

Renal Cell Carcinoma Treatment Regimens

Clinical Trials: The NCCN 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 healthcare 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 becomes 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 National Comprehensive Cancer Network 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.

► Adjuvant Therapy for Patients With Clear Cell Histology and High-Risk Disease¹

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

REGIMEN	DOSING
Sunitinib (Category 2B) ²⁻⁶	Sunitinib 50 mg orally once daily with or without food for 4 weeks, followed by 2 weeks off for 1 year.

► Relapse or Stage IV: First-line Therapy for Patients with Clear Cell Histology¹

Pembrolizumab + Axitinib (Category 2A; preferred for favorable risk); (Category 1; preferred for poor/intermediate risk) ^{7,8}	Day 1: Pembrolizumab 200mg IV AND Days 1-21: Axitinib 5mg orally twice daily. ^a Repeat cycle every 3 weeks.
Pazopanib (Category 2A; preferred for favorable risk); (Category 1 for poor/intermediate risk) ^{9,12}	Pazopanib 800mg orally once daily without food.
Sunitinib (Category 2A; preferred for favorable risk); (Category 1 for poor/intermediate risk) ^{2,13,14}	Sunitinib 50mg orally once daily with or without food for 4 weeks, followed by 2 weeks off.
Bevacizumab + IFN alfa-2B (Category 1) ¹⁵⁻¹⁷	Day 1: Bevacizumab 10mg/kg IV AND Days 1,3,5,8,10,12: Interferon alfa-2B 9 million units subcutaneous every 2 weeks.
Temsirolimus (Category 1 for poor/intermediate risk) ¹⁸⁻²⁰	Temsirolimus 25mg IV over 30–60 minutes once weekly.
Nivolumab/Ipilimumab Followed by Nivolumab (Category 1 [preferred] for poor/intermediate risk); Category 2A for favorable risk) ²¹⁻²³	Day 1: Nivolumab 3mg/kg IV over 30 minutes AND Day 1: Ipilimumab 1mg/kg IV over 30 minutes every 3 weeks for 4 cycles FOLLOWED BY Day 1: Nivolumab 240mg IV every 2 weeks OR Day 1: Nivolumab 480mg IV every 4 weeks.
High-dose Aldesleukin (IL-2) (for patients with excellent performance status and normal organ function) ^{25,26}	Days 1-5 and 15-19: IL-2 600,000 units/kg IV over 15 minutes every 8 hours (max 14 doses on days 1-5 and 14 doses on days 15-19 for a max 28 total doses per cycle). Repeat cycle every 12 weeks for a max of 3 cycles.
Cabozantinib (Category 2A; preferred for poor/intermediate risk); (Category 2B for favorable risk) ²⁷⁻²⁹	Cabozantinib 60mg orally once daily on an empty stomach.
Axitinib (Category 2B) ^{30-32,b}	Axitinib 5mg orally twice daily with or without food.

► Relapse or Stage IV: Subsequent Therapy for Patients with Clear Cell Carcinoma¹

Cabozantinib (Category 1; preferred) ²⁷⁻³⁰	Cabozantinib 60mg orally once daily on an empty stomach.
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Renal Cell Carcinoma Treatment Regimens

► Relapse or Stage IV: Subsequent Therapy for Patients with Clear Cell Carcinoma¹ (continued)

REGIMEN	DOSING
Nivolumab (Category 1; preferred) ^{22,33,34}	Day 1: Nivolumab 240mg IV over 30 minutes every 2 weeks OR Day 1: Nivolumab 480mg IV over 30 minutes every 4 weeks.
Axitinib (Category 1) ^{30-32,35,b}	Axitinib 5mg orally twice daily with or without food.
Lenvatinib + Everolimus (Category 1) ³⁶⁻³⁸	Lenvatinib 18mg orally once daily with or without food.
Nivolumab/Ipilimumab (Category 2A; preferred) ²¹⁻²⁴	Day 1: Nivolumab 3mg/kg IV over 30 minutes AND Day 1: Ipilimumab 1mg/kg IV over 30 minutes every 3 weeks for 4 cycles FOLLOWED BY Day 1: Nivolumab 240mg IV every 2 weeks OR Day 1: Nivolumab 480mg IV every 4 weeks.
Pembrolizumab + Axitinib ^{7,8}	Day 1: Pembrolizumab 200mg IV AND Days 1-21: Axitinib 5mg orally twice daily. ^a Repeat cycle every 3 weeks.
Everolimus ^{37,39,40}	Everolimus 10mg orally once daily with or without food.
Pazopanib ^{9,12}	Pazopanib 800mg orally once daily without food.
Sunitinib ^{2,41,42}	Sunitinib 50mg orally once daily with or without food for 4 weeks, followed by 2 weeks off.
Bevacizumab (Category 2B) ^{15,43}	Bevacizumab 10mg/kg IV every 2 weeks.
Sorafenib (Category 2B) ⁴⁴⁻⁴⁸	Sorafenib 400mg orally twice daily without food.
High-dose Aldesleukin (IL-2) (for patients with excellent performance status and normal organ function) (Category 2B) ^{23,24}	Days 1-5 and 15-19: IL-2 600,000 units/kg IV over 15 minutes every 8 hours (max 14 doses on days 1-5 and 14 doses on days 15-19 for a max 28 total doses per cycle). Repeat cycle every 12 weeks for a max of 3 cycles.
Temsirolimus (Category 2B) ^{18,49,50}	Temsirolimus 25mg IV over 30-60 minutes weekly.
Doxorubicin/Gemcitabine (for patients with disease characterized by predominant sarcomatoid features) (Category 2B) ^{51,52}	Day 1: Doxorubicin 50mg/m ² IV push FOLLOWED BY Day 1: Gemcitabine 1500-2000mg/m ² IV over 60 minutes every 2 or 3 weeks.
Gemcitabine/Sunitinib (for patients with disease characterized by predominant sarcomatoid features) (Category 2B) ⁵³	Days 1 and 8: Gemcitabine 1000mg/m ² IV over 30 minutes AND Days 1-14: Sunitinib 37.5mg orally once daily with or without food every 3 weeks.

► Relapse or Stage IV: Systemic Therapy for Patients with Non-Clear Cell Histology¹

Sunitinib (preferred) ^{2,42,54}	Sunitinib 50mg orally once daily with or without food for 4 weeks, followed by 2 weeks off.
Temsirolimus (Category 1: poor-prognosis patients; Category 2A: selected patients of other risk groups) ^{18-20,49,50}	Temsirolimus 25mg IV over 30-60 minutes weekly.
Cabozantinib ^{27,28}	Cabozantinib 60mg orally once daily on an empty stomach.
Everolimus ^{37,39,40}	Everolimus 10mg orally once daily with or without food.
Axitinib ^{30,31,b}	Axitinib 5mg orally twice daily with or without food.
Bevacizumab ^{15,43,54}	Bevacizumab 15mg/kg IV every 3 weeks.
Erlotinib ^{56,57}	Erlotinib 150mg orally once daily on an empty stomach.

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Renal Cell Carcinoma Treatment Regimens

► Relapse or Stage IV: Systemic Therapy for Patients with Non-Clear Cell Histology¹ (continued)

REGIMEN	DOSING
Lenvatinib + Everolimus ³⁶⁻³⁸	Lenvatinib 18mg orally once daily with or without food AND Everolimus 5mg orally once daily with or without food.
Nivolumab ^{22,33,34}	Day 1: Nivolumab 240mg IV over 30 minutes every 2 weeks OR Day 1: Nivolumab 480mg IV over 30 minutes over 4 weeks.
Pazopanib ^{9,12,58}	Pazopanib 800mg orally once daily without food.
Bevacizumab + Erlotinib (for selected patients with advanced papillary RCC including HLRCC ^{15,59,60,c})	Days 1 and 15: Bevacizumab 10mg/kg IV AND Days 1-28: Erlotinib 150mg orally once daily on empty stomach. Repeat cycle every 28 days.
Bevacizumab + Everolimus ^{15,37,61}	Days 1 and 15: Bevacizumab 10mg/kg IV AND Days 1-28: Everolimus 10mg orally once daily with or without food. Repeat cycle every 28 days.
Doxorubicin/Gemcitabine (for patients with disease characterized by predominant sarcomatoid features) (Category 2B) ^{51,52,d}	Day 1: Doxorubicin 50mg/m ² IV push FOLLOWED BY Day 1: Gemcitabine 1500-2000mg/m ² over 60 minutes every 2 or 3 weeks.
Gemcitabine/Sunitinib (for patients with disease characterized by predominant sarcomatoid features) (Category 2B) ⁵³	Days 1 and 8: Gemcitabine 1000mg/m ² IV over 30 minutes AND Days 1-14: Sunitinib 37.5mg orally once daily with or without food every 3 weeks.
Gemcitabine/Carboplatin (for patients with collecting duct or medullary subtypes only; Category 2A) ⁶²	Days 1 and 8: Gemcitabine 1250mg/m ² IV over 30 minutes AND Day 1: Carboplatin AUC5 IV over 30 minutes every 3 weeks for 6 cycles.
Paclitaxel/Carboplatin (for patients with collecting duct or medullary subtypes only; Category 2A) ⁶³	Day 1: Paclitaxel 175mg/m ² IV over 3 hours FOLLOWED BY Day 1: Carboplatin AUC5-6 IV over 30 minutes every 3 weeks for 6 cycles.
Gemcitabine/Cisplatin (for patients with collecting duct or medullary subtypes only; Category 2A) ⁶²	Days 1 and 8: Gemcitabine 1250mg/m ² over 30 minutes AND Day 1: Cisplatin 70mg/m ² IV over 60 minutes every 3 weeks for 6 cycles.

^a The dose of axitinib can be increased to 7mg, then 10mg, twice daily if safety criteria are met and reduced to 3mg, then 2mg, twice daily to manage toxic effects.

^b The dose of axitinib is typically started at 5mg twice daily and then titrated to a maximum of 10mg twice daily based on response or toxicity.

^c HLRCC: Hereditary leiomyomatosis and renal cell cancer.

^d Continue until disease progression or unacceptable toxicity including reaching a lifetime cumulative anthracycline dose.

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