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| cLINICAL UTILITY OF MOLECULAR TESTING IN  AML in morphological remission  Mutations detected at low variant allele frequency in a remission bone marrow sample may represent the presence of low level residual disease or alternatively the presence of a pre-leukaemic clone. Mutations found at high variant allele frequency in a remission sample most likely represent the presence of a pre-leukaemic clone.  Mutations in *DNMT3A*, *TET2* and *ASXL1* (‘DTA’ mutations) commonly persist in remission of AML and do not adversely impact on relapse rate or survival outcomes1,2.  In contrast, persistent non-DTA mutations regardless of variant allele frequency, are associated with an increased risk of relapse and inferior overall survival1,2.  Molecular MRD monitoring by RT-qPCR assays is routinely recommended in AML subtypes where validated MRD markers are available: *PML-RARA*, *RUNX1-RUNX1T1*, *CBFB-MYH11* and *NPM1* mutations3.  Other rare gene fusions in AML potentially feasible for MRD tracking include: *KMT2A* fusions, *DEK-NUP214* and *BCR-ABL1*4.  Ultra-deep sequencing by NGS5 may be performed for the MRD monitoring of other mutations such as *NPM1* (non-type A/B/D).  Detectable MRD by NGS pre- and post-transplant is predictive of relapse and survival, and may help refine transplantation and post-transplantation management in AML6-8.  Some mutations have a potential for germline predisposition to haematological malignancy: *CEBPA*, *DDX41*, *RUNX1*, *ANKRD26*, *ETV6*, *GATA2* and *TP53*. The persistence of these mutations in remission at a variant allele frequency ~50% should prompt consideration of germline sample testing in the appropriate clinical context.  References  **1.** Jongen-Lavrencic M, et al. Molecular Minimal Residual Disease in Acute Myeloid Leukemia. *N Engl J Med* 2018; **378**(13): 1189-99. **2.** Morita K, et al. Clearance of Somatic Mutations at Remission and the Risk of Relapse in Acute Myeloid Leukemia. *J Clin Oncol* 2018; **36**(18): 1788-97. **3.** Schuurhuis GJ, et al. Minimal/measurable residual disease in AML: a consensus document from the European LeukemiaNet MRD Working Party. *Blood* 2018; **131**(12): 1275-91. **4.** Grimwade D, Freeman SD. Defining minimal residual disease in acute myeloid leukemia: which platforms are ready for "prime time"? *Blood* 2014; **124**(23): 3345-55. **5.** Blombery P, et al. Sensitive NPM1 Mutation Quantitation in Acute Myeloid Leukemia Using Ultradeep Next-Generation Sequencing in the Diagnostic Laboratory. *Arch Pathol Lab Med* 2018; **142**(5): 606-12. **6.** Thol F, et al. Measurable residual disease monitoring by NGS before allogeneic hematopoietic cell transplantation in AML. *Blood* 2018; **132**(16): 1703-13. **7.** Hourigan CS, et al. Impact of Conditioning Intensity of Allogeneic Transplantation for Acute Myeloid Leukemia With Genomic Evidence of Residual Disease. *J Clin Oncol* 2020; **38**(12): 1273-83. **8.** Heuser M, et al. Posttransplantation MRD monitoring in patients with AML by next-generation sequencing using DTA and non-DTA mutations. *Blood Adv* 2021; **5**(9): 2294-304. |