RENAL CELL CARCINOMA TREATMENT REGIMENS (Part 1 of 2)

Clinical Trials: The National Comprehensive Cancer Network recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced health care team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data become available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

General treatment notes:[1]

- Targeted therapy using tyrosine kinase inhibitors and anti-vascular endothelial growth factor antibodies is now widely used as first- and second-line treatments in renal cell carcinoma (RCC). To date, seven such agents have been approved by the FDA for the treatment of advanced RCC: sunitinib, sorafenib, pazopanib, axitinib, temsirolimus, everolimus, and bevacizumab in combination with interferon.
- Prior to targeted therapies, systemic treatment options were limited to cytokine therapy, notably IL-2 and interferon-α-2A (IFN-α-2a).

First-line Therapy for Patients with Predominantly Clear Cell Histology[1]

Note: All recommendations are Category 2A unless otherwise indicated.
Regimens listed alphabetically by category and preference.

REGIMEN	DOSING
Pazopanib (Category 1; preferred)[2,3]	Pazopanib 800mg orally once daily without food.
Sunitinib (Category 1; preferred)[4,5]	Sunitinib 50mg orally daily with or without food for 4 weeks, followed by 2 weeks off.
Bevacizumab + IFN-α (Category 1)[6-8]	Bevacizumab 10mg/kg IV every 2 weeks + IFN-α.
Temsirolimus (Category 1: poor-prognosis patients; Category 2B: selected patients of other risk groups)[9,10]	Temsirolimus 25mg IV over 30–60 minutes once weekly until disease progression or unacceptable toxicity.
Axitinib[11,12,a]	Axitinib 5mg orally every 12 hours.
Cabozantinib (for poor- and intermediate-risk groups)[13]	Cabozantinib 60mg orally once daily.
High-dose IL-2 (for selected patients with excellent performance status and normal organ function)[13,14,b]	**Days 1–5 and 15–19:** IL-2 600,000 IU/kg IV every 8 hours (max 14 doses). Repeat cycle every 4 weeks for max 3 cycles.

Subsequent Therapy for Patients with Predominantly Clear Cell Carcinoma[1]

Cabozantinib (Category 1; preferred)[16,d]	Cabozantinib 60mg orally once daily without food until disease progression or unacceptable toxicity.
Nivolumab (Category 1; preferred)[17,18,d]	Nivolumab 240mg IV every 2 weeks until disease progression or unacceptable toxicity.
Axitinib (Category 1)[11,12,a]	Axitinib 5mg orally every 12 hours.
Lenvatinib + everolimus (Category 1)[19]	Lenvatinib 18 mg orally once daily + everolimus 5 mg orally once daily with or without food until disease progression or unacceptable toxicity.
Everolimus[20,21]	Everolimus 10mg orally once daily with or without food.
Pazopanib[2,3]	Pazopanib 800mg orally once daily without food.
Sorafenib[22-25]	Sorafenib 400mg orally twice daily without food.
Sunitinib[4,26,27]	Sunitinib 50mg orally daily with or without food for 4 weeks, followed by 2 weeks off.
Bevacizumab (Category 2B)[28]	Bevacizumab 10mg/kg IV every 2 weeks.
High-dose IL-2 (for selected patients with excellent performance status and normal organ function) (Category 2B)[14,15,b]	**Days 1–5 and 15–19:** IL-2 600,000 IU/kg IV every 8 hours (max 14 doses). Repeat cycle every 4 weeks for max 3 cycles.
Temsirolimus (Category 2B)[31,32]	Temsirolimus 25mg IV over 30-60 minutes weekly until disease progression or unacceptable toxicity.

Systemic Therapy for Patients with Non-Clear Cell Histology[1]

Sunitinib (preferred)[4,26,27]	Sunitinib 50mg orally daily with or without food for 4 weeks, followed by 2 weeks off.
Axitinib[11,12,a]	Axitinib 5mg orally every 12 hours.
Bevacizumab[28]	Bevacizumab 10mg/kg IV every 2 weeks.
Bevacizumab + erlotinib (for selected patients with advanced papillary RCC including HLRCC)[29,f]	**Day 1:** Bevacizumab 10mg/kg IV **Days 1-14:** Erlotinib 150mg orally once daily. Repeat cycle every 14 days.

continued

RENAL CELL CARCINOMA TREATMENT REGIMENS (Part 2 of 2)

Systemic Therapy for Patients with Non-Clear Cell Histology[1] (continued)

REGIMEN	DOSING
Bevacizumab + everolimus (for selected patients with advanced papillary RCC including HLRCC)[30,f]	**Day 1:** Bevacizumab 10mg/kg IV **Days 1-14:** Everolimus 10mg orally once daily. Repeat cycle every 14 days.
Cabozantinib[16,d]	Cabozantinib 60mg orally once daily without food until disease progression or unacceptable toxicity.
Erlotinib[33,e]	Erlotinib 150mg orally once daily without food.
Everolimus[20,21]	Everolimus 10mg orally once daily with or without food.
Lenvatinib + everolimus[19]	Lenvatinib 18 mg orally once daily + everolimus 5 mg orally once daily with or without food until disease progression or unacceptable toxicity.
Nivolumab[17,18,d]	Nivolumab 240mg IV every 2 weeks until disease progression or unacceptable toxicity.
Pazopanib[2,3]	Pazopanib 800mg orally once daily without food.
Sorafenib[22-25]	Sorafenib 400mg orally twice daily without food.
Temsirolimus (Category 1: poor-prognosis patients; Category 2A: selected patients of other risk groups)[27,28]	Temsirolimus 25mg IV over 30–60 minutes weekly until disease progression or unacceptable toxicity.

a May increase to 7mg every 12 hours after 2 weeks based on criteria; may increase to 10mg every 12 hours after 2 weeks based on criteria.

b Treatments divided into 60-day courses, with each IV treatment course consisting of 2 cycles of therapy, separated by approximately 7–10 days of rest with no other therapy during the remainder of the 60 days.

c Patients who progressed were dose-escalated to 600 mg twice daily.

d Based on the results of phase III trials, eligible patients should preferentially receive this agent over everolimus.

e Erlotinib is used off-label for RCC. The NCCN guidelines include it as an optional first-line therapy for patients with relapsed or medically unresectable stage IV non-clear cell carcinoma.

f HLRCC: Hereditary leiomyomatosis and renal cell cancer.

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