AML: classification, biology and prognosis

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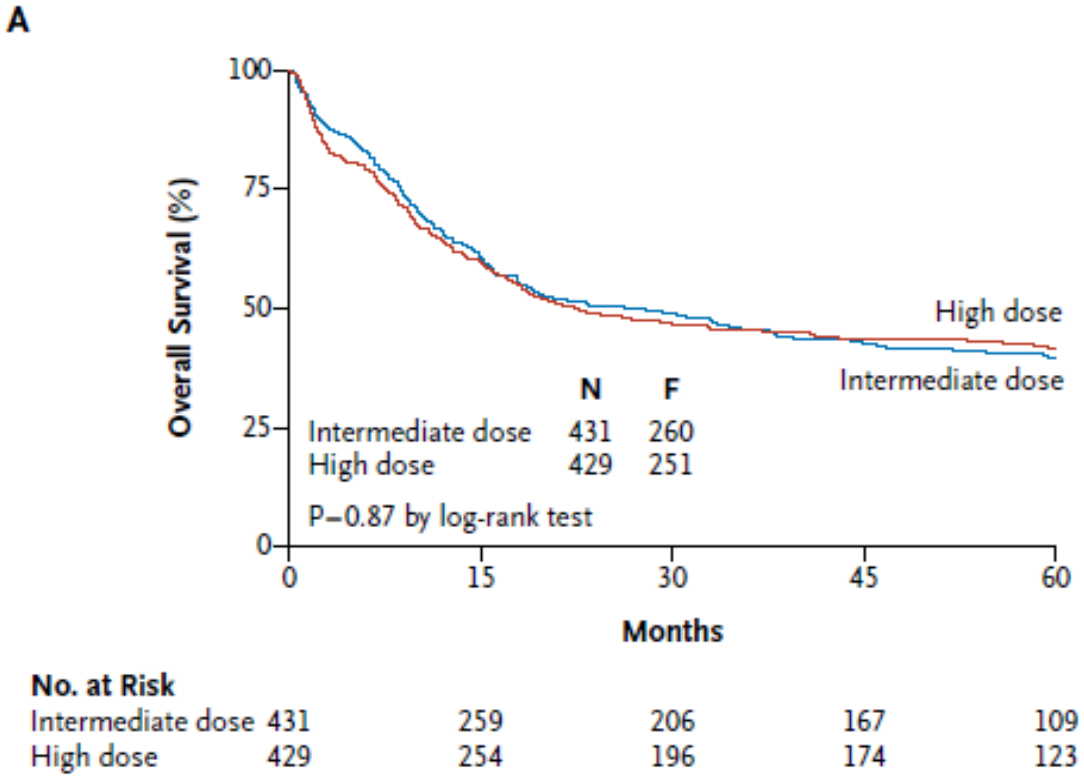
Ziekenhuis Netwerk Antwerpen

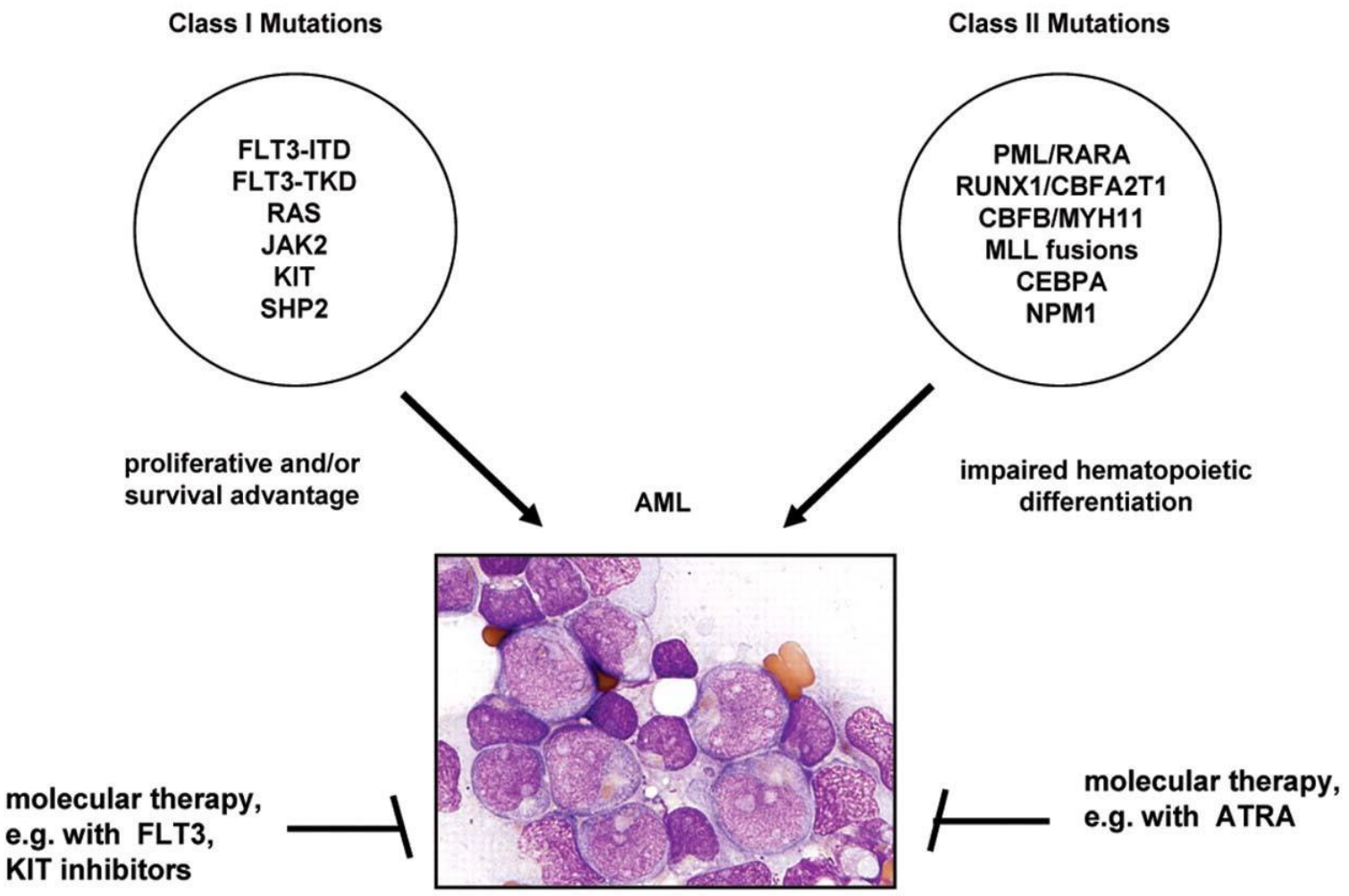
Acute myeloid leukemia

- Clonal expansion of undifferentiated myeloid precursors
- Impaired hematopoiesis and bone marrow failure
- Heterogeneous response to treatment and prognosis



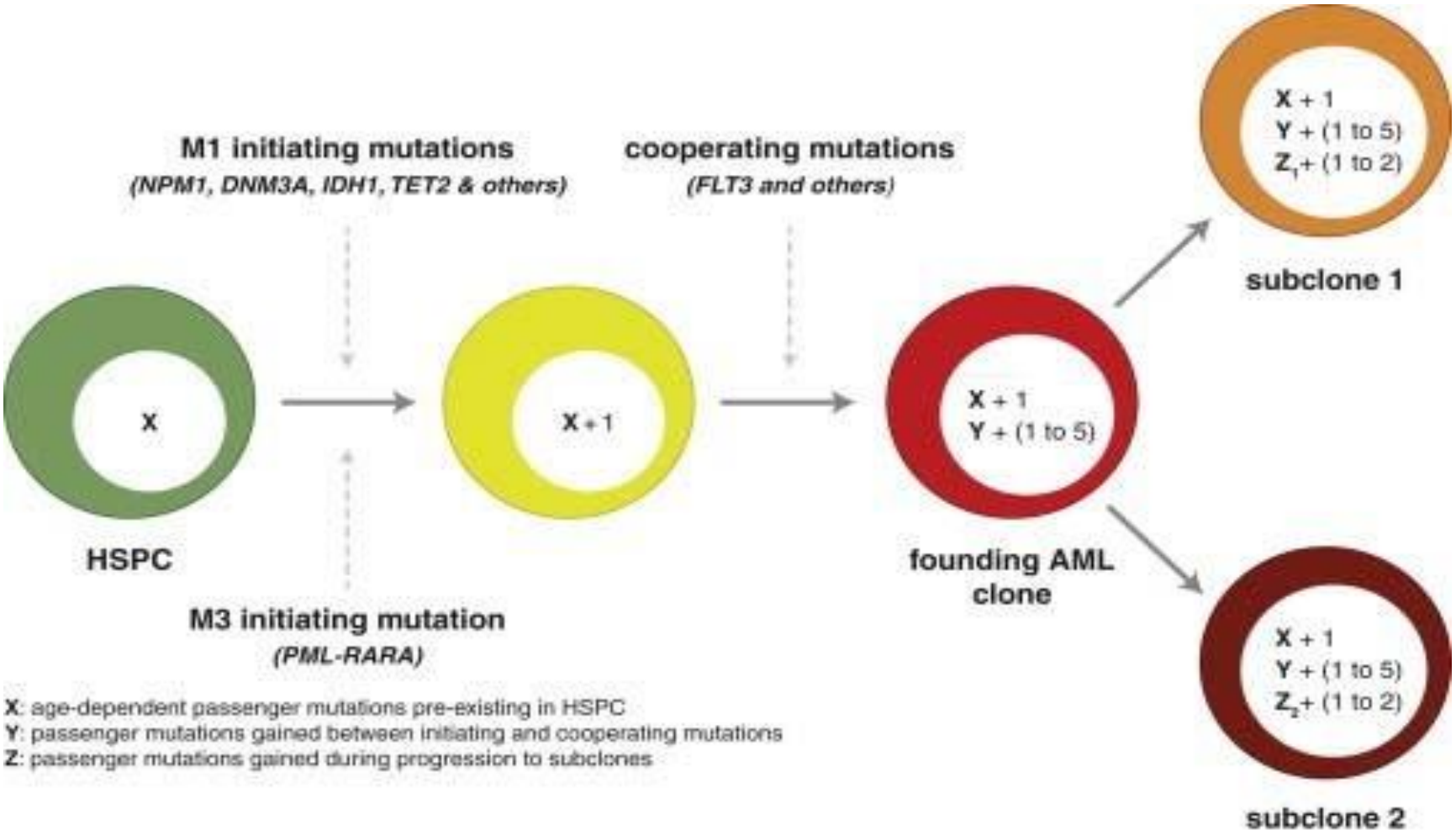
Löwenberg et al, NEJM, 2011

Two cooperating classes of mutations in AML



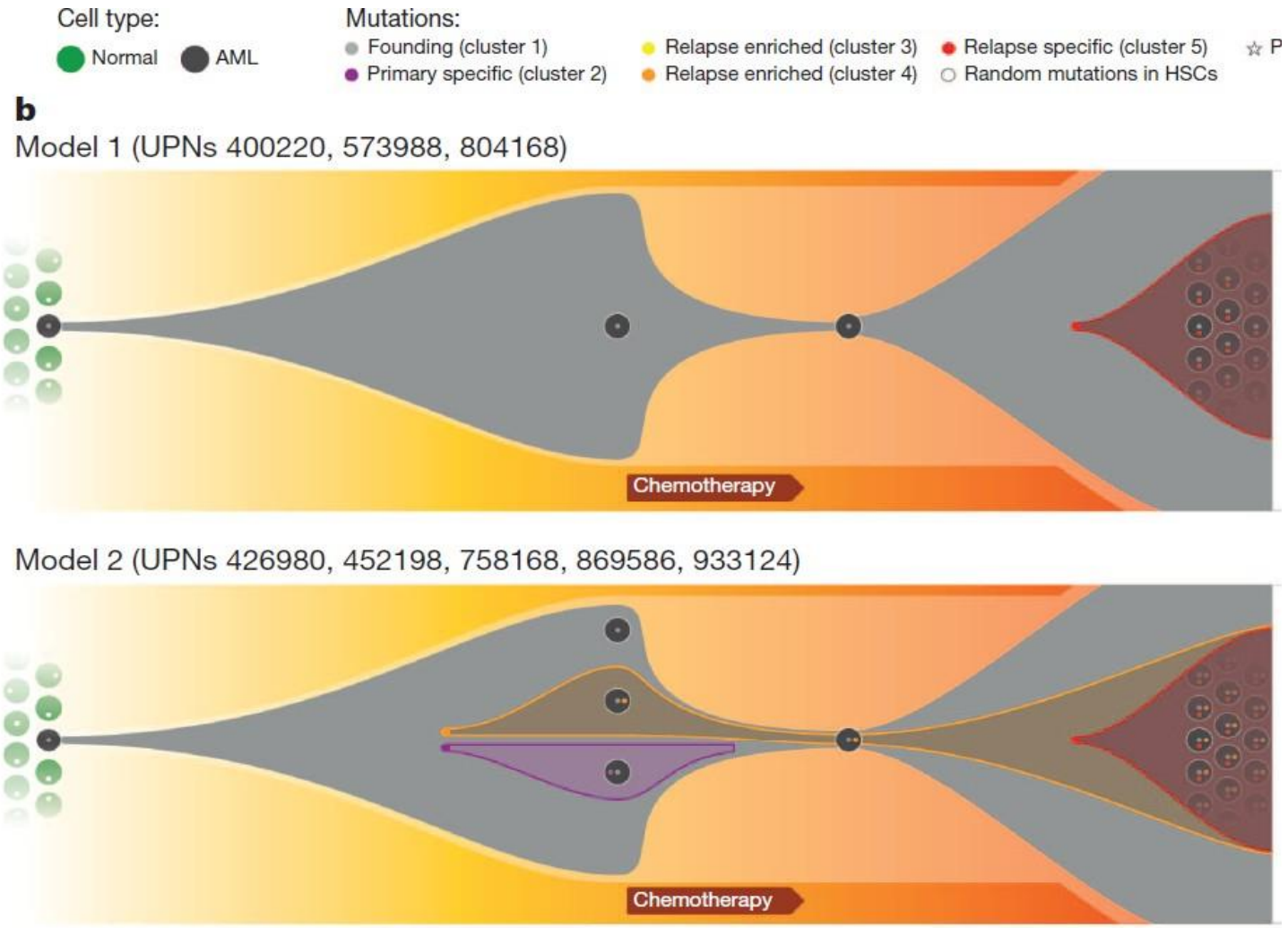
Adapted from Speck & Gilliland, Nat Rev Cancer. 2002

Evolution of mutations in AML



Welch et al, Cell, 2012

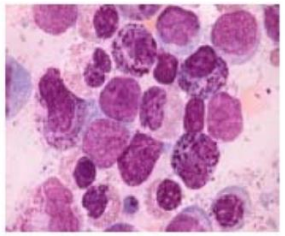
Patterns of relapse in AML



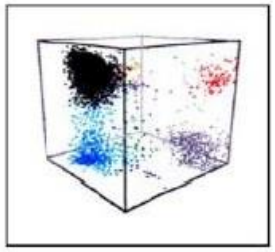
Ding et al, Nature, 2012

Modern diagnosis of AML

Morphology

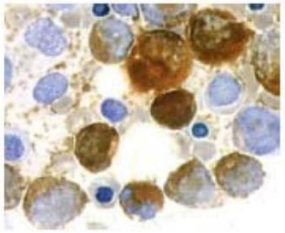


Immunophenotyping

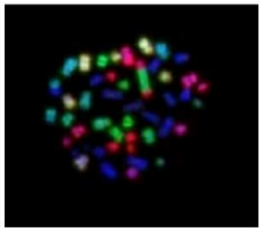


Cytogenetics

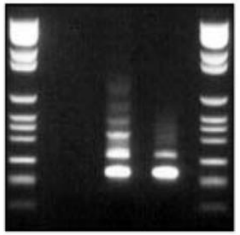
Cytochemistry



FISH



Molecular Biology



FAB classification of AML (morphology)

FAB classification of acute myeloblastic leukaemia

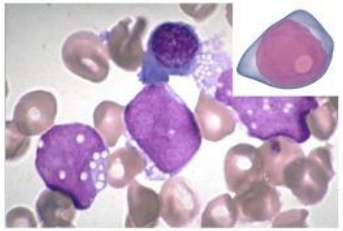


Photo courtesy of: Acute myeloid leukemia pathophysiology, 2012

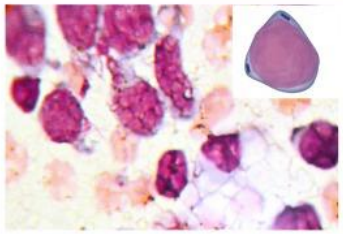
M0 Acute myeloblastic leukaemia with minimal differentiation

Morphology:

Can resemble LLA-L2 blasts. Medium-sized blasts, rounded nucleus, fine chromatin, basophilic non-granular cytoplasm, prominent nucleoli.

Immunophenotype

- CD13 +
- CD33 +
- CD11b +
- CD11c +
- CD14 +
- CD15 +



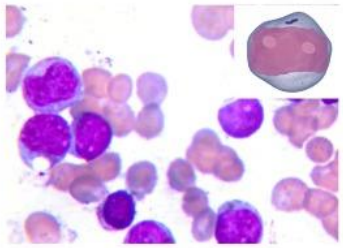
M1 Acute myeloblastic leukaemia without maturation

Morphology:

Medium-sized blasts with high nucleo:cytoplasm (n:c) ratio, rounded nuclei with immature, dispersed chromatin with one or more prominent nucleoli. Blasts can show fine azurophilic granulation or isolated Auer rods in the cytoplasm in 5% to 10% of cases

Immunophenotype

- MPO +
- CD13 +
- CD33 +
- CD117+
- CD34 +/-



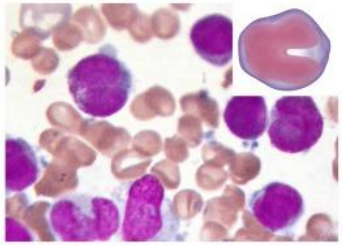
M2 Acute myeloblastic leukaemia with maturation

Morphology:

Small to medium-sized blasts with high nucleo: cytoplasm (n:c) ratio and rounded nuclei sometimes located in a corner of the cytoplasm. The nucleus shows dispersed, immature chromatin with one or more nucleoli. The cytoplasm is basophilic and can contain traces of primary azurophilic granulation or isolated Auer rods.

Immunophenotype

- MPO +
- CD34 +/-
- CD13 +
- CD15 +
- HLA-DR +/-
- Sudan black +
- CD117 +/-



M3 Promyelocytic leukaemia

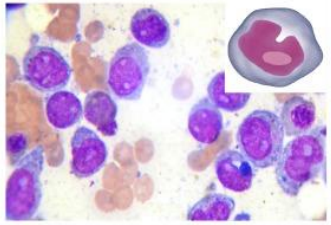
Morphology:

Abundant, intensely azurophilic granulation. The nucleus is usually monocytic in appearance (reniform) and is either irregular or bilobed with a deep cleft. Scarcely basophilic cytoplasm due to the proliferation of azurophilic granulation. Some atypical promyelocytes also contain elongated or splinter-shaped crystalline cytoplasmic inclusions specific to this type of leukaemia.These usually form clumps, but differ from Auer rods in that they show a tubular substructure on electronic microscopy.

Immunophenotype

- CD13 +
- CD33 +
- HLA-DR -
- CD34 -

FAB classification of acute myeloblastic leukaemia



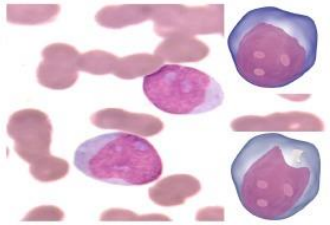
M4 Acute myelomonocytic leukaemia

Morphology:

Large blasts, moderate nucleo:cytoplasm (n:c) ratio and variable basophilia. The nucleus may be rounded, kidney-shaped or irregular. Nucleoli are usually prominent.

Immunophenotype

- CD13 +
- CD15 +
- CD33 +
- CD11b +
- CD11c +
- CD14 +
- CD64 +
- CD4 +

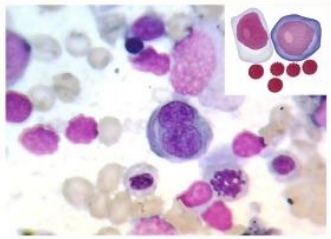


M5 Acute monocytic leukaemia

M5a acute monoblastic leukaemia:
Large blasts with rounded nucleus and dispersed, immature chromatin (1-3 nucleoli) and moderately large and intensely basophilic cytoplasm. The cytoplasm may show some Auer rods and/or prolongations and granulations.
M5b acute monocytic leukaemia
Promonocytes have a rounded or kidney-shaped nucleus with a less basophilic cytoplasm that is more highly granulated than monoblasts and contains some vacuoles. A findings of erythrophagocytosis together with monocytic blasts suggests a t(8;16) translocation.

Immunophenotype

- CD14 +
- CD68 +
- CD4 +
- CD11c +
- HLA-DR +
- CD64 +

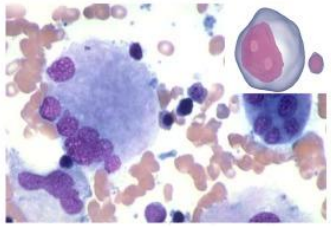


M6 Acute erythroid leukaemia

M6a erythroid leukaemia with proliferation of mixed blasts:
Over 50% erythroid precursors and around 30% myeloblasts. Morphology of erythrocytes in peripheral blood is greatly changed, with schistocytes, "pincered" or mushroom-shaped cells, and spiculated echinocyte and acanthocyte cells.
M6b pure erythroid leukaemia:
Erythroids make up 80% of bone marrow cells, with less than 3% myeloid cells. Erythrocytes in peripheral blood consist of macrocytes, basophilic stippling, Howell-Jolly bodies or Cabot rings.

Immunophenotype

- CD13 +
- CD33 +
- CD15 +
- Glycophorin A +
- Glycophorin C +



M7 Acute megakaryocytic leukaemia

Morphology:

Highly immature, polymorphic blasts. The nucleus is eccentric with dispersed, reticulated chromatin and 1-3 prominent nucleoli. The cytoplasm is non-granular, basophilic, and very similar in appearance to platelets, with pseudopods or granulations. Micromegakaryocytes and fragments of megakarioblasts are seen in peripheral blood (giant platelets, some highly degranulated).

Immunophenotype

- CD41 +
- CD61 +
- CD42 +
- CD13 +
- CD33 +
- CD34 +

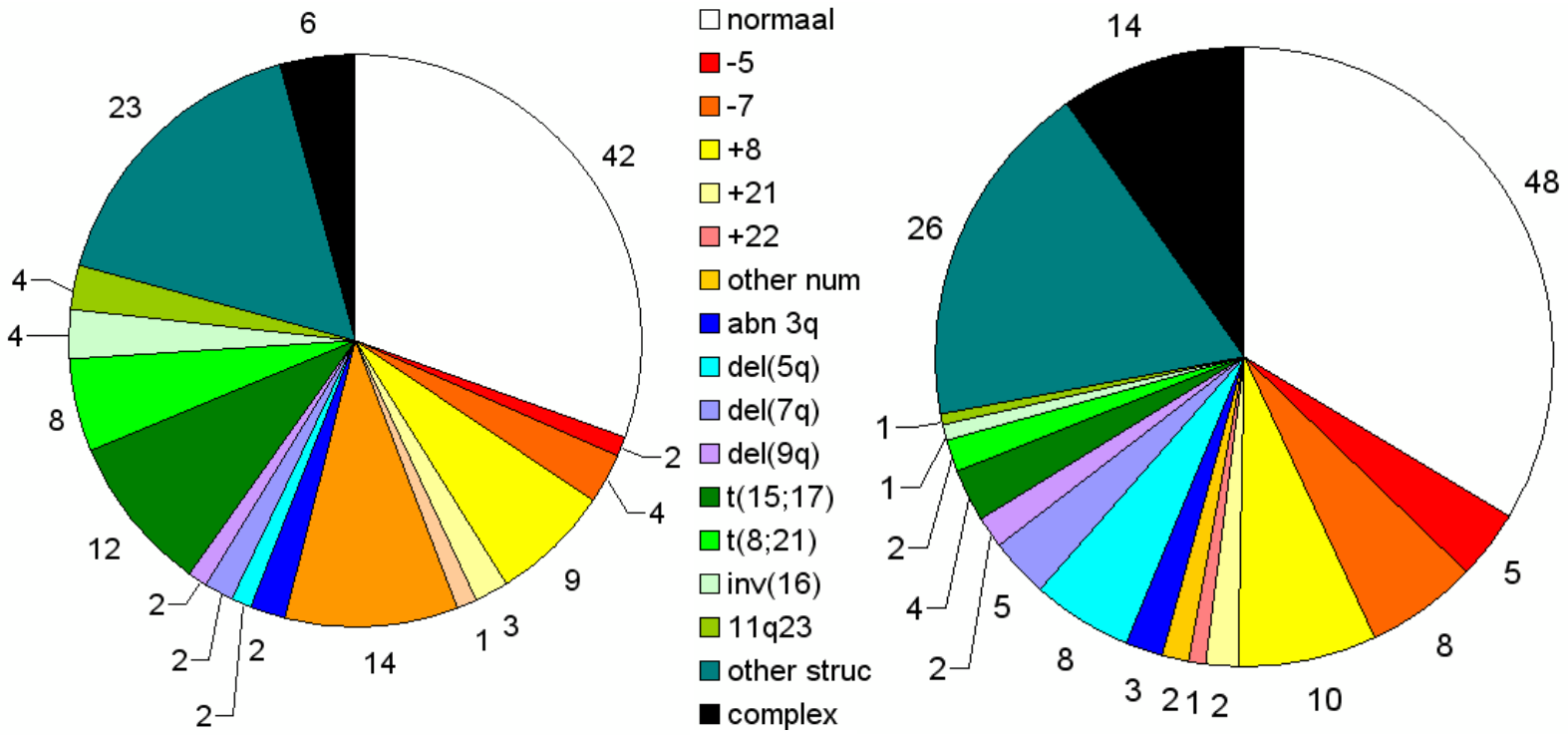
Bennett et al et al, BJH, 1976

Markers for the diagnosis of AML and MPAL

Expression of cell-surface and cytoplasmic markers	
Diagnosis of AML[*]	
Precursors[†]	CD34, CD117, CD33, CD13, HLA-DR
Granulocytic markers[‡]	CD65, cytoplasmic MPO
Monocytic markers[§]	CD14, CD36, CD64
Megakaryocytic markers[‖]	CD41 (glycoprotein IIb/IIIa), CD61 (glycoprotein IIIa)
Erythroid markers	CD235a (glycophorin A), CD36
Diagnosis of MPAL[¶]	
Myeloid lineage	MPO (flow cytometry, immunohistochemistry, or cytochemistry) or monocytic differentiation (at least 2 of the following: nonspecific esterase cytochemistry, CD11c, CD14, CD64, lysozyme)
T-lineage	Strong[#] cytoplasmic CD3 (with antibodies to CD3 ε chain) or surface CD3
B-lineage[**]	Strong[#] CD19 with at least 1 of the following strongly expressed: cytoplasmic CD79a, cCD22, or CD10 or weak CD19 with at least 2 of the following strongly expressed: CD79a, cCD22, or CD10

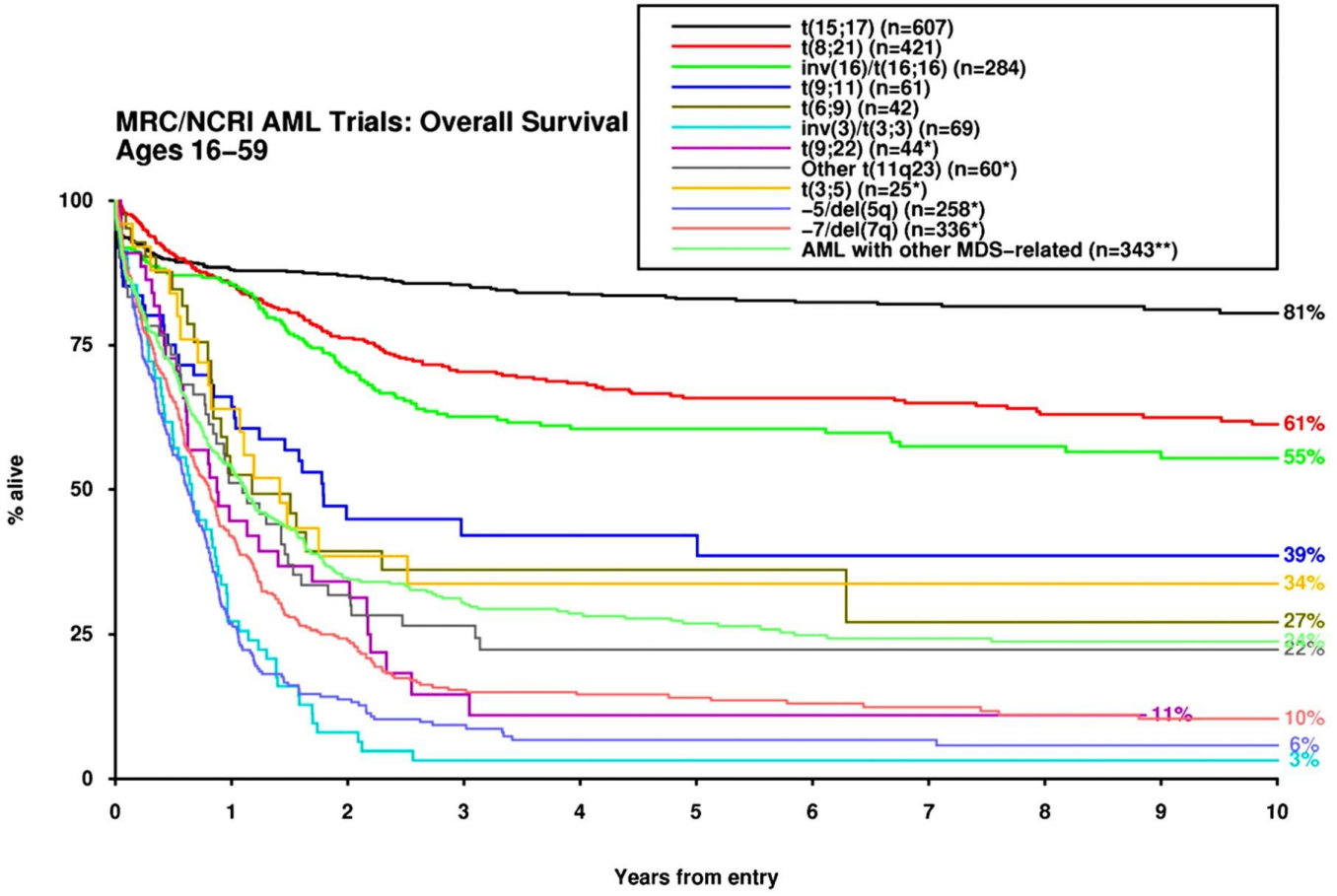
Blood, 2017, Döhner et al.

Cytogenetic distribution of AML



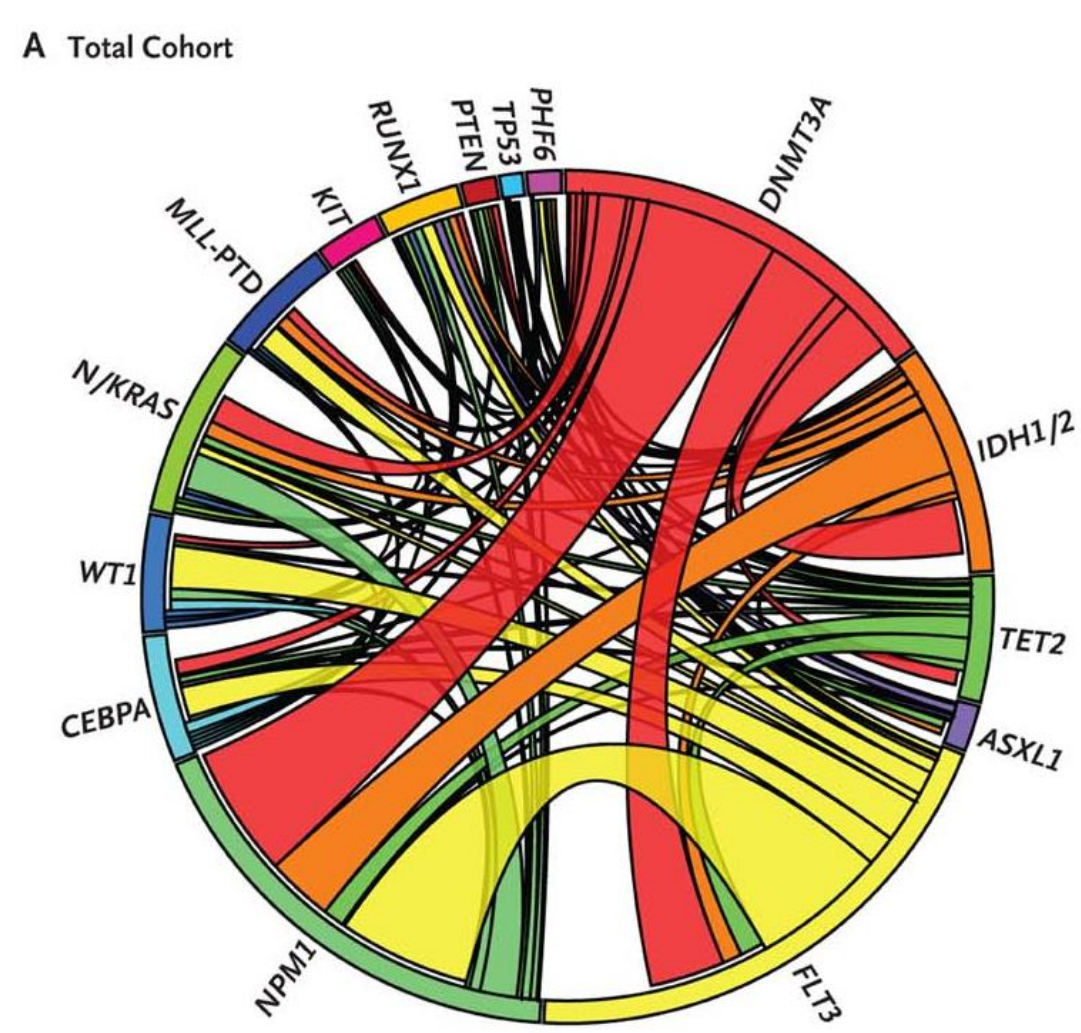
Based on Grimwade et al, Blood 1998;
Grimwade et al, Blood, 2001

Impact of specific genetic aberrations on survival in AML



Grimwade et al, Blood 2010

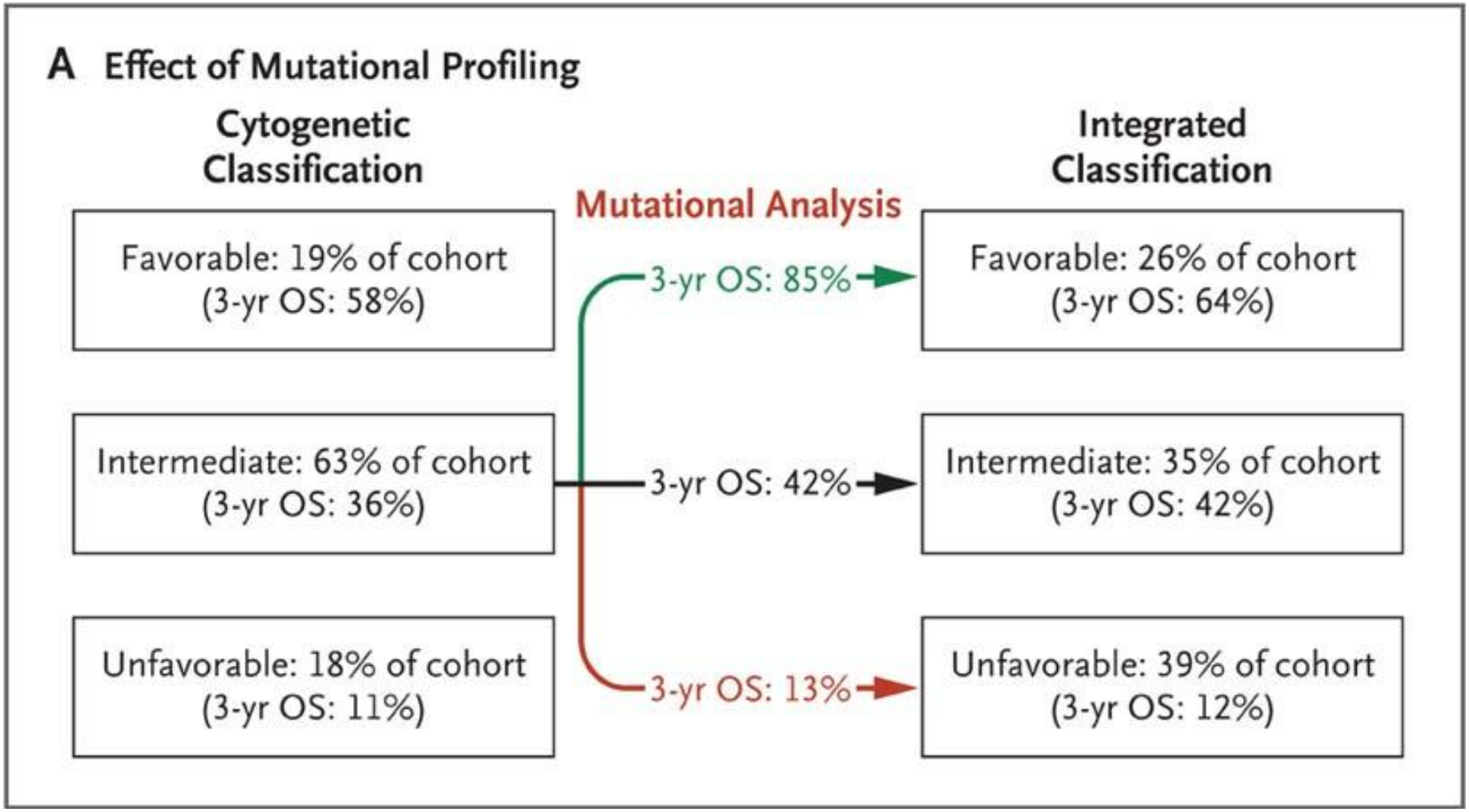
Mutational complexity of AML



Gene	Overall Frequency (%)
FLT3 (ITD, TKD)	37 (30, 7)
NPM1	29
DNMT3A	23
NRAS	10
CEBPA	9
TET2	8
WT1	8
IDH2	8
IDH1	7
KIT	6
RUNX1	5
MLL-PTD	5
ASXL1	3
PHF6	3
KRAS	2
PTEN	2
TP53	2
HRAS	0
EZH2	0

Patel JP et al. N Engl J Med 2012;366:1079-1089

Comprehensive mutational profiling for risk stratification and clinical management of AML.



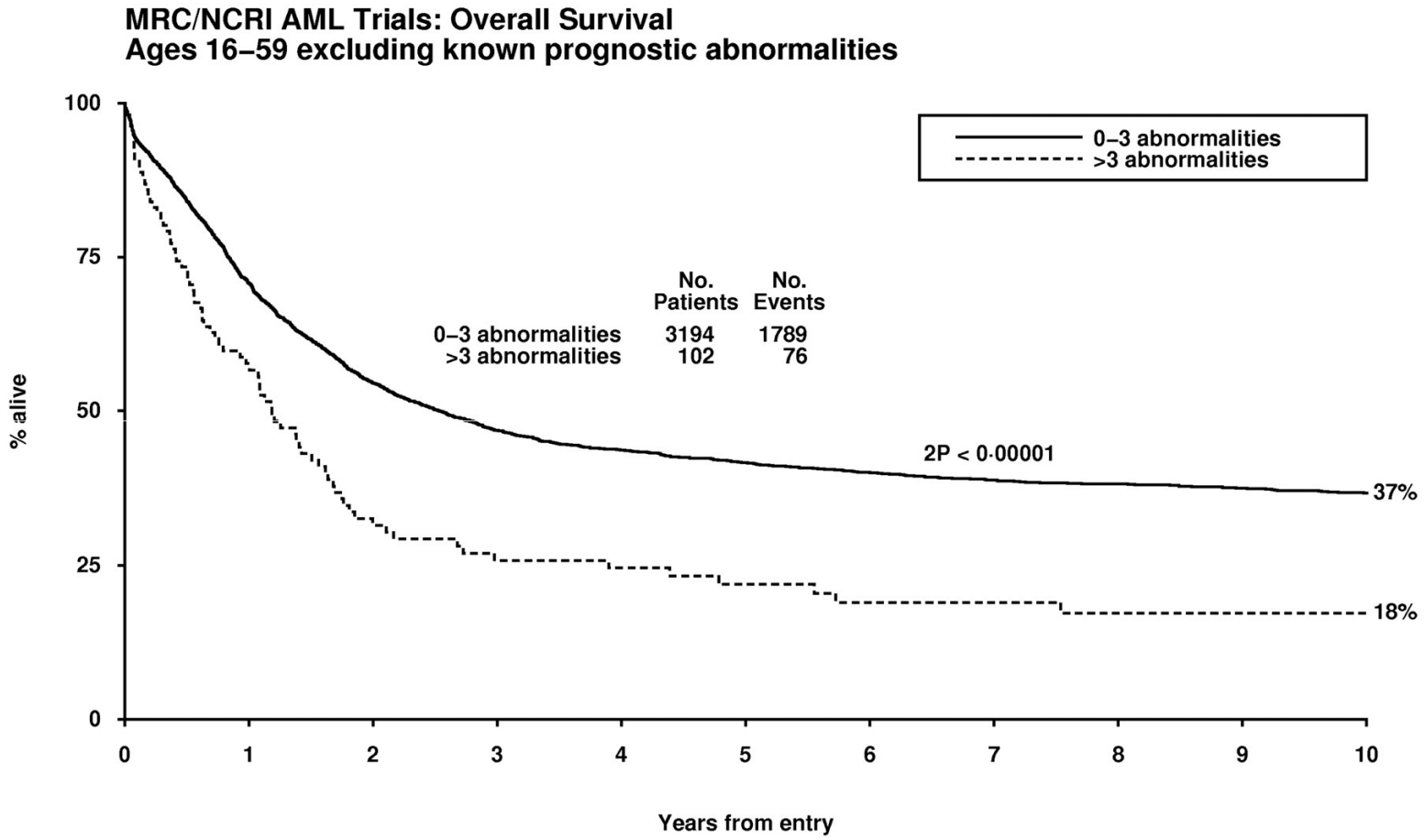
Patel JP et al. N Engl J Med 2012;366:1079-1089

2022 ELN risk genetic stratification

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* without *FLT3*-ITD
	bZIP in-frame mutated *CEBPA*
Intermediate	Mutated *NPM1* and *FLT3*-ITD
	Wild-type *NPM1* with *FLT3*-ITD (without adverse-risk genetic lesions)
	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)(p11.2;p13.3)/*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, and/or ZRSR2*
	Mutated *TP53*

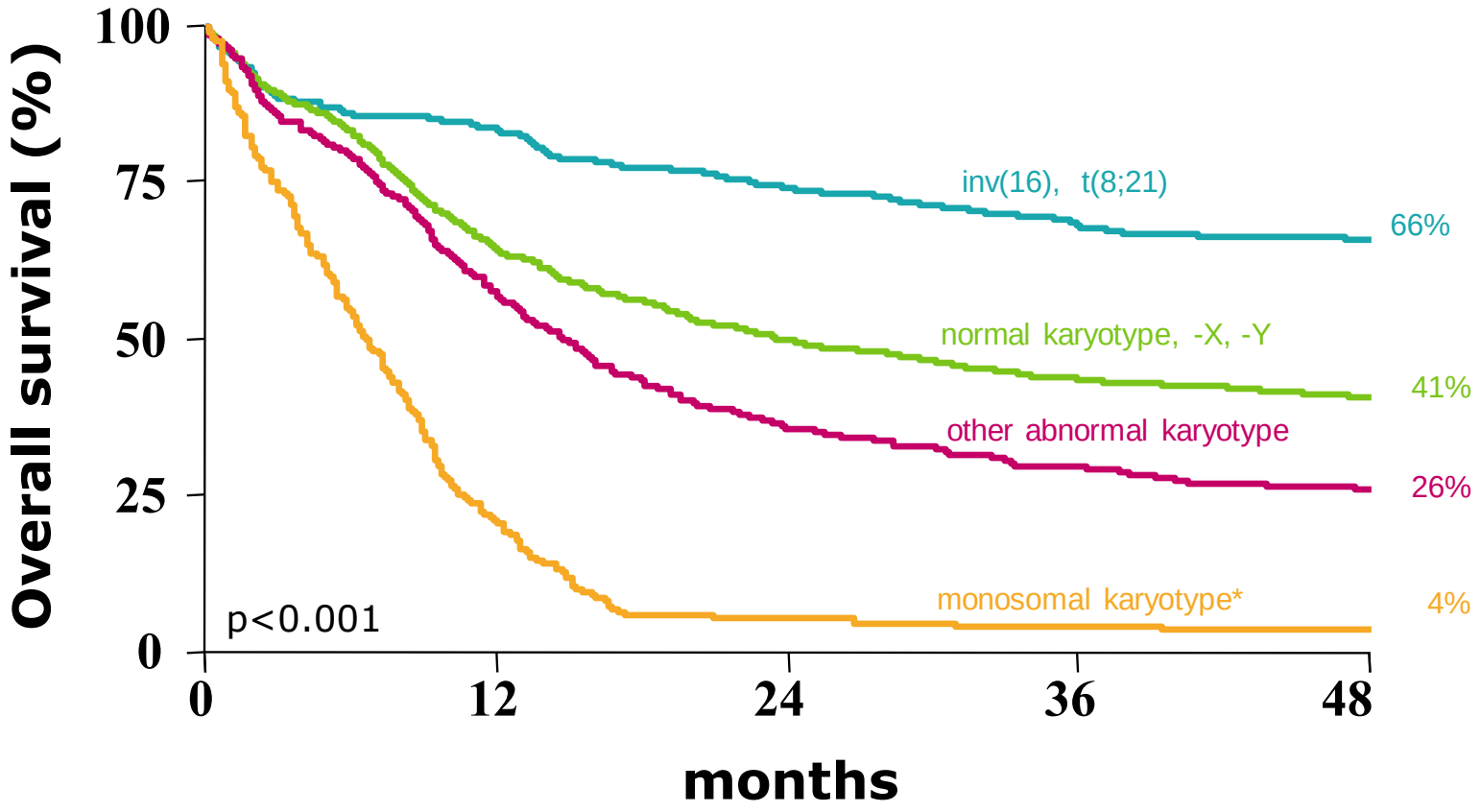
Blood, 2022, Döhner et al.

Impact of karyotype complexity on survival for AML patients not belonging to favourable subgroups



Grimwade et al, Blood 2010

Overall survival in AML patients categorized into favourable, intermediate, adverse and very adverse cytogenetic risk groups



Two or more autosomal monosomy or
1 auto monosomy with structural abn (n=184)
= monosomal karyotype*

Breems et al. J Clin Oncol 2008

Acute myeloid leukemia
Prognosis according age

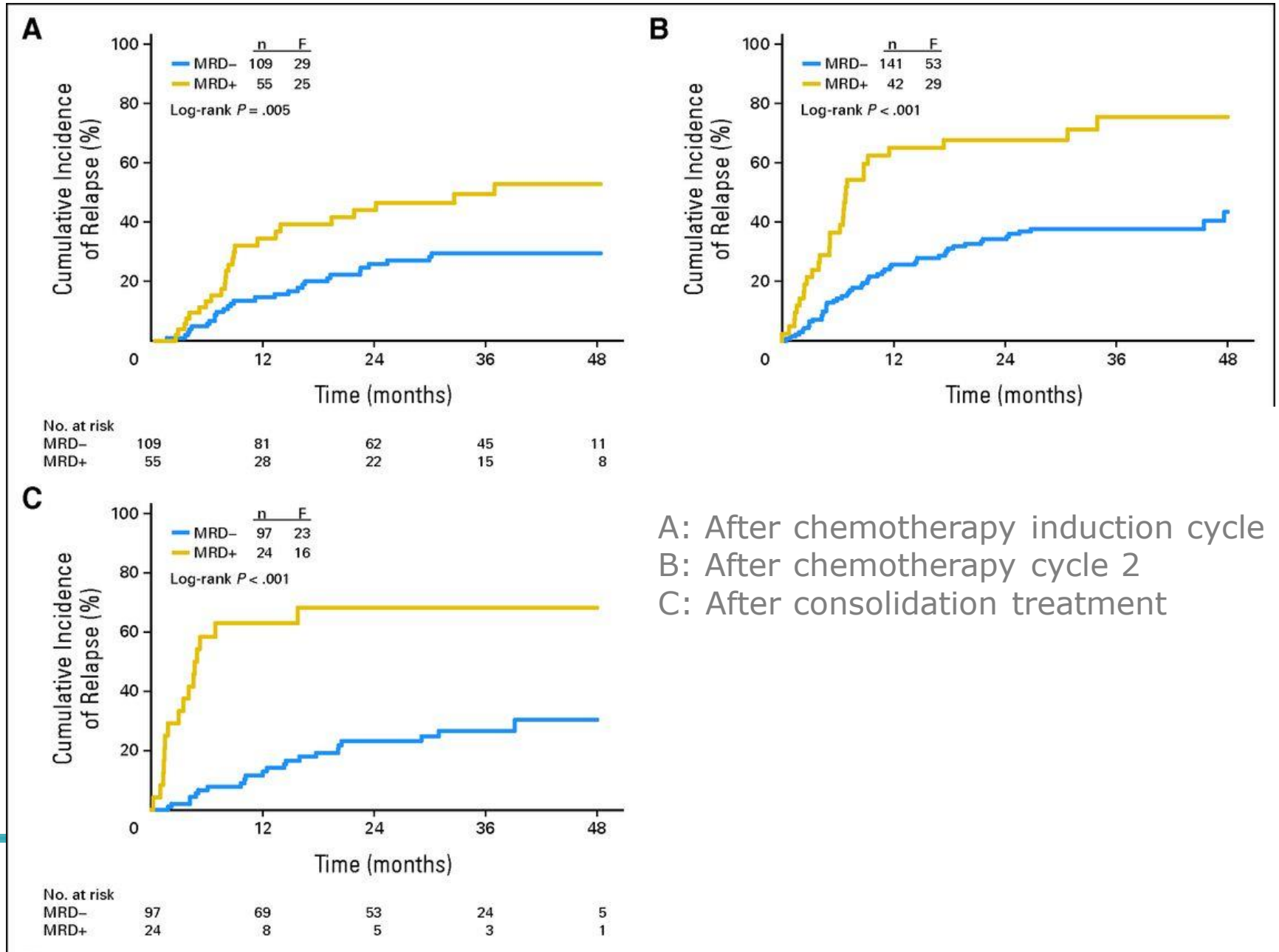
Age	Complete remission	Overall survival
18 - 60 years	**80%**	**40% at 5 years**
>60 years	**65%**	**28% at 2 years**

Prognostic value of minimal residual disease detection in AML with flowcytometry

- 517 AML patients, 18-60 years
- 85% of all AMLs:
  - Leukemia-associated phenotype by immunoflow cytometry is determined at diagnosis
  - Minimal residual disease assessment in complete remission:
    - After chemotherapy induction cycle 1
    - After chemotherapy cycle 2
    - After consolidation treatment

Terwijn et al. J Clin Oncol 2013

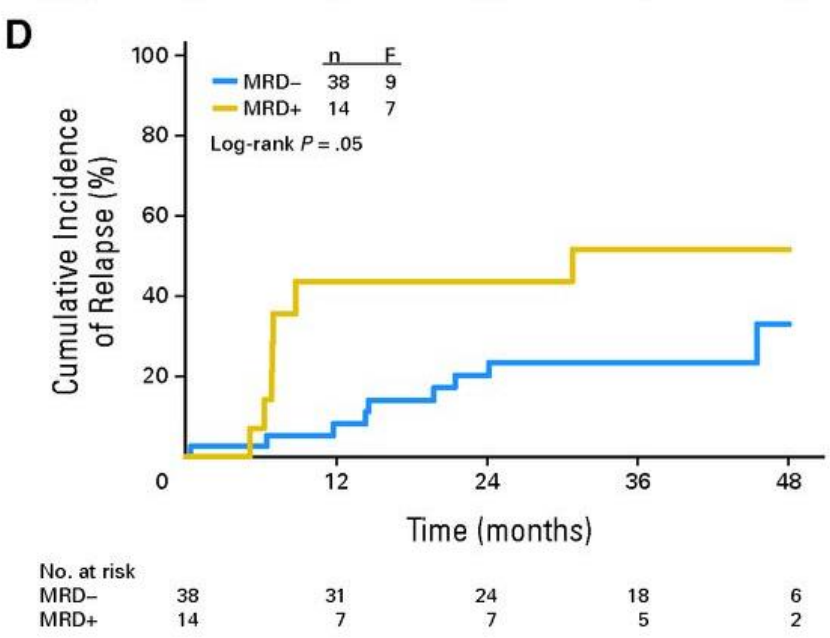
Relapse incidence by minimal residual disease

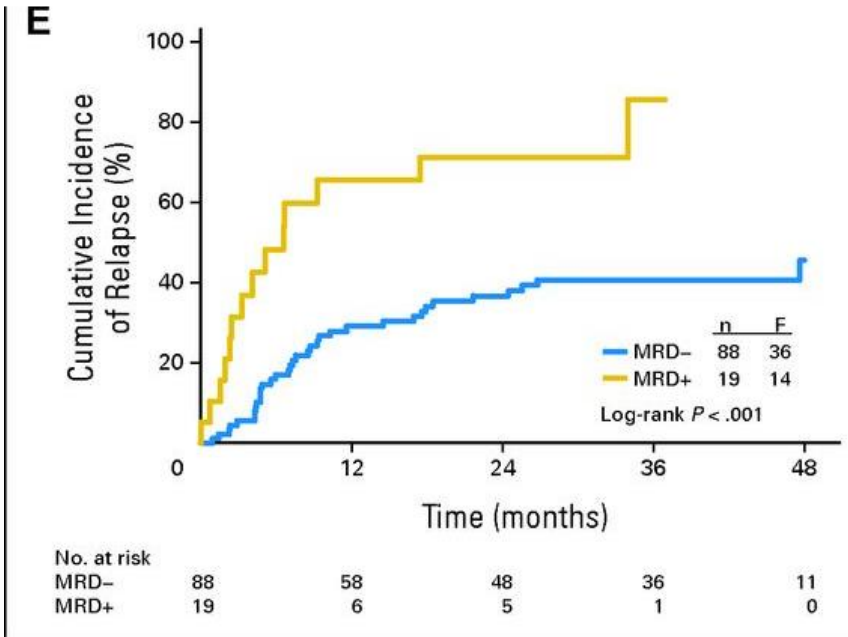


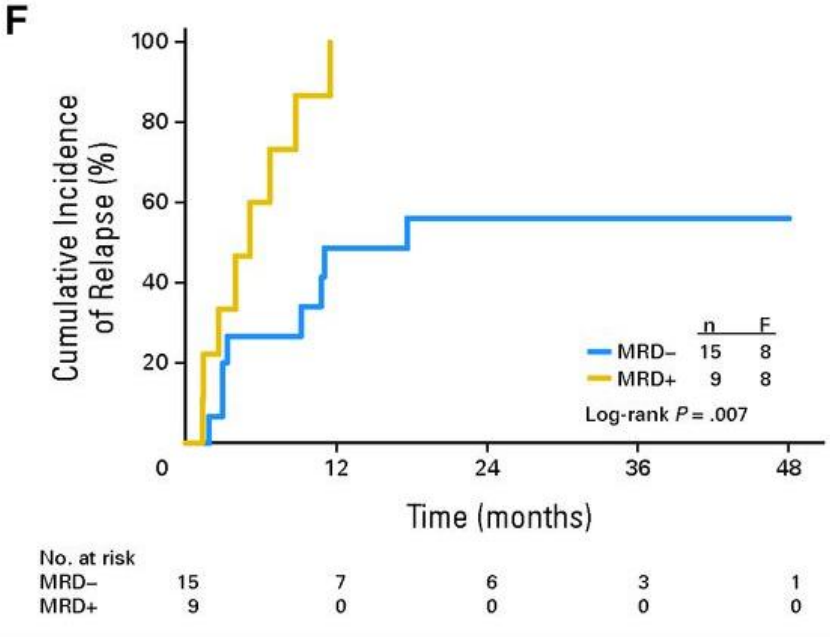
A: After chemotherapy induction cycle 1
B: After chemotherapy cycle 2
C: After consolidation treatment

Relapse incidence by minimal residual disease

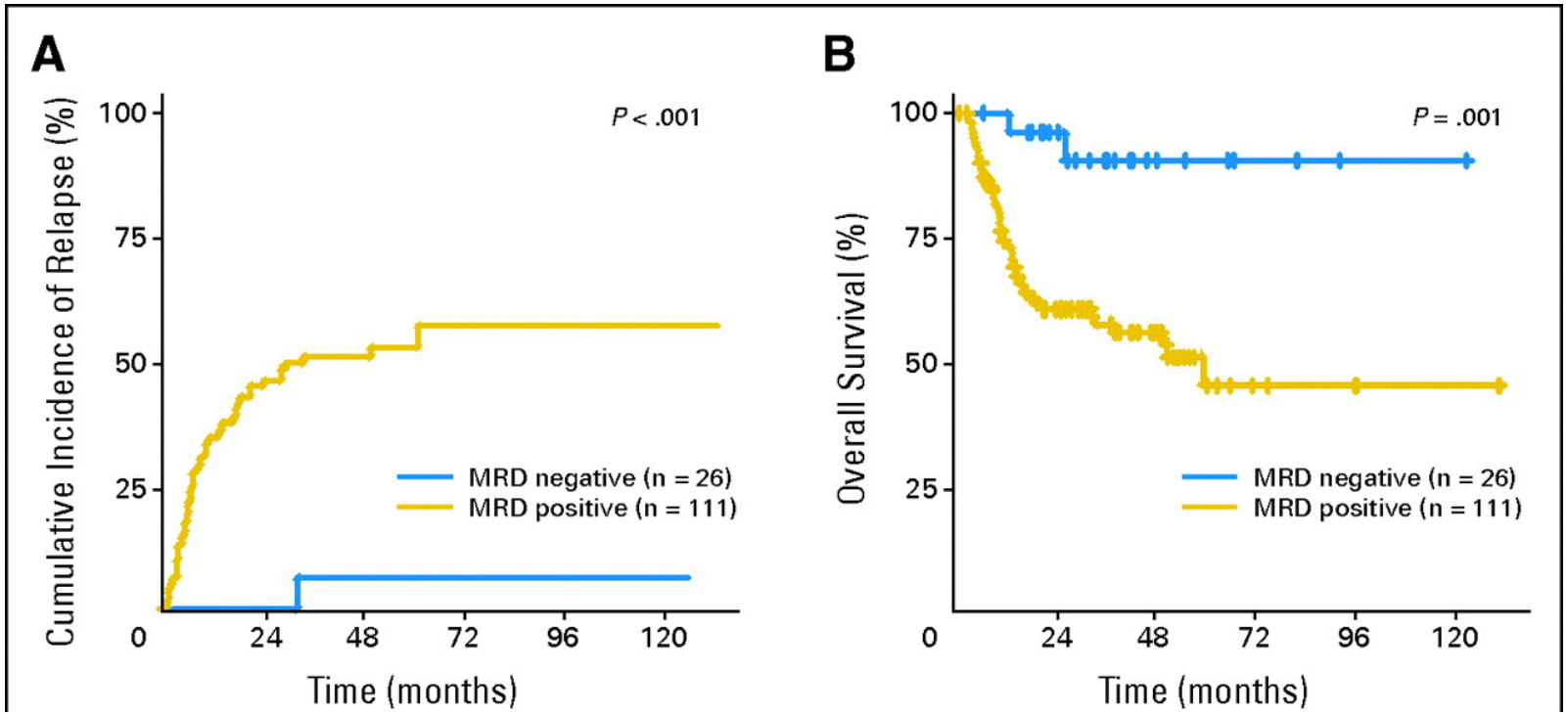
After chemotherapy cycle 2
D: Good risk
C: Intermediate risk
F: Poor risk





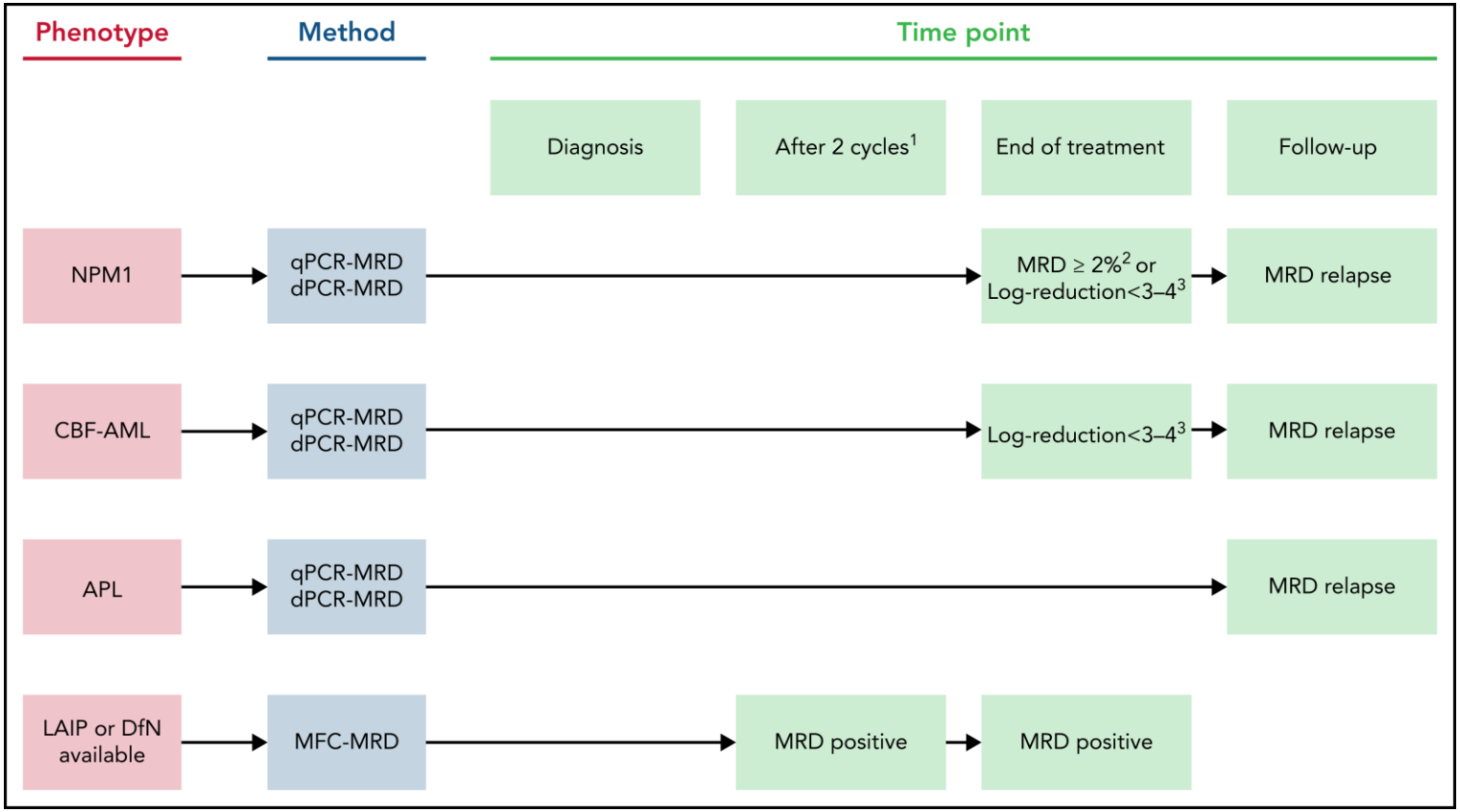


Prognostic value of minimal residual disease detection in NPM1-mutated AML



Krönke J et al, J Clin Oncol 2011

2021 Update on MRD in acute myeloid leukemia: a consensus document from the European LeukemiaNet MRD Working Party



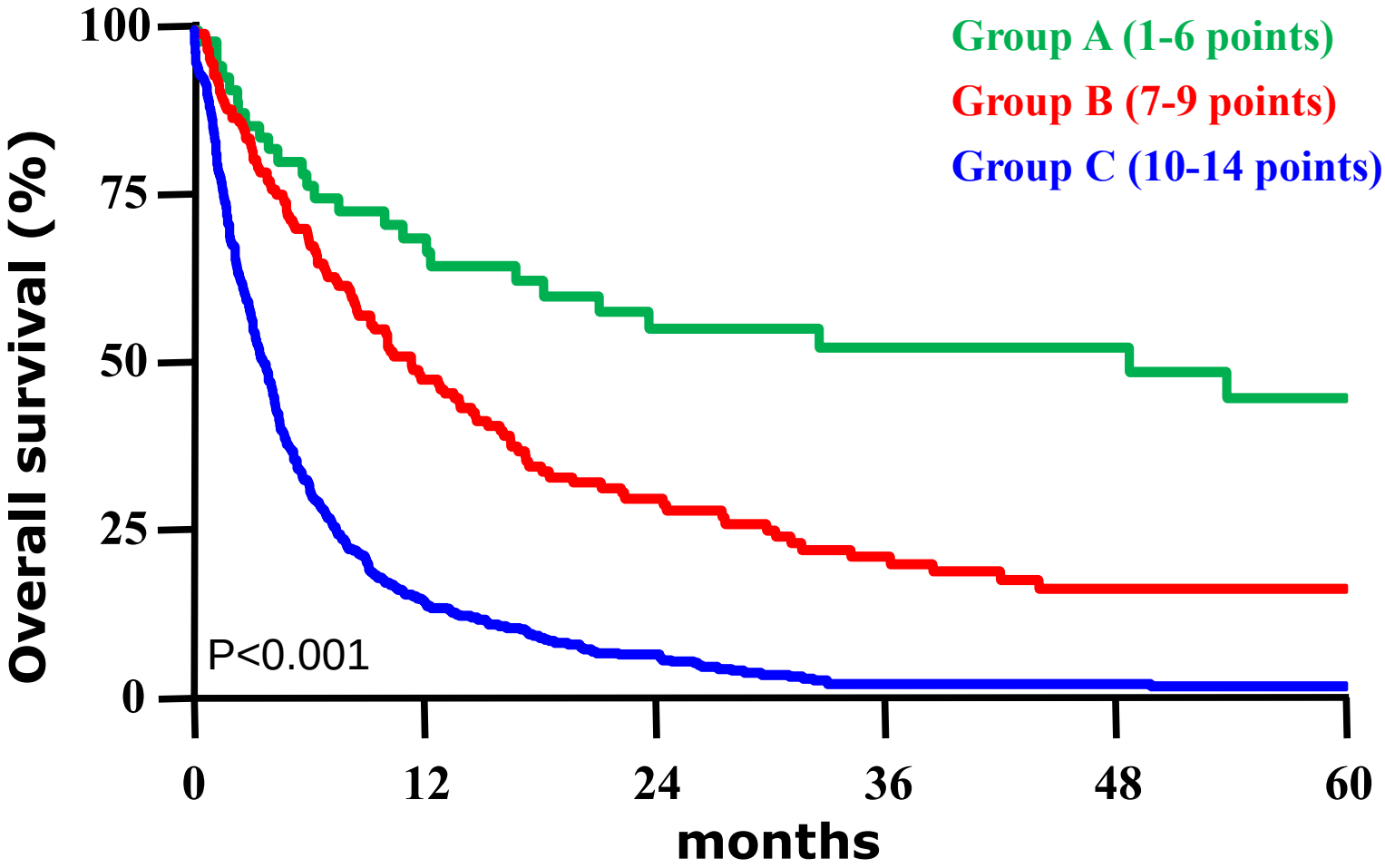
Heuser et al, Blood, 2021

Prognostic score (0 – 14 points) for AML at first relapse

Prognostic factor		Coefficient	Points
Relapse free interval from first CR	>18 months	0	**0**
	7 to 18 months	0.69	**3**
	<=6 months	1.28	**5**
Cytogenetics at diagnosis	t(16;16) or inv(16)	0	**0**
	t(8;21)	0.68	**3**
	Other	1.19	**5**
Age at first relapse	<=35 years	0	**0**
	36 to 45 years	0.21	**1**
	>45 years	0.47	**2**
STC before first relapse	No	0	**0**
	Yes	0.49	**2**

Breems et al. J Clin Oncol 2005

Overall survival among patients with AML in first relapse according to prognostic group



Breems et al. J Clin Oncol 2005

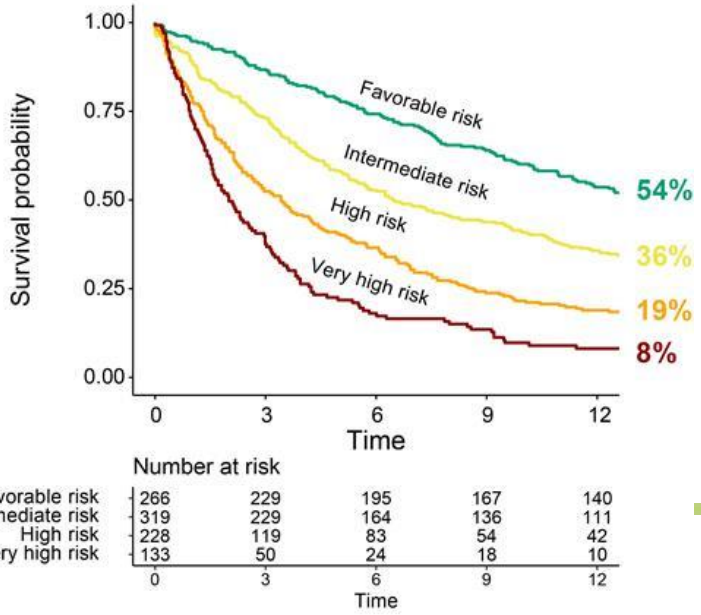
Novel prognostic model for patients with AML in first relapse with improved prognostic accuracy

A

Variable	Points
Clinical data	
Age ≥ 60 (years)	2
Relapse free interval ≤ 1 (year)	2
WBC ≥ 10 (x10e9/L)	1
Previous allo-SCT	2
Cytogenetic data	
CK/MK	2
No t(16;16) or t(8;21)	3
t(v;11q23)	2
Molecular data	
TP53	2
FLT3-ITD	1

Favorable risk: **≤5 points**
Intermediate risk **6-7 points**
High risk **8-9 points**
Very high risk **≥10 points**

B

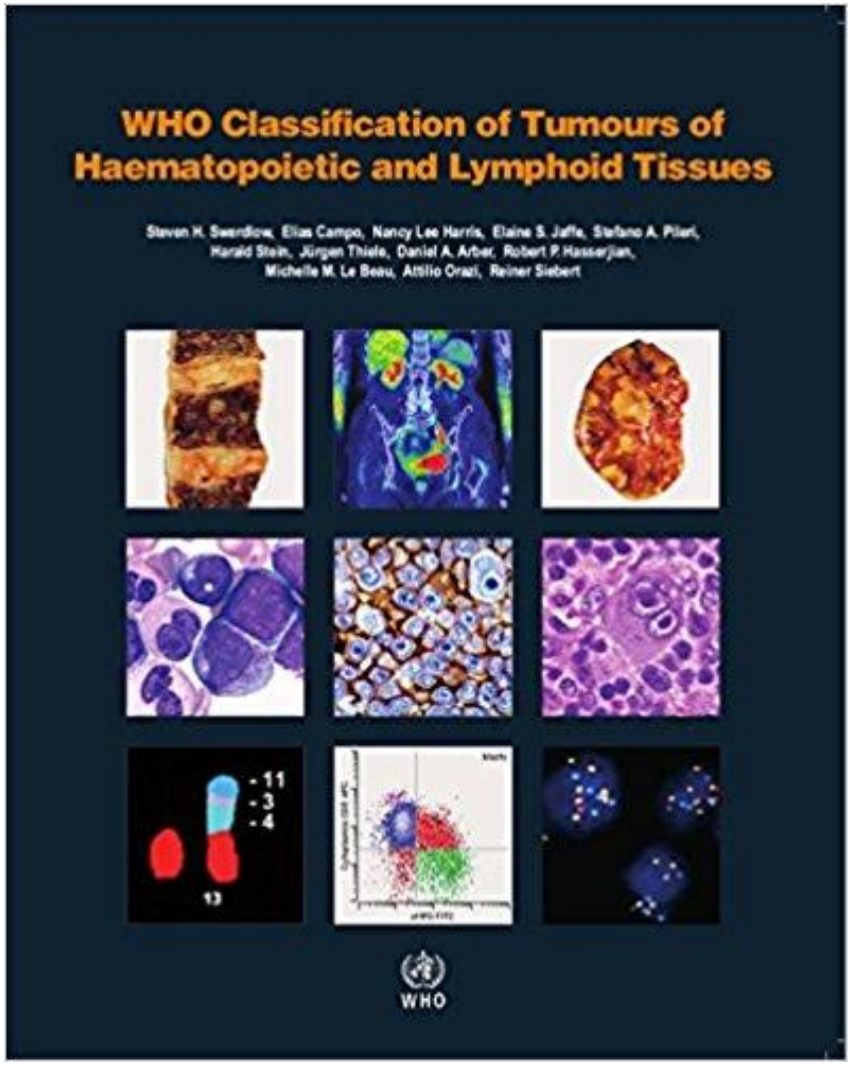


Van Der Maas, Breems et al, ASH 2023

Identification of molecular abnormalities have therapeutic consequences

Abnormality	Treatment option
PML-RARA gene fusion	Retenoic acid (ATRA)
FLT3 mutations	FLT3-inhibitors
IDH1 mutations	IDH1 inhibitors
IDH2 mutations	IDH2 inhibitors
KMT2A rearrangements	Menin/KMT2A inhibitors
NPM1 mutations	Menin/KMT2A inhibitors

WHO classification



Swerdlow et al, Revised 4th Edition, 2017

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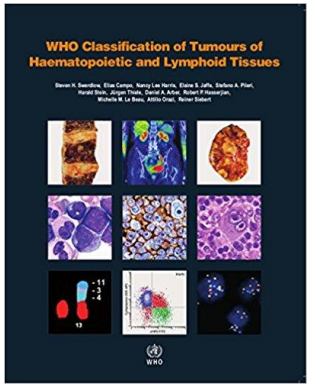
Chapter 8: Acute myeloid leukemia and related precursor neoplasms

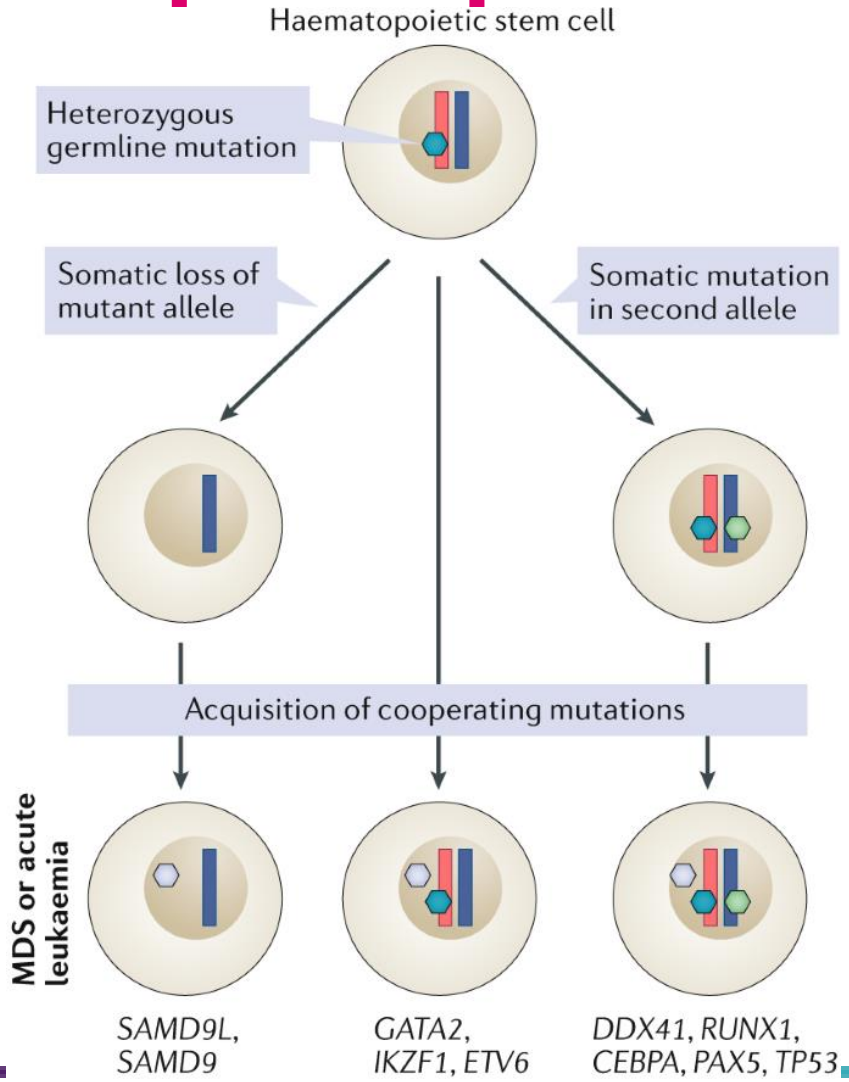
Chapter 9: Blastic plasmacytoid dendritic neoplasm

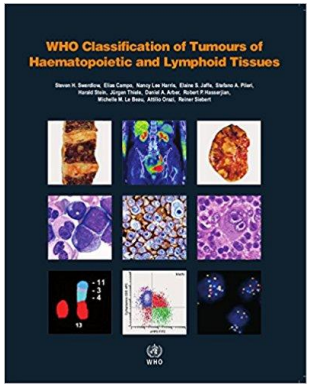
Chapter 10: Acute leukemias of ambiguous lineage

Mixed phenotype acute leukemia (MPAL)



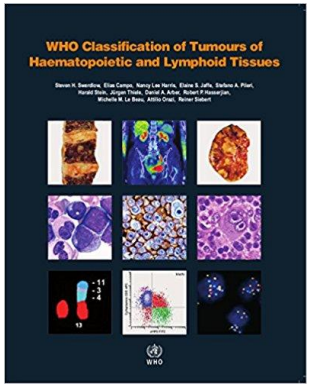
7: Myeloid neoplasms with germline predisposition





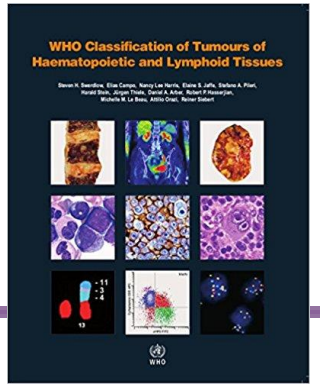
8: Acute myeloid leukemia and related precursor neoplasms

- AML with recurrent genetic abnormalities
- AML with myelodysplasia-related changes
- Therapy-related myeloid neoplasms
- AML not otherwise specified
- Myeloid sarcoma
- Myeloid proliferations associated with Down syndrome



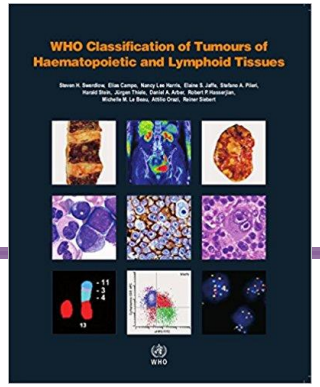
AML with recurrent genetic abnormalities

- AML with t(8;21)(q22;q22); *RUNX1-RUNX1T1*
- AML with inv(16)(p13.1;1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
- Acut promyelocytic leukemia with *PML-RARA* FAB M3
- AML with t(9;11)(p21.3;q23.3); *KMT2A-MLLT3*
- AML with t(6;9)(p23;q34.1); *DEK-NUP214*
- AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM (=EVI1)*
- AML (megakaryoblastic) with t(1;22)(p13.3;q13.1); *RBM15-MKL1*
- AML with *BCR-ABL1*
- AML with with gene mutations
  - AML with mutated *NPM1*
  - AML with biallelic mutation of *CEBPA*
  - AML with mutated *RUNX1*



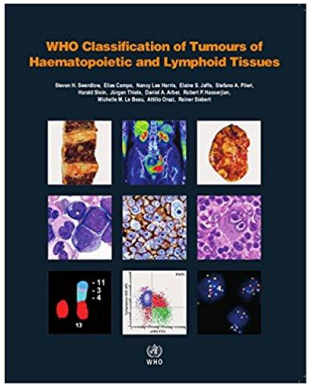
AML, myelodysplasia-related

- ≥ 20% blasts in PB or BM
- AND one of the following:
  - History of MDS or MDS/MPN
  - Defining cytogenetic abnormalities
  - Multilineage dysplasia: dysplasia in ≥50% of cells in ≥2 myeloid lineages
- AND absence of both prior cytotoxic therapy for unrelated disease and aforementioned recurring genetic abnormalities



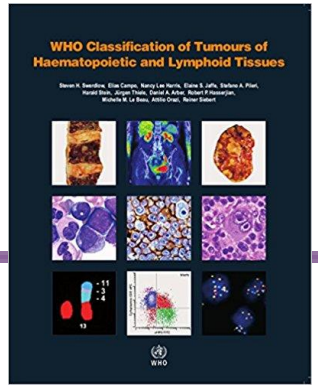
Therapy-related myeloid neoplasms

- t-AML, t-MDS or t-MDS/MPN
- Excluded: progression from MPN or evolution of primary MDS or MDS/MPN to AML (secondary AML)
- Cytotoxic agents implicated in therapy-related myeloid neoplasms
  - Alkylating agents
  - Ionizing radiation therapy
  - Topoisomerase II inhibitors
  - Others



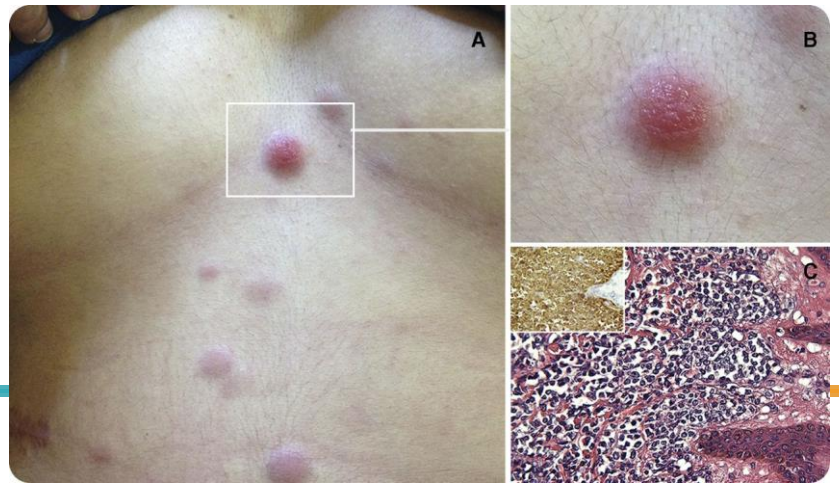
AML not other specified

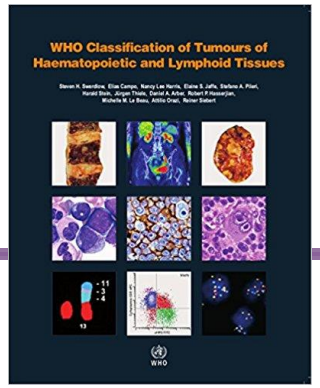
- AML with minimal differentiation — FAB M0
  - MPO negative, CD13+, CD117+, CD33+ (60%)
- AML without maturation — FAB M1
  - >90% blasts of NEC
- AML with maturation — FAB M2
- Acute myelomonocytic leukemia — FAB M4
- Acute monoblastic/monocytic leukemia — FAB M5a/b
- Acute erythroid leukemia — FAB M6
- Acute megakaryoblastic leukemia — FAB M7
- Acute basophilic leukemia
- Acute panmyelosis with myelofibrosis



Myeloid sarcoma

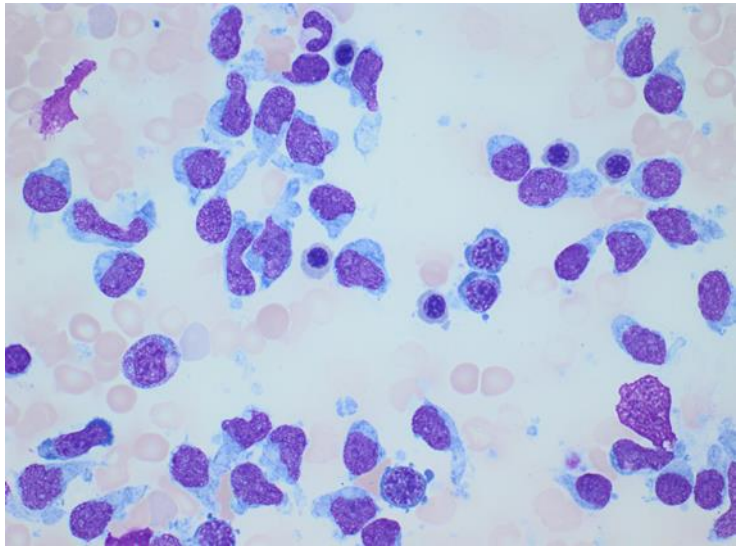
- Tumor mass consisting of myeloid blasts with or without maturation
- Occurring in other anatomical site than bone marrow
- Not: Infiltration of any site of the body by myeloid blasts in a patient with AML
- Localization, any site, most frequent:
  - Skin, lymph nodes, GI tract, bone, soft tissue, testes

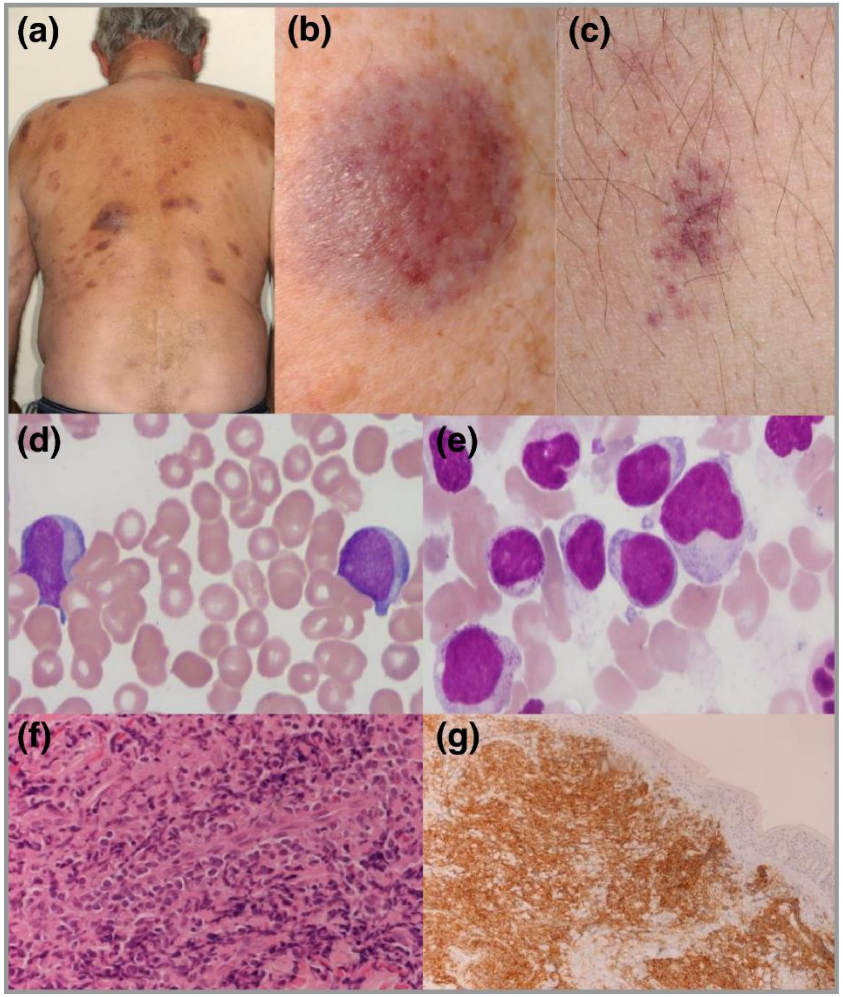




9: Blastic plasmacytoid dendritic neoplasm (BPDCN)

- Aggressive tumor derived from precursors fo plasmacytoid dendritic cells
- High frequency of cutaneous and bone marrow involvement and leukemic dissemination





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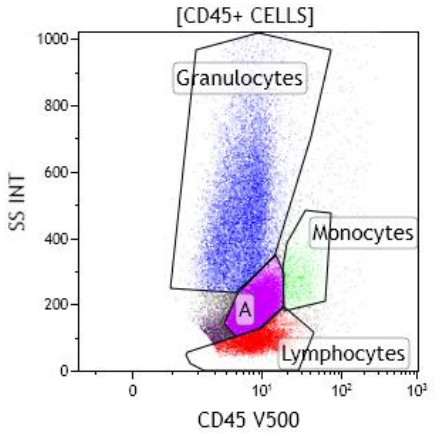
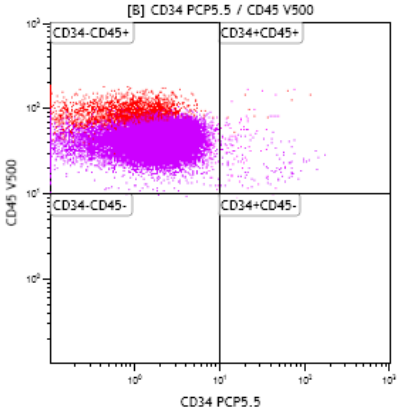
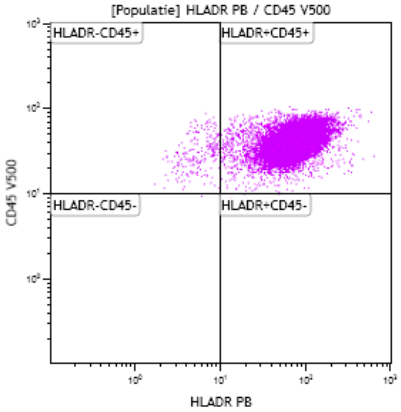
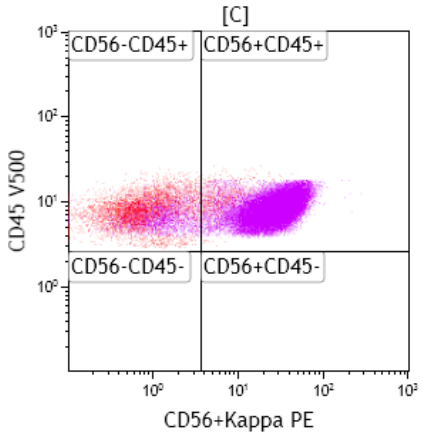
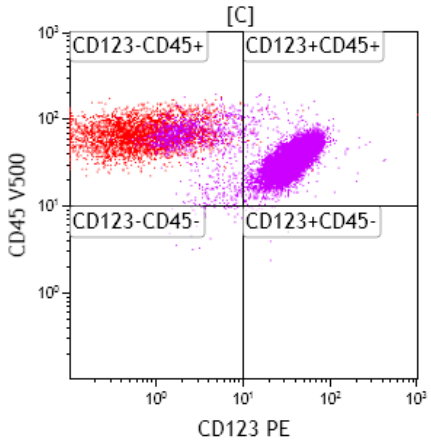


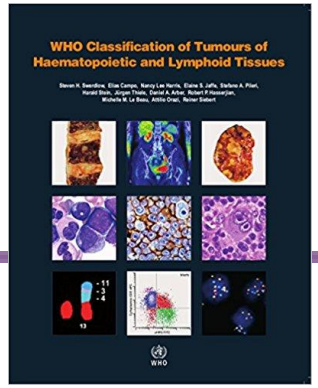








Populatie A
CD45+ HLADR+ CD56+ CD4+(LD) CD123+
CD34- CD19- CD3- cytCD3- cytCD79a- cytTdT- cytMPO-



10: Acute leukemias of ambiguous lineage

Acute Leukemia of Ambiguous Lineage (ALAL)

Encompasses those leukemias that show no clear evidence of differentiation along a single lineage

AUL

Expresses no markers specific for either lymphoid or myeloid lineage. Blasts often express HLA-DR, CD34 and/or CD38 and may be positive for terminal deoxynucleotidyl transferase

MPAL

It includes leukemias with blasts that express antigens of more than one lineage to such a degree that it is not possible to assign the leukemias to any one lineage with certainty

Requirements for assigning more than one lineage to a single blast population

Myeloid lineage

Myeloperoxidase or Monocytic differentiation (at least 2 of the following: NSE, CD11c, CD14, CD64, lysozyme)

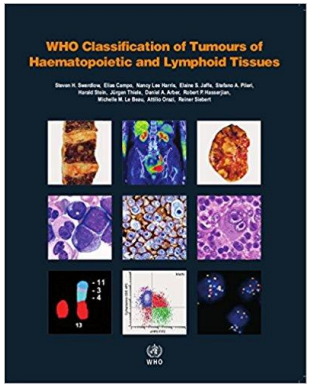
B lineage

Strong CD19 with at least 1 of the following strongly expressed: CD79a, cytoplasmic CD22, CD10 or

Weak CD19 with at least 1 of the following strongly expressed: CD79a, cytoplasmic CD22, CD10

T lineage

Cytoplasmic CD3 or surface CD3



But, Summer 2022…

The 5th edition of the WHO classification of haematolymphoid tumors: Myeloid and histiocytic dendritic neoplasm

Khoury et al. Leukemia 2022 Jul; Jul;36(7):1703-1719.

International Consensus Classification of myeloid neoplasms and acute leukemias: integrating morphologic, clinical and genomic data

Arber et al. Blood 2022 Sep 15;140(11):1200-1228.

The 5th edition of the WHO classification of haematolymphoid tumors: Myeloid and histiocytic dendritic neoplasm

Khoury et al. Leukemia 2022 Jul; Jul;36(7):1703-1719.

- AML with defining genetic abnormalities
- AML with myelodysplasia-related changes
- Therapy-related myeloid neoplasms
- AML defined by differentiation
- Myeloid sarcoma
- Myeloid proliferations associated with Down syndrome

AML with recurrent genetic abnormalities, no blast cutoff

- Acut promyelocytic leukemia with *PML-RARA* fusion
- AML with *RUNX1-RUNX1T1* fusion
- AML *CBFB-MYH11* fusion
- AML with *DEK-NUP214* fusion
- AML with *RBM15-MRTFA* *fusion*
- AML with *BCR-ABL1* fusion, ≥20% blasts
- AML with *KMT2A* rearrangement
- AML with *MECOM* rearrangement
- AML with *NUP98* rearrangement
- AML with *NPM1* mutation
- AML with *CEBPA* mutation, ≥20% blasts
- AML with other defined genetic alterations
- AML myelodysplasia-related, ≥20% blasts, updated definition

AML, myelodysplasia-related

- ≥ 20% blasts in PB or BM
- AND one of the following:
  - History of MDS or MDS/MPN
  - Defining cytogenetic abnormalities
    - Complex karyotype: 3 or more chromosomal abnormalities
    - Unbalanced abnormalities: -7, del(7q), del(5q), i(17q), -13, del(13q), del(11q), del(12p), t(12p) or del(17p)
    - Loss of 5q, 7q, 12p or 17p due to unbalanced translocation
  - Defining somatic mutations
    - ASXL1, BCOR, EZH2, SF3B1, SRSF2, STAG2, U2AF1, ZSRS2
- AND absence of both prior cytotoxic therapy for unrelated disease and aforementioned recurring genetic abnormalities

Therapy-related myeloid neoplasms

t-AML, t-MDS or t-MDS/MPN

Excluded: progression from MPN or evolution of primary MDS or MDS/MPN to AML (secondary AML)

Cytotoxic agents implicated in therapy-related myeloid neoplasms

- Alkylating agents
- Ionizing radiation therapy
- Topoisomerase II inhibitors
- Others

AML defined by differentiation

- AML with minimal differentiation — FAB M0
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International Consensus Classification of myeloid neoplasms and acute leukemias: integrating morphologic, clinical and genomic data

Arber et al. Blood 2022 Sep 15;140(11):1200-1228.

- MDS/AML (previously MDS-EB2, 10-19% blasts)
- More genetically defined integrated classification
  - AML with recurrent genetic abnormalities
  - AML with myelodysplasia-related changes
  - ~~Therapy-related myeloid neoplasms~~
  - AML not otherwise specified
  - Myeloid sarcoma
- Myeloid proliferations associated with Down syndrome

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

Classification of AML with % blasts (1)

- Acute promyelocytic leukemia with t15;17)(q24.1;g21.2); *PML-RARA* ≥10%
- APL with other *RARA* rearrangements ≥10%
- AML with t(8;21)(q22;q22); *RUNX1-RUNX1T1* ≥10%
- AML with inv(16)(p13.1;1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11* ≥10%
- AML with t(9;11)(p21.3;q23.3); *KMT2A-MLLT3* ≥10%
- AML with other *KMT2A* rearrangements ≥10%
- AML with t(6;9)(p23;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 (supplemental table) ≥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* (MDS/AML 10-19 blasts, AML ≥20%)

Classification of AML (2)

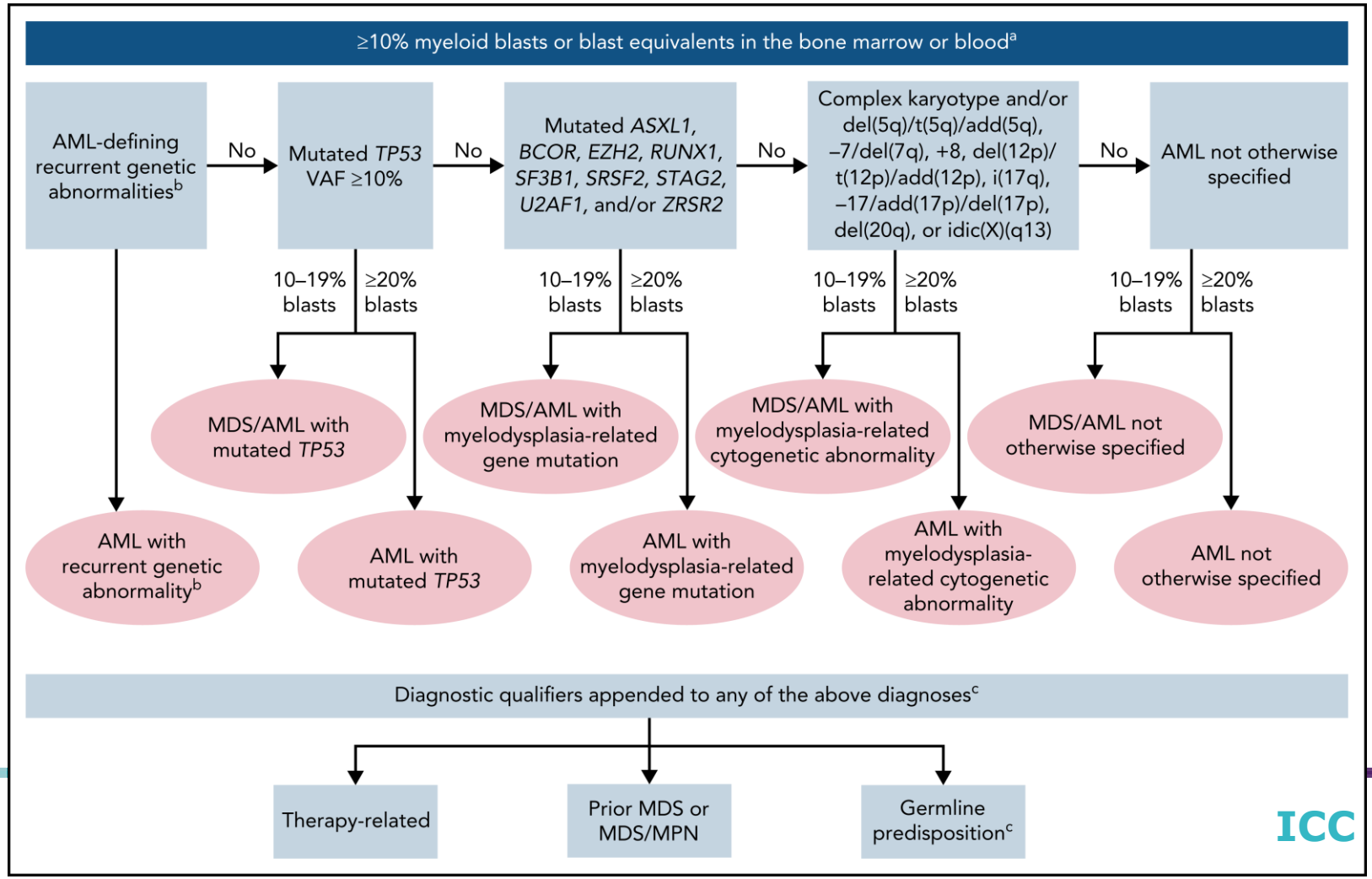
- **Supplemental Table: AML with other rare recurring translocations**
- AML with t(1;3)(p36.3;q21.3)/PRDM16::RPN1
- AML with t(3;5)(q25.3;q35.1)/NPM1::MLF1
- AML with t(8;16)(p11.2;p13.3)/KAT6A::CREBBP
- AML (megakaryoblastic) with t(1;22)(p13.3;q13.1)/RBM15::~~MKL1~~MRTF1
- AML with t(5;11)(q35.2;p15.4/ NUP98::NSD1
- AML with t(11;12)(p15.4;p13.3)/NUP98::KMD5A
- AML with NUP98 and other partners
- AML with t(7;12)(q36.3;p13.2)/ETV6::MNX1
- AML with t(10;11)(p12.3;q14.2)/PICALM::MLLT10
- AML with t(16;21)(p11.2;q22.2)/FUS::ERG
- AML with t(16;21)(q24.3;q22.1)/RUNX1::CBFA2T3
- AML with inv(16)(p13.3q24.3)/CBFA2T3::GLIS2

Classification of AML with % blasts (3)

- AML and MDS/AML with myelodysplasia-related gene mutations (MDS/AML 10-19 blasts, AML ≥20%) Defined by mutations in ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1 or ZSRS2
- AML with myelodysplasia-related cytogenetic abnormalities (MDS/AML 10-19 blasts, AML ≥20%) 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) (MDS/AML 10-19 blasts, AML ≥20%)
- Myeoid sarcoma

Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the European LeukemiaNet

Döhner et al. Blood 2022 Sep 22;140(12):1345-1377



ICC 2022

Literature AML

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