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| Clinical utility of molecular testing in  acute myeloid leukaemia  Diagnostic Utility  Acute myeloid leukaemia (AML) with defining genetic abnormalities includes AML with specific gene fusions (e.g. *RUNX1*::*RUNX1T1*), gene rearrangements (*KMT2A*, *MECOM* and *NUP98*), and gene mutations (*NPM1, CEBPA* and myelodysplasia-related [MR])1*.*  AML-MR include mutations in *ASXL1*, *BCOR, EZH2*, *SF3B1*, *SRSF2*, *STAG2, U2AF1, ZRSR2* (WHO and ICC)1,2and *RUNX1* (ICC)2.  AML with *BCR*::*ABL1* fusion is a rare *de novo* AML, or alternatively represents blast phase of chronic myeloid leukaemia.  *KIT* mutations are rarely observed in non-core binding factor AML3; testing for t(8;21) and inv(16) should be considered.  *JAK2* Val617Phe mutations are infrequent in *de novo* AML; a preceding myeloproliferative neoplasm should be considered3.  *RUNX1* mutations are rare in BPDCN but are more typical of AML with plasmacytoid dendritic cell expansion (pDC-AML)4,5,6.  Acute erythroid leukaemia is characterised by a high prevalence of multi-hit *TP53* alterations and complex karyotype7.  *UBTF*-TD are associated with dysplasia, normal karyotype or trisomy 8, and mutations in *WT1* and *FLT3*-ITD8,9.  In-frame insertion mutations in *CBFB* are similar to inv(16) AML but without the *CBFB*::*MYH11* fusion10.  Some mutations have potential germline predisposition: *CEBPA*, *DDX41*, *RUNX1*, *ANKRD26*, *ETV6*, *GATA2* and *TP53*. Testing a remission and/or germline sample in the appropriate clinical context should be considered.  Prognostic Utility  ELN 2022 and proposed 2024 risk stratifications are used for patients treated with intensive11 and less-intensive12 therapies (Table) (the later applicable to patients receiving HMA monotherapy, HMA/VEN, or AZA/IVO [for *IDH1* mut AML]). Beat-AML 2024 is an alternative risk model for AML treated with less-intensive therapies13.  MRD assessment may be a more potent independent predictor of outcome compared to the baseline molecular profile14,15.  *UBTF*-TD8,9 and *NUP98-*rearranged16,17 AML are associated with inferior outcomes.    BIOMARKERS OF RESPONSE TO THERAPY  *FLT3* mutations are the target of midostaurin18 (*FLT3*-ITD and TKD) (clinical trials included only TKD mutations at Asp835 and Ile836 codons), quizartinib (*FLT3*-ITD only)19 in newly diagnosed AML, and gilteritinib20 in relapsed/refractory AML.  *FLT3* testing should be repeated at relapse/progression as ~20% of patients have a gain or loss in mutation status21.  *IDH1* (Arg132) and *IDH2* (both Arg140 and Arg172) mutations are the target of IDH1 and IDH2 inhibitors, respectively22.  AML with *UBTF*-TD, *DEK*::*NUP214*, or *NUP98* rearrangement have a transcriptional signature similar to *KMT2A*-rearranged AML, including *HOX* gene dysregulation, and are potentially targetable by menin inhibitors23,24.  Acquired resistance to targeted inhibitors have been described with *FLT3* Phe691Leu (FLT3 inhibitors)25, second-site *IDH1*/*IDH2* mutations (IDH1/IDH2 inhibitors)26, *BAX* (BCL2 inhibitors)27, and *MEN1* (menin inhibitors)28.  References  **1.** WHO Classification of Tumours Editorial Board. Haematolymphoid tumours. Lyon (France): International Agency for Research on Cancer; 2024. 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