

Kidney Cancer 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 only provided 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 National Comprehensive Cancer Network 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.

Note: All recommendations are category 2A unless otherwise indicated.

► Adjuvant Therapy for Patients With Grade 4 Tumors With Clear Cell Histology +/- Sarcomatoid Features¹

| REGIMEN | DOSING |
|------------------------------|--|
| Stage II Disease | |
| Pembrolizumab ²⁻⁵ | Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 17 cycles. OR Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year. |

► Adjuvant Therapy for Patients With Clear Cell Histology¹

| | |
|--|--|
| Stage III Disease | |
| Pembrolizumab ²⁻⁵ | Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 17 cycles. OR Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year. |
| Sunitinib (Category 3) ⁶⁻¹⁰ | Days 1-28: Sunitinib 50mg orally once daily. Repeat cycle every 6 weeks (4 weeks on followed by 2 weeks off treatment) for 1 year. |

► Relapse or Stage IV: First-line Therapy for Clear Cell Histology^{1,a}

| Favorable Risk | |
|--|--|
| Preferred Regimens | |
| Axitinib + Pembrolizumab (Category 1) ^{2,5,11,12,b} | Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years, concurrent with: Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks. OR Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for up to 2 years, concurrent with: Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks. |
| Cabozantinib + Nivolumab (Category 1) ^{3,15,c} | Days 1-28: Cabozantinib 40mg orally once daily. Day 1 and 15: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 4 weeks for up to 2 years, conditionally followed by: Days 1-28: Cabozantinib 40mg orally daily. Repeat cycle every 4 weeks. OR Days 1-28: Cabozantinib 40mg orally once daily. Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for up to 2 years, conditionally followed by: Days 1-28: Cabozantinib 40mg orally daily. Repeat cycle every 4 weeks. |

continued

Kidney Cancer Treatment Regimens

► Relapse or Stage IV: First-line Therapy for Clear Cell Histology^{1,a} (continued)

| REGIMEN | DOSING |
|--|--|
| Favorable Risk (continued) | |
| Preferred Regimens (continued) | |
| Lenvatinib + Pembrolizumab (Category 1) ^{2,16-18} | <p>Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years, concurrent with:</p> <p>Days 1-21: Lenvatinib 20mg orally once daily. Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for up to 2 years, concurrent with:</p> <p>Days 1-42: Lenvatinib 20mg orally once daily. Repeat cycle every 6 weeks.</p> |
| Other Recommended Regimens | |
| Axitinib + Avelumab ^{11,19,20,b} | <p>Days 1 and 15: Avelumab 800mg IV over 60 minutes.</p> <p>Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks.</p> |
| Cabozantinib (Category 2B) ^{13,21-23,c} | <p>Days 1-28: Cabozantinib 60mg orally once daily. Repeat cycle every 4 weeks.</p> |
| Nivolumab + Ipilimumab Followed by Nivolumab ^{15,24-27} | <p>Day 1: Nivolumab 3mg/kg IV over 30 minutes, followed by:</p> <p>Day 1: Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, followed by:</p> <p>Day 1: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks.</p> <p>OR</p> <p>Day 1: Nivolumab 3mg/kg IV over 30 minutes, followed by:</p> <p>Day 1: Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, followed by:</p> <p>Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.</p> |
| Pazopanib ²⁸⁻³² | <p>Days 1-28: Pazopanib 800mg orally once daily. Repeat cycle every 4 weeks.</p> |
| Sunitinib ⁶⁻¹⁰ | <p>Days 1-28: Sunitinib 50mg orally once daily. Repeat cycle every 6 weeks (4 weeks on followed by 2 weeks off treatment).</p> |
| Useful Under Certain Circumstances | |
| Axitinib (Category 2B) ^{11,33-35,b} | <p>Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks.</p> |
| High-dose Aldesleukin (Interleukin-2) (Category 2B) ^{36,37,d} | <p>Days 1-5 and 15-19: Aldesleukin (interleukin-2) 600,000units/kg IV over 15 minutes every 8 hours for a maximum of 14 doses (maximum of 28 total doses per cycle). Repeat cycle every 12 weeks for a maximum of 3 cycles.</p> |
| Poor/Intermediate Risk | |
| Preferred Regimens | |
| Axitinib + Pembrolizumab (Category 1) ^{2,5,11,12,b} | <p>Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years, concurrent with:</p> <p>Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks.</p> <p>OR</p> <p>Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for up to 2 years, concurrent with:</p> <p>Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks.</p> |
| Cabozantinib ^{13,21-23,c} | <p>Days 1-28: Cabozantinib 60mg orally once daily. Repeat cycle every 4 weeks.</p> |

continued

Kidney Cancer Treatment Regimens

► Relapse or Stage IV: First-line Therapy for Clear Cell Histology^{1,a} (continued)

| REGIMEN | DOSING |
|--|---|
| Poor/Intermediate Risk (continued) | |
| Preferred Regimens (continued) | |
| Cabozantinib + Nivolumab (Category 1) ^{3,15,c} | <p>Days 1-28: Cabozantinib 40mg orally once daily. Day 1 and 15: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 4 weeks for up to 2 years, conditionally followed by: Days 1-28: Cabozantinib 40mg orally daily. Repeat cycle every 4 weeks.</p> <p>OR</p> <p>Days 1-28: Cabozantinib 40mg orally once daily. Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for up to 2 years, conditionally followed by: Days 1-28: Cabozantinib 40mg orally daily. Repeat cycle every 4 weeks.</p> |
| Lenvatinib + Pembrolizumab (Category 1) ^{2,16,18} | <p>Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years, concurrent with: Days 1-21: Lenvatinib 20mg orally once daily. Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for up to 2 years, concurrent with: Days 1-42: Lenvatinib 20mg orally once daily. Repeat cycle every 6 weeks.</p> |
| Nivolumab + Ipilimumab Followed by Nivolumab (Category 1) ^{14,21,27} | <p>Day 1: Nivolumab 3mg/kg IV over 30 minutes, followed by: Day 1: Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, followed by: Day 1: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks.</p> <p>OR</p> <p>Day 1: Nivolumab 3mg/kg IV over 30 minutes, followed by: Day 1: Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, followed by: Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.</p> |
| Other Recommended Regimens | |
| Axitinib + Avelumab ^{11,19,20,b} | <p>Days 1 and 15: Avelumab 800mg IV over 60 minutes. Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks.</p> |
| Pazopanib ²⁸⁻³² | <p>Days 1-28: Pazopanib 800mg orally once daily. Repeat cycle every 4 weeks.</p> |
| Sunitinib ⁶⁻¹⁰ | <p>Days 1-28: Sunitinib 50mg orally once daily. Repeat cycle every 6 weeks (4 weeks on followed by 2 weeks off treatment).</p> |
| Useful Under Certain Circumstances | |
| Axitinib (Category 2B) ^{11,33-35,b} | <p>Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks.</p> |
| High-dose Aldesleukin (Interleukin-2) (Category 3) ^{36,37,d} | <p>Days 1-5 and 15-19: Aldesleukin (interleukin-2) 600,000units/kg IV over 15 minutes every 8 hours for a maximum of 14 doses (maximum of 28 total doses per cycle). Repeat cycle every 12 weeks for a maximum of 3 cycles.</p> |
| Temsirolimus (Category 3) ³⁸⁻⁴⁰ | <p>Day 1: Temsirolimus 25mg IV over 30-60 minutes. Repeat cycle weekly.</p> |

continued

Kidney Cancer Treatment Regimens

► Relapse or Stage IV: Subsequent Therapy for Clear Cell Histology¹

| Preferred Regimens | |
|--|--|
| Cabozantinib (Category 1) ^{13,21-23,c} | Days 1-28: Cabozantinib 60mg orally once daily. Repeat cycle every 4 weeks. |
| Lenvatinib + Everolimus (Category 1) ^{16,41,42} | Days 1-28: Everolimus 5mg orally once daily Days 1-28: Lenvatinib 18mg orally once daily. Repeat cycle every 4 weeks. |
| Nivolumab (Category 1) ^{15,43-45} | Day 1: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. OR Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks. |
| Other Recommended Regimens | |
| Axitinib (Category 1) ^{11,33-35,b} | Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks. |
| Axitinib + Avelumab (Category 3) ^{11,33-35,b} | Days 1 and 15: Avelumab 800mg IV over 60 minutes Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks. |
| Axitinib + Pembrolizumab ^{2,5,11,12,b} | Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years, concurrent with: Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks. OR Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for up to 2 years, concurrent with: Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks. |
| Cabozantinib + Nivolumab ^{13-15,c} | Days 1-28: Cabozantinib 40mg orally once daily. Day 1 and 15: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 4 weeks for up to 2 years, conditionally followed by: Days 1-28: Cabozantinib 40mg orally daily. Repeat cycle every 4 weeks. OR Days 1-28: Cabozantinib 40mg orally once daily. Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for up to 2 years, conditionally followed by: Days 1-28: Cabozantinib 40mg orally daily. Repeat cycle every 4 weeks. |
| Lenvatinib + Pembrolizumab ^{2,16-18} | Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years, concurrent with: Days 1-21: Lenvatinib 20mg orally once daily. Repeat cycle every 3 weeks. OR Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for up to 2 years, concurrent with: Days 1-42: Lenvatinib 20mg orally once daily. Repeat cycle every 6 weeks. |
| Nivolumab + Ipilimumab Followed by Nivolumab ^{14,24-27} | Day 1: Nivolumab 3mg/kg IV over 30 minutes, followed by: Day 1: Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, followed by: Day 1: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. OR Day 1: Nivolumab 3mg/kg IV over 30 minutes, followed by: Day 1: Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for 4 cycles, followed by: Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks. |

continued

Kidney Cancer Treatment Regimens

► Relapse or Stage IV: Subsequent Therapy for Clear Cell Histology¹ (continued)

| Other Recommended Regimens (continued) | |
|--|--|
| Pazopanib ²⁸⁻³² | Days 1-28: Pazopanib 800mg orally once daily. Repeat cycle every 4 weeks. |
| Sunitinib ⁶⁻¹⁰ | Days 1-28: Sunitinib 50mg orally once daily. Repeat cycle every 6 weeks (4 weeks on followed by 2 weeks off treatment). |
| Tivozanib ⁴⁶⁻⁴⁸ | Days 1-21: Tivozanib 1.34mg orally once daily. Repeat cycle every 4 weeks. |
| Useful Under Certain Circumstances | |
| Bevacizumab (Category 2B) ^{49-51.e} | Day 1: Bevacizumab 10mg/kg IV. Repeat cycle every 2 weeks. OR Day 1: Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks. |
| Everolimus ^{41,52-54} | Days 1-28: Everolimus 10mg orally once daily. Repeat cycle every 4 weeks. |
| High-dose Aldesleukin (Interleukin-2) (Category 2B) ^{36,37.d} | Days 1-5 and 15-19: Aldesleukin (interleukin-2) 600,000units/kg IV over 15 minutes every 8 hours for a maximum of 14 doses (maximum of 28 total doses per cycle). Repeat cycle every 12 weeks for a maximum of 3 cycles. |
| Sorafenib (Category 3) ⁵⁵⁻⁵⁷ | Days 1-28: Sorafenib 400mg orally twice daily. Repeat cycle every 4 weeks. |
| Temsirolimus (Category 2B) ³⁸⁻⁴⁰ | Day 1: Temsirolimus 25mg IV over 30-60 minutes. Repeat cycle weekly. |

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

| Preferred Regimens | |
|--|---|
| Cabozantinib ^{13,21-23.c} | Days 1-28: Cabozantinib 60mg orally once daily. Repeat cycle every 4 weeks. |
| Sunitinib ⁶⁻¹⁰ | Days 1-28: Sunitinib 50mg orally once daily. Repeat cycle every 6 weeks (4 weeks on followed by 2 weeks off treatment). |
| Other Recommended Regimens | |
| Lenvatinib + Everolimus ^{16,41,42} | Days 1-28: Everolimus 5mg orally once daily Days 1-28: Lenvatinib 18mg orally once daily. Repeat cycle every 4 weeks. |
| Nivolumab ^{124,43-45} | Day 1: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. OR Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks. |
| Pembrolizumab ²⁻⁵ | Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years. OR Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for up to 2 years. |
| Useful Under Certain Circumstances | |
| Axitinib ^{11,32-34.b} | Days 1-28: Axitinib 5-10mg orally twice daily. Repeat cycle every 4 weeks. |
| Bevacizumab ^{49-51.e} | Day 1: Bevacizumab 10mg/kg IV. Repeat cycle every 2 weeks. OR Day 1: Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks. |
| Doxorubicin/Gemcitabine (for renal medullary carcinoma) ^{58-60.f} | Day 1: Doxorubicin 50mg/m ² IV push. Day 1: Gemcitabine 1,500mg/m ² IV over 30 minutes. Repeat cycle every 2 weeks. |

continued

Kidney Cancer Treatment Regimens

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

| Useful Under Certain Circumstances (continued) | |
|---|---|
| Erlotinib ^{61,62} | Days 1-28: Erlotinib 150mg orally once daily. Repeat cycle every 4 weeks. |
| Erlotinib + Bevacizumab ^{49,61,63,64} | Days 1-28: Erlotinib 150mg orally once daily. Days 1 and 15: Bevacizumab 10mg/kg IV. Repeat cycle every 4 weeks. |
| Everolimus ^{41,52-54} | Days 1-28: Everolimus 10mg orally once daily. Repeat cycle every 4 weeks. |
| Everolimus + Bevacizumab (for selected patients with advanced papillary renal cell carcinoma) ^{41,49,65,e} | Days 1-28: Everolimus 10mg orally once daily Days 1 and 15: Bevacizumab 10mg/kg IV. Repeat cycle every 4 weeks. |
| Gemcitabine/Carboplatin (for patients with collecting duct or medullary subtypes) ^{59,66,67} | Days 1 and 8: Gemcitabine 1,250mg/m ² IV over 30 minutes. Day 1: Carboplatin AUC 5 IV over 30 minutes. Repeat cycle every 3 weeks for 6 cycles. |
| Gemcitabine/Cisplatin (for patients with collecting duct or medullary subtypes) ^{59,67,68,g} | Days 1 and 8: Gemcitabine 1,250mg/m ² over 30 minutes Day 1: Cisplatin 70mg/m ² IV over 60 minutes. Repeat cycle every 3 weeks for 6 cycles. |
| Paclitaxel/ Carboplatin (for patients with collecting duct or medullary subtypes) ⁶⁸⁻⁷⁰ | Day 1: Paclitaxel 175mg/m ² IV over 3 hours, followed by: Day 1: Carboplatin AUC 5-6 IV over 30 minutes. Repeat cycle every 3 weeks for 6 cycles. |
| Pazopanib ²⁸⁻³² | Days 1-28: Pazopanib 800mg orally once daily. Repeat cycle every 4 weeks. |
| Temsirolimus (Category 1 for poor-prognosis risk group; Category 2A for other risk groups) ³⁸⁻⁴⁰ | Day 1: Temsirolimus 25mg IV over 30-60 minutes. Repeat cycle weekly. |

► Kidney-Specific Systemic Therapy for Confirmed Hereditary Renal Cell Carcinoma¹

| Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC) | |
|--|--|
| Useful Under Certain Circumstances | |
| Erlotinib + Bevacizumab ^{49,61,63,64} | Days 1-28: Erlotinib 150mg orally once daily. Days 1 and 15: Bevacizumab 10mg/kg IV. Repeat cycle every 4 weeks. |
| Tuberous Sclerosis Complex (TSC) | |
| Useful Under Certain Circumstances | |
| Everolimus ^{41,52-54} | Days 1-28: Everolimus 10mg orally once daily. Repeat cycle every 4 weeks. |
| von Hippel-Lindau Disease (VHL) | |
| Preferred Regimen | |
| Belzutifan ^{71,72} | Days 1-28: Belzutifan 120mg orally once daily. Repeat cycle every 4 weeks. |
| Useful Under Certain Circumstances | |
| Pazopanib ²⁸⁻³² | Days 1-28: Pazopanib 800mg orally once daily. Repeat cycle every 4 weeks. |

^a Adjuvant pembrolizumab (200mg IV over 30 minutes, repeat cycle every 3 weeks for up to 2 years OR 400mg IV over 30 minutes, repeat cycle every 6 weeks for up to 2 years)2-5 after metastasectomy within 1 year of nephrectomy is an option for patients with disease characterized by clear cell histology.

^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 Cabozantinib (Cabometyx[®]) tablets and cabozantinib (Cometriq[®]) capsules are not interchangeable products. The dosage strengths of each product and dosing recommendations for specific indications differ.

^d For patients with excellent performance status and normal organ function.

^e An FDA-approved biosimilar is an appropriate substitute for bevacizumab.

^f Doxorubicin is an anthracycline. Cumulative anthracycline dosage should be monitored.

^g Hydration is required with supplemental electrolytes pre- and post-administration of Cisplatin.

continued

Kidney Cancer Treatment Regimens

References

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