Molecular Testing

Provisional Recommendations

Provisional recommendations are for tumor types where an oncology clinical pathway has not yet been published. These recommendations are closely aligned with standard of care recommendations where testing is informative in making treatment decisions.

April 2025 – V1.2025

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Cervical Carcinoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Adenocarcinoma	ISH	HPV	Local VA	No	Tumor Tissue
Persistent, Recurrent, or Metastatic Disease	IHC	PD-L1 clone 22C3 with CPS	Local VA or locally contracted vendor	No	Tumor Tissue
	IHC	MLH1, MSH2, MSH6, PMS2	Local VA or locally contracted vendor	No	Tumor Tissue
	PCR	Microsatellite instability (MSI) status by PCR	Regional Testing Center (GLA)	Yes	Tumor Tissue, Blood
	Methylation Testing	MLH1 promoter hypermethylation testing (in the setting of loss of MLH1 or PMS2 expression by IHC). Hypermethylation suggests somatic mutation. Unmethylated calls for Germline Lynch testing.	Local VA or locally contracted vendor	No	Tumor Tissue
	Germline	If full germline testing not performed, perform Germline Lynch testing if: 1) MSH2 or MSH6 loss by IHC; 2) MLH1 or PMS2 loss by IHC and MLH1 unmethylated; or 3) MSI-H without IHC testing and MLH1 unmethylated	Fulgent Genetics	Yes	Blood, Saliva

Ovarian, Fallopian Tube, & Primary Peritoneal Carcinomas

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Epithelial Tumor, Endometrioid Histology, Stage I	IHC	MLH1, MSH2, MSH6, PMS2	Local VA or locally contracted vendor	No	Tumor Tissue
	PCR	Microsatellite instability (MSI) status by PCR	Regional Testing Center (GLA)	Yes	Tumor Tissue, Normal Tissue, Blood
Epithelial Tumor, All Histologies, Stage II-IV	IHC	MLH1, MSH2, MSH6, PMS2	Tempus	Yes	Tumor Tissue
	IHC	Folate Receptor alpha (FOLR1)	Foundation Medicine when ordered with NGS	Yes	Tumor Tissue
	IHC	HER2	Foundation Medicine when ordered with NGS	Yes	Tumor Tissue
	Somatic NGS	CGP using both DNA and RNA based methodology	Tempus Foundation Medicine	Yes Yes	Tumor Tissue, Blood
Epithelial Tumor, Mucinous Histologies, All Stages	PGx	DPYD*	Fulgent	Yes	Blood, Saliva
Epithelial Tumor, All Histologies, All Stages	Germline NGS	Germline NGS panel (VA POC recommended)	Fulgent	Yes	Blood, Saliva

* Perform DPYD Testing If not already Performed; if DPYD PGx results return predicted phenotypes of either intermediate or poor metabolizer, please consult your local PGx pharmacist or submit an IFC Pharmacogenomics e-consult for assistance with therapeutic recommendation; a clinician may proceed without DPYD testing if withholding chemotherapy for 2-3 weeks may gravely endanger patient's life; for example, if the disease burden is very high and it involves a large portion of vital organs such as liver, etc.

Paraganglioma or Pheochromocytoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Paraganglioma or Pheochromocytoma	Germline NGS	Germline NGS panel (VA POC recommended)	Fulgent	Yes	Blood, Saliva

Anaplastic Large Cell Lymphoma (ALCL)

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Anaplastic Large Cell Lymphoma (ALCL)	IHC	1) ALK, CD30 2) T-cell markers to confirm lineage 3) PAX5 to exclude B-cell lineage	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
ALK-Negative Anaplastic Large Cell Lymphoma (ALCL)	FISH	FISH for TP63, DUSP22 rearrangement	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood

B-Cell Acute Lymphoblastic Leukemia/Lymphoma (B-ALL/LBL)

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
B-Cell Acute Lymphoblastic Leukemia/Lymphoma (B-ALL/LBL)	Flow Cytometry	Leukemia/lymphoma panel. If able, chose a lab with B-ALL minimal residual disease (MRD) testing capability for future testing.	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	FISH B-ALL standard panel that includes t(9;22) BCR-ABL1; Optional probes for normal/uninformative karyotype: 11q23 KMT2A (MLL) rearrangement; +4, +10, +17, t(1;19) TCF3-PBX1; 14q32 IGH rearrangement; del(9p) CDKN2A deletion	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Karyotyping	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Quantitative PCR	BCR-ABL1 quantitative PCR including both p190 and p210 isoforms	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Somatic NGS	Consider CGP if no driver mutation detected (Foundation Heme)	Foundation Medicine	Yes	Bone Marrow Biopsy, Blood

Burkitt Lymphoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Burkitt Lymphoma	IHC or Flow Cytometry	Immunophenotyping including CD10, CD19, CD20, CD43, BCL2, BCL6, Ki-67, MYC, TdT, and surface immunoglobulin light chains kappa and lambda	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	FISH	FISH for IGH::MYC. If negative, consider FISH for IGK::MYC or IGL::MYC	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	ISH	EBER in-situ hybridization	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Morphologically and Phenotypically Consistent with Burkitt Lymphoma, but Negative for MYC Fusion	Array CGH or FISH	Evaluate for 11q abnormalities to rule out Burkitt-like lymphoma	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood

Chronic Myelomonocytic Leukemia (CMML) and Other Myelodysplastic/Myeloproliferative Neoplasms (MDS/MPN)

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical Suspicion of Myelodysplastic Syndrome/Myeloproliferative Neoplasm (MDS/MPN)	Flow Cytometry	Consider monocyte subset analysis in addition to leukemia/lymphoma flow panel	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH*	BCR-ABL1 t(9;22) (to rule out CML)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Bone marrow karyotype	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
Bone Marrow Morphology Consistent with Myelodysplastic Syndrome/Myeloproliferative Neoplasm (MDS/MPN)	Somatic NGS**	Targeted myeloid NGS panel including ASXL1, BCOR, BCOR1, CBL, CUX1, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, KRAS, NPM1, NRAS, PHF6, RAD21, RUNX1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, ZRSR2, JAK2, CALR, MPL, SETBP1, ETNK1, PTPN11, and NF1. Optional: DDX41.	GLA Foundation Medicine	GLA Grant*** Yes	Bone Marrow Biopsy, Blood
* Depending on pathology and karyotype findings, FISH and molecular studies may be performed on a subsequent peripheral blood sample if needed; However, it is understood that in certain resource limited areas this type of reflex testing algorithm may not be possible; In those circumstances, it may be in the best interest of the patient to order FISH and molecular testing up front in order to avoid excessive delays in diagnosis					
** Can be performed on subsequent peripheral blood sample					
*** Reach out to GLA for information on use of NGS testing under a VA sponsored grant, with no cost to your local facility					

Eosinophil Related Malignancies

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical Suspicion for Eosinophil-Related Malignancy	Flow Cytometry	Leukemia/lymphoma panel on bone marrow (include blast/myeloid lineage phenotyping and T□cell phenotyping to rule out lymphocytic variant-HES)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	FISH (Bone marrow or peripheral blood)* a. BCR-ABL1 t(9;22) (to rule out CML) b. Optional (if concerned for AML) inv(16) or t(16;16) CBFB/MYH11	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Bone marrow karyotype	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
Abnormal T-cells Detected by Flow Cytometry	Molecular Testing	T-cell clonality	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
Bone Marrow Morphology Consistent with a Chronic Myeloproliferative Neoplasm or Mixed Myeloproliferative and Lymphoid Neoplasm	Somatic NGS**	a. Targeted myeloid NGS panel for MDS/MPN genes: ASXL1, BCOR, BCOR1, CBL, CUX1, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, KRAS, NPM1, NRAS, PHF6, RAD21, RUNX1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, ZRSR2, JAK2, CALR, MPL, SETBP1, ETNK1, PTPN11, and NF1. Optional: DDX41. b. RNA based Fusion panel including: PDGFRA, PDGFRB, FGFR1, JAK2, ABL1, ABL2, FLT3, and ETV6.	Foundation Medicine	Yes	Bone Marrow Biopsy, Blood
* FISH and molecular studies may be performed on a subsequent peripheral blood sample if needed; However, it is understood that in certain resource limited areas this type of reflex testing algorithm may not be possible; In those circumstances, it may be in the best interest of the patient to order FISH and molecular testing up front in order to avoid excessive delays in diagnosis					
** Can be performed on subsequent peripheral blood sample					

Immunosuppression – Related/HHV8/EBV – Related Lymphoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Immunosuppression-Related/HHV8/EBV-Related Lymphoma	Serology	Consider HIV testing	Local VA or locally contracted vendor	No	Blood

Mixed Lineage Blasts – Mixed Phenotype Acute Leukemia (MPAL) or Undifferentiated Leukemia

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Mixed Lineage Blasts – Mixed Phenotype Acute Leukemia (MPAL) or Undifferentiated Leukemia	Flow Cytometry	Leukemia/lymphoma panel on bone marrow	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	BCR::ABL1 and KMT2A rearrangement; -5/5q; -7/7q rearrangement	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Molecular Testing	qPCR for BCR::ABL1 (if positive for BCR::ABL1 FISH)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Bone marrow karyotype	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Rapid Molecular Tests (<1 week TAT)	FLT3 ITD and TKD, IDH1/2, NPM1, CEBPA (optional)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Somatic NGS	RNA and DNA based CGP	Foundation Medicine	Yes	Bone Marrow Biopsy, Blood

Post-Transplant Lymphoproliferative Disorder

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Post-Transplant Lymphoproliferative Disorder	IHC	CD30	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	ISH	EBER in-situ hybridization	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood

Systemic Mastocytosis

Eligibility	Test Category	Test Type*	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical Suspicion for Systemic Mastocytosis	Serology	Serum Tryptase	Local VA or locally contracted vendor	No	Blood
	IHC	CD117, tryptase, CD2, CD25, CD30 IHC on bone marrow	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Flow Cytometry	Leukemia/lymphoma panel on bone marrow. Include mast cell phenotyping if available.	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Bone marrow karyotype	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Molecular Testing	KIT D816V mutation (high sensitivity single gene test)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
Bone Marrow Morphology Consistent with Systemic Mastocytosis	Somatic NGS*	Targeted myeloid NGS panel to include: MDS/MPN genes: (ASXL1, BCOR, BCOR1, CBL, CUX1, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, KRAS, NPM1, NRAS, PHF6, RAD21, RUNX1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, ZRSR2, JAK2, CALR, MPL, SETBP1, ETNK1, PTPN11, and NF1. Optional: DDX41)	GLA Foundation Medicine	GLA Grant** Yes	Bone Marrow Biopsy, Blood
Systemic Mastocytosis with Significant Eosinophilia	Somatic NGS	a. Targeted myeloid NGS panel for MDS/MPN genes: ASXL1, BCOR, BCOR1, CBL, CUX1, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, KRAS, NPM1, NRAS, PHF6, RAD21, RUNX1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, ZRSR2, JAK2, CALR, MPL, SETBP1, ETNK1, PTPN11, and NF1. Optional: DDX41. b. RNA based Fusion panel including: PDGFRA, PDGFRB, FGFR1, JAK2, ABL1, ABL2, FLT3, and ETV6.	Foundation Medicine	Yes	Bone Marrow Biopsy, Blood

* Can be performed on subsequent peripheral blood sample

** Reach out to GLA for information on use of NGS testing under a VA sponsored grant, with no cost to your local facility

T-Cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL/LBL)

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
T-Cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL/LBL)	Flow Cytometry	Leukemia/lymphoma panel	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	Consider FISH T-ALL panel including rearrangements in TRB or TRD; loss of CDKN2A	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Karyotyping	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Somatic NGS	Consider CGP (Foundation Heme) if unresponsive to standard therapy	Foundation Medicine	Yes	Bone Marrow Biopsy, Blood

T-Cell and NK-Cell Leukemias/Lymphomas

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
T-Prolymphocytic Leukemia/Lymphoma (TPLL)	IHC or Flow Cytometry	Sufficient T-cell markers to confirm lineage, including TCL1a	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	FISH	Consider FISH for TCL1a rearrangements	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Molecular Testing*	Consider T-cell clonality if needed for diagnosis	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Adult T-cell Leukemia/Lymphoma (ATLL)	IHC or Flow Cytometry	Sufficient T-cell markers to confirm lineage, including T-regulatory antigens such as CD25 and FOXP3	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Serology	Serology for HLTV-1	Local VA or locally contracted vendor	No	Blood
	Molecular Testing*	Consider T-cell clonality if needed for diagnosis	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Angioimmunoblastic T-cell Lymphoma (AITL) and other Follicular T-Helper Lymphomas	IHC or Flow Cytometry	Sufficient T-cell markers to confirm lineage, including TFH antigens such as CD10, BCL6, PD1, CXCL13, and ICOS	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	ISH	EBER in situ hybridization	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Molecular Testing*	Consider T-cell clonality if needed for diagnosis	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
T-Cell Large Granular Lymphocytic Leukemia (T-LGLL)	IHC or Flow Cytometry	Sufficient T-cell markers to confirm lineage, including CTL antigens such as CD8, CD56, CD16, CD57, granzyme B, Peroforin, TIA1, granzyme M	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Molecular Testing*	Consider T-cell clonality if needed for diagnosis	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Hepatosplenic T-Cell Leukemia (HSTCL)	IHC or Flow Cytometry	Sufficient T-cell markers to confirm lineage, such as TCRab, TCRgd, CD8, CD56, granzyme B, granzyme M, perforin, TIA1	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Molecular Testing*	Consider T-cell clonality if needed for diagnosis	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Aggressive NK-Cell Leukemia (ANKL)	IHC or Flow Cytometry	Sufficient NK-cell markers to confirm lineage, such as CD2, CD7, CD16, CD56, granzyme B, granzyme M, perforin, TIA1, KIRs	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	ISH	EBER in situ hybridization	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Molecular Testing*	T-cell clonality to rule out T-cell leukemia	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Extranodal NK/T-Cell Lymphoma (ENKTL)	IHC or Flow Cytometry	Sufficient NK-cell markers to confirm lineage, such as CD2, CD7, CD16, CD56, granzyme B, granzyme M, perforin, TIA1, KIRs	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	ISH	EBER in situ hybridization	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
NK-Cell Large Granular Lymphocytic Leukemia (NK-LGL)	IHC or Flow Cytometry	Sufficient NK-cell markers to confirm lineage, such as CD2, CD7, CD16, CD56, granzyme B, granzyme M, perforin, TIA1, KIRs	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Molecular Testing*	T-cell clonality to rule out T-LGLL	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood

* If sample via bone marrow, molecular testing can be performed on non-decalcified clot section or subsequent peripheral blood sample