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| Clinical Utility of MOLECULAR Testing in  Core Binding Factor ACUTE MYELOID Leukaemia  Diagnostic Utility  AML with t(8;21)(q22;q22.1); RUNX1-RUNX1T1 and AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11 are commonly referred to as core binding factor AML (CBF-AML). Upon detection of these disease-defining chromosomal translocations or gene fusions, the diagnosis of AML can be made regardless of blast count1.  >90% of CBF-AML harbor additional secondary gene mutations, most commonly affecting KIT, NRAS and FLT32-4.  KIT mutations are rarely observed in non-CBF AML4.  Recurrent mutations in chromatin modifiers (e.g. ASXL1, ASXL2) and cohesin complex genes (e.g. RAD21) are enriched in AML with t(8;21) but are uncommon in AML with inv(16)2,3,5.  Both RUNX1-RUNX1T1 and CBFB-MYH11 are suitable markers for measurable residual disease (MRD) monitoring.  Prognostic UTILITY  CBF-AML is considered to have a favourable prognosis relative to other AML subtypes4,6.  KIT mutations have been associated with higher risk of relapse in t(8;21) AML but not in inv(16)/t(16;16)7,8. However MRD level after therapy may be a more relevant predictor of relapse for CBF-AML than baseline gene mutations9,10.  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 midostaurin11 (in newly diagnosed AML) and gilteritinib12 (in relapsed/refractory AML) however these clinical studies generally included few patients with CBF-AML.  References  **1.** Swerdlow S, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues (revised 4th edition). Lyon: IARC; 2017. **2.** Jahn N, et al. Genomic heterogeneity in core-binding factor acute myeloid leukemia and its clinical implication. *Blood Adv* 2020; **4**(24): 6342-52. **3.** Duployez N, et al. Comprehensive mutational profiling of core binding factor acute myeloid leukemia. *Blood* 2016; **127**(20): 2451-9. **4.** Papaemmanuil E, et al. Genomic Classification and Prognosis in Acute Myeloid Leukemia. *N Engl J Med* 2016; **374**(23): 2209-21. **5.** Opatz S, et al. The clinical mutatome of core binding factor leukemia. *Leukemia* 2020; **34**(6): 1553-62. **6.** Dohner H, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood* 2017; **129**(4): 424-47. **7.** Ishikawa Y, et al. Prospective evaluation of prognostic impact of KIT mutations on acute myeloid leukemia with RUNX1-RUNX1T1 and CBFB-MYH11. *Blood Adv* 2020; **4**(1): 66-75. **8.** Boissel N, et al. Incidence and prognostic impact of c-Kit, FLT3, and Ras gene mutations in core binding factor acute myeloid leukemia (CBF-AML). *Leukemia* 2006; **20**(6): 965-70. **9.** Jourdan E, et al. Prospective evaluation of gene mutations and minimal residual disease in patients with core binding factor acute myeloid leukemia. *Blood* 2013; **121**(12): 2213-23. **10.** Pollyea DA, et al. NCCN Guidelines Insights: Acute Myeloid Leukemia, Version 2.2021: Featured Updates to the NCCN Guidelines. *Journal of the National Comprehensive Cancer Network J Natl Compr Canc Netw* 2021; **19**(1): 16-27. **11.** Stone RM, et al. Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a FLT3 Mutation. *N Engl J Med* 2017; **377**(5): 454-64. **12.** Perl AE, et al. Gilteritinib or Chemotherapy for Relapsed or Refractory FLT3-Mutated AML. *N Engl J Med* 2019; **381**(18): 1728-40. |