Biomarkers - MD Anderson Approved

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The Molecular Testing Evaluation Committee (MTEC) is responsible for the review and approval of requests for biomarker testing based on evaluating published data and determining if there is sufficient scientific and clinical interest for their use in standard care of patients at MD Anderson. The committee reports up to Medical Practice and the Executive Committee for the Medical Staff. Biomarkers approved by MTEC and available through Pathology and Laboratory Medicine using CLIA-compliant molecular diagnostic tests that satisfy the institutionally defined criteria are included in this document.

The following exception criteria must be met for orders which are not included in this document; additionally, the request must be approved by the internal MDACC Single Use Order Set Committee.

**Exception criteria:**
- The test is clinically justifiable: Molecular test results will guide treatment decisions, and the results will identify treatment selection among currently available therapies.
- The patient is appropriate for such therapies: The patient has a performance status of ECOG of 0 or 1 and is expected to live for at least three months.
- The patient has locally advanced or metastatic disease not appropriate for other therapies.
<table>
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<tr>
<th>DISEASE SITE</th>
<th>CELL TYPE</th>
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<td>• MSI (MLH1, MSH2, MSH6, PMS2)</td>
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1 For DCIS specimens, ER and PR should be performed on the final surgical specimen and not the core biopsy since there may be invasive cancer in the surgical specimen in which case all biomarkers should be done on the invasive cancer (ER, PR, HER2/neu, Ki-67). If no invasive cancer seen, then ER and PR should be performed on the DCIS specimen.
2 For metastatic breast cancer cases, ER, PR, HER2/neu and Ki-67 should be obtained if ordered by the requesting physician as clinically indicated.
3 HER2/neu by FISH will only be performed if a 2+ or greater result is obtained by HER2/neu IHC, or in select 1+ IHC results as judged by the pathologist on the case, or if requested by the ordering or treating physicians as clinically indicated.

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<td>*p53</td>
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### Gastrointestinal Stomach & Esophagogastric Junction Adenocarcinoma
- **HER2/neu**
- **MET**
- **MSI** (MLH1, MSH2, MSH6, PMS2)

- **NTRK1** fusion
- **NTRK2** fusion
- **NTRK3** fusion

### Colorectal Adenocarcinoma
- **HER2/neu**
- **BRAF V600E**
- Immunohistochemistry for DNA mismatch repair enzymes (MLH1, MSH2, MSH6, PMS2)
  - Note: MLH1 promoter hypermethylation analysis and **BRAF** mutation analysis will also be performed if immunohistochemistry shows loss of MLH1 and if sufficient tumor DNA is available for analysis.
- **HER2/neu**

- **BRAF** mutation
- **KRAS** mutation
- **MLH1** promoter hypermethylation analysis and **BRAF** mutation analysis (only if immunohistochemistry for DNA mismatch repair enzymes has already been performed and shows loss of MLH1)
- **MSI** by PCR

- **NTRK1** fusion
- **NTRK2** fusion
- **NTRK3** fusion

- **PIK3CA** mutation

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1. **HER2/neu by FISH** will only be performed if a 2+ or greater result is obtained by **HER2/neu IHC**

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<td>∙ NTRK3 fusion</td>
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¹May also be used for prognostic determination (single use)
²May also be for optional follow-up sample, to estimate treatment response (single use)
³May also be for estimating treatment response baseline sample (single use)
⁴May also be for clinical suspicion for treatment resistance

PMP = Pseudomyxoma Peritonei
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*ALL* = acute lymphocytic/lymphoblastic leukemia

*AML/MDS* = acute myelogenous leukemia/myelodysplastic syndrome
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APL = acute promyelocytic leukemia
CLL = chronic lymphocytic leukemia

These guidelines have been specifically developed for MD Anderson and are not intended to replace the independent medical or professional judgment of physicians or other health care providers.
### Biomarkers - MD Anderson Approved

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<td>EZH2 mutation</td>
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<td>JAK2 v617F mutation</td>
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<td>KIT mutation</td>
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<td>MPL mutation</td>
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<td>TET2 mutation</td>
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<td>TP53 mutation</td>
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<td>FIP1L1-PDGFR fusion</td>
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<td>t(9;22) BCR-ABL1 quantitative PCR</td>
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</table>

**CML** = chronic myeloid leukemia  **HES** = hypereosinophilic syndrome  **CMML** = chronic myelomonocytic leukemia  **MPN** = myeloproliferative neoplasms
## Biomarkers - MD Anderson Approved

These guidelines have been specifically developed for MD Anderson and are not intended to replace the independent medical or professional judgment of physicians or other health care providers.

<table>
<thead>
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<th>DISEASE SITE</th>
<th>DIAGNOSIS</th>
<th>CYTOGENETICS</th>
<th>FLOW</th>
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<td>MF - Peripheral Blood</td>
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<td>CD34</td>
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<td>PV, ET, MF</td>
<td>Conventional chromosome analysis</td>
<td>Acute Leukemia screen</td>
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<td>T Cell Disorders - Peripheral Blood</td>
<td>Conventional chromosome analysis</td>
<td>CD4/CD8 Ratio</td>
<td>(9,22) BCR/ABL1</td>
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<td>T Cell Disorders</td>
<td>Conventional chromosome analysis</td>
<td>TCRB clonality</td>
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<td>T-Cell</td>
<td>STAT5B</td>
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<td>T-Prolymphocytic Leukemia (T-PLL)</td>
<td>FISH - 14q32</td>
<td>TCRG clonality</td>
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<td>T-Large Granular Lymphocytic Leukemia (T-LGL)</td>
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<td>STAT5B</td>
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</table>

MF = Mycosis fungoides  
PV = Polycythemia Vera  
ET = Essential thrombocytopenia
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<th>DISEASE SITE</th>
<th>DIAGNOSIS</th>
<th>CYTOGENETICS</th>
<th>FLOW CYTOMETRY</th>
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<td>Lymphoma</td>
<td>Burkitt Lymphoma</td>
<td>• Conventional chromosome analysis</td>
<td>B-Cell Lymphoma Panel</td>
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<td>• FISH - MYC</td>
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<td>• IGH clonality</td>
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<td>Burkitt Lymphoma Peripheral Blood</td>
<td>FISH - MYC</td>
<td>CD4/CD8 Ratio</td>
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<td>Diffuse Large B-Cell Lymphoma</td>
<td>Conventional chromosome analysis</td>
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<td>• CD79A</td>
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<td>• FISH – CCND1 MYEVOY</td>
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<td>• FISH – MYC</td>
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<td>• EZH2 (codon 646)</td>
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<td>• FISH – TP53 CEP17</td>
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<td>• MYD88 (codon 265)</td>
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<td>Mantle Cell Lymphoma</td>
<td>Conventional chromosome analysis</td>
<td>B-Cell Lymphoma Panel</td>
<td>• BIRC3 – Exons 6-9</td>
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<td>• FISH – CCND1 MYEVOY</td>
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<td>• FISH – MYC</td>
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<td>• IGH Gene Rearrangement</td>
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<td>• NOTCH1 – Exons 26, 27, 34</td>
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<td>Myeloma</td>
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<td>• MYD88 (codon 265)</td>
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</table>
Biomarkers - MD Anderson Approved

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SUGGESTED READINGS

NOTE: suggested readings represent the evidence used when the biomarker was first presented for approval

All Solid Tumor Types

Molecular: NTRK1, NTRK2, and NTRK3 Fusion Analysis


Immunohistochemistry: Microsatellite Instability (MSI) (MLH1, MSH2, MSH6, PMS2)


Continued on next page
SUGGESTED READINGS

NOTE: suggested readings represent the evidence used when the biomarker was first presented for approval

All Solid Tumor Types – continued

**Immunohistochemistry: Microsatellite Instability (MSI) (MLH1, MSH2, MSH6, PMS2)**


**Brain/Neuro-Oncology**

**Diffuse Glioma**

**FISH/p19q:**

Bouvier, C., et al. (2004). Deletions of chromosomes 1p and 19q are detectable on frozen smears of gliomas by FISH: usefulness for stereotactic biopsies. *Journal of Neuro-Oncology, 68*(2), 141-149


**Immunohistochemistry/BRAF:**


**Immunohistochemistry/EGFR528:**


SUGGESTED READINGS – continued

**Brain/Neuro-Oncology – continued**

**Diffuse Glioma**

**Molecular/IDH1/IDH2:**
Capper, D., Sahm, F., Hartmann, C., et al. (2010). Application of mutant IDH1 antibody to differentiate diffuse glioma from nonneoplastic central nervous system lesions and therapy-induced changes. *American Journal of Surgical Pathology, 34*(8), 1199-1204. doi: http://dx.doi.org/10.1097/PAS.0b013e3181e7740d.


Continued on next page
SUGGESTED READINGS – continued

Brain/Neuro-Oncology – continued

Diffuse Glioma

Molecular/IDH1/Multigene predictor:

Molecular/PIK3CA:

Immunohistochemistry/PTEN:

Molecular/CIMP:

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Continued on next page
SUGGESTED READINGS – continued

Low Grade Glioma

Molecular/BRAF:


Molecular/MGMT:


FISH/1p/19q:


SUGGESTED READINGS – continued

Breast

Immunohistochemistry/ER and Immunohistochemistry/PR:


Immunohistochemistry/Ki67:


Immunohistochemistry/HER2/NEU and Immunohistochemistry/FISH/HER2/NEU:


Continued on next page
SUGGESTED READINGS – continued

Breast - continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Molecular/ESR1:**


**Molecular/FGFR:**


**Molecular/MammaPrint:**


Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Breast – continued

Molecular/Oncotype:

Molecular/PIK3CA:

Molecular/TP53:

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Department of Clinical Effectiveness V5
Approved by the Executive Committee of the Medical Staff on 12/17/2019
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Endocrine

Adrenocortical Neoplasm

Immunohistochemistry/Ki67:

Anaplastic, Follicular, Papillary Thyroid Carcinoma

Molecular/BRAF:

Molecular/KRAS HRAS NRAS:
CNS SUPERSEDED Local Coverage Determination (LLCD): https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35396&ContrId=338&ver=20&ContrVer=1&Keyword=biomarker&KeywordSearchType=Or&PolicyType=Both&ArticleType=SAD%7cEd&Cntrctr=338*1&Date=&KeyWordLookUp=Doc&SearchType=Advanced&CoverageSelection = Both&kq=true&bc=IAAAABAAAAAAA%3d%3d&

Continued on next page
Molecular/BRAF:
CMS SUPERSEDED Local Coverage Determination (LLCD): https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35396&ContrId=338&ver=20&ContrVer=11&Keyword=biomarker&KeywordSearchType=Or&PolicyType=Both&ArticleType=SAD%7cEd&Cntrctr=3381&Date=&KeyWordLookUp=Doc&SearchType=Advanced&CoverageSelection=Both&kq=true&bc=1AAAAABAAAAA%3d%3d&

Molecular/KRAS HRAS NRAS:
CMS SUPERSEDED Local Coverage Determination (LLCD): https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35396&ContrId=338&ver=20&ContrVer=11&Keyword=biomarker&KeywordSearchType=Or&PolicyType=Both&ArticleType=SAD%7cEd&Cntrctr=3381&Date=&KeyWordLookUp=Doc&SearchType=Advanced&CoverageSelection=Both&kq=true&bc=1AAAAABAAAAA%3d%3d&

Molecular/PIK3CA:

Note: suggested readings represent the evidence used when the biomarker was first presented for approval.

**SUGGESTED READINGS – continued**
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Endocrine

Anaplastic, Follicular, Papillary Thyroid Carcinoma

Immunohistochemistry/PTEN:


Medullary Thyroid Carcinoma

Molecular/RET mutation status:


Molecular/HRAS KRAS & NRAS mutation status:


Sherman et al. (2013). Demonstrating patients with somatic RAS or RET mutation in MTC have better response to TKI therapy with cabozantinib than those lacking mutations. ASCO presentation #6000.

FISH CDKN2C:


Continued on next page
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SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Endocrine – continued

Anaplastic, Follicular, Papillary Thyroid Carcinoma

FISH CDKN2C - continued:

Parathyroid Carcinoma

Immunohistochemistry/Ki67:

Pituitary Neoplasm

Immunohistochemistry/Ki67:

Immunohistochemistry/p53:

Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Gastrointestinal

Stomach and Esophagogastric Junction Adenocarcinoma

**Immunohistochemistry/HER2/neu and FISH/HER2/neu:**


Small Intestinal Adenocarcinoma

**Immunohistochemistry/DNA mismatch repair enzymes and Molecular/MSI PCR, MLH1 promoter methylation, KRAS, BRAF:**
Small bowel and appendiceal adenocarcinoma may be treated with systemic chemotherapy according to the NCCN Guidelines for Colon Cancer. *NCCN Guidelines*, Version 3.2013, Colon Cancer, Page COL-1.


Colorectal Adenocarcinoma

**Immunohistochemistry/IHC mmr enzymes and Colorectal Adenocarcinoma/Molecular/MSI PCR:**


The panel recommends that MMR protein testing be performed for all patients younger than 50 years old with colon cancer, based on an increased likelihood of Lynch syndrome in this population. MMR testing should also be considered for all patients with stage II disease, because stage II MSH-H patients may have a good prognosis and do not benefit from 5-FU adjuvant therapy. *NCCN Guidelines*, Version 3.2013, Colon Cancer, Page COL-A 4 of 5.


**Molecular/BRAF:**


Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Gastrointestinal - continued

Colorectal Adenocarcinoma - continued

Molecular/KRAS:

Carcinoma of the Anal Canal

Immunohistochemistry/p16:

Immunohistochemistry/HPV:

Neuroendocrine

Immunohistochemistry/CDX2:

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Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Gastrointestinal - continued

Neuroendocrine - continued

Immunohistochemistry/TTF:


Immunohistochemistry/Ki67:


Immunohistochemistry/DAXX, ATRX:


DAXX, ATRX, MEN1, PTEN, PIK3CA, TSC2:

Continued on next page
SUGGESTED READINGS – continued

Gastrointestinal – continued

Neuroendocrine – continued

Immunohistochemistry/MEN1:

MGMT Methylation:

Molecular/18Q LOH:

Molecular/PTEN, TSC2:


Pseudomyxoma Peritonei

Molecular/IKRAS:

Genitourinary/Urology

Hepatic Adenoma

Molecular/Beta Catenin:

Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Genitourinary/Urology - continued

Prostate

Immunohistochemistry/PSA:

Immunohistochemistry/PAP:

Immunohistochemistry/CgA:

Molecular/RB1, TP53, PTEN, AR:

Molecular/RB1, TP53, AR:

Molecular/RB1, TP53:

Use of platinum-based chemotherapy in aggressive variant prostate carcinomas:
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Genitourinary/Urology - continued

Testicular, Suspected Testicular

Immunohistochemistry/bHCG and AFP:

Upper Urinary Tract and Renal Pelvis Urothelial Carcinoma

FISH/HER2/neu:

Immunohistochemistry and Molecular/MSI panel and MLH1 promoter methylation assay and PCR based MSI testing:
DOI - 10.1097/01.MP.0000024263.25043.0C

Continued on next page
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SUGGESTED READINGS – continued
Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Gynecology

Ovarian and Uterine

**FISH/Her2/neu:**
AID - 10.1111/j.1525-1438.2007.00946.x [doi]

Continued on next page
Gynecology – continued

Ovarian and Uterine - continued

Immunohistochemistry/Her2/neu:

Note: suggested readings represent the evidence used when the biomarker was first presented for approval.
Gynecology - continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Ovarian and Uterine - continued

Immunohistochemistry/HPV:

Immunohistochemistry/MSI:
Murphy, M. A., & Wentzensen, N. (2011). Frequency of mismatch repair deficiency in ovarian cancer: a systematic review This article is a US Government work and, as such, is in the public domain of the United States of America. International Journal of Cancer, 129(8), 1914-1922. doi: http://dx.doi.org/10.1002/ijc.25835
Gynecology - continued

Ovarian and Uterine - continued

Immunohistochemistry/PTEN:


SUGGESTED READINGS – continued
Note: suggested readings represent the evidence used when the biomarker was first presented for approval
SUGGESTED READINGS – continued

Gynecology - continued

Ovarian and Uterine - continued

Molecular/BRAF:

Continued on next page
SUGGESTED READINGS – continued
Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Gynecology - continued**

**Ovarian and Uterine - continued**

**Molecular/KRAS:**


Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Gynecology - continued**

**Ovarian and Uterine - continued**

**Molecular/MLH1 promoter methylation:**


*Continued on next page*
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Gynecology - continued

Ovarian and Uterine - continued

Molecular/MSI PCR:

Continued on next page
Gynecology - continued

Ovarian and Uterine - continued

Molecular/P3K AKT:

SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval
Gynecology - continued

Ovarian and Uterine - continued

Molecular/PTEN:

SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Head and Neck**

**Oropharynx/Nasopharynx/Oral Cavity**

**HPV and P16:**


**Nasopharynx Cancer and Salivary Cancer**

**EBV and erB-2 and HER2/neu:**


**Salivary Cancer**

**c-kit and EGFR and Androgen Receptor:**


*Continued on next page*
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SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Liquid Biopsies

Breast: AKT1, BRCA1, BRCA2, ERBB2, ESR1, PIK3CA

AKT1


BRCA1/BRCA2


ERBB2


Continued on next page
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SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Liquid Biopsies – continued**

**Breast: AKT1, BRCA1, BRCA2, ERBB2, ESR1, PIK3CA – continued**

**ESR1**


**PIK3CA**


Continued on next page
Liquid Biopsies – continued
Endocrine:

Anaplastic Thyroid: BRAF, EML4/ALK, HRAS, KRAS, MTOR, NRAS, NTRK1, RET
Medullary Thyroid: RET
Papillary Thyroid: BRAF

ALK fusions, NTRK1 fusions, RET fusions

BRAF
Atezolizumab Combinations With Chemotherapy for Anaplastic and Poorly Differentiated Thyroid Carcinomas, Trial NCT03181100 https://clinicaltrials.gov/ct2/show/NCT03181100

BRAF, HRAS, KRAS, MTOR, NRAS

SUGGESTED READINGS – continued
Note: suggested readings represent the evidence used when the biomarker was first presented for approval
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Liquid Biopsies – continued

Endocrine, Thyroid – continued

BRAF, HRAS, KRAS, NRAS


Iyer, P., Cote, G. J., Dadu, R., Ferrarotto, R., Busaidy, N., Hofmann, M., … Cabanillas, M. E. Circulating BRAF V600E Cell-Free DNA Detected by Droplet-Digital PCR (ddPCR) as a Biomarker in the Management of Anaplastic Thyroid Carcinoma (ATC) Patients. 87th Annual Meeting of the American Thyroid Association, Victoria, BC, 10/2017


A phase II Trial of CUDC-907 Treatment in People with Metastatic and Locally Advanced Thyroid Cancer, Trial NCT03002623 https://clinicaltrials.gov/ct2/show/NCT03002623.

MTOR


NTRK1


RAS

SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Liquid Biopsies – continued**

**Gastrointestinal:** Colorectal adenocarcinoma, Small Intestinal Adenocarcinoma, Appendiceal Adenocarcinoma, Pseudomyosoma Pentonei (PMP)

**APC, BRAF, KRAS, NRAS, PIC3CA, TP53**


SUGGESTED READINGS — continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Liquid Biopsies – continued

Genitourinary

Prostate

ATM, BRCA2


ATM, BRCA2, PTEN, RB1, TP53


ATM, BRCA2, TP53


BRCA2


PTEN, RB1, TP53


Continued on next page
SUGGESTED READINGS – continued

**Liquid Biopsies – continued**

**Genitourinary – continued**

**Urothelial**

**ERBB2**


**FGFR3**


**Melanoma: BRAF, GNA11, GNAQ, KIT, NRAS**


**Thoracic, Non-Small Cell Lung: BRAF, EGFR, EML4/ALK, ERBB2, MET, RET, ROS1**


Continued on next page
SUGGESTED READINGS – continued

Leukemia

Cytogenetics/Multiplex PCR (all subtypes):

Molecular-Genetics (Overview):

Molecular-Genetics (Philadelphia negative - all types):

Molecular-Genetics (Philadelphia negative B-lineage):

Burkitt subtype (c-myc):

Philadelphia positive subtype (BCR-ABL1) - Overlap CML:

Philadelphia positive subtype (Mutations) - Overlap CML:

Note: suggested readings represent the evidence used when the biomarker was first presented for approval
SUGGESTED READINGS – continued

Leukemia – continued

ALL - continued

IgH/TCR (all subtypes):

TP53 Mutations:
Chiaretti S, Brugnoletti F, Tavolaro, S et al. TP53 mutations are frequent in adult acute lymphoblastic leukemia cases negative for recurrent fusion genes and correlate with poor response to induction therapy. Haematologica 2013 May;98(5):e59-61

NOTCH1 and FBXW7:

Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Leukemia – continued

AML/MDS

Molecular CD33:


Molecular RUNX1:


Molecular SF3B1:
SUGGESTED READINGS – continued

Leukemia – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

AML/MDS

Molecular SF3B1, SRSF2, U2AF1, ZRSR2:


AML/MDS/CMML/Aplastic Anemia

Cytogenetics:


Molecular/DNMT3A:


Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Leukemia – continued

AML/MDS/CMML/Aplastic Anemia - continued

Molecular/FLT3:


Continued on next page
SUGGESTED READINGS – continued

Leukemia – continued

AML/MDS/CMML/Aplastic Anemia – continued

CEBPA:


IDH1/IDH2:


JAK2/MPL:

Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Leukemia** – continued

**AML/MDS/CMML/Aplastic Anemia - continued**

**KIT:**


**NPM1:**


**RAS:**


Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Leukemia – continued**

**Additional CMML:**


**APL**

**Cytogenetics/FISH:**


**FLT3:**


*Continued on next page*
Leukemia – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

APL - continued

IDH1/IDH2:


KIT:


NPM1:


RAS:


SUGGESTED READINGS – continued

Leukemia – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval.

CLL  Blood or bone marrow can be used for any of these tests. There are leukemia cells sampled by blood draw or bone marrow aspirate

Metaphase karyotype:


FISH for 11q del, 17p del, +12, 13q del:


IGHV mutation status:


Hamblin TJ, Davis Z, Gardiner A, Oscier DG, Stevenson FK. Unmutated Ig V(H) genes are associated with a more aggressive form of chronic lymphocytic leukemia Blood. 1999 Sep 15;94(6):1848-54. PubMed PMID: 10477713

TP53 sequencing and ATM sequencing, TP53, BIRC3, BTK, NOTCH1, PLCG2, SF3B1:


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SUGGESTED READINGS – continued

Leukemia – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

CLL - continued

TP53 sequencing and ATM sequencing, TP53, BIRC3, BTK, NOTCH1, PLCG2, SF3B1:


Continued on next page
SUGGESTED READINGS – continued

**Leukemia – continued**

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**CLL**

TP53 sequencing and ATM sequencing, TP53, BIRC3, BTK, NOTCH1, PLCG2, SF3B1:


**CML**


**Hairy Cell Leukemia**


**HES, Mastocytosis, MF, PV, ET**


**Note**

Continued on next page
SUGGESTED READINGS – continued

Leukemia – continued

T-Cell Disorders

TCRB clonality, TCRG clonality, FISH - 14q32:


Large Granular Lymphocytic Leukemia (T-LGL)

Somatic STAT3:


Prolymphocytic Leukemia (T-PLL)

JAK1, JAK3, STAT5B, IL2RG:


Lymphoma

Diffuse Large B-Cell Lymphoma


SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Lymphoma – continued

Mantle Cell

MRD, t(11;14) IGH-BCL1:


MYC (FISH):


NOTCH1:


NOTCH2, BTK, BIRC3:


Somatic Hypermutation:


TP53:


Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Melanoma


Continued on next page
SUGGESTED READINGS – continued

Melanoma - continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Acral, Mucosal, Uveal, and Unknown Primary Melanoma**

*Immunohistochemistry, PTEN:*


**Myeloma**

*Plasma Cell*


**Sarcoma**

*Desmoid fibromatosis*

**Molecular/CTNNBI:**


*Gastrointestinal stromal tumor*

**Molecular/CKIT and PDGFR:**


**Neuroblastoma**

**FISH/NMYC:**


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Biomarkers - MD Anderson Approved

These guidelines have been specifically developed for MD Anderson and are not intended to replace the independent medical or professional judgment of physicians or other health care providers.

SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Sarcoma - continued

Soft Tissue and Primary Bone:

Immunohistochemistry/ NY-ESO-1:


Continued on next page

Department of Clinical Effectiveness V5

Approved by the Executive Committee of the Medical Staff on 12/17/2019
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Soft Tissue and Primary Bone - continued:**

**Immunohistochemistry/**NY-ESO-1 continued:


Continued on next page
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

**Sarcoma - continued**

**Soft Tissue and Primary Bone - continued:**

**Immunohistochemistry/NY-ESO-1 continued:**


**Continued on next page**
SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Thoracic – continued

Non Small Cell Lung Cancer

**Immunohistochemistry/PD-L1 22C3:**


**FISH**:


**FISH/Non Small Cell Lung Cancer/BRAF:**

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Biomarkers - MD Anderson Approved

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SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Thoracic – continued

Non Small Cell Lung Cancer – continued

Molecular/BRAF V600E:

Molecular/EGFR:
Biomarkers - MD Anderson Approved

SUGGESTED READINGS – continued

Note: suggested readings represent the evidence used when the biomarker was first presented for approval

Thoracic – continued

Non Small Cell Lung Cancer - continued

Molecular/ELM4-ALK:


Molecular/KRAS:


Biomarkers - MD Anderson Approved

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DEVELOPMENT CREDITS

This practice consensus document was reviewed in conjunction with disease site representatives listed below. It was approved by the Molecular Testing Evaluation Committee (MTEC) at The University of Texas MD Anderson Cancer Center. The information is updated at least every two years or as new evidence emerges and is presented to MTEC for review and approval.

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