# Renal Cell Carcinoma





## TABLE OF CONTENTS

# Renal Cell Carcinoma





**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

Renal mass
(excluding Wilms tumor)

- Chest x-ray or CT chest
- CT abdomen and optional CT pelvis
- MRI abdomen, if iodinated IV contrast not possible
- CBC with differential, CMP, LDH, and UA
- Lifestyle risk assessment[1]

Potential metastatic lesion identified[2]?
- Yes → See metastatic disease on Page 5
- No → Increased alkaline phosphatase or symptoms of bone pain?
  - Yes → Bone scan or bone survey and plain films of any symptomatic or suspicious areas → Lesion identified?
    - Yes
      - Further imaging as needed
      - Consider biopsy of lesion
      - → See metastatic disease on Page 5
    - No
  - No

Mass in contralateral kidney (multifocal disease, ipsilateral and/or contralateral)?
- Yes → See multifocal renal masses on Page 4
- No → Clinical suspicion of urothelial carcinoma?
  - Yes
    - Biopsy
    - Urine cytology
    - → See Urothelial Carcinoma of Bladder and Upper Tract algorithm
  - No → Impaired renal function or morphologically abnormal contralateral kidney?
    - Yes
      - Split renal function test
      - Consider Nephrology consult
      - Consider cystatin-C with eGFR in cases of possible impaired kidney function
    - No → See Page 3

## FURTHER WORKUP

CMP = comprehensive metabolic panel
eGFR = estimated glomerular filtration rate
LDH = lactate dehydrogenase
UA = urinalysis

[1] See Physical Activity, Nutrition, Obesity Screening and Management, and Tobacco Cessation Treatment algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
[2] Retroperitoneal lymph nodes up to 3 cm do not imply unresectable disease. Lymph node biopsy not indicated.



Department of Clinical Effectiveness V12
Approved by The Executive Committee of the Medical Staff on 02/18/2025

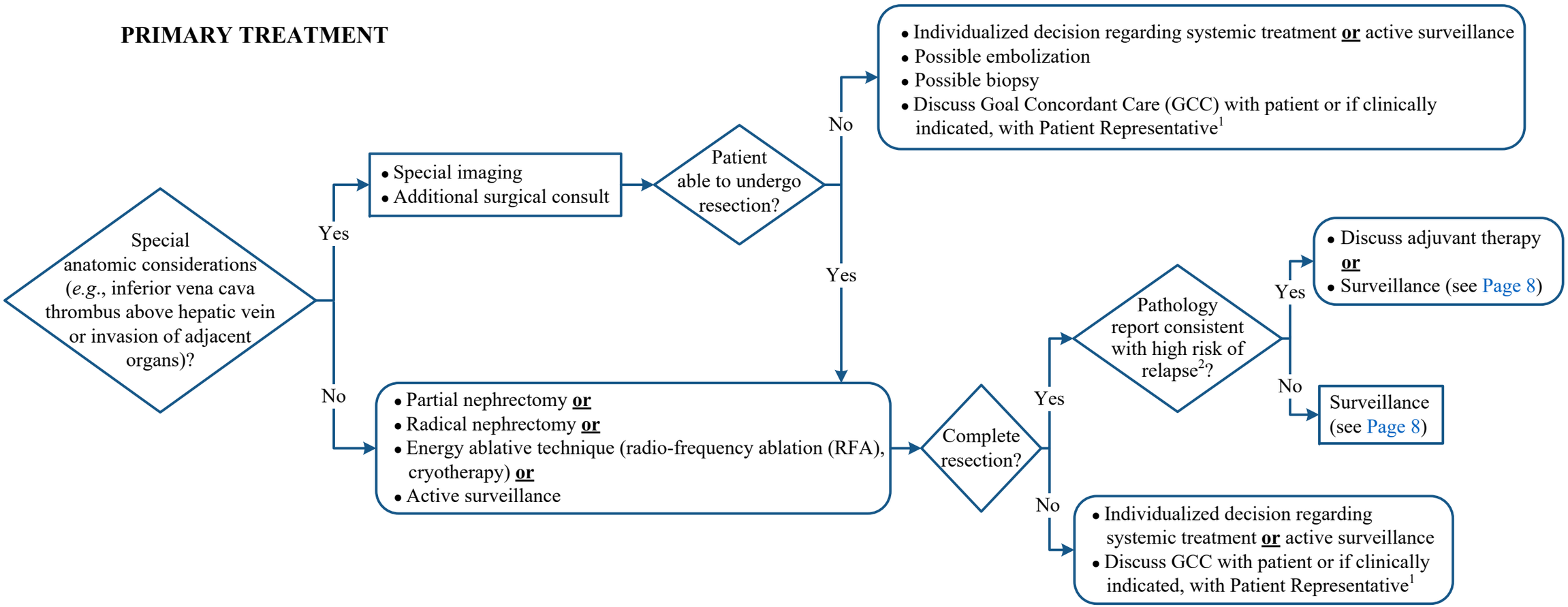
# Renal Cell Carcinoma





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

## PRIMARY TREATMENT




NED = no evidence of disease

[1] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

[2] High risk of relapse include clear cell histology, pT2G4, any pT3, pT4, pN1, or M1 who became NED after resection of metastases



Department of Clinical Effectiveness V12
Approved by The Executive Committee of the Medical Staff on 02/18/2025

# Renal Cell Carcinoma





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

## FURTHER WORKUP

Multifocal renal masses

Complete staging:
- CT chest, abdomen and pelvis
- MRI brain (if signs or symptoms are present)
- Bone scan or bone survey (if signs or symptoms are present)
- CBC with differential, CMP, LDH, and UA
- Split renal function test

Clinical evidence and/or family history of hereditary renal cell carcinoma syndrome[1]?

- Yes → Refer to Genitourinary Genetics clinic at MD Anderson
- No → Metastasis identified?
  - Yes → See metastatic disease on Page 5
  - No
    - Unilateral lesion → • Nephron-sparing approaches or nephrectomy depending on anatomy **or** • Active surveillance
    - Bilateral lesions → Lesions amenable to nephron-sparing approaches?
      - Yes → • Nephron-sparing approaches **or** • Active surveillance
      - No → Nephrology consult → Individualized decision regarding bilateral nephrectomy, systemic treatment, **or** active surveillance

CMP = comprehensive metabolic panel
LDH = lactate dehydrogenase
UA = urinalysis

[1] Features of von Hippel-Lindau disease includes:
- Major features:
  - Hemangioblastomas of the retina, spine, or brain
  - Clear Cell (cc) RCC diagnosed < 40 years of age or multiple/bilateral ccRCC tumors at any age
  - Pheochromocytoma
  - Paraganglioma of abdomen, thorax, or neck
  - Retinal angiomas
- Minor features:
  - Endolymphatic sac tumors
  - Papillary cystadenomas of the epididymis or broad ligament
  - Pancreatic serous cystadenoma (> 1)
  - Pancreatic neuroendocrine tumor or multiple pancreatic cysts (> 1)
- Other hereditary RCC syndromes include:
  - Hereditary Papillary Renal Carcinoma (HPRC) / *MET* gene
  - Birt-Hogg-Dube syndrome (BDHS) / *FLCN* gene
  - Tuberous Sclerosis Complex (TSC) / *TSC1, TSC2* genes
  - Hereditary Leiomyomatosis and RCC (HLRCC) / *FH* gene
  - BAP1 Tumor Predisposition Syndrome (TPDS) / *BAP1* gene
  - Hereditary Paraganglioma / Pheochromocytoma (PCL/PCC) syndromes / *SDHA/B/C/D* genes



Department of Clinical Effectiveness V12
Approved by The Executive Committee of the Medical Staff on 02/18/2025

# Renal Cell Carcinoma





**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, CMP, LDH, and UA
- MRI brain if clinically indicated
- Bone scan or bone survey if clinically indicated
- Consider biopsy

## TREATMENT

Multiple Metastases

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

Yes

Consider appropriate consultations:
- Surgery
- Radiation therapy
- Energy ablation
- Embolization

No

- Consider cytoreductive nephrectomy if primary tumor in place, after appropriate multidisciplinary discussion
- Biopsy if not surgical candidate

Refer to systemic regimens, see Page 6 for clear cell and Page 7 for non-clear cell

Solitary metastasis

Metastasis surgically resectable?

No

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

If primary in place, consider cytoreductive nephrectomy, after appropriate multidisciplinary discussion

Yes

- Resect metastasis
- If primary in place, consider cytoreductive nephrectomy, after appropriate multidisciplinary discussion

Surgically NED?

Yes

- Discuss adjuvant therapy[1] **or**
- Surveillance (see Page 8)

No

Refer to systemic regimens, see Page 6 for clear cell and Page 7 for non-clear cell

CMP = comprehensive metabolic panel
LDH = lactate dehydrogenase
NED = no evidence of disease
UA = urinalysis

[1] For stage M1 with NED after nephrectomy or resection of metastatic lesions, consider clinical trial or adjuvant pembrolizumab for up to a year



Department of Clinical Effectiveness V12
Approved by The Executive Committee of the Medical Staff on 02/18/2025

# Renal Cell Carcinoma





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

## PATHOLOGY

Clear cell

- Frontline agents: Favorable risk[2]
  - Preferred regimens
    - Axitinib plus pembrolizumab
    - Cabozantinib[3] plus nivolumab
    - Lenvatinib plus pembrolizumab
    - Ipilimumab plus nivolumab
  - Other recommended regimens
    - Axitinib plus avelumab
    - Cabozantinib[3]
    - Pazopanib
    - Sunitinib
  - Useful in certain circumstances
    - Active surveillance
    - Axitinib

- Frontline agents: Intermediate or poor risk[2]
  - Preferred regimens
    - Axitinib plus pembrolizumab
    - Cabozantinib[3] plus nivolumab
    - Ipilimumab plus nivolumab
    - Lenvatinib plus pembrolizumab
    - Cabozantinib[3]
  - Other recommended regimens
    - Axitinib plus avelumab
    - Pazopanib
    - Sunitinib
  - Useful in certain circumstances
    - Axitinib

## SYSTEMIC TREATMENT[1]

### A

Subsequent therapy agents based on prior immunotherapy exposure:

- For immunotherapy naïve patients:
  - Other recommended regimens[4]
    - Axitinib plus pembrolizumab
    - Cabozantinib[3]
    - Cabozantinib[3] plus nivolumab
    - Everolimus plus lenvatinib
    - Ipilimumab plus nivolumab
    - Lenvatinib plus pembrolizumab
    - Nivolumab
  - Useful in certain circumstances:
    - Axitinib
    - Everolimus
    - Pazopanib
    - Sunitinib
    - Tivozanib[3,5]
    - Belzutifan[3]
    - Bevacizumab
    - Axitinib plus avelumab

- For patients treated with immunotherapy:
  - Other recommended regimens[4]
    - Axitinib
    - Belzutifan[3]
    - Cabozantinib[3]
    - Everolimus plus Lenvatinib
    - Tivozanib[3]
  - Useful in certain circumstances:
    - Axitinib plus pembrolizumab
    - Cabozantinib[3] plus nivolumab
    - Everolimus
    - Ipilimumab plus nivolumab
    - Lenvatinib plus pembrolizumab
    - Pazopanib
    - Sunitinib
    - Bevacizumab
    - Axitinib plus avelumab

Prolonged period of stabilization and/or regression of lesions?

Yes
- Consider surgical consolidation **or**
- Observation **or**
- Continue therapy **or**
- Change therapy (see Box A on this page)

No
- Change therapy (see Box A on this page)
- Discuss GCC with patient or if clinically indicated, with Patient Representative[6]

[1] See Appendix A for drug dosing and schedule

[2] International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) criteria:
- Favorable risk: meets none of the features below
- Intermediate risk: meets 1-2 features below
- Poor risk: meets 3 or more features below

Features include:
- Time from diagnosis to treatment < 1 year
- Karnofsky Performance Status < 80%
- Hypercalcemia (total calcium corrected for albumin)
- Anemia
- Neutrophilia
- Thrombocytosis

[3] Not on MD Anderson formulary

[4] Other recommended regimens are listed in alphabetical order

[5] Indicated after at least two lines of prior systemic therapy

[6] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).



Department of Clinical Effectiveness V12
Approved by The Executive Committee of the Medical Staff on 02/18/2025

# Renal Cell Carcinoma





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

**PATHOLOGY**

**SYSTEMIC TREATMENT[1]**

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

**A**

- Preferred:
  - Clinical trial
  - Cabozantinib[2]
  - Cabozantinib[2] plus nivolumab
  - Lenvatinib plus pembrolizumab
- Other recommended regimens:
  - Sunitinib
  - Nivolumab
  - Pembrolizumab
  - Erlotinib plus bevacizumab (HLRCC related RCC and/or advanced papillary RCC)
  - Lenvatinib plus everolimus
- Useful in certain circumstances:
  - Axitinib
  - Everolimus
  - Bevacizumab plus everolimus
  - Ipilimumab plus nivolumab

Response?

Yes → Continue treatment to maximum response →
- Consider surgical consolidation **or**
- Observation **or**
- Change therapy (see Box A on this page)

No →
- Change therapy
- Discuss GCC with patient or if clinically indicated, with Patient Representative[3]

HLRCC = hereditary leiomyomatosis and renal cell cancer
RCC = renal cell carcinoma

[1] See Appendix A for drug dosing and schedule
[2] Not on MD Anderson formulary
[3] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).



Department of Clinical Effectiveness V12
Approved by The Executive Committee of the Medical Staff on 02/18/2025

## SURVEILLANCE

### Risk Classification

If final microscopic surgical margins are positive for cancer, the risk category should be considered at least one level higher, and increased clinical vigilance should be exercised

| |
|---|
| Low Risk (LR): pT1 and Grade 1/2 |
| Intermediate Risk (IR): pT1 and Grade 3/4, or pT2 any Grade |
| High Risk (HR): pT3 any Grade |
| Very High Risk (VHR): pT4 or pN1, or sarcomatoid/rhabdoid dedifferentiation, or macroscopic positive margin |

**Recommended follow-up schedule after surgery for renal cancer (in months)[1]**

| Risk | 3 | 6 | 9 | 12 | 18 | 24 | 30 | 36 | 48 | 60 | 72-84 | 96-120 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LR | - | - | - | X | - | X | - | - | X | X | X | X |
| IR | - | X | - | X | - | X | - | X | X | X | X | X |
| HR | - | X | - | X | X | X | X | X | X | X | X | X |
| VHR | X | X | X | X | X | X | X | X | X | X | X | X |

**Recommended follow-up schedule after thermal ablation (in months)[1,2]**

| Months after ablation | 3 | 6 | 9 | 12 | 18 | 24 | 30 | 36 | 48 | 60 | 72-84 | 96-120 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Follow up | - | X | - | X | - | X | - | X | X | X | X | X |

[1] Follow-up timeline is approximate and allows flexibility to accommodate reasonable patient, caregiver, and institutional needs. Each follow-up visit should include relevant history, physical examination, laboratory testing, and abdominal and chest imaging. Overall, 30% of renal cancer recurrences after surgery are diagnosed beyond 60 months. Informed/shared decision-making should guide surveillance decisions beyond 60 months.

[2] Patients undergoing ablative procedures with biopsy that confirmed malignancy or was non-diagnostic should undergo pre- and post-contrast cross-sectional abdominal imaging within 6 months (if not contraindicated). Subsequent follow-up should be according to the recommendations for the intermediate risk postoperative protocol.

## APPENDIX A: Drug Dosing

| Drug | Dose and Schedule |
|---|---|
| Axitinib | 5 mg PO twice daily |
| Axitinib plus avelumab | • Axitinib 5 mg PO twice daily<br>• Avelumab 800 mg IV every 2 weeks |
| Axitinib plus pembrolizumab | • Axitinib 5 mg PO twice daily<br>• Pembrolizumab 200 mg IV every 3 weeks **or** 400 mg IV every 6 weeks |
| Belzutifan[1] | 120 mg PO daily |
| Bevacizumab | 10 mg/kg IV every 2 weeks **or** 15 mg/kg IV every 3 weeks |
| Cabozantinib[1] | 60 mg PO daily |
| Cabozantinib[1] plus nivolumab | • Cabozantinib 40 mg PO daily<br>• Nivolumab 240 mg IV every 2 weeks **or** 480 mg IV every 4 weeks |
| Erlotinib plus bevacizumab | • Erlotinib 150 mg PO daily<br>• Bevacizumab 10 mg/kg IV every 2 weeks **or** 15 mg/kg IV every 3 weeks |
| Everolimus | 10 mg PO daily |
| Ipilimumab plus nivolumab | • Ipilimumab 1 mg/kg IV plus nivolumab 3 mg/kg (maximum dose 240 mg) IV every 3 weeks for 4 doses, **then**<br>• Nivolumab 6 mg/kg (maximum dose 480 mg) IV every 4 weeks |
| Lenvatinib plus everolimus | • Lenvatinib 18 mg PO daily<br>• Everolimus 5 mg PO daily |
| Lenvatinib plus pembrolizumab | • Lenvatinib 20 mg PO daily<br>• Pembrolizumab 200 mg IV every 3 weeks **or** 400 mg IV every 6 weeks |
| Nivolumab | 6 mg/kg (maximum dose 480 mg) IV every 4 weeks **or** 3 mg/kg (maximum dose 240 mg) IV every 2 weeks |
| Pazopanib | 800 mg PO daily |
| Pembrolizumab | 200 mg IV every 3 weeks **or** 400 mg IV every 6 weeks |
| Sunitinib | 50 mg PO daily for 4 weeks on/2 weeks off **or** 2 weeks on/1 week off |
| Tivozanib[1] | 1.34 mg PO daily on days 1 to 21 of a 28-day cycle |

[1] Not on MD Anderson formulary

## SUGGESTED READINGS

Brett, A. S. (2023). How should we interpret differences between cystatin C–based and creatinine-based GFR estimates? *NEJM Journal Watch*, 1. Retrieved from https://www.proquest.com/docview/2890682820?accountid=7135&pq-origsite=primo&sourcetype=Scholarly%20Journals

Campbell, S. C., Clark, P. E., Chang, S. S., Karam, J. A., Souter, L., & Uzzo, R. G. (2021). Renal mass and localized renal cancer: Evaluation, management, and follow-up: AUA Guideline: Part I. *The Journal of Urology, 206*(2), 199-208. https://doi.org/10.1097/JU.0000000000001911

Campbell, S. C., Uzzo, R. G., Karam, J. A., Chang, S. S., Clark, P. E., & Souter, L. (2021). Renal mass and localized renal cancer: Evaluation, management, and follow-up: AUA Guideline: Part II. *The Journal of Urology, 206*(2), 209-218. https://doi.org/10.1097/JU.0000000000001912

Choueiri, T. K., Escudier, B., Powles, T., Tannir, N. M., Mainwaring, P. N., Rini, B. I., . . . Motzer, R. J. (2016). Cabozantinib versus everolimus in advanced renal cell carcinoma (METEOR): Final results from a randomised, open-label, phase 3 trial. *The Lancet Oncology, 17*(7), 917-927. https://doi.org/10.1016/S1470-2045(16)30107-3

Choueiri, T. K., Halabi, S., Sanford, B. L., Hahn, O., Michaelson, M. D., Walsh, M. K., . . . Morris, M. J. (2017). Cabozantinib versus sunitinib as initial targeted therapy for patients with metastatic renal cell carcinoma of poor or intermediate risk: The Alliance A031203 CABOSUN Trial. *Journal of Clinical Oncology, 35*(6), 591-597. https://doi.org/10.1200/JCO.2016.70.7398

Choueiri, T. K., Motzer, R. J., Rini, B. I., Haanen, J., Campbell, M. T., Venugopal, B., . . . Albiges, L. (2020). Updated efficacy results from the JAVELIN Renal 101 trial: First-line avelumab plus axitinib versus sunitinib in patients with advanced renal cell carcinoma. *Annals of Oncology, 31*(8), 1030-1039. https://doi.org/10.1016/j.annonc.2020.04.010

Choueiri, T. K., Powles, T., Burotto, M., Escudier, B., Bourlon, M. T., Zurawski, B., . . . Motzer, R. J. (2021). Nivolumab plus cabozantinib versus sunitinib for advanced renal-cell carcinoma. *The New England Journal of Medicine, 384*(9), 829-841. https://doi.org/10.1056/NEJMoa2026982

Choueiri, T. K., Tomczak, P., Park, S. H., Venugopal, B., Ferguson, T., Chang, Y.-H., . . . Powles, T. (2021). Adjuvant pembrolizumab after nephrectomy in renal-cell carcinoma. *The New England Journal of Medicine, 385*(8), 683-694. https://doi.org/10.1056/NEJMoa2106391

Heng, D. Y. C., Xie, W., Regan, M. M., Warren, M. A., Golshayan, A. R., Sahi, C., . . . Choueiri, T. K. (2009). Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor-targeted agents: Results from a large, multicenter study. *Journal of Clinical Oncology, 27*(34), 5794-5799. https://doi.org/10.1200/JCO.2008.21.4809

Jonasch, E., Donskov, F., Iliopoulos, O., Rathmell, W. K., Narayan, V. K., Maughan, B. L., . . . Srinivasan, R. (2021). Belzutifan for renal cell carcinoma in von Hippel-Lindau Disease. *The New England Journal of Medicine, 385*(22), 2036-2046. https://doi.org/10.1056/NEJMoa2103425

Lee, C.-H., Shah, A. Y., Rasco, D., Rao, A., Taylor, M. H., Di Simone, C., . . . Motzer, R. J. (2021). Lenvatinib plus pembrolizumab in patients with either treatment-naive or previously treated metastatic renal cell carcinoma (Study 111/KEYNOTE-146): A phase 1b/2 study. *The Lancet Oncology*, *22*(7), 946-958. https://doi.org/10.1016/S1470-2045(21)00241-2

McDermott, D. F., Regan, M. M., Clark, J. I., Flaherty, L. E., Weiss, G. R., Logan, T. F., . . . Atkins, M. B. (2005). Randomized phase III trial of high-dose interleukin-2 versus subcutaneous interleukin-2 and interferon in patients with metastatic renal cell carcinoma. *Journal of Clinical Oncology, 23*(1), 133-141. https://doi.org/10.1200/JCO.2005.03.206

MD Anderson Institutional Policy #CLN1202 - Advance Care Planning Policy
Advance Care Planning (ACP) Conversation Workflow (ATT1925)

*Continued on next page*

## SUGGESTED READINGS - continued

Messing, E. M., Manola, J., Wilding, G., Propert, K., Fleischmann, J., Crawford, E. D., . . . Trump, D. (2003). Phase III study of interferon alfa-NL as adjuvant treatment for resectable renal cell carcinoma: An eastern cooperative oncology Group/Intergroup trial. *Journal of Clinical Oncology, 21*(7), 1214-1222. https://doi.org/10.1200/JCO.2003.02.005

Mickisch, G. H. J., Garin, A., van Poppel, H., de Prijck, L., & Sylvester, R. (2001). Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: A randomised trial. *The Lancet, 358*(9286), 966-970. https://doi.org/10.1016/S0140-6736(01)06103-7

Motzer, R., Alekseev, B., Rha, S.-Y., Porta, C., Eto, M., Powles, T., . . . Choueiri, T. K. (2021). Lenvatinib plus pembrolizumab or everolimus for advanced renal cell carcinoma. *The New England Journal of Medicine*, *384*(14), 1289-1300. https://doi.org/10.1056/NEJMoa2035716

Motzer, R. J., Bacik, J., Murphy, B. A., Russo, P., & Mazumdar, M. (2002). Interferon-alfa as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. *Journal of Clinical Oncology, 20*(1), 289-296. https://doi.org/10.1200/JCO.2002.20.1.289

Motzer, R. J., Hutson, T. E., Glen, H., Michaelson, M. D., Molina, A., Eisen, T., . . . Larkin, J. (2015). Lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma: A randomised, phase 2, open-label, multicentre trial. *The Lancet Oncology*, *16*(15), 1473-1482. https://doi.org/10.1016/S1470-2045(15)00290-9

Motzer, R. J., Hutson, T. E., Tomczak, P., Michaelson, M. D., Bukowski, R. M., Rixe, O., . . . Figlin, R. A. (2007). Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *The New England Journal of Medicine, 356*(2), 115-124. https://doi.org/10.1056/NEJMoa065044

Motzer, R. J., Michaelson, M. D., Redman, B. G., Hudes, G. R, Wilding, G., Figlin, R. A., . . . Rini, B. I. (2006). Activity of SU11248, a multitargeted inhibitor of vascular endothelial growth factor receptor and platelet-derived growth factor receptor, in patients with metastatic renal cell carcinoma. *Journal of Clinical Oncology, 24*(1), 16-24. https://doi.org/10.1200/JCO.2005.02.2574

Motzer, R. J., Tannir, N. M., McDermott, D. F., Arén Frontera, O., Melichar, B., Choueiri, T. K., . . . Escudier, B. (2018). Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. *The New England Journal of Medicine*, *378*(14), 1277-1290. https://doi.org/10.1056/NEJMoa1712126

National Comprehensive Cancer Network. (2024). *Kidney Cancer* (NCCN Guideline Version 2.2025). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf

Rini, B. I., Pal, S. K., Escudier, B. J., Atkins, M. B., Hutson, T. E., Porta, C., . . . McDermott, D. F. (2020). Tivozanib versus sorafenib in patients with advanced renal cell carcinoma (TIVO-3): A phase 3, multicentre, randomised, controlled, open-label study. *The Lancet Oncology, 21*(1), 95-104. https://doi.org/10.1016/S1470-2045(19)30735-1

Rini, B. I., Plimack, E. R., Stus, V., Gafanov, R., Hawkins, R., Nosov, D., . . . Powles, T. (2019). Pembrolizumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. *The New England Journal of Medicine, 380*(12), 1116-1127. https://doi.org/10.1056/NEJMoa1816714

Shlipak, M. G., Matsushita, K., Ärnlöv, J., Inker, L. A., Katz, R., Polkinghorne, K. R., . . . Gansevoort, R. T. (2013). Cystatin C versus creatinine in determining risk based on kidney function. *The New England Journal of Medicine, 369*(10), 932-943. https://doi.org/10.1056/NEJMoa1214234

Spencer, S., Desborough, R., Mehta, S., Ives, N., & Bhandari, S. (2024). Cystatin C vs creatinine eGFR in advanced CKD: An analysis of the STOP-ACEi trial. *Clinical Kidney Journal, 17*(9), 1-12. https://doi.org/10.1093/ckj/sfae268

van der Poel, H., Roukema, J., Horenblas, S., van Geel, A., & Debruyne, F. (1999). Metastasectomy in renal cell carcinoma: A multicenter retrospective analysis. *European Urology, 35*(3), 197-203. https://doi.org/10.1159/000019849

Yang, J. C., Haworth, L., Sherry, R. M., Hwu, P., Schwartzentruber, D. J., Topalian, S. L., . . . Rosenberg, S. A. (2003). A randomized trial of bevacizumab, an anti-vascular endothelial growth factor antibody, for metastatic renal cancer. *The New England Journal of Medicine, 349*(5), 427-434. https://doi.org/10.1056/NEJMoa021491

Yang, J. C., Sherry, R. M., Steinberg, S. M., Topalian, S. L., Schwartzentruber, D. J., Hwu, P., . . . Rosenberg, S. A. (2003). Randomized study of high-dose and low-dose interleukin-2 in patients with metastatic renal cancer. *Journal of Clinical Oncology, 21*(16), 3127-3132. https://doi.org/10.1200/JCO.2003.02.122

## DEVELOPMENT CREDITS

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

### Core Development Team Leads

Eric Jonasch, MD (Genitourinary Medical Oncology)
Jose Antonio Karam, MD (Urology)

### Workgroup Members

Matthew Campbell, MD (Genitourinary Medical Oncology)
Henry Cao, PharmD (Pharmacy Clinical Programs)
Seungtaek Choi, MD (Genitourinary Radiation Oncology)
Brittney Cotta, MD (Urology)
Wendy Garcia, BS♦
Brittnee Macintyre, MSN, APRN, FNP-C♦
Surena Matin, MD (Urology)
Pavlos Msaouel, MD, PhD (Genitourinary Medical Oncology)
Chaan Ng, MD (Abdominal Imaging)
Quynh-Nhu Nguyen, MD (Radiation Oncology)
Van Nguyen, PharmD♦
Raquel Sanchez, MS♦
Nizar Tannir, MD (Genitourinary Medical Oncology)
Emily Wang, PharmD (Pharmacy Clinical Programs)

♦Clinical Effectiveness Development Team