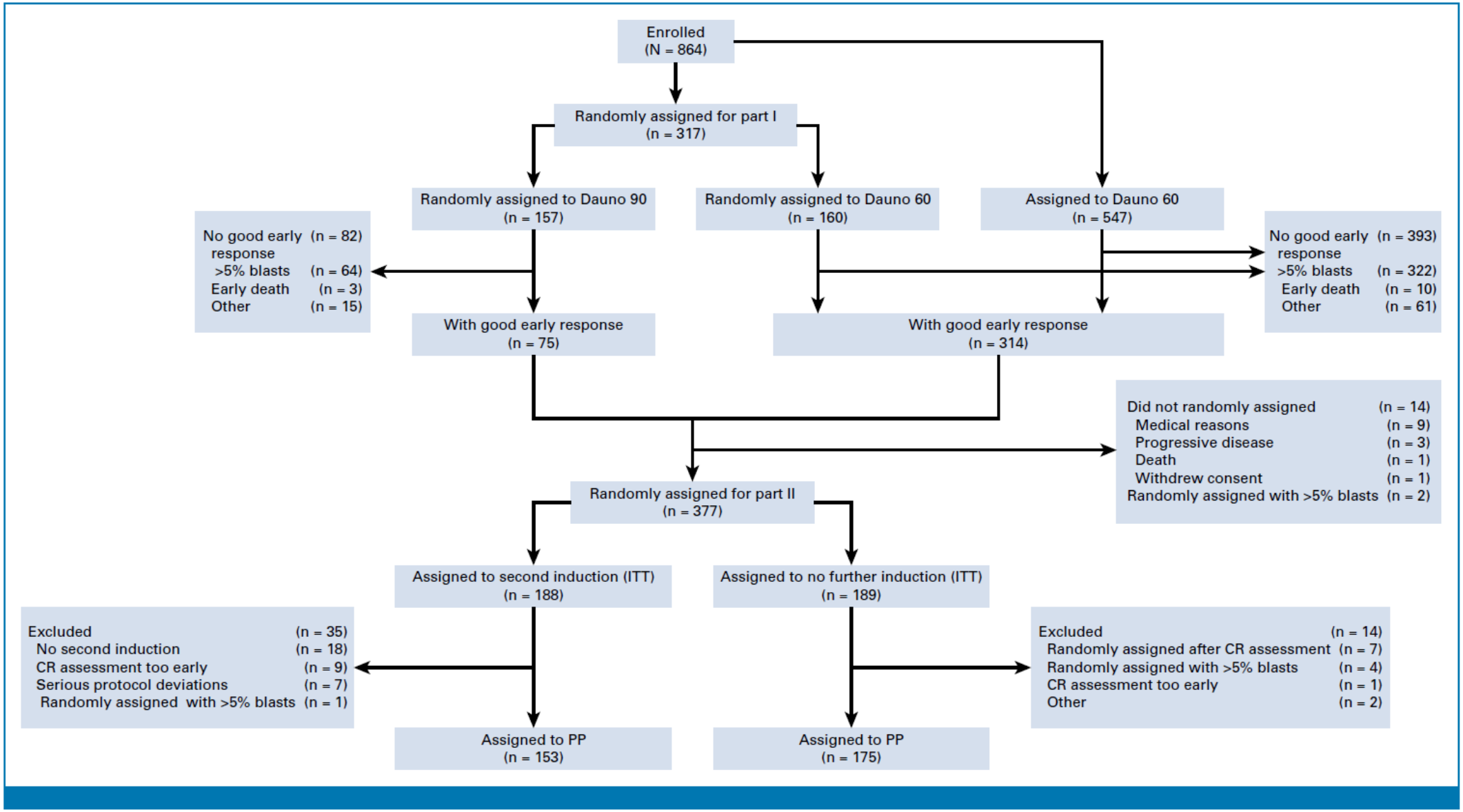
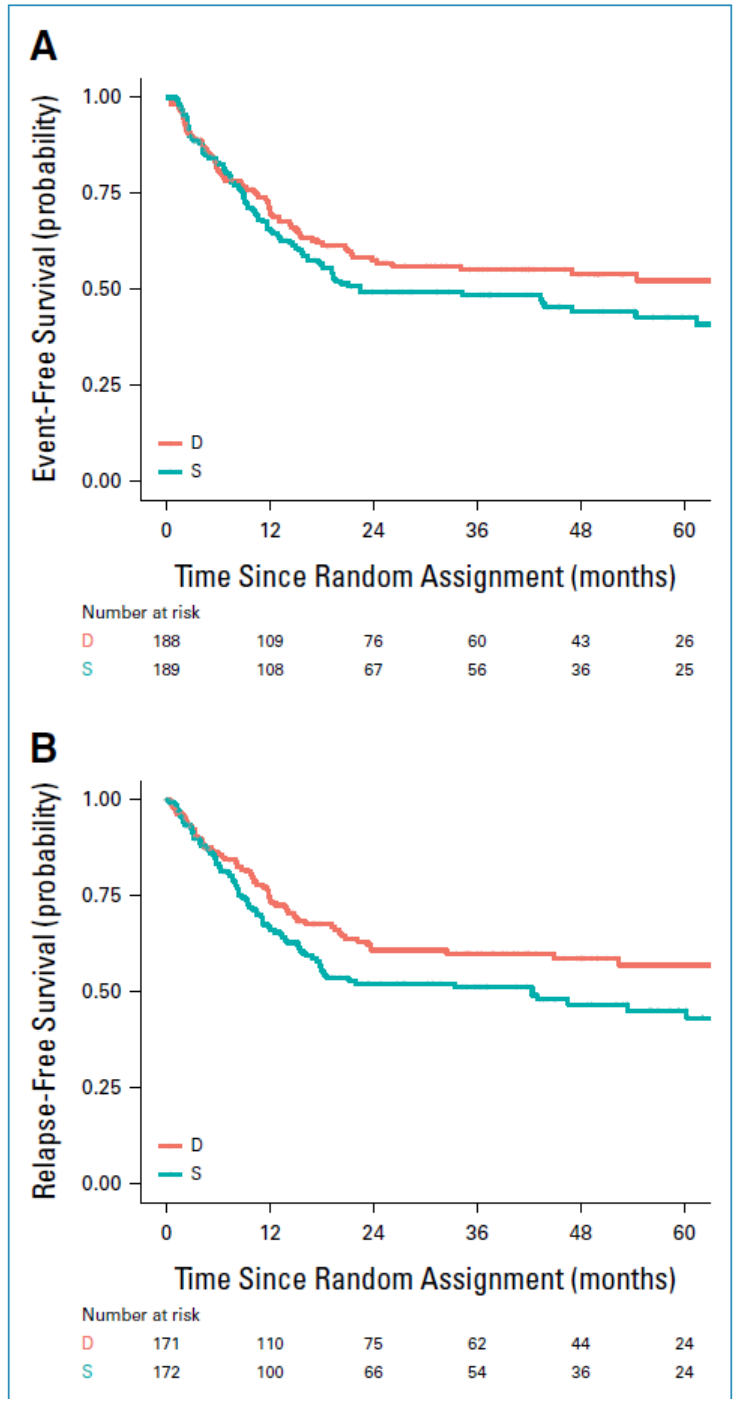
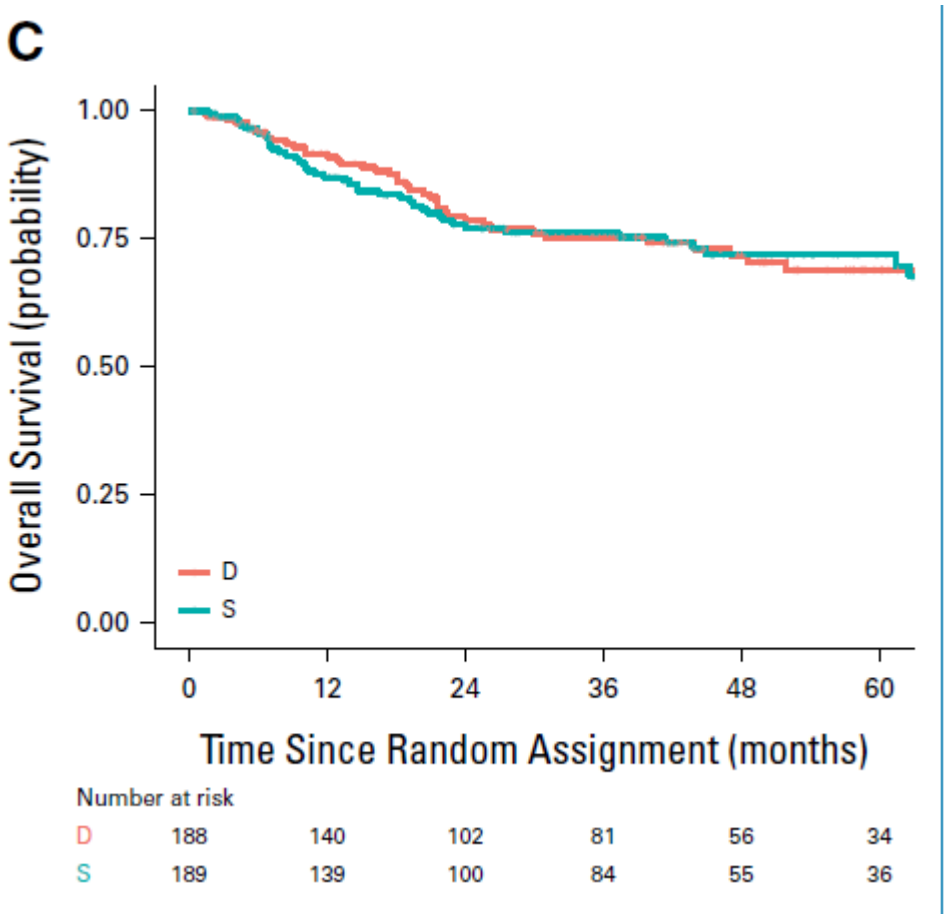


FIG 1. CONSORT diagram on random assignment and treatment. CR, complete remission; ITT, intent-to-treat principle in the full analysis set; PP, per-protocol analysis set.


A
Event-Free Survival (probability)
1.00
0.75
0.50
0.25
0.00
D
S
0
12
24
36
48
60
Time Since Random Assignment (months)
Number at risk
D 188 109 76 60 43 26
S 189 108 67 56 36 25
B
Relapse-Free Survival (probability)
1.00
0.75
0.50
0.25
0.00
D
S
0
12
24
36
48
60
Time Since Random Assignment (months)
Number at risk
D 171 110 75 62 44 24
S 172 100 66 54 36 24


C
Overall Survival (probability)
1.00
0.75
0.50
0.25
0.00
D
S
0
12
24
36
48
60
Time Since Random Assignment (months)
Number at risk
D 188 140 102 81 56 34
S 189 139 100 84 55 36

AML Summary fit

- Induction fit
- 7 +3 (5+2 ?)
- Study when possible
- FLT3+: + Midostaurin
- t-AML, AML-MRC: CPX-351
- CD33+: Gemtuzumab Ozogamicin bei CBF oder NPM1mut/FLT3wt
- Consolidation:
- Good: 3 Zyklus Chemo (Mitoxantron/Etopside. HD-Cytarabine bei CBF-AML)
- Bad: allo-HSCT
- Intermediate: allo-HSCT. donor availibilty ? MRD ?
- Maintenance
- CC-486 in CR (CAVE Zulassung)
- Post-allo: Sorafenib bei FLT3+
- Azacitidine/Venetoclax (prä-HSCT Persistenz). Decitabine (bei TP53) (CAVE Zulassung)
- ± DLI

AML Summary unfit

- Azacitidine/Venetoclax
- IDH1 Inhibitor/Azacitidine
- FLT3+: Midostaurin
- IDH2 Inhibitor (Cave Zulassung)
- LDAC
- LDAC + Glasdegib
- CC-486 in CR

Thank you for your attention