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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* mutations3,4.  Other rare gene fusions in AML potentially feasible for MRD tracking include: *KMT2A* fusions, *DEK*::*NUP214* and *BCR*::*ABL1*5.  Detectable *FLT3*-ITD by deep NGS after chemotherapy or pre-transplant is associated with increased risk and reduced overall survival6,7. However, the role of serial *FLT3*-ITD monitoring is not established. A proportion of patients (~20%) could also lose *FLT3*-ITD at the time of AML relapse8.  Detectable MRD by NGS pre- and post-transplant is predictive of relapse and survival, and may help refine transplantation and post-transplantation management in AML9-11.  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.** Heuser M, et al. 2021 Update on MRD in acute myeloid leukemia: a consensus document from the European LeukemiaNet MRD Working Party. *Blood* 2021; **138**(26): 2753-67. **5.** 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. **6.** Loo S, et al. Pretransplant FLT3-ITD MRD assessed by high-sensitivity PCR-NGS determines posttransplant clinical outcome. *Blood* 2022; **140**(22): 2407-11. **7.** Grob T, et al. Prognostic Value of FLT3-Internal Tandem Duplication Residual Disease in Acute Myeloid Leukemia. *J Clin Oncol* 2023; **41**(4): 756-65. **8.** Cloos J, et al. Stability and prognostic influence of FLT3 mutations in paired initial and relapsed AML samples. *Leukemia* 2006; **20**(7): 1217-20. **9.** Thol F, et al. Measurable residual disease monitoring by NGS before allogeneic hematopoietic cell transplantation in AML. *Blood* 2018; **132**(16): 1703-13. **10.** Hourigan CS, et al. Impact of Conditioning Intensity of Allogeneic Transplantation for Acute Myeloid Leukemia With Genomic Evidence of Residual Disease. *Journal of Clinical Oncology* 2020; **38**(12): 1273-83. **11.** 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. |