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| cLINICAL UTILITY OF MOLECULAR TESTING IN  HIGH GRADE b-CELL LYMPHOMA  DIAGNOSTIC utility  Diffuse large B-cell lymphoma (DLBCL) is a genomically and clinically heterogeneous disease. Gene expression profiling has identified two distinct subtypes based on cell of origin (COO): germinal centre B-cell (GCB) and activated B-cell (ABC) however approximately 10-20% of cases are unclassified using this method1,2. Genomic subclassification of DLBCL is on-going and to date there is no unifying subcategorisation however several groups have published overlapping models3-5.  *CD79B* and *MYD88* Leu265Pro mutations frequently co-occur and are enriched in ABC-DLBCL. This group is variously known as the MCD/C5/MYD88 subtype3-5. *MYD88* Leu265Pro mutations are highly recurrent in DLBCL occurring at immune-privileged sites e.g. CNS and testicular.  *NOTCH1* mutations define the N1 subtype and are seen almost exclusively in ABC-DLBCL3.  The BN2/C1/NOTCH2 subtype is characterised by the co-occurrence of *BCL6* fusions and *NOTCH2* mutations3-5. This subtype is not associated with any COO. It shares mutational similarity to MZL but is not enriched for cases of transformed MZL3,4.  *EZH2* mutations together with *BCL2* translocations define the EZB/C3/BCL2 subtype and are predominantly GCB-DLBCL3-5. This subytpe is enriched for mutations in *TNFRSF14, CREBBP, EP300,* and *KMT2D3,4.*  Histological transformation of follicular lymphoma (FL) may show typical mutations observed in FL such as *KMT2D, CREBBP*, *EP300*, *EZH2* and *STAT6* (also seen in the EZB/C3/BCL2 DLBCL subtype4) along with aberrant somatic hypermutation, biallelic loss of *CDKN2A/B* and/or *TP53* and *MYC* rearrangement6.  Primary mediastinal B-cell lymphoma (PMBL) has both a gene expression profile and mutational profile distinct from DLBCL but similar to classical Hodgkin lymphoma (cHL)7-9. PMBL is characterised by constitutive activation of JAK-STAT and NF-kB signalling pathways as well as amplification or translocation of 9p24.1. This region contains *JAK2, CD274* (PD-L1) and *PDCD1LG2* (PD-L2)genes whose co-amplification likely cooperates in the pathogenesis of PMBL10,11.  Recurrently observed mutations in PMBL include *SOCS1* inactivating mutations (~60% cases), *STAT6* (~35%), *TNFAIP3* (~35%), *PTPN1* (~20%) and *XPO1* (~25%)9,12-15.  Some cases of nodal DLBCL share molecular overlap with PMBL (SOCS1/SGK1 subgroup)4,16.  Mutations in *ID3, TCF3, CCND3* and *TP53* are commonly observed in Burkitt lymphoma17-19.  Plasmablastic lymphoma is characterised by a high frequency of *MYC* translocations and RAS/MAPK pathway mutations (*KRAS, NRAS* and *BRAF*), in addition to mutations in *STAT3* and *TP53*20.  PROGNOSTIC utility  HGBL with *MYC* and *BCL2* and/or *BCL6* rearrangements (double hit lymphoma) is associated with inferior outcomes21.  *TP53* mutations are associated with inferior overall and progression-free survival in *de novo* DLBCL patients treated with R-CHOP22.  BIOMARKERS OF RESPONSE TO THERAPY  Clinico-molecularly defined relapsed/refractory PMBL shows high response rates to pembrolizumab (anti-PD1 monoclonal antibody)23. Similar to cHL, biomarker analysis suggests PD-L1/PD-L2 over-expression in PMBL renders the tumour sensitive to PD-1 blockade23.  REFERENCES  **1.** Alizadeh AA, et al. Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling. *Nature* 2000; **403**(6769): 503-11. **2.** Rosenwald A, et al. The use of molecular profiling to predict survival after chemotherapy for diffuse large-B-cell lymphoma. *N Engl J Med* 2002; **346**(25): 1937-47. **3.** Schmitz R, et al. 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