Renal Cell Carcinoma

INITIAL EVALUATION

Renal mass (excluding Wilms tumor)
- Chest x-ray or CT chest
- CT abdomen and optional CT pelvis
- CBC, sodium, potassium, carbon dioxide, BUN, creatinine, alkaline phosphatase, calcium, albumin

Potential metastatic lesion identified?
- Yes → See Metastatic Disease on Page 4
- No → See Bladder Cancer Algorithm

Increased alkaline phosphatase or symptoms of bone pain?
- Yes → Bone scan and plain films of any symptomatic or suspicious areas
- No → Lesion identified?
  - Yes → Lesion identified?
    - Yes → See Metastatic Disease on Page 4
    - No → See Bladder Cancer Algorithm
  - No → Mass in contralateral kidney (multifocal disease, ipsilateral and/or contralateral)?
    - Yes → See Multifocal Renal Masses on Page 3
    - No → Clinical suspicion of transitional cell carcinoma (TCC)?
      - Yes → Biopsy, Urine cytology
      - No → Impaired renal function or morphologically abnormal contralateral kidney?
        - Yes → See Bladder Cancer Algorithm
        - No → No

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

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.

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Renal Cell Carcinoma

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

If you have special anatomic considerations, e.g., inferior vena cava thrombus above hepatic vein or invasion of adjacent organs?

Yes
- Special imaging
- Additional surgical consultation

Patient able to undergo resection?

Yes
- Partial nephrectomy
- Radical nephrectomy
- Laparoscopic approach to radical or partial nephrectomy
- Energy ablative technique [radio-frequency ablation (RFA), cryotherapy]
- Watchful waiting or active surveillance

No

Special imaging

No

Individualized decision regarding systemic treatment or observation

Possible embolization

Pathology report consistent with high risk of relapse?

Yes
- Clinical trial of adjuvant therapy if available or
- Observation

No
- Observation

Complete resection?

Yes

Individualized decision regarding systemic treatment or observation

No

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

**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

  - **Multiple metastases**

  - **Solitary metastasis**

  - **Metastasis surgically resectable?**

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

**METASTASES AT PRESENTATION OR RECURRENCE**

- **Consider local control modalities:**
  - Surgery
  - Radiation therapy
  - Energy ablation
  - Embolization

- **Consider cytoreductive nephrectomy if primary tumor in place or**
  - Neoadjuvant therapy in setting of clinical trials
  - Biopsy if not surgical candidate

- **If primary in place, consider cytoreductive nephrectomy**

- **Resect metastasis**

  - 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

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Page 4 of 11

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### PATHOLOGY

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

### SYSTEMIC TREATMENT

- 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

- Consider surgical consolidation or
- Observation or
- Change therapy

- 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

- Prolonged period of stabilization and/or regression of lesions?
  - Yes
    - Consider surgical consolidation or
    - Observation or
    - Change therapy
  - No
    - Change therapy

---

1 See Appendix A for dosing
Renal Cell Carcinoma

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

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
  - 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)
  - No
    - Consider embolization to control primary if symptomatic
    - Systemic therapy

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

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
# Renal Cell Carcinoma

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## SURVEILLANCE

### Stage I:

<table>
<thead>
<tr>
<th>Examination</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
<td>3 6 12 18 24 30 36 48 60</td>
</tr>
<tr>
<td>Physical exam</td>
<td>- - x - x - x x x</td>
</tr>
<tr>
<td>CT of abdomen</td>
<td>- - - - - - - -</td>
</tr>
<tr>
<td>CXR or CT chest</td>
<td>- - x - x - x x x</td>
</tr>
<tr>
<td>Blood tests(^1)</td>
<td>- - x - x - x x x</td>
</tr>
</tbody>
</table>

### Stage II:

<table>
<thead>
<tr>
<th>Examination</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
<td>3 6 12 18 24 30 36 48 60</td>
</tr>
<tr>
<td>Physical exam</td>
<td>- - x - x - x x x</td>
</tr>
<tr>
<td>CT of abdomen</td>
<td>- - - - x - - -</td>
</tr>
<tr>
<td>CXR or CT chest</td>
<td>- x x x x x x x</td>
</tr>
<tr>
<td>Blood tests(^1)</td>
<td>- x x x x x x x</td>
</tr>
</tbody>
</table>

### Stage III:

<table>
<thead>
<tr>
<th>Examination</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
<td>3 6 12 18 24 30 36 48 60</td>
</tr>
<tr>
<td>Physical exam</td>
<td>x x x x x x x x x</td>
</tr>
<tr>
<td>CT of abdomen</td>
<td>- x x x - x x x</td>
</tr>
<tr>
<td>CXR or CT chest</td>
<td>x x x x x x x</td>
</tr>
<tr>
<td>Blood tests(^1)</td>
<td>x x x x x x x</td>
</tr>
</tbody>
</table>

### Stage IV:

<table>
<thead>
<tr>
<th>Examination</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td></td>
</tr>
</tbody>
</table>

---

\(^1\)Blood tests include CBC, calcium, liver function tests, and alkaline phosphatase
APPENDIX A: Suggested Guide for Dosing Options

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

*Non-formulary

1 For clear cell renal cell carcinoma
SUGGESTED READINGS


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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