Cancer Of Unknown Primary

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

Note: Consider Clinical Trials as treatment options for eligible patients.
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**FINDINGS**

Adenocarcinoma\(^1\), poorly differentiated carcinoma (65%)

**FURTHER WORK-UP**

- Immunohistochemical markers to help suggest most “likely” primary site (See Table 1)
- Estrogen Receptor/Progesterone Receptor in women
- Alpha Fetoprotein (αFP) and beta-human chorionic (βHCG) gonadotropin for poorly differentiated carcinoma to rule out germ cell (See Table 1, Figure 1)
- See Notes below

**ADDITIONAL FINDINGS**

- Disseminated cancer, two or more sites involved
- Women with peritoneal carcinoma (typically, serous papillary pathology) in the presence of normal ovaries: check Cancer Antigen-125
- Solitary site of metastasis
- Isolated axillary nodes in women
- MRI Breast if mammogram and ultrasound are negative

**TREATMENT**

- Chemotherapy if good performance status
- If suggestive of primary peritoneal cancer, refer to ovarian cancer algorithm. Palliative measures, as needed, for small bowel obstruction.
- If resectable, resect with or without prior chemotherapy, chemoradiation.
- If unresectable, chemotherapy, radiation or chemoradiation PET/CT recommended.
- MRI negative, no surgery, consider radiation
- Chemotherapy for breast cancer
- MRI positive, breast surgery or
- Radiation therapy and chemotherapy
- Refer to Breast Cancer Algorithm

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**NOTES:**

- Gene Expression Profiling to identify the putative primary cancer profile (tissue of origin) is an emerging diagnostic test; currently experimental and studies are ongoing.
- Appropriate mutation analysis studies where indicated.
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<table>
<thead>
<tr>
<th>Likely Primary Site</th>
<th>Stain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>Estrogen receptor (ER), Gross cystic disease fluid fibrous protein-15 (GCDFP-15), mammaglobin, Her-2 neu, GATA-3</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>Thyroid transcription factor (TTF-1), surfactant protein A, Napsin A</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>PSA, PAP, Alpha-methylacyl CoA racemase/P504S (AMACR/P504S), Prostein</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Leukocyte common antigen (LCA), CD3, CD 4, CD 5, CD10, CD20, CD45, PAX5, Bcl-2, Bcl-6,cyclin D1</td>
</tr>
<tr>
<td>Mullerian/Ovarian</td>
<td>Estrogen receptor (ER), WT-1, PAX8</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>Desmin$^1$, factor VIII$^2$, CD31, Smooth muscle actin for Leiomyosarcoma, MyoD1, myogenin for Rhabdomyosarcoma</td>
</tr>
<tr>
<td>Neuroendocrine Tumor</td>
<td>Chromogranin, Synaptophysin, CD56</td>
</tr>
<tr>
<td>Germ Cell Tumor</td>
<td>βHCG, αFP, OCT3/4, CKIT, SALL4, CD30 (embryonal)</td>
</tr>
<tr>
<td>Urothelial Malignancies</td>
<td>CK7, CK20, Thrombomodulin, GATA-3</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>CK7, CK20, CDX-2, carcinoembryonic antigen (CEA). SATB2</td>
</tr>
<tr>
<td>Renal</td>
<td>RCC, CD10, PAX8</td>
</tr>
<tr>
<td>Hepatocellular Carcinoma</td>
<td>HepPar-1, CD10, Glypican-3, Arginase-1</td>
</tr>
<tr>
<td>Melanoma</td>
<td>S100, HMB-45, Tyrosinase and Melan-A, SOX10</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Thyroglobulin, TTF-1, PAX8</td>
</tr>
</tbody>
</table>

1 Positive in desmoid tumors, rhabdomyosarcomas, and leiomyosarcomas

2 Positive in angiosarcomas

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Approach to Cytokeratin (CK7 and CK20) markers used in Cancer of Unknown Primary

FIGURE 1

CK7          CK20

CK7 positive, CK20 positive
Urothelial tumors
Ovarian mucinous adenocarcinoma
Pancreatic adenocarcinoma
Cholangiocarcinoma
Stomach carcinoma

CK7 positive, CK20 negative
Lung adenocarcinoma
Breast carcinoma
Thyroid carcinoma
Endometrial carcinoma
Cervical carcinoma
Salivary gland carcinoma
Cholangiocarcinoma
Pancreatic carcinoma
Stomach carcinoma
Esophageal carcinoma

CK7 negative, CK20 positive
Colorectal carcinoma
Merkel cell carcinoma
(dot-like pattern)

CK7 negative, CK20 negative
Hepatocellular carcinoma
Renal cell carcinoma
Prostate carcinoma
Squamous cell and small cell lung carcinoma
Head and neck carcinoma

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SUGGESTED READINGS


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DEVELOPMENT CREDITS

This practice consensus algorithm is based on majority expert opinion of the Gastrointestinal Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following medical, radiation, radiologists, and pathologists.

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