Cancer Of Unknown Primary[1]

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.

EVALUATION

- History and physical including pelvic and/or rectal exam
- Hemoccult test
- CBC, LFTs, comprehensive metabolic profile, prostate specific antigen (PSA), other directed serum tumor markers
- CT chest, abdomen and pelvis
- Mammogram
- Endoscopy when indicated
- MRI brain
- Bone scan if symptomatic
- PET/CT (optional)
- Lifestyle risk assessment[2]

Fine needle aspiration (FNA) or core biopsy (preferred) of most accessible lesion[3] if not already performed, or if insufficient tissue is available for diagnosis and/or predictive/prognostic markers and/or molecular analysis

FINDINGS

Squamous cell carcinoma[4] (5%)

FURTHER WORK-UP

Metastatic cervical adenopathy

- Ultrasound
- FNA or core needle biopsy (preferred)
- CT head and neck
- Consider PET/CT

Localized to head and neck?

Yes

Head and neck surgery:
- Triple endoscopy
- Consider tonsillectomy

Refer to Head and Neck Service for further treatment recommendations

No, disseminated disease

Chemotherapy if good performance status

Metastatic inguinal adenopathy

- Perineal exam, anoscopy if needed
- Pelvic examination in a woman[4]
- PET/CT optional
- Cystoscopy/urologic evaluation if indicated

- If localized, lymph node dissection or local radiation therapy (or both in selected cases)
- Neoadjuvant chemotherapy in selected cases

Disseminated, visceral metastases

Directed invasive tests as needed

- Chemotherapy if good performance status
- Radiation therapy as indicated

Undifferentiated carcinoma, neuroendocrine tumor/carcinoma, undifferentiated neoplasm (30% all included), see Page 2

Adenocarcinoma[1], poorly differentiated carcinoma (65%), see Page 3

[1] See MD Anderson approved biomarkers (click here)
[2] See Physical Activity, Nutrition, and Tobacco Cessation Algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
[3] The biopsied lesion may be the primary site
[4] If suspecting head and neck, cervical, or anal malignancy, consider testing for HPV in situ hybridization

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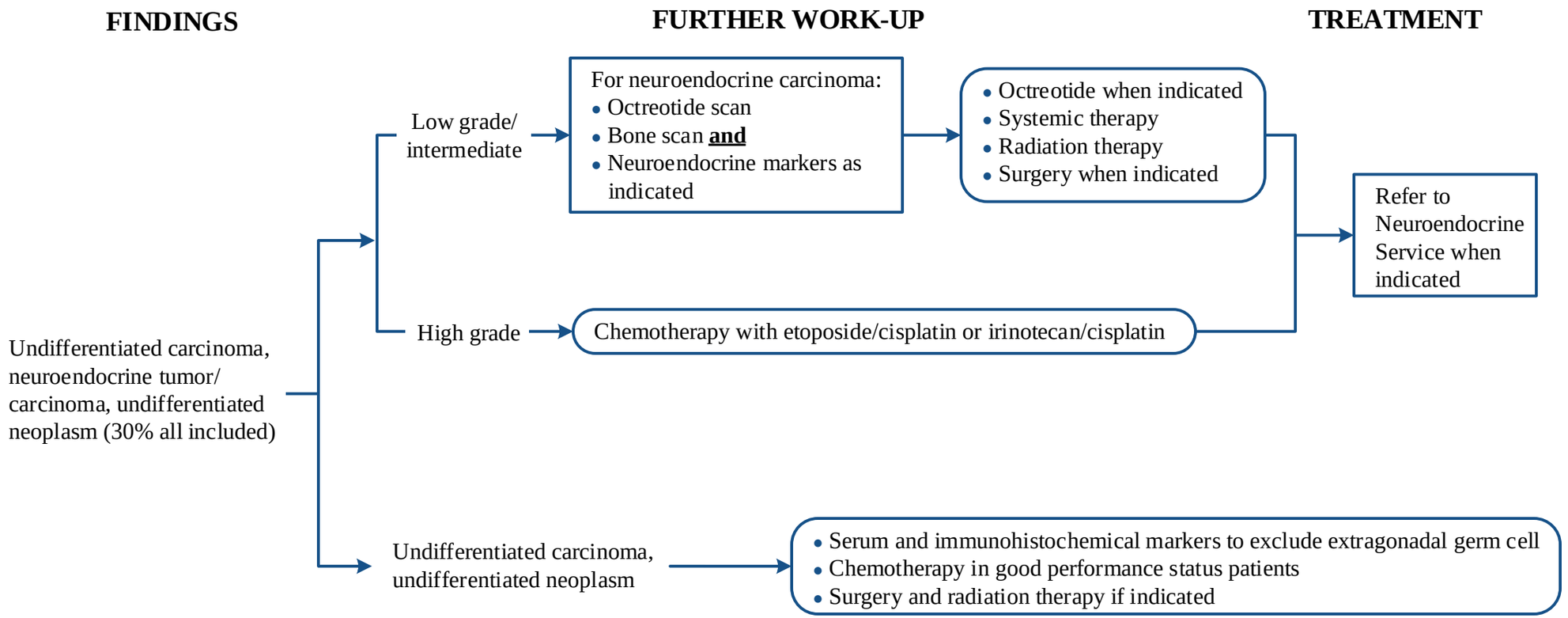

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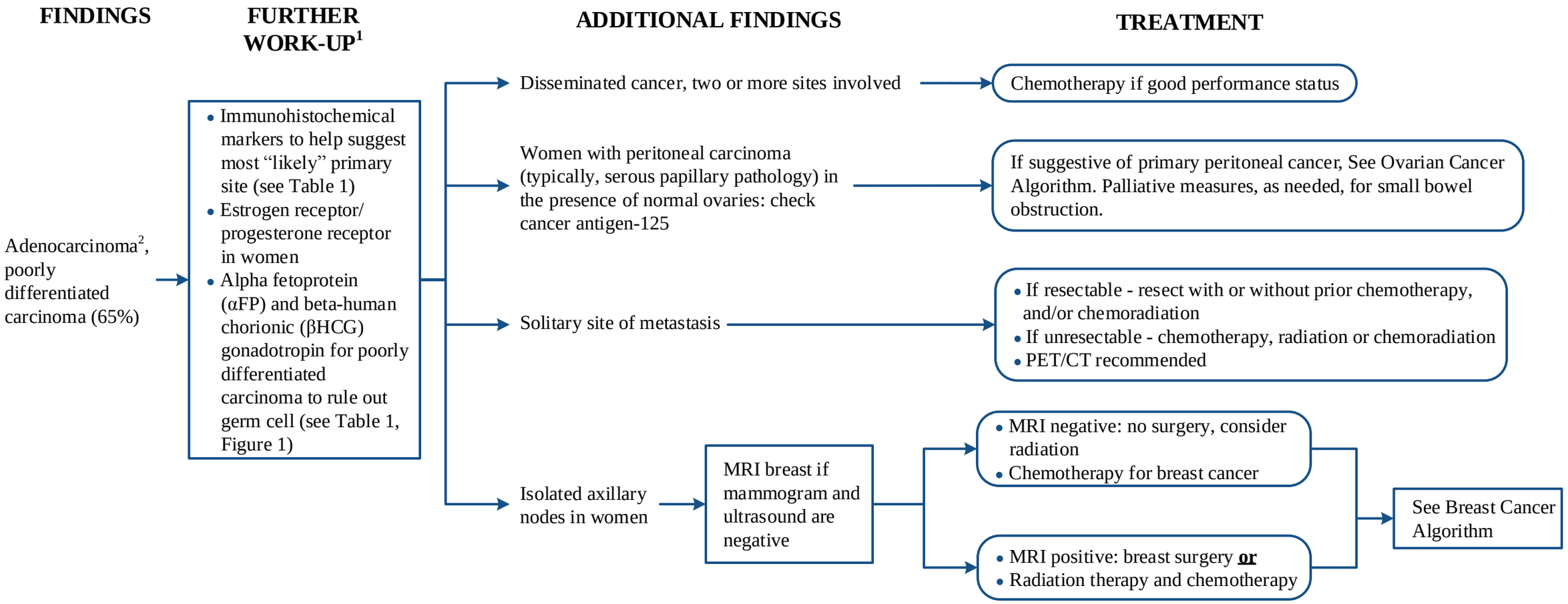

[1] Further work-up:
- Gene expression profiling to identify the putative primary cancer profile (tissue of origin) is an emerging diagnostic test; currently experimental and studies are ongoing
- Appropriate mutation analysis studies where indicated

[2] See MD Anderson approved biomarkers (click here)

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TABLE 1: Commonly utilized immunoperoxidase stains to assist in the differential diagnosis of poorly diferentiated neoplasms

Likely primary site	Stain
Breast Cancer	Estrogen receptor (ER), gross cystic disease fluid fibrous protein-15 (GCDFP-15), mammaglobin, HER-2 neu, GATA-3
Lung Cancer	Thyroid transcription factor (TTF-1), surfactant protein A, napsin A
Prostate Cancer	PSA, prostatic acid phosphatase (PAP), alpha-methylacyl CoA racemase/P504S (AMACR/P504S) protein
Lymphoma	Leukocyte common antigen (LCA), CD3, CD4, CD5, CD10, CD20, CD45, PAX5, Bcl-2, Bcl-6, cyclin D1
Mullerian/Ovarian	Estrogen receptor (ER), WT-1, PAX8
Sarcoma	Desmin[1], factor VIII[2], CD31, smooth muscle actin for leiomyosarcoma, MyoD1, myogenin for rhabdomyosarcoma
Neuroendocrine Tumor	Chromogranin, synaptophysin, CD56
Germ Cell Tumor	βHCG, αFP, OCT3/4, CKIT, SALL4, CD30 (embryonal)
Urothelial Malignancies	CK7, CK20, thrombomodulin, GATA-3
Colorectal Cancer	CK7, CK20, CDX-2, carcinoembryonic antigen (CEA), SATB2
Renal	Renal cell carcinoma (RCC), CD10, PAX8
Hepatocellular Carcinoma	HepPar-1, CD10, glypican-3, arginase-1
Melanoma	S100, HMB-45, tyrosinase and melan-A, SOX10
Thyroid	Thyroglobulin, thyroid transcription factor (TTF-1), PAX8

[1] Positive in desmoid tumors, rhabdomyosarcomas, and leiomyosarcomas

[2] Positive in angiosarcomas

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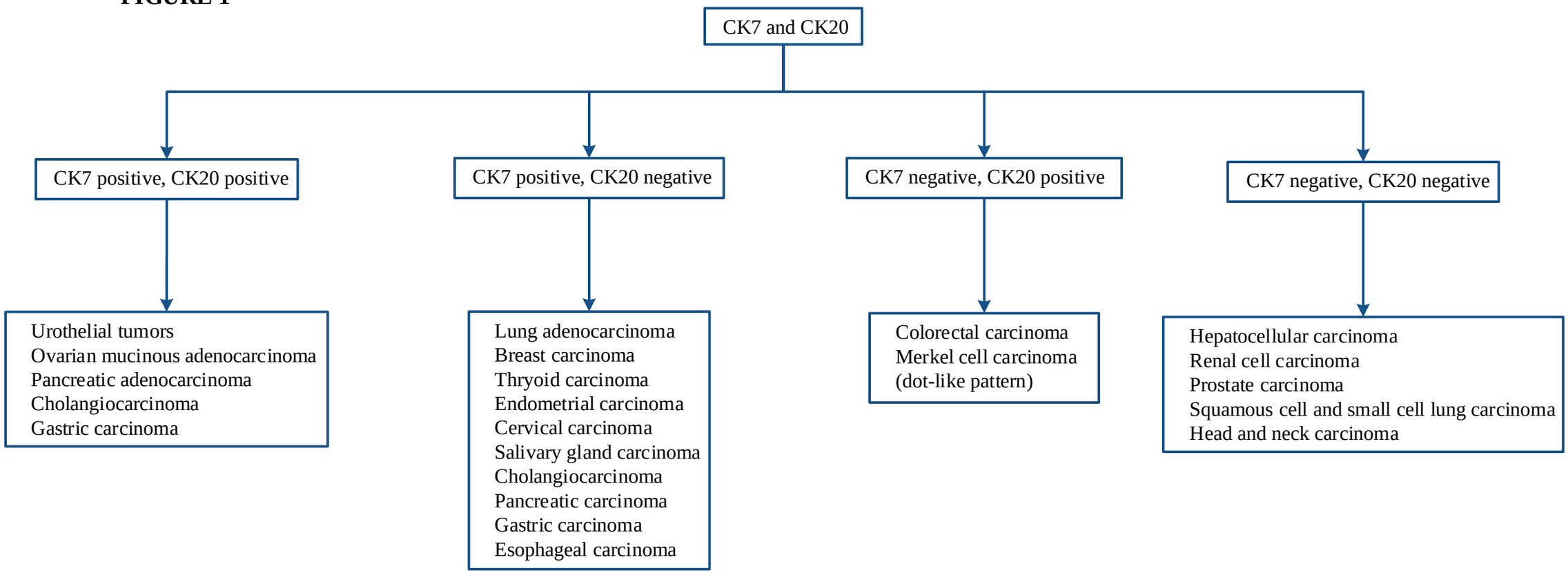
Approach to cytokeratin (CK7 and CK20) markers used in cancer of unknown primary

FIGURE 1



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DEVELOPMENT CREDITS

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

Beth Chasen, MD (Nuclear Medicine)
Wendy Garcia, BS♦
Firoze Jameel, MSN, RN, OCN♦
Aurelio Matamoros, MD (Diagnostic Radiology-Body Imaging)
Kanwal Raghav, MD (GI Medical Oncology)
Asif Rashid, MD (Pathology, Anatomical)
Melissa Taggart, MD (Pathology, Anatomical)
Gauri Varadhachary, MD (GI Medical Oncology)Ŧ

Ŧ Core Development Team

♦ Clinical Effectiveness Development Team