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| CLINICAL Utility of Molecular Testing in  MYELOID NEOPLASMS POST CYTOTOXIC THERAPY  Diagnostic Utility  Myeloid neoplasms post cytotoxic therapy (MN-pCT) encompass myelodysplastic neoplasms (MDS), myelodysplastic/myeloproliferative neoplasms (MDS/MPN), and acute myeloid leukaemia (AML) that arise in a patient with a history of exposure to DNA-damaging cytotoxic chemotherapy and/or large-field radiation therapy1.  In contrast to the WHO 5th edition, the international consensus classification (ICC) of myeloid neoplasms and acute leukaemia has eliminated a stand-alone category of MN-pCT and instead “therapy-related” is applied as a secondary diagnostic qualifier to be used following a specific MDS, AML (or MDS/AML) diagnosis2.  *TP53* mutations (frequently multi-hit), along with del(5q), -7/del(7q) and a complex karyotype are significantly over-represented in MN-pCT and are associated with prior alkylating therapy and/or ionizing radiation1,3.  Recurrent balanced translocations, frequently involving 11q23 (*KMT2A*)*,* are associated with prior topoisomerase II inhibitor therapy, a short latency period and presentation with overt AML without a preceding MDS phase1.  Other gene mutations more frequently observed in MN-pCT include *PPM1D* (~15%) and other DNA damage response genes4,5.  Exposure to PARP1 inhibitors is now recognised as a qualifying criterion for MN-pCT, while methotrexate exposure has been excluded1.  MN-pCT generally arise within 10 years of last exposure to cytotoxic therapy, and the origin of cases with very long latency periods may be unrelated to therapy6.  A subset of MN-pCT patients, especially those with a strong family history of cancer, may have inherited germline mutations in genes involved in DNA damage response pathways3.  A subset of AML-pCT have secondary-type mutations (*SRSF2*, *SF3B1*, *U2AF1*, *ZRSR2*, *ASXL1, EZH2*,or *STAG2*) which resemble AML, myelodysplasia-related (AML-MR) following a known history of MDS or MDS/MPN7.  Prognostic Utility  Whilst the prognosis of patients with MN-pCT is generally poor, patients with complex karyotype, abnormalities of chromosomes 5 and/or 7 and TP53 mutations have particularly inferior outcomes.  BIOMARKERS OF RESPONSE TO THERAPY  *FLT3* mutations are the target of midostaurin8 (*FLT3*-ITD and TKD) (clinical trials included only TKD mutations at Asp835 and Ile836 codons), quizartinib (*FLT3*-ITD only)9 in newly diagnosed AML, and gilteritinib10 in relapsed/refractory AML.  *FLT3* testing should be repeated at relapse/progression as ~20% of patients have a change (gain or loss) in mutation status11.  *IDH1* (Arg132) and *IDH2* (both Arg140 and Arg172) mutations are the target of IDH1 and IDH2 inhibitors, respectively12.  AML with *UBTF*-TD, *DEK*::*NUP214*, or *NUP98* rearrangement have a transcriptional signature similar to *KMT2A*-rearranged AML, including HOX gene dysregulation, and is potentially targetable by menin inhibitors13,14.  Several mutations have been described in patients with acquired resistance to targeted inhibitors such as *FLT3* Phe691Leu (FLT3 inhibitors)15, second-site IDH1/IDH2 mutations (IDH1/IDH2 inhibitors)16, *BAX* (BCL2 inhibitors)17, and *MEN1* (menin inhibitors)18.  References  **1.** WHO Classification of Tumours Editorial Board. Haematolymphoid tumours. Lyon (France): International Agency for Research on Cancer; forthcoming. (WHO classification of tumours series, 5th ed.; vol. 11). https://publications.iarc.fr. **2.** Arber DA, et al. International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: integrating morphologic, clinical, and genomic data. *Blood* 2022; **140**(11): 1200-28. **3.** McNerney ME, et al. 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