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| Clinical utility of molecular testing in  acute myeloid leukaemia  Diagnostic Utility  In the WHO revised 4th edition classification, acute myeloid leukaemia (AML) with recurrent genetic abnormalities includes AML with mutated *NPM1*, AML with biallelic mutation of *CEBPA*, and AML with mutated *RUNX1* (provisional)*1.*  The presence of a mutation in *SRSF2*, *SF3B1*, *U2AF1*, *ZRSR2*, *ASXL1*, *EZH2*, *BCOR* or *STAG2* has been shown to be highly specific (>95%) for a diagnosis of secondary AML, even without a known antecedent MDS diagnosis3.  *KIT* mutations are rarely observed in non-core binding factor AML2 and therefore if detected, specific testing for t(8;21) and inv(16) should be considered.  *JAK2* Val617Phe mutations are infrequent in *de novo* AML (approximately 1%) and therefore a preceding myeloproliferative neoplasm should be considered if detected2.  AML with plasmacytoid dendritic cell expansion (pDC-AML) is a recently described entity representing a subset of AML with pDC expansion and high frequency of *RUNX1* mutations (70%)4.  The molecular profile of blastic plasmacytoid dendritic cell neoplasm (BPDCN) is not specific and resembles that of other myeloid neoplasms such as MDS and CMML, however *RUNX1* mutations are rarely observed5,6.  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.  **Table. 2022 European LeukemiaNet (ELN) risk classification**  cid:image001.jpg@01D8BEB8.44339240Prognostic Utility  The ELN 2022 risk stratification incorporates baseline cytogenetic and molecular factors (Table)7. Major changes include *CEBPA* in-frame mutations in the bZIP domain, secondary AML-like gene mutations, and removal of the allelic ratio threshold for *FLT3*-ITD.  Other examples of prognostication models include the knowledge bank approach and the AML Classification and Risk Stratification Calculator8,9.  MRD assessment is an independent prognostic indicator post therapy for AML, and may be a more potent predictor of outcome compared to the baseline clinical and molecular profile10,11.  *TP53* mutations and complex karyotype provide independent and additive prognostic information, with the combination having the worst outcome2.  BIOMARKERS OF RESPONSE TO THERAPY  *FLT3*-ITD and *FLT3*-TKD mutations (clinical trials included only TKD mutations at Asp835 and Ile836 codons) are the target of midostaurin12 (in newly diagnosed AML) and gilteritinib13 (in relapsed/refractory AML).  Repeat *FLT3* testing at relapse or disease progression is recommended as ~20% of patients have a change (gain or loss) in *FLT3* mutation status14.  *IDH1* (Arg132) and *IDH2* (both Arg140 and Arg172) mutations are the target of IDH1 and IDH2 inhibitors, respectively15.  Second-site *IDH1*/*IDH2* mutations have been described in patients with acquired resistance to IDH1/IDH2 inhibitors16.  References  **1.** Swerdlow S, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues (revised 4th edition). Lyon: IARC; 2017. **2.** Papaemmanuil E, et al. Genomic Classification and Prognosis in Acute Myeloid Leukemia. *N Engl J Med* 2016; **374**(23): 2209-21. **3.** Lindsley RC, et al. Acute myeloid leukemia ontogeny is defined by distinct somatic mutations. *Blood* 2015; **125**(9): 1367-76. **4.** Xiao W, et al. 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