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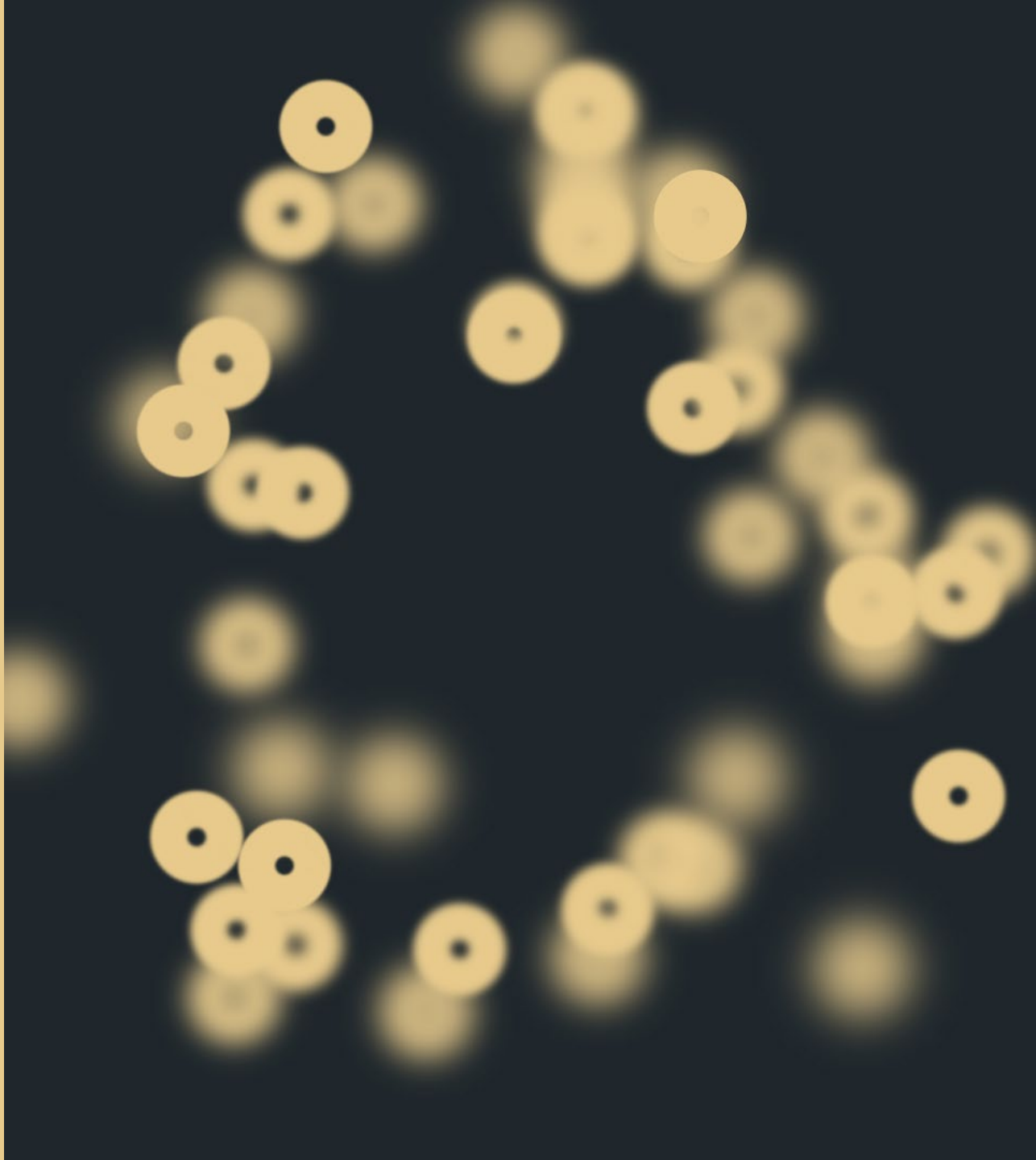
EHA-SWG Scientific Meeting on Recent Advances in the Pathogenesis and Treatment of Secondary Acute Myeloid Leukemias

Berlin, Germany
April 25-26, 2025



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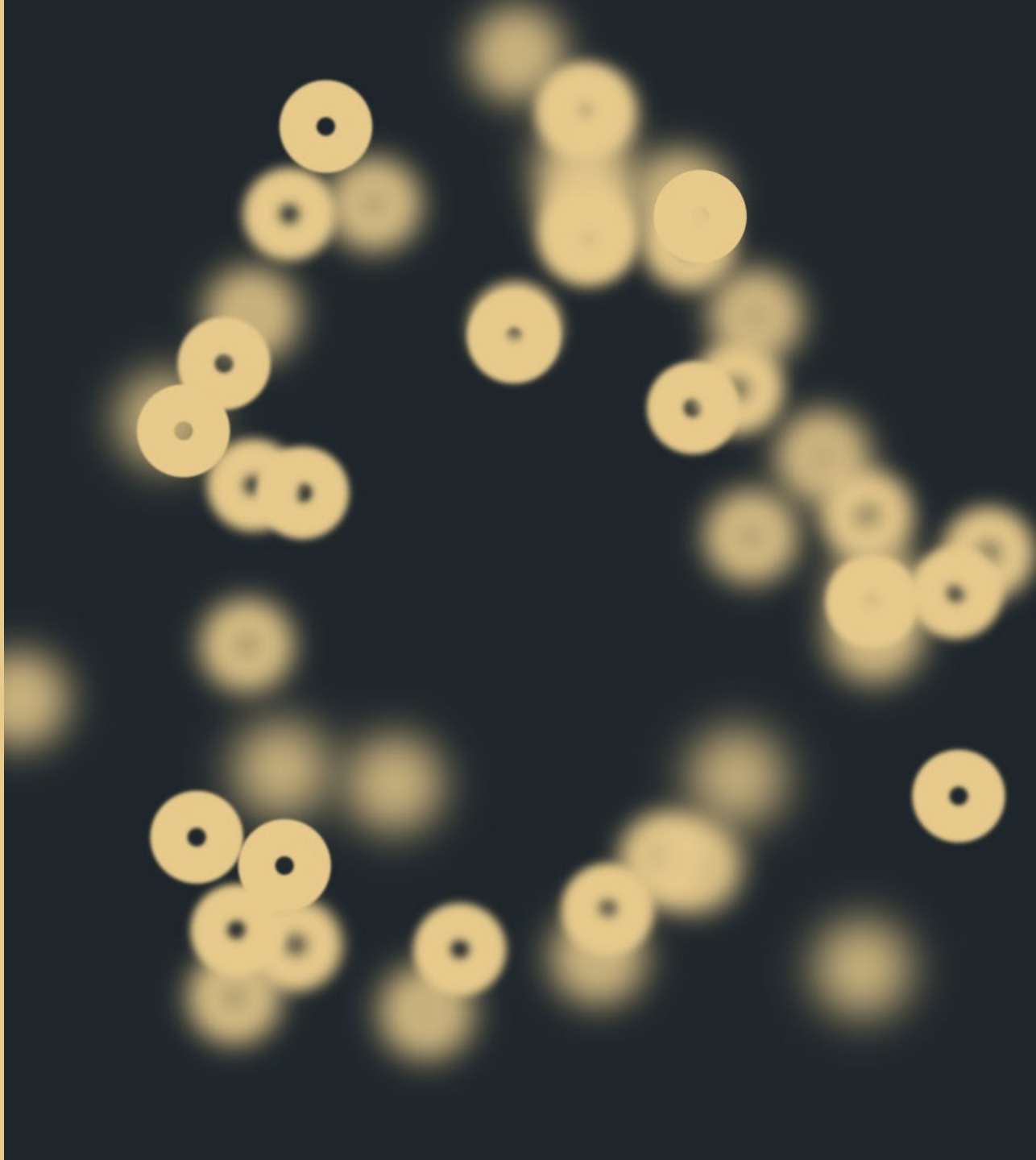
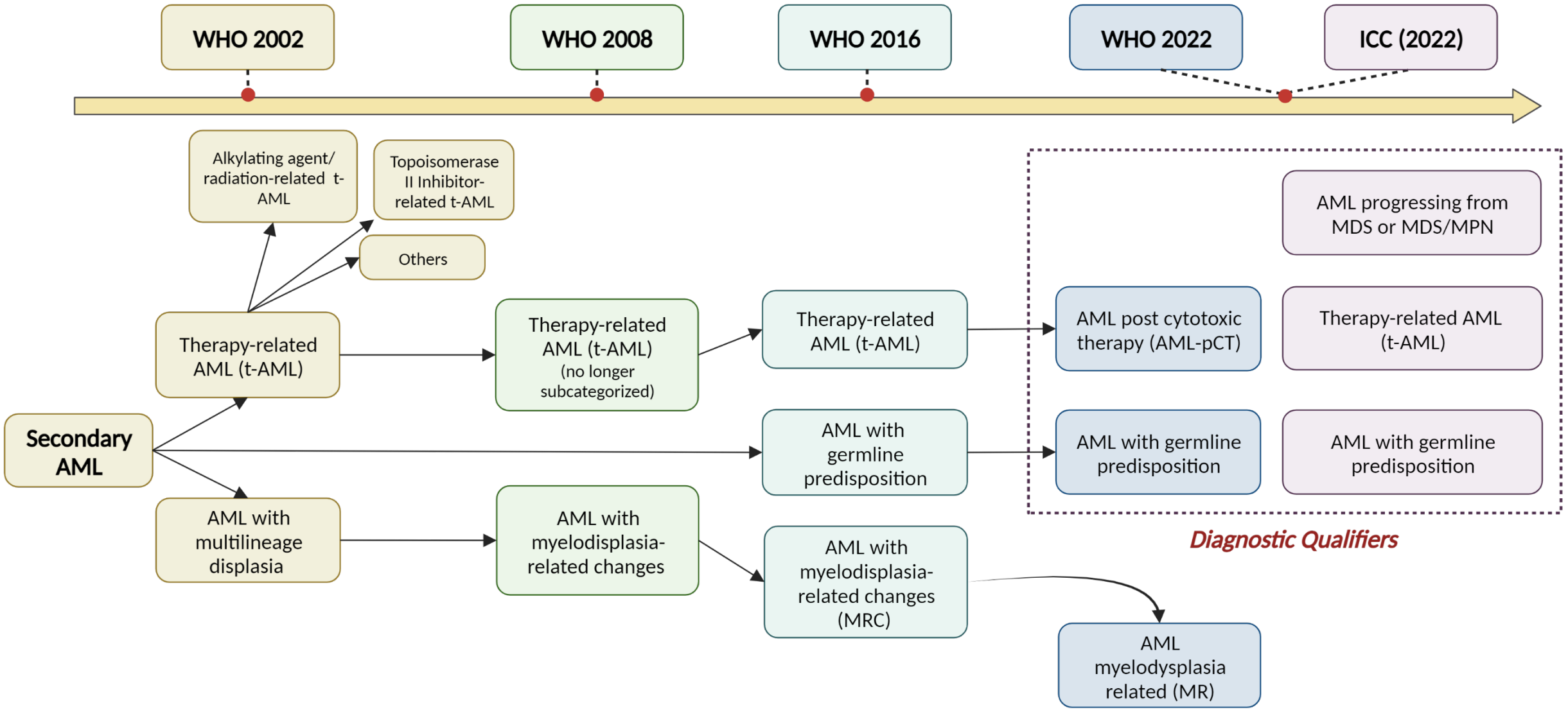
Navigating the borderland of secondary AML: refining the diagnostic qualifiers and evaluating the impact of 20% blast threshold

Enrico Attardi, MD, PhD

University of Rome Tor Vergata,
Department of Biomedicine and Prevention



Evolution of secondary AML classification



Modified from Guarnera L

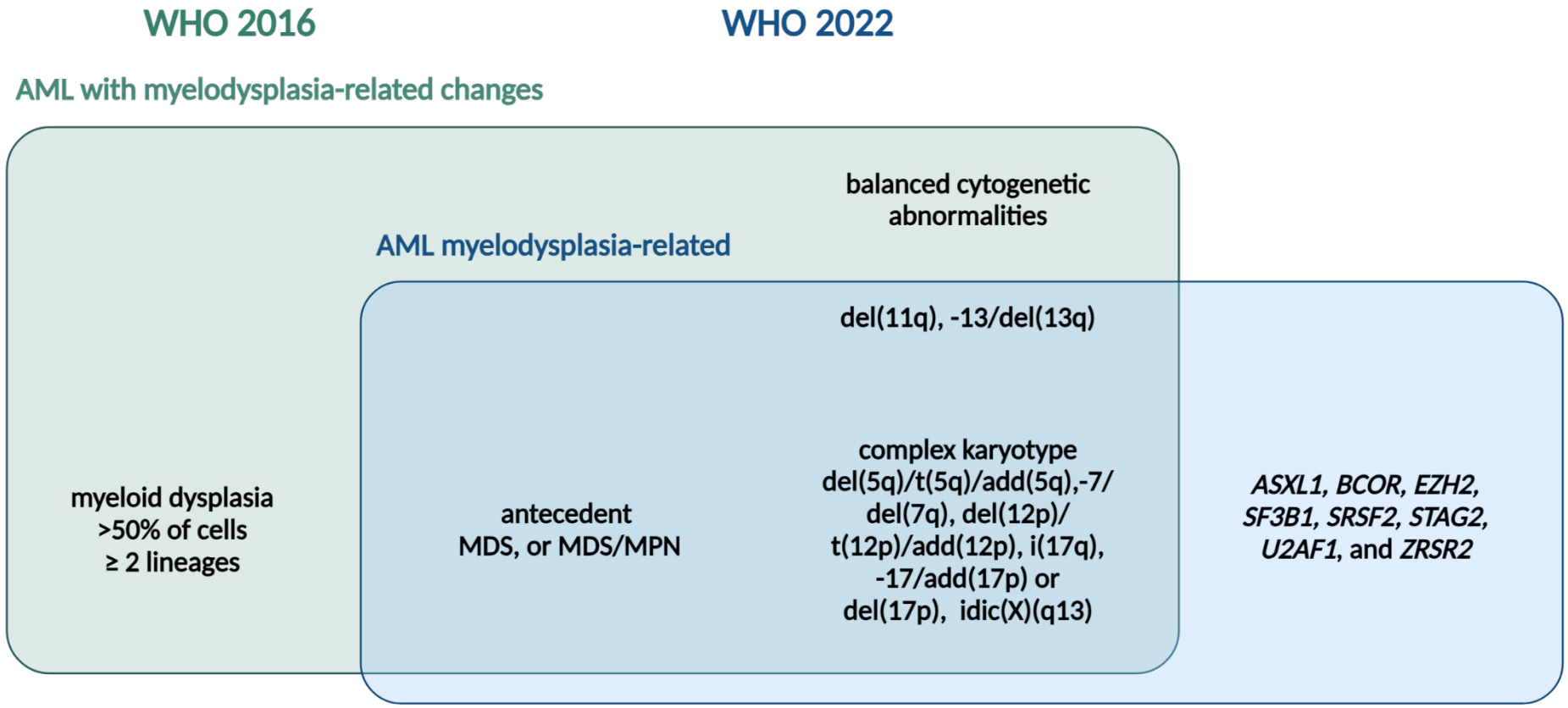
AML myelodysplasia related

WHO 2016

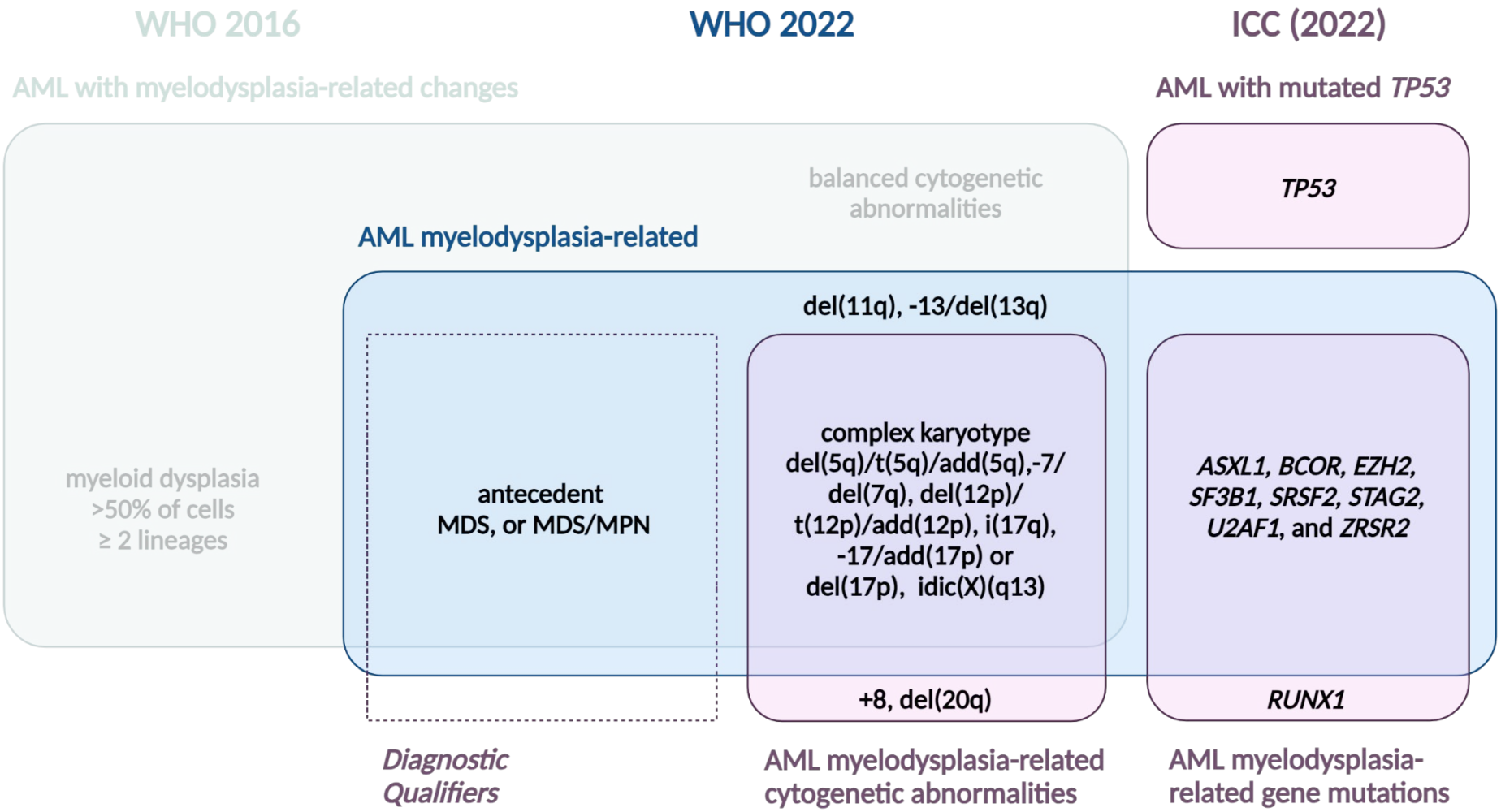
AML with myelodysplasia-related changes

		balanced cytogenetic abnormalities
		del(11q), -13/del(13q)
myeloid dysplasia >50% of cells ≥ 2 lineages	antecedent MDS, or MDS/MPN	complex karyotype del(5q)/t(5q)/add(5q),-7/ del(7q), del(12p)/ t(12p)/add(12p), i(17q), -17/add(17p) or del(17p), idic(X)(q13)

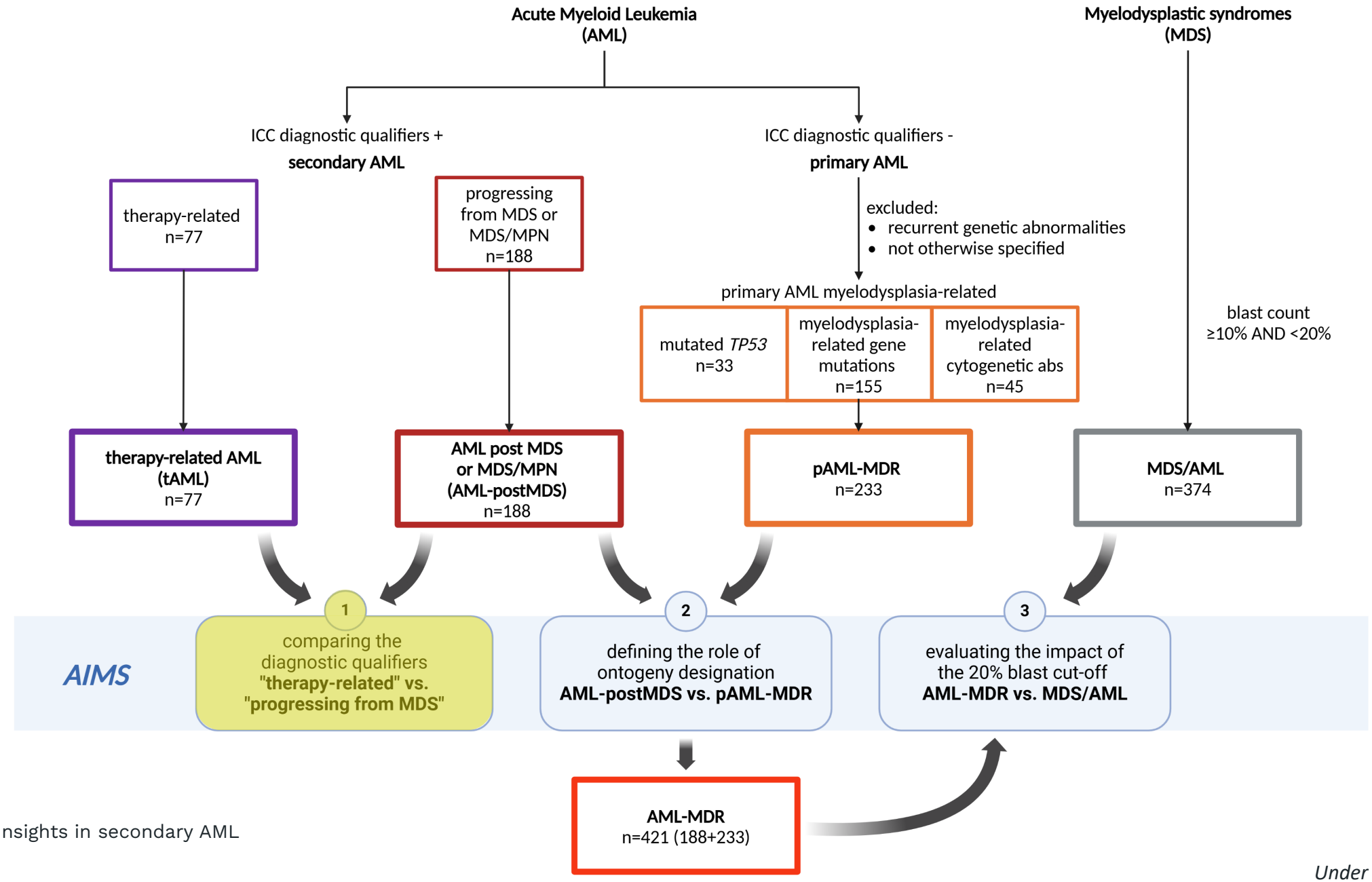
AML myelodysplasia related



AML myelodysplasia related



Study population and aims



Diagnostic classification of AML-postMDS and tAML

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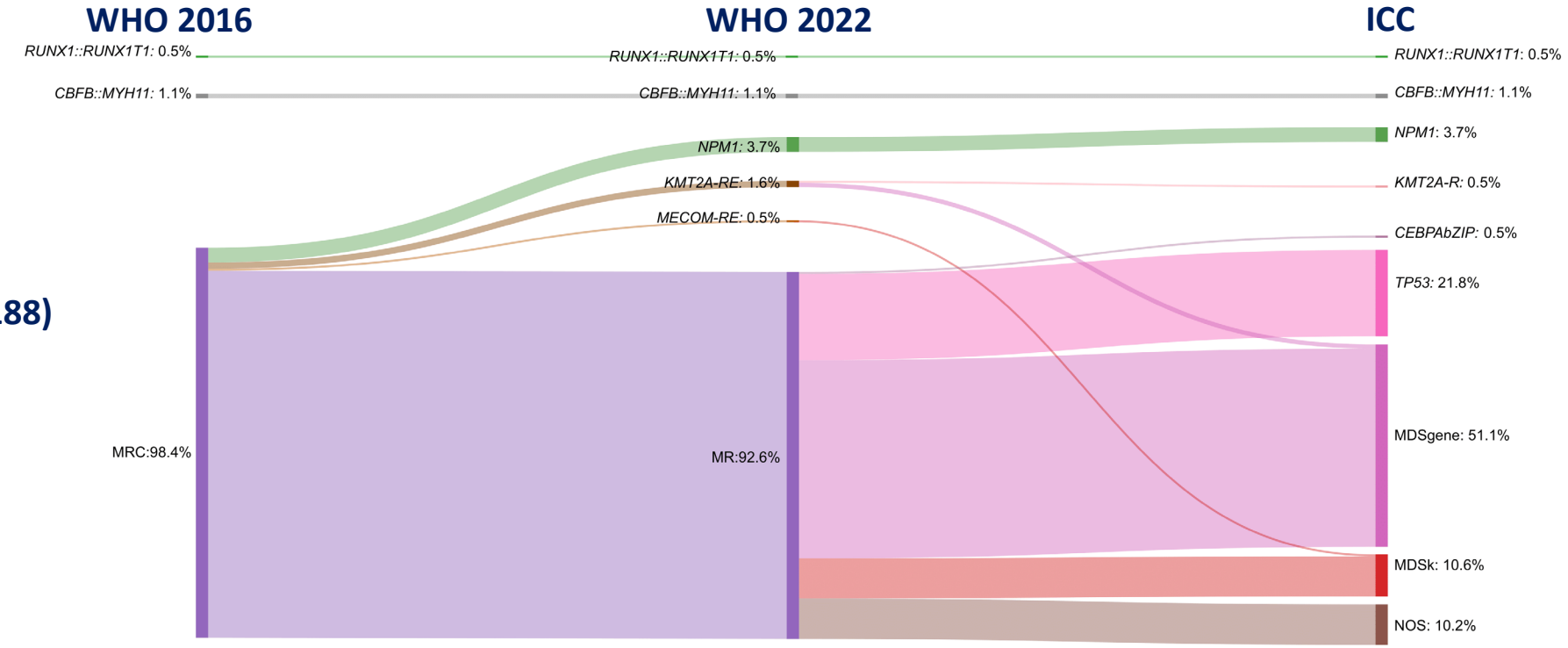
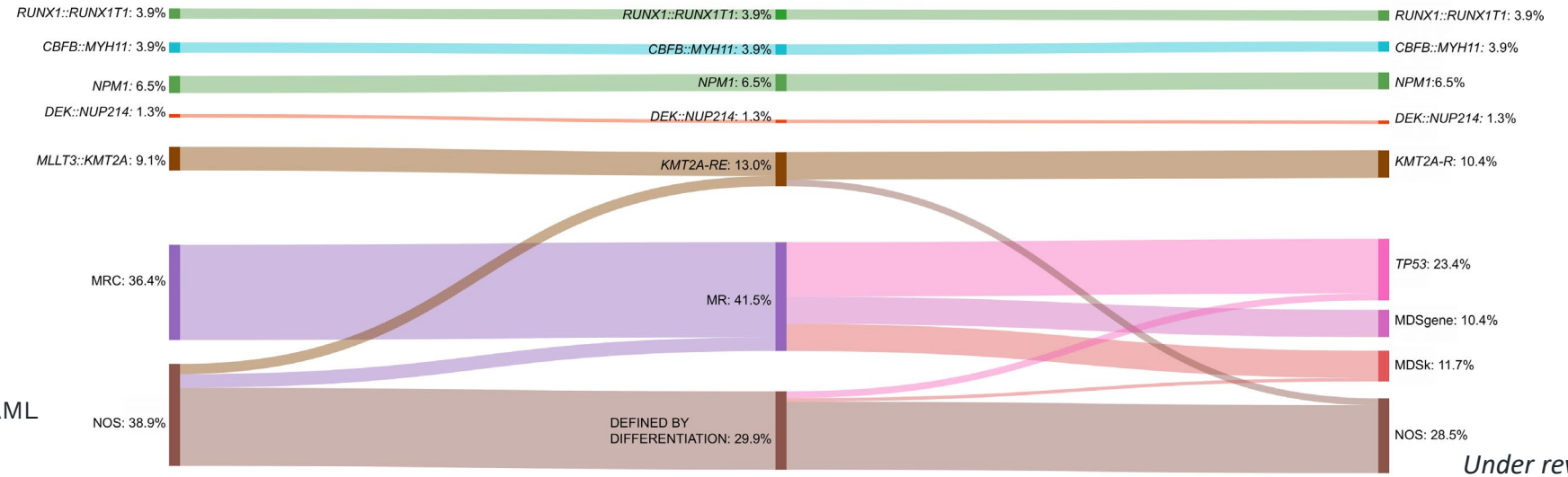
AML-postMDS (n=188)



tAML (n=77)



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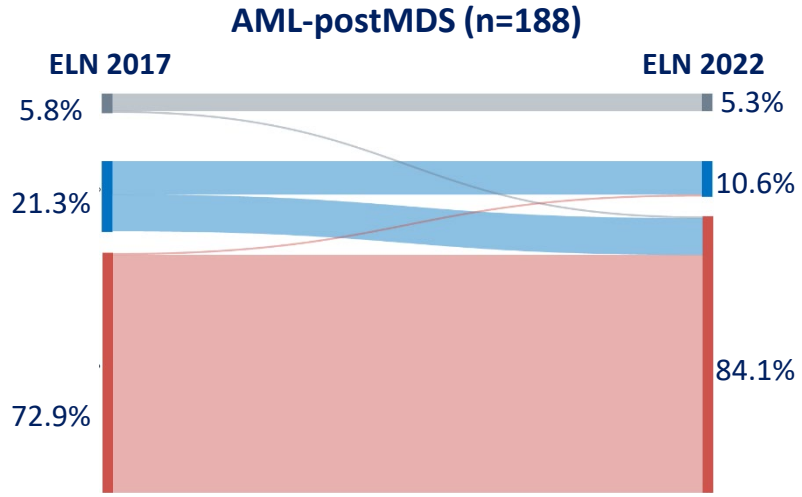
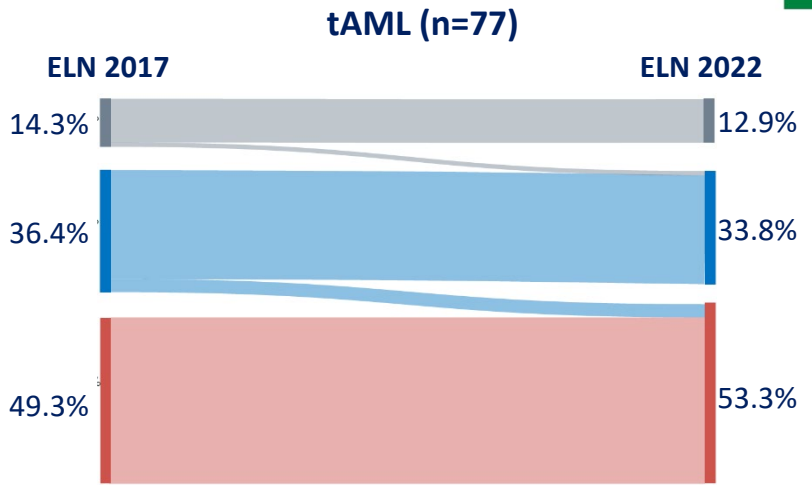
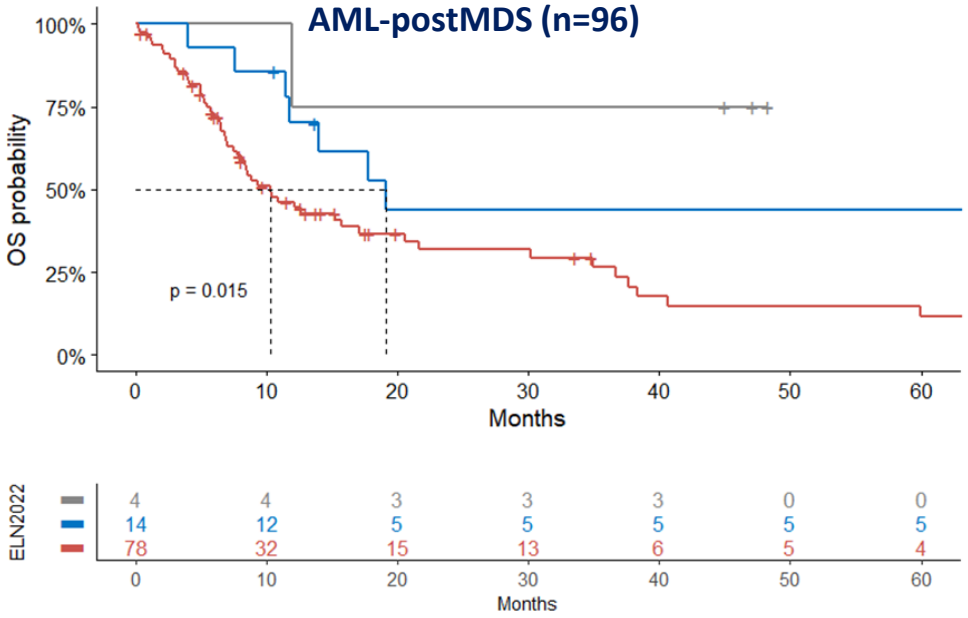
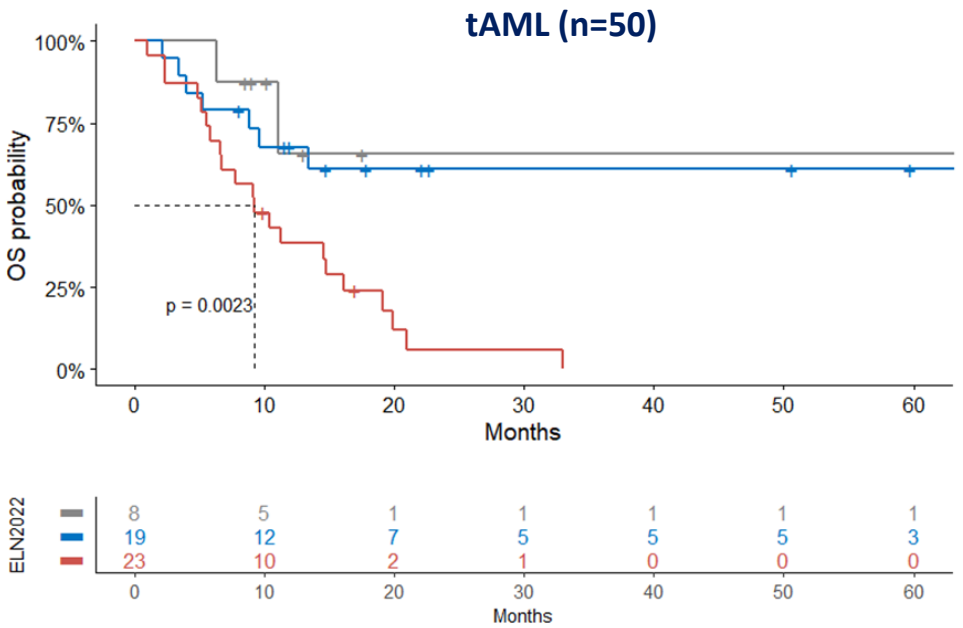
Stratification and outcome of AML-postMDS and tAML





Risk categorIes: Favorable Intermediate Adverse

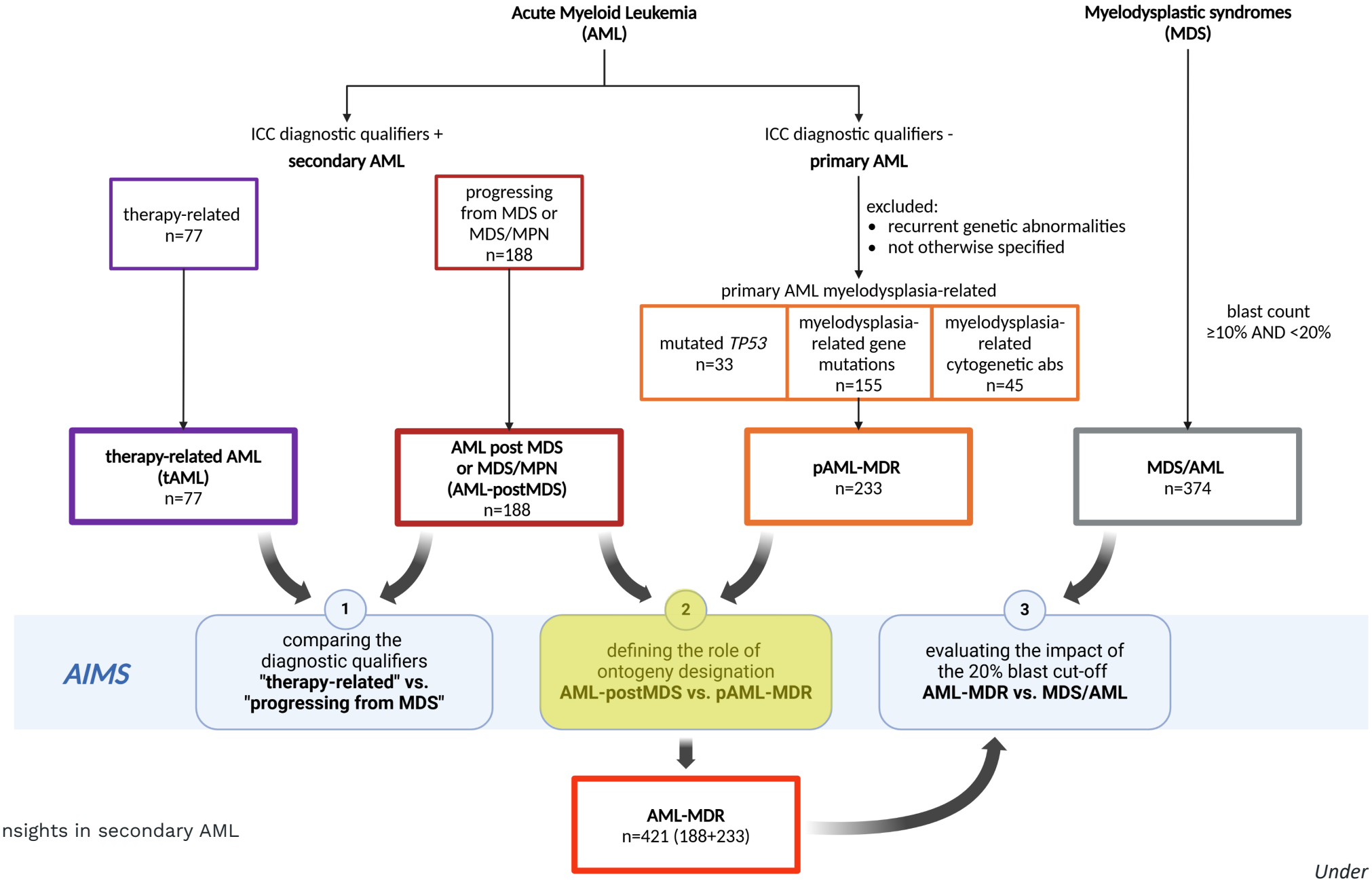




Log-rank test pairwise Intermediate-Adverse: **p=0.059**

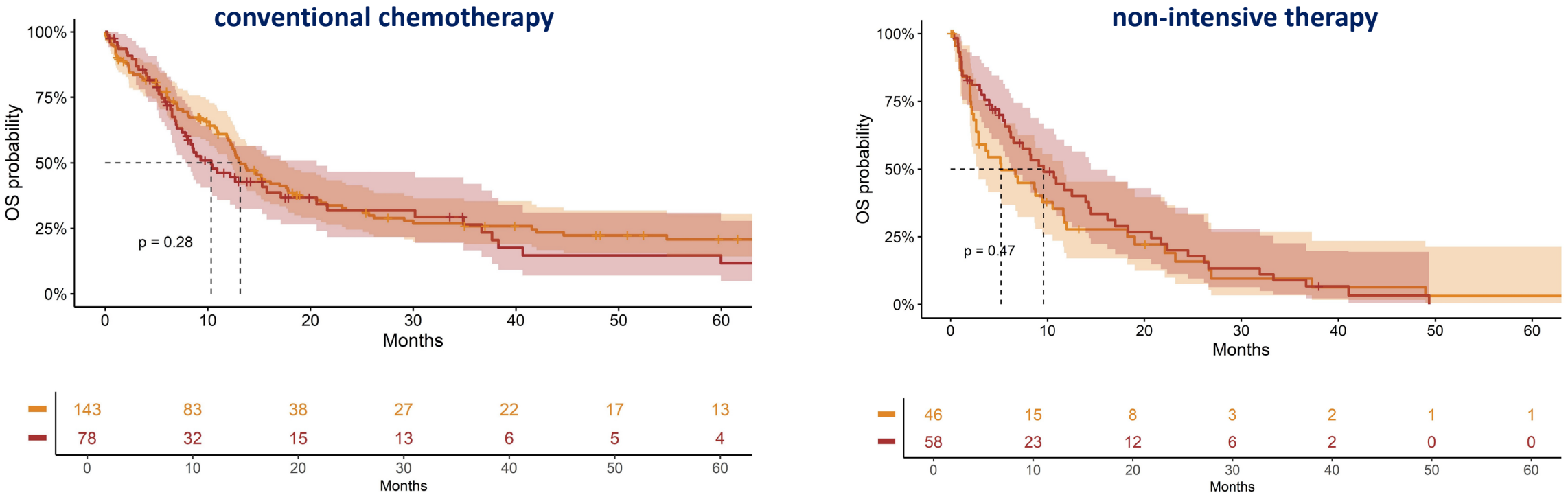
Log-rank test pairwise Intermediate-Adverse: **p=0.007**

Study population and aims



Anamnestically vs. genetically-defined secondary AML

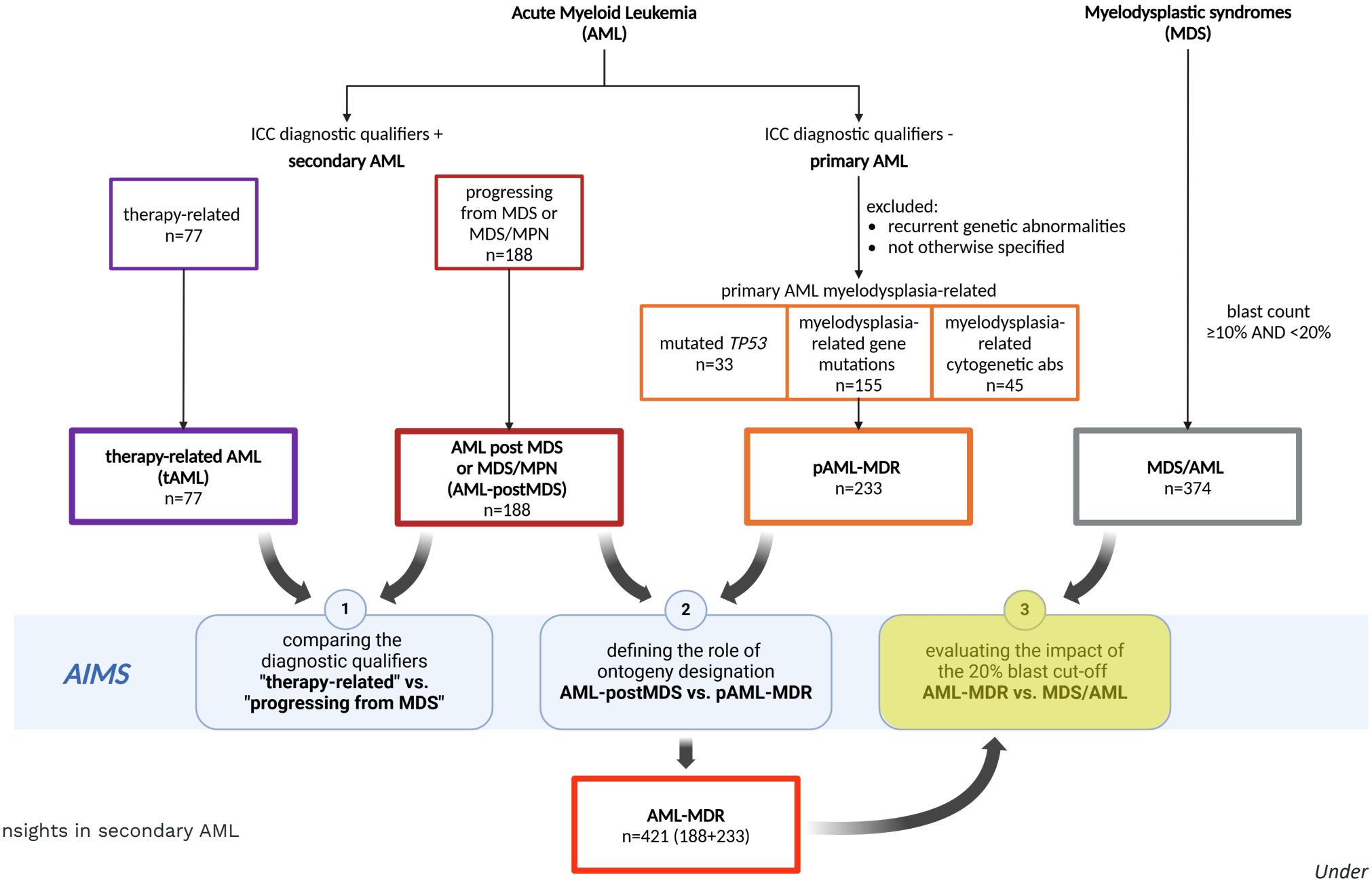
No significant differences in terms of number of mutations, frequency of genetic alterations (gene mutations and MDR cytogenetic abnormalities) and the clone size of MDR gene mutations, except for *TP53*$_{mut}$ (↑ in AML-postMDS)



Adverse ELN 2022 pAML-MDR AML-postMDS

Anamnestically vs. genetically-defined secondary AML are also similar in the outcome

Study population and aims



Navigating the MDS and AML boundaries: 20% blast threshold

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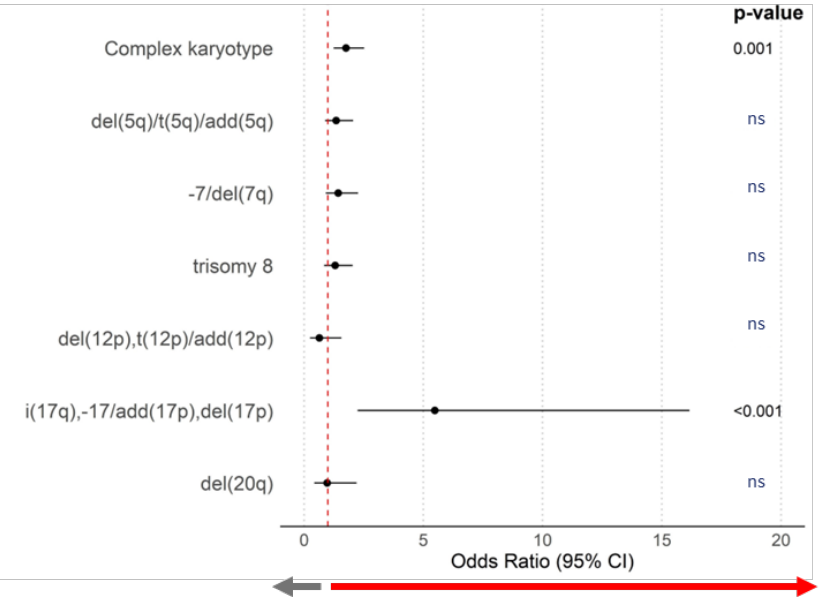
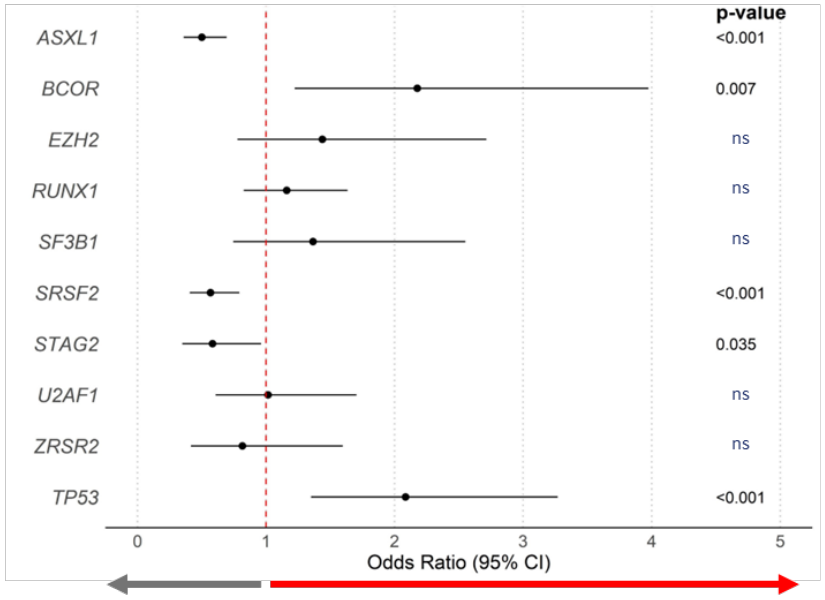
MDR cytogenetic abnormalities



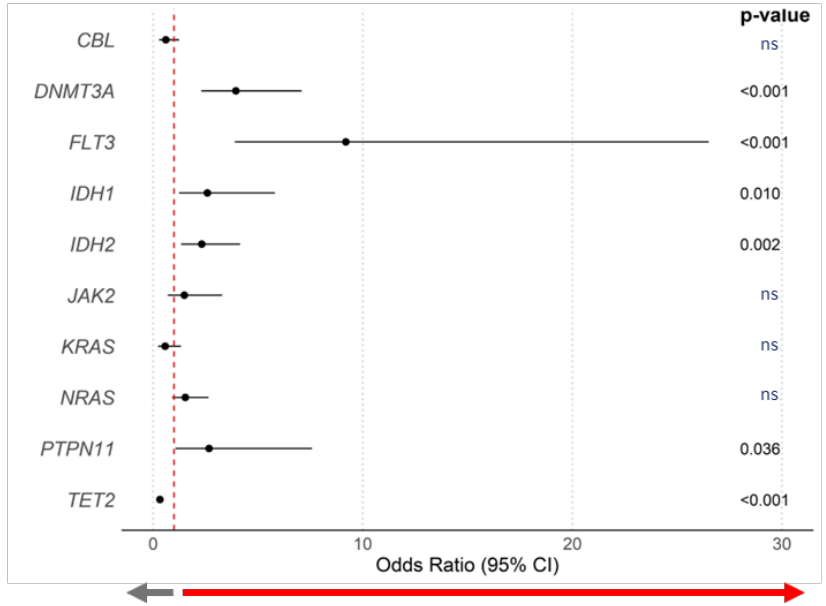
MDS/AML n=374 — AML-MDR n=421

TP53 and MDR gene mutations



MDS/AML — AML-MDR

Other myeloid mutations



MDS/AML — AML-MDR

The 20% blast threshold remains a complemental diagnostic and prognostic tool,
as MDS/AML and AML categories exhibit specific differences in their biological profiles…

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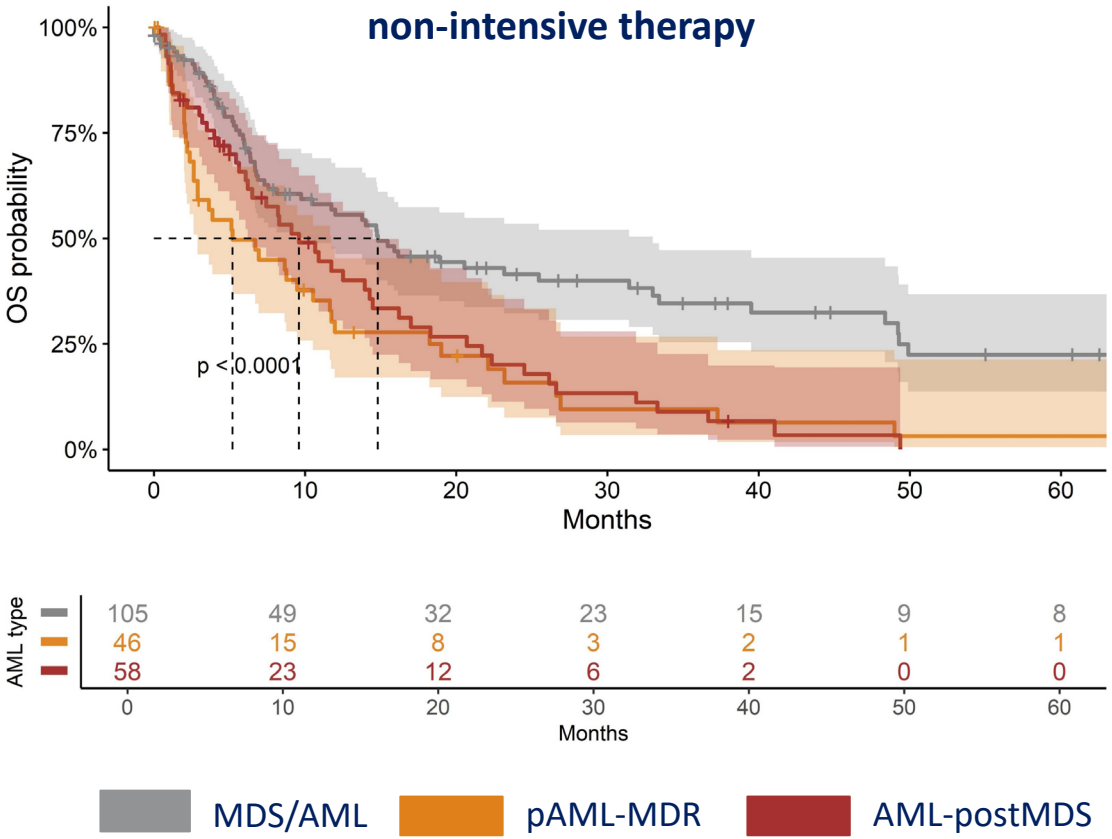
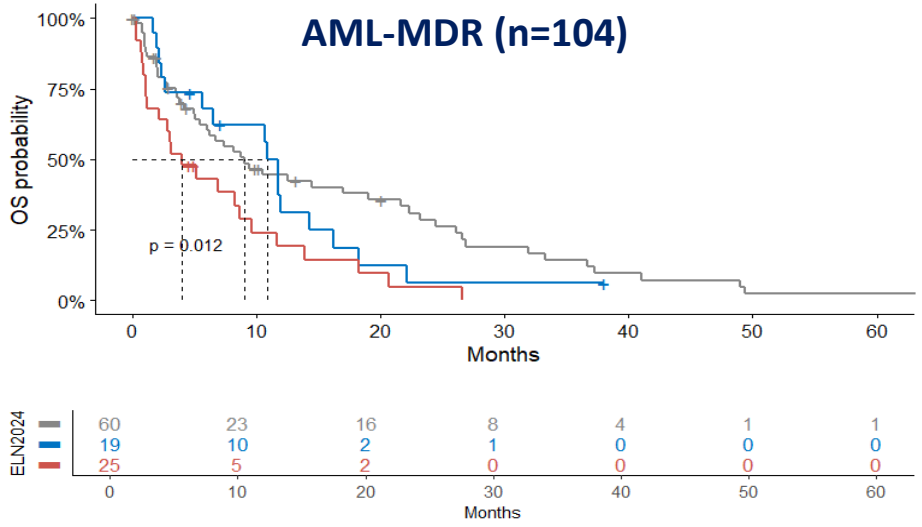
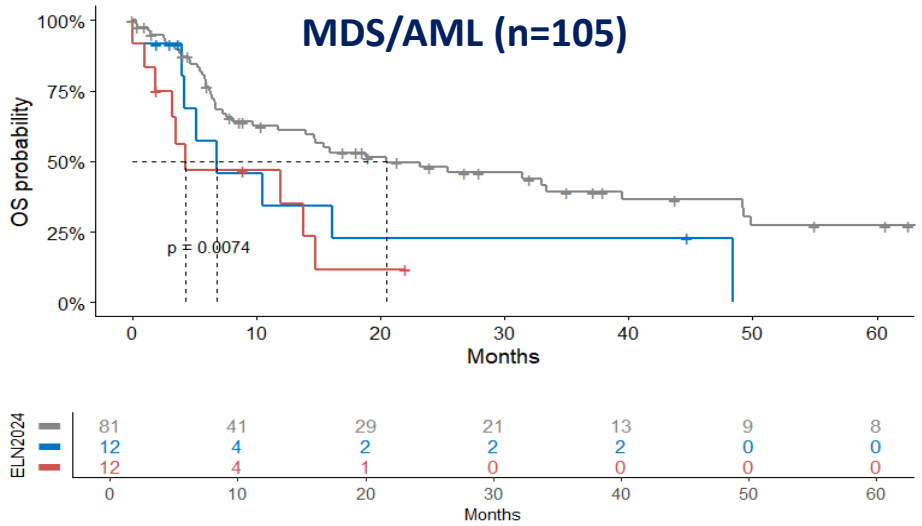
Navigating the MDS and AML boundaries: 20% blast threshold







MDS/AML vs. pAML-MDR HR:2.26, 95%CI 1.51-3.38, p<0.001

MDS/AML vs. AML-postMDS HR:1.90, 95%CI 1.30-2.79, p<0.001

…and differences in their clinical outcomes.

Conclusion

- Even when excluding a history of MDS or MDS/MPN as a “classifier”, over 80% of AML-postMDS cases fell within the “myelodysplasia-related” ICC categories, and into the ELN 2022 adverse risk category. This qualifier, may suggest unfavorable outcomes from the very first day of diagnosis.

- Therapy-related AML should be diagnostically approached as "second" neoplasms, rather than being categorized as “secondary” AML.

- Overlap between genetically vs. anamnestically defined secondary AML suggests that the ontogeny designation is not the real “watershed” of AML subcategories, and that genetic signature plays a dominant role.

- Conversely, the 20% blast threshold remains a complemental diagnostic and prognostic tool, as MDS/AML and AML categories exhibit specific differences in their biological profiles.

- In this “transition era”, our analysis emphasized the importance of incorporating clinical and genetic characteristics, for an integrated diagnostic approach of secondary AML and MDS/AML.

Acknowledgements

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