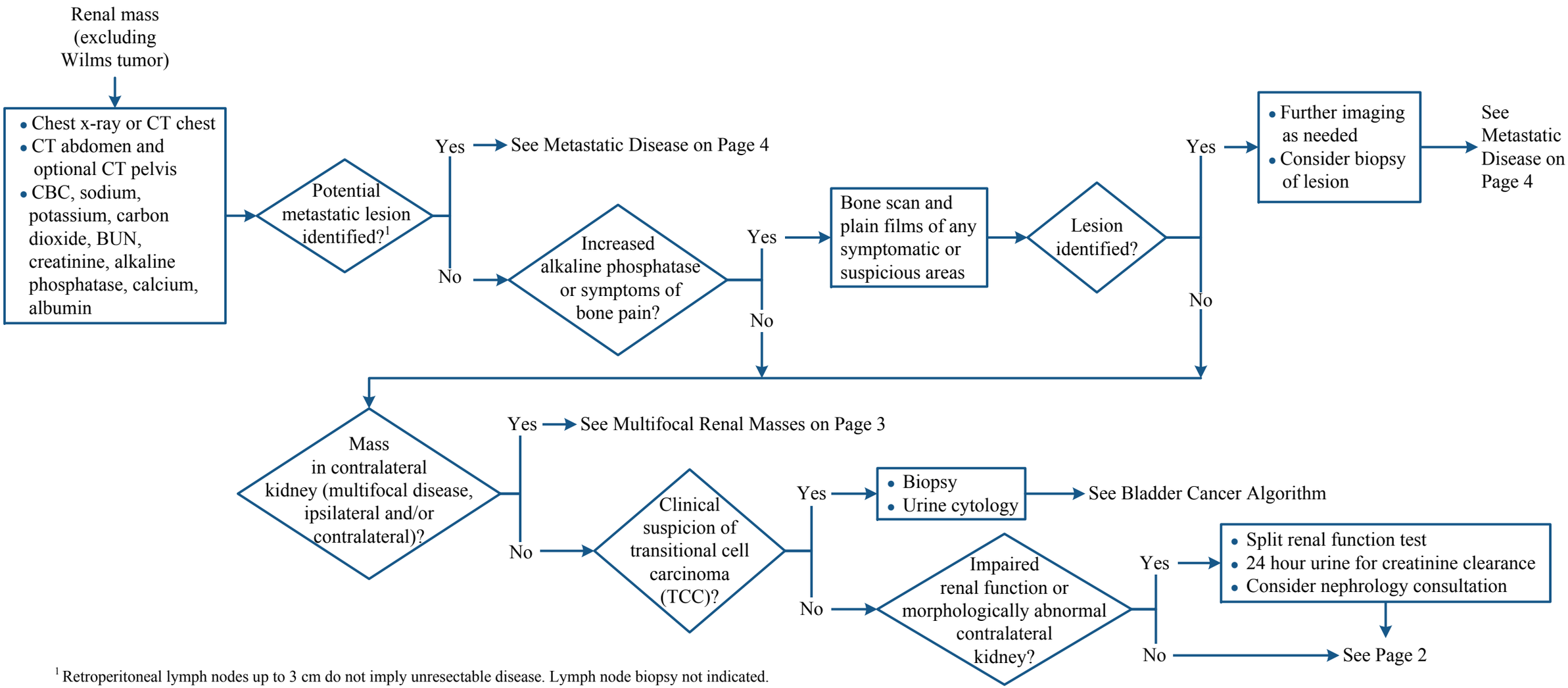
Renal Cell Carcinoma

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.

Patients with Renal Cell Carcinoma (RCC) diagnosed before age 46, regardless of histology, should be referred for genetic counseling and consideration of hereditary RCC syndromes.

INITIAL EVALUATION



[1] Retroperitoneal lymph nodes up to 3 cm do not imply unresectable disease. Lymph node biopsy not indicated.

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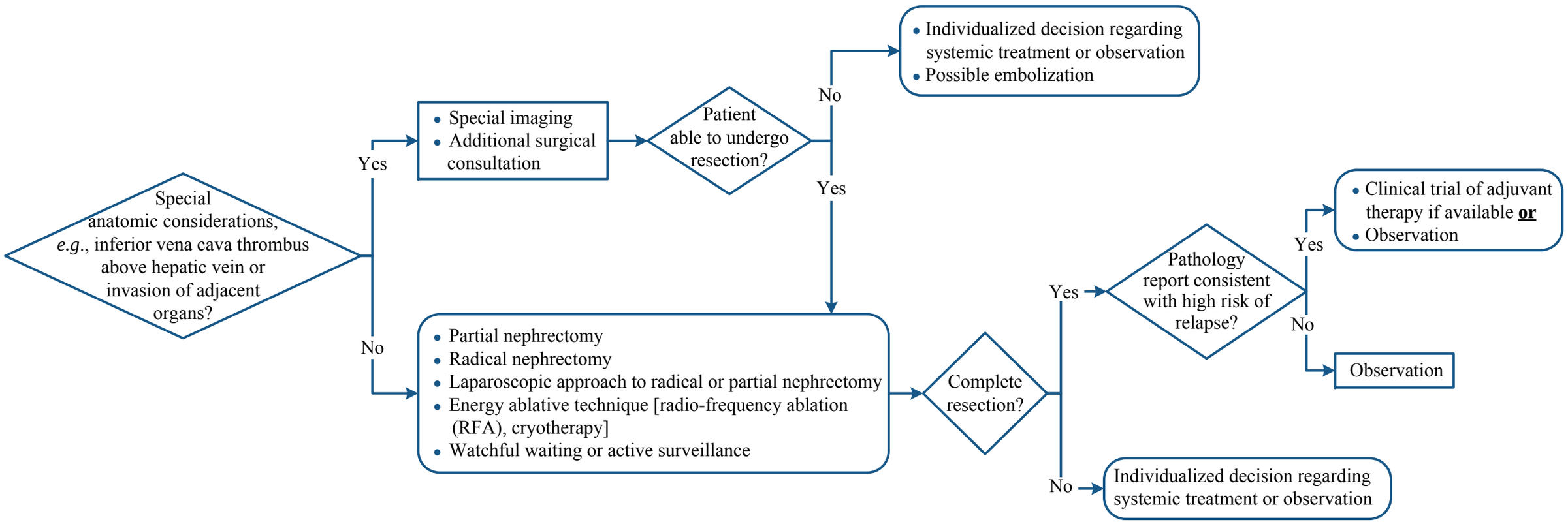

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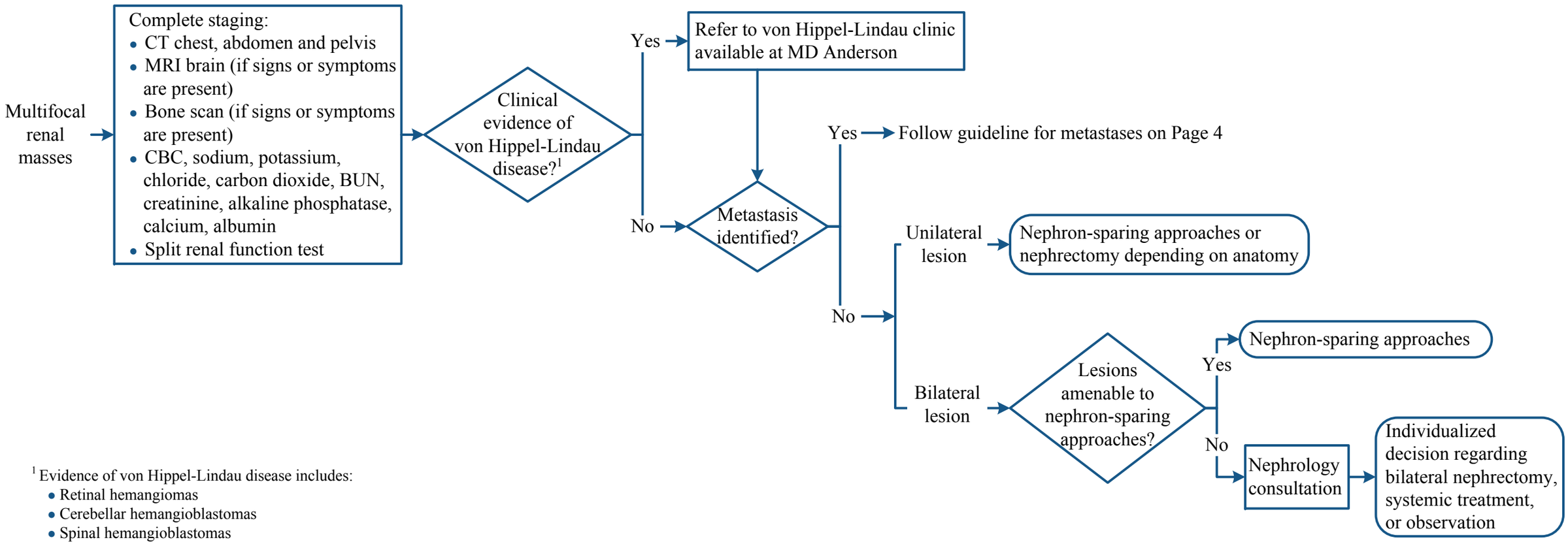

[1] Evidence of von Hippel-Lindau disease includes:
- Retinal hemangiomas
- Cerebellar hemangioblastomas
- Spinal hemangioblastomas
- Renal cell carcinoma
- Pheochromocytoma
- Pancreatic cysts
- Pancreatic neuroendocrine tumors
- Endolymphatic sac tumors
- Round ligament cysts (females)
- Epididymal cysts (males)

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CLINICAL PRESENTATION

Suspicion of metastatic disease

Staging:
- CT chest, abdomen, and pelvis
- CBC with differential, sodium, potassium, chloride, LDH, carbon dioxide, BUN, creatinine, alkaline phosphatase, calcium, albumin, AST
- MRI brain if clinically indicated
- Bone scan if clinically indicated

METASTASES AT PRESENTATION OR RECURRENCE

Multiple metastases

Anatomically threatening, (e.g., brain lesion, imminent pathologic fracture, or biliary obstruction)?

- Yes → Consider local control modalities:
  - Surgery
  - Radiation therapy
  - Energy ablation
  - Embolization
- No →
  - Consider cytoreductive nephrectomy if primary tumor in place **or**
  - Neoadjuvant therapy in setting of clinical trials
  - Biopsy if not surgical candidate

Solitary metastasis

Metastasis surgically resectable?

- No → Consider local control modalities:
  - Surgery
  - Radiation therapy
  - Energy ablation
  - Embolization

  → If primary in place, consider cytoreductive nephrectomy
- Yes → Anatomically threatening, (e.g., brain lesion, imminent pathologic fracture, or biliary obstruction)?
  - Yes → Resect metastasis
  - No →
    - Partial nephrectomy
    - Radical nephrectomy
    - Laparoscopic approach to radical or partial nephrectomy
    - Energy ablative technique (RFA, cryotherapy)

    → Restage
    - Surgically NED → Consider observation versus adjuvant therapy In setting of clinical trial
    - Solitary metastasis → Resect solitary metastasis
    - Multiple metastases → Refer to multiple metastasis above

Refer to Systemic Regimens on Page 5

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

PATHOLOGY | **SYSTEMIC TREATMENT**[1]

Clear cell

- Clinical trial
- Frontline agents – good/intermediate risk:
  - Pazopanib
  - Sunitinib
  - Bevacizumab plus interferon alpha-2b
  - Interleukin-2
- Frontline agent – poor risk:
  - Temsirolimus
- Second-line agents:
  - Nivolumab
  - Cabozantinib
  - Lenvatinib plus everolimus
  - Axitinib
  - Everolimus
  - Sorafenib
  - Previously unused frontline agent
  - Chemotherapy: gemcitabine and fluorouracil, gemcitabine and capecitabine

→ Prolonged period of stabilization and/or regression of lesions?

- Yes → Consider surgical consolidation **or** Observation **or** Change therapy
- No → Change therapy

Non-clear cell (papillary, chromophobe, medullary, translocation carcinoma, collecting duct)

- Clinical trial
- Antiangiogenic agents: sunitinib, cabozantinib bevacizumab plus interferon alpha-2b, axitinib, sorafenib, pazopanib, **or**
- mTOR inhibitors: temsirolimus, everolimus **or**
- Immunomodulatory agents: nivolumab
- Consider empiric individualized therapy with available agents

→ Response?

- Yes → Continue treatment to maximum response → Consider surgical consolidation **or** Observation **or** Change therapy
- No → Change therapy

[1] See Appendix A for dosing

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

EVALUATION

- Chest x-ray or CT chest
- CT abdomen and optional CT pelvis
- MRI abdomen
- CBC, sodium, potassium, carbon dioxide, BUN, creatinine, alkaline phosphatase, calcium, albumin
- MRI/CT brain if clinically indicated
- Central nervous system imaging if clinically indicated

SUMMARY BY STAGE

Clinical Stage I T1a T1b less than or equal to 7 cm → Good surgical candidate?

- Yes → Consider biopsy if atypical radiographic findings → Partial nephrectomy (if anatomically feasible); Radical nephrectomy
- No → Consider biopsy → Energy ablation; Active surveillance

Clinical Stage II greater than 7 cm → Good surgical candidate?

- Yes → Consider biopsy if atypical radiographic findings → Partial nephrectomy (if anatomically feasible); Radical nephrectomy
- No → Consider biopsy → Active surveillance; Embolization

Clinical Stage III T3a/T3b/N+ → Good surgical candidate?

- Yes → Consider biopsy if atypical radiographic findings → Partial nephrectomy; Radical nephrectomy → Clinical trial for adjuvant treatment
- No → Consider biopsy → Active surveillance; Embolization

Clinical Stage IV M+ → Good surgical candidate?

- Yes → Medical oncology consult → Cytoreductive nephrectomy (resection of single metastasis if possible) → Systemic therapy[1] **or**; Clinical trial
- No → Consider embolization to control primary if symptomatic → Systemic therapy[1]

[1] Systemic therapy:

- Antiangiogenic agents: sunitinib, bevacizumab plus interferon alpha-2b, axitinib, sorafenib, pazopanib **or**
- mTOR inhibitors: temsirolimus, everolimus **or**
- Chemotherapy: gemcitabine and fluorouracil, gemcitabine and capecitabine **or**
- Immunotherapy: interleukin-2

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SURVEILLANCE

Stage I:

	Months								
Examination	3	6	12	18	24	30	36	48	60
History	-	-	x	-	x	-	x	x	x
Physical exam	-	-	x	-	x	-	x	x	x
CT of abdomen	-	-	-	-	-	-	-	-	-
CXR or CT chest	-	-	x	-	x	-	x	x	x
Blood tests[1]	-	-	x	-	x	-	x	x	x

Stage II:

	Months								
Examination	3	6	12	18	24	30	36	48	60
History	-	x	x	x	x	x	x	x	x
Physical exam	-	x	x	x	x	x	x	x	x
CT of abdomen	-	-	-	-	x	-	-	-	x
CXR or CT chest	-	x	x	x	x	x	x	x	x
Blood tests[1]	-	x	x	x	x	x	x	x	x

Stage III:

	Months								
Examination	3	6	12	18	24	30	36	48	60
History	x	x	x	x	x	x	x	x	x
Physical exam	x	x	x	x	x	x	x	x	x
CT of abdomen	-	x	x	x	x	-	x	x	x
• then yearly after 2 years									
CXR or CT chest	x	x	x	x	x	x	x	x	-
Blood tests[1]	x	x	x	x	x	x	x	x	x

Stage IV:

History and physical exam, CT of abdomen, CXR, blood tests[1] every 3 months for years 1 and 2; every 4 months for years 3 and 4; every 6 months for year 5; then yearly.

CXR = chest x-ray

[1]Blood tests include CBC, calcium, liver function tests, and alkaline phosphatase

APPENDIX A: Suggested Guide for Dosing Options

Drug	Line of Therapy[1]	Dosing
Pazopanib	1st	800 mg PO daily
Sunitinib	1st	50 mg PO, 4 weeks on/2 weeks off or 2 weeks on/1 week off
Bevacizumab plus interferon alpha-2b	1st	Bevacizumab 10 mg/kg IV every 2 weeks, interferon 9 million units subcutaneously 3 times a week
Interleukin-2	1st	720,000 international units/kg IV every 8 hours (maximum 14 doses)
Temsirolimus	1st	25 mg IV weekly
Nivolumab	2nd	240 mg IV every 2 weeks
Cabozantinib*	2nd	60 mg PO daily (Cabometyx™ tablet formulation)
Lenvatinib* plus everolimus	2nd	Lenvatinib 18 mg PO daily, everolimus 5 mg PO daily
Axitinib	2nd	5 mg PO twice a day
Everolimus	2nd	10 mg PO daily
Sorafenib	2nd	400 mg PO twice a day

*Non-formulary

[1] For clear cell renal cell carcinoma

SUGGESTED READINGS

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Continued on Next Page

SUGGESTED READINGS - *continued*

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DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Genitourinary Center 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, and urologic oncologists:

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