

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.

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Basal Cell Carcinoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Basal Cell Carcinoma	No molecular testing is currently required for standard prognostication and therapy.				

Central Nervous System Malignancies

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Gliial Neoplasms	IHC	IDH1 R132 mutation ATRX TP53	Local VA or locally contracted vendor	No	Tumor Tissue
	FISH	1p/19q FISH for codeletion CDKN2A/B homozygous loss	Local VA or locally contracted vendor	No	Tumor Tissue, Blood
	Molecular Testing	Mutation testing for ATRX, BRAF, H3-3A, IDH1, IDH2, TERT promoter, TP53	Tempus Foundation Medicine	Yes	Tumor Tissue
	Molecular/Cytogenetic	Chromosomal microarray	Local VA or locally contracted vendor	No	Tumor Tissue
	Methylation Testing	MGMT promoter methylation testing	Local VA or locally contracted vendor	No	Tumor Tissue
Meningiomas	FISH	CDKN2A/B homozygous loss	Local VA or locally contracted vendor	No	Tumor Tissue, Blood
	Molecular Testing	TERT promoter mutation testing	Local VA or locally contracted vendor	No	Tumor Tissue
	Molecular/Cytogenetic	Chromosomal microarray	Local VA or locally contracted vendor	No	Tumor Tissue

Cervical Carcinoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
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

Gastrointestinal Stromal Tumor (GIST)

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Gastrointestinal Stromal Tumor (GIST)	Molecular Testing	KIT PCR, with reflex to PDGFRA PCR	Local VA or locally contracted vendor	No	Tumor Tissue



Melanoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Cutaneous Melanoma	Molecular Testing	BRAF V600E/K PCR	Local VA or locally contracted vendor	No	Tumor Tissue, Blood
	IHC	BRAF V600E mutation	Local VA or locally contracted vendor	No	Tumor Tissue
Mucosal Melanoma	Molecular Testing	BRAF V600E/K PCR KIT PCR	Local VA or locally contracted vendor	No	Tumor Tissue, Blood
	IHC	BRAF V600E mutation	Local VA or locally contracted vendor	No	Tumor Tissue
Ocular (Uveal) Melanoma	Gene Expression Profiling*	Gene expression profiling for risk stratification	Local VA or locally contracted vendor	No	Blood
	Chromosomal Micro Array*	Chromosomal micro array for risk stratification	Local VA or locally contracted vendor	No	Blood, Saliva
	Somatic NGS*	Comprehensive genomic profiling (CGP) for risk stratification including GNAQ, GNA11, BAP1, PLCB4, CYSLTR2, SF3B1, EIF1AX	Tempus Foundation Medicine	Yes Yes	Tumor Tissue, Blood
	Genotyping	High resolution testing for HLA-A*02:01 for recurrent metastatic uveal melanoma only	Local VA or locally contracted vendor	No	Blood, Saliva
Acral/Lentiginous Melanoma	Molecular Testing	BRAF V600E/K PCR KIT PCR	Local VA or locally contracted vendor	No	Tumor Tissue, Blood
	IHC	BRAF V600E mutation	Local VA or locally contracted vendor	No	Tumor Tissue

* Risk stratification for Ocular melanoma could be done either by gene expression profiling, chromosomal micro array or CGP

Merkel Cell Carcinoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Merkel Cell Carcinoma	No molecular testing is currently required for standard prognostication and therapy.				



Mesothelioma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Mesothelioma	No molecular testing is currently required for standard prognostication and therapy.				



Ovarian, Fallopian Tube, & Primary Peritoneal Carcinomas

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
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, Blood
All Histologies, Stage II-IV	IHC	MLH1, MSH2, MSH6, PMS2	Tempus	Yes	Tumor Tissue
	Somatic NGS	Comprehensive Genomic Profiling with HRD analysis	Tempus Foundation	Yes Yes	Tumor Tissue, Blood
All Histologies, All Stages	Germline NGS	Germline NGS panel (VA POC recommended)	Fulgent	Yes	Blood, Saliva



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



Soft Tissue Sarcoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Soft Tissue Sarcoma Other Than GIST	Somatic NGS	DNA and RNA-based Comprehensive genomic profiling (CGP)	Tempus Foundation Medicine (Heme panel)	Yes Yes	Tumor Tissue, Blood



Squamous Cell Carcinoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Squamous Cell Carcinoma	No molecular testing is currently required for standard prognostication and therapy.				



Thyroid Carcinoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Advanced or Metastatic Carcinoma	Somatic NGS	Comprehensive Genomic Profiling	Tempus Foundation	Yes Yes	Tumor Tissue, Blood
Medullary Thyroid Carcinoma, Any Stage	Germline	Germline NGS panel (VA POC recommended)	Fulgent	Yes	Blood, Saliva



Uterine Carcinoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Uterine Carcinoma All Stages, Histologies	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 NGS	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
Metastatic/Recurrent Endometrioid	IHC	ER	Local VA or locally contracted vendor	No	Tumor Tissue
Stage III/IV or Recurrent Serous Carcinoma	IHC	HER2 IHC with reflex to FISH if 2+ on IHC	Local VA or locally contracted vendor	No	Tumor Tissue
	FISH	HER2 FISH if 2+ on IHC	Local VA or locally contracted vendor	No	Tumor Tissue, Blood
Endometrioid AND < age 50	Germline NGS	Germline NGS panel	Fulgent Genetics	Yes	Blood, Saliva
Endometrioid AND Personal or Family History of Other Lynch-Related Cancers	Germline NGS	Germline NGS panel	Fulgent Genetics	Yes	Blood, Saliva

Acute Leukemia (Mixed Phenotype or Undifferentiated Leukemia)

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Acute Leukemia (Mixed Phenotype or Undifferentiated Leukemia)	Flow Cytometry	Leukemia/lymphoma panel	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Karyotyping	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	-5/-5q, -7/-7q, KMT2A, t(8;21) RUNX1::RUNX1T1, t(15;17) PML::RARA, t(16;16) or inv(16) CBFB::MYH11; t(9;22) BCR::ABL1; TP53	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Rapid Molecular Tests (<1 week TAT)	FLT3 ITD and TKD, IDH1/2, NPM1 (quantitative preferred), 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

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) CBFβ/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

Essential Thrombocythemia (ET)

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical Suspicion of Essential Thrombocythemia (ET)	Stain	Reticulin staining on *bone marrow biopsy	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	FISH (Peripheral blood or Bone marrow) to rule out t(9;22) BCR-ABL1	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	MPN reflex test: JAK2 V617F --> CALR (if JAK2 V617F negative) --> MPL (if CALR negative)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
Bone Marrow Morphology Consistent with Pre-Fibrotic Primary Myelofibrosis	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
Essential Thrombocythemia (ET) with Myelofibrosis and/or Increased Blasts	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

* For clinically well patients who will only be observed if diagnosis is confirmed, some clinicians prefer to limit workup to peripheral blood and MPN reflex testing only However, bone marrow biopsy is essential to distinguish ET from prefibrotic primary myelofibrosis and is strongly recommended to document baseline fibrosis

** 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

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



Lymphoplasmacytic Lymphoma

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Lymphoplasmacytic Lymphoma*	Molecular Testing	Targeted sequencing for MYD88 and CXCR4 mutations	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood

* Karyotype and FISH are not informative



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



Myelofibrosis

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical Suspicion for Myelofibrosis	Stain	a. Reticulin stain b. Consider Trichrome stain if reticulin is moderate or marked	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Flow Cytometry	Flow cytometry (Bone marrow) – Leukemia/lymphoma panel	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	FISH (Bone marrow or peripheral blood) for t(9;22) BCR-ABL1	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 Myeloid Neoplasm with Myelofibrosis	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
* Here, “secondary myelofibrosis” refers specifically to post-essential thrombocythemia myelofibrosis (post-ET-MF) and post polycythemia vera myelofibrosis (post-PV-MF); non-myeloid diseases may present with fibrosis and should be worked up as the causal disease; for example, Hairy cell leukemia, metastatic breast cancer, and classic Hodgkin lymphoma can cause marrow fibrosis but should not be worked up as a myeloid neoplasm					
** 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					

Polycythemia Vera (PV)

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical Suspicion of Polycythemia Vera (PV)	Stain	Reticulin staining on *bone marrow biopsy	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	FISH (Peripheral blood or Bone marrow) to rule out t(9;22) BCR-ABL1	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	JAK2 V617F with reflex to JAK2 sequencing of exons 12 - 15	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
Polycythemia Vera (PV) with Myelofibrosis and/or Increased Blasts	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
* For clinically well patients who will only be observed if diagnosis is confirmed, workup can be limited to peripheral blood and JAK2 reflex testing only; however, bone marrow biopsy and targeted NGS panel are recommended for complete baseline disease characterization and prognostication					
** 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					

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
Peripheral T-Cell Lymphoma (PTCL), NOS	IHC or Flow Cytometry	Sufficient T-cell markers to confirm lineage and exclude specific entities	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-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, Perforin, 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

Questions?

Contact VHAOncologyPathways@va.gov



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