Society for Hematopathology

Webinar Q&A: June 17, 2026

"RUNX1-Mutated Acute Myeloid Leukemia: Phenotypic Heterogeneity And Classification Dilemma"

Speaker:
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1. **Question**: When you mention the increased pDC what is your cut-off and does the increase in number go hand in hand with prognosis, so 2% pDC has better prognosis than 4% pDC?
   Answer: We have not done this analysis but we should as we have accumulated more cases by now.

2. **Question:** If RUNX1 mutation is required for pDC differentiation, why are the allele frequencies of RUNX1 mutation in AML-pDC <100%?
   Answer: Most cases have heterozygous mutation, therefore, 40-50% VAF of RUNX1 mutation means every single sorted blast carries the mutation.

3. **Question:** Is TCL1 only a marker of BPDCN or can that be seen on normal PDCs?
   Answer: TCL1 can be seen in normal pDCs but its expression is upregulated in BPDCN.

4. **Question:** pDC-AML in the setting of post-cytotoic therapy, how to classify? Its prognosis vs. prognosis of AML, PCT?
   Answer: pDC-AML can be seen in therapy-related or post cytotoxic setting. As we move towards genomic classification, I would say pDC-AML has a better prognosis than AML with mutated TP53, but likely similar to or slightly worse than AML MR. We should get this comparison done in our next study.

5. **Question:** Based on these new findings you shared, how do you classify increased blasts <20% with mutated TP53?
   Answer: Currently, ICC classifies these as MDS/AML with mutated TP53. Increasing evidence suggests that for TP53, patients with 10-19% blasts vs >=20% blasts show similar inferior outcomes and they should be classified and managed similarly.

6. **Question:** Would an AML with deletion 17p (incl TP53 locus) but no P53 mutation by NGS be best classified as AMl-MR (and not AML with mutated TP53)?
   Answer: Current classifications would support AML MR designation in this situation. A multicenter study may be required to evaluate the significance of del17p without TP53.

7. **Question:** You mentioned that complex karyotype does not change the prognosis so why do you propose keeping it as a classifier for AML-MR?
   Answer: Sorry if I was not clear on this. CK comes as different forms.
   A, if CK is concurrent with a driver fusion such as BCR-ABL1, BCR-ABL1 fusion will supersedes CK. We do not reclassify such cases from BCR-ABL1 MPAL to AML MP.
   B, if CK is hyperdiploid karyotypes with three or more trisomies (or polysomies) without structural abnormalities, these should not reclassify MPAL to AML MP.
   C. if CK involves del5/5q, del7/7q, and/or del17/d17p, these are real MR CK. In the absence of other drivers, these CK would classify MPAL to AML MP.

8. **Question:** could you further discuss if there were any differences (OS, genetics) between T/myeloid vs B/Myeloid in cases that you ultimately classified as AML-MP vs MPAL from your 2025 study? also were you using WHO4R/ICC or WHO5 criteria for MPAL classification?
   Answer: We did not perform that analysis but it is a good question. We should do it for our next study.
   For 2025 study, we started with WHO4R, and compared to ICC and WHO5 (data not shown in the paper). Eventually we proposed a genomic approach. More work needs to be done to validate the genomic approach.

9. **Question:** With regards to AMLs with increased PDCs did you also compare them to AML cases with increased CD123 expression. If yes, were their any differences? Also did the myeloid balsts in pDC-AML show increased CD123 expression?
   Answer: Good point! No, but we should do it.

10. **Question:** If a patient has acute leukemia, complex karyotype and have mixed phenotype. Would it be AML-MP or MPAL. Does the complex karyotype differ if it has an MDS defining cytogenetic abnormality?
    Answer: Please refer to question 7.

11. **Question:** Does your proposed algorithm apply to MPAL with two distinct myeloid and lymphoid blast populations? How about Acute undifferentiated leukemia?
    Answer: We did not separate biphenotypic from ambiguous lineage. AUL was not included in our study.

12. **Question:** Is the lineage dominance among blast population (e.g. % of blasts being myeloid vs lymphoid lineage) by flow cytometry useful to distinguish between AML-MP and MPAL?
    Answer: No. MPAL can (and often) have myeloid predominance.

13. **Question:** What´s the WHO approach if you have for example AML with a big myeloid clone and a small additional clone with different phenotype, i.e. B/T-phenotype? Would you call it AML-MP or AML with small clone with B/T-phenotype, like suggested in ICC?
    Answer: Depending how small the additional clone is. We still do not have a consensus on the percent cutoff of blast population. In our practice, we prioritize the genomics. For example, in a patient with TP53 mutation and no other drivers, we would call it AML despite mixed phenotype.
    In comparison, in a patient with PICALM::MLLT10 fusion, BM can show pure myeloid blasts, while skin or lymph node show pure lymphoid blasts, and sometimes, another biopsy shows a mixed phenotype with myeloid or lymphoid as the predominant population. Regardless, this is MPAL.
    In a patient without such drivers, for example, only with RUNX1/IDH2 mutation and no other significant aberrations, flow shows 95% blasts are myeloid and 5% immature T or B, we would still classify it MPAL. However, we would note the myeloid predominance in our report and clinician may treat the patients with myeloid regimen. How to treat MPAL is a different topic.