Towards individualized therapy for metastatic renal cell carcinoma

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Corrected: Author Correction
Supplementary Table 1 | Selected ongoing studies in renal cell carcinoma. Combination strategies have shown increased response rates compared with single-agent sunitinib but might have also increased side effect profiles, highlighting that optimal pairing is key for clinical benefit and the reduction of adverse events.

<table>
<thead>
<tr>
<th>Investigated agents and study</th>
<th>Phase, disease setting and comparator</th>
<th>Primary end points</th>
<th>Efficacy and comments</th>
</tr>
</thead>
</table>
| Ipilimumab + nivolumab        | III Untreated disease Sunitinib       | ORR, OS and PFS in patients with intermediate or poor risk disease | Intermediate or poor-risk disease:  
- ORR (investigator assessed): 42% versus 29% \( (P = 0.0001) \)  
- mOS: NR versus 26.6 months (HR 0.66; \( P < 0.0001 \))  
- mPFS (investigator assessed): 8.2 months versus 8.3 months (HR 0.77; \( P = 0.001 \))  
Favourable-risk disease:  
- ORR (investigator assessed): 39% versus 50% \( (P = 0.14) \)  
- mOS: NR versus NR (HR 1.22; \( P = 0.44 \))  
- mPFS (investigator assessed): 13.9 months versus 19.9 months (HR 1.23; \( P = 0.189 \)) 2 of 3 primary end points were met |
| CheckMate214 (REF. \(^1\); NCT02231749) |                                      |                    |                      |
| Pembrolizumab + axitinib      | III Untreated disease Sunitinib       | PFS and OS evaluation by IRC in ITT population | 12-month OS: 89.9% versus 78.3% \( (HR 0.53; P < 0.0001) \)  
mPFS: 15.1 months versus 11.1 months (HR 0.69; \( P < 0.001 \))  
ORR: 59.3% versus 35.7% |
| KEYNOTE-426 (REF. \(^3\); NCT02853331) |                                      |                    |                      |
| Avelumab + axitinib           | III Untreated disease Sunitinib       | PFS and OS evaluated by IRC in PD-L1\(^+\) population | mPFS: 13.8 months versus 7.2 months (HR 0.61; \( P < 0.001 \))  
ORR in PD-L1\(^+\): 55.2% versus 25.5%  
OS not yet reported |
| JAVELIN Renal-101 (REF. \(^4\); NCT02684006) |                                      |                    |                      |
| Atezolizumab + bevacizumab    | III Untreated disease Sunitinib       | ORR, PFS and OS in PD-L1\(^+\) population | ORR in PD-L1\(^+\): 43% (35–50%) versus 35% (28–42%)  
PFS in PD-L1\(^+\): 11.2 months versus 7.7 months (HR 0.74; \( P = 0.0217 \))  
OS not yet reported |
<p>| IMmotion151 (REF. (^5); NCT02420821) |                                      |                    |                      |
| Lenvatinib + pembrolizumab    | III Untreated disease Lenvatinib plus | PFS evaluated by IRC in ITT population | Results not yet reported |
| CLEAR (REF. (^6); NCT03147288) |                                      |                    |                      |</p>
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Treatment</th>
<th>Phase</th>
<th>Disease Status</th>
<th>Safety/Timing</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT02811861</td>
<td>everolimus or sunitinib</td>
<td>III</td>
<td>Untreated disease Sunitinib</td>
<td>PFS evaluated by IRC</td>
<td>Results not yet reported</td>
</tr>
<tr>
<td>Cabozantinib + Nivolumab CheckMate-9ER (REF. 7; NCT03141177)</td>
<td>II</td>
<td>Untreated disease Atezolizumab or sunitinib</td>
<td>PFS in ITT population and in PD-L1* population</td>
<td>ITT population: - ORR: 32%, 25% and 29% with combination, atezolizumab and sunitinib, respectively - mPFS: 11.7 months, 6.1 months and 8.4 months with combination, atezolizumab and sunitinib, respectively PD-L1* population: - ORR: 46%, 28% and 27% with combination, atezolizumab and sunitinib, respectively - mPFS: 14.7 months, 5.5 months and 7.8 months with combination, atezolizumab and sunitinib, respectively</td>
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<tr>
<td>Lenvatinib + pembrolizumab Study 111 (REF. 9; NCT02501096)</td>
<td>Ib/II</td>
<td>Untreated or previously treated disease No comparator</td>
<td>Phase Ib: MTD Phase II: ORR at week 24</td>
<td>Median PFS: 13.8 months IRR ORR at 24 weeks: 66.4% mPFS 17.7 months (9.6 months–NR)</td>
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<tr>
<td>Axitinib + pembrolizumab KEYNOTE-06 (REF. 10; NCT02853331)</td>
<td>Ib</td>
<td>Untreated disease No comparator</td>
<td>DLT for MTD and/or RP2D of combination therapy</td>
<td>ORR: 73% (59–84.4%), CR: 8%, PR 65%</td>
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<tr>
<td>Cabozantinib + atezolizumab COSMIC-021 (REF. 11; NCT03170960)</td>
<td>Ib</td>
<td>Untreated disease No comparator</td>
<td>ORR in each cohort (4 expansion cohorts involving patients with genitourinary and thoracic malignancies) Safety and tolerability of combination regimen</td>
<td>ORR: 50% (12 patients reported) Cabozantinib dose escalation: 40 mg and 60 mg</td>
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<tr>
<td>Tivozanib + nivolumab AV-951-16-119 (NCT03136627)</td>
<td>Ib/II</td>
<td>Previously treated disease No comparator</td>
<td>MTD of combination regimen</td>
<td>Results pending</td>
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<tr>
<td>Pazopanib + pembrolizumab KEYNOTE-018 (REF. 12; NCT02014636)</td>
<td>I/II</td>
<td>Untreated disease No comparator</td>
<td>Phase I: DLT and MTD Phase II: PFS</td>
<td>ORR: 45% (9 of 20 patients) Cohorts split by pazopanib dose (run-in sequence)</td>
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<tr>
<td>Pazopanib or sunitinib +</td>
<td></td>
<td></td>
<td>Safety and tolerability of</td>
<td>Pazopanib or sunitinib:</td>
<td></td>
</tr>
</tbody>
</table>
| nivolumab CheckMate-016 (REF. 13; NCT01472081) | Untreated and previously treated disease No comparator | combination regimens | - ORR: 54.5%  
- mOS: NR  
Pazopanib plus nivolumab:  
- ORR: 45%  
- mOS: 27.9 months |
|---|---|---|---|
| Cabozantinib + ipilimumab + nivolumab CaboNivo and CaboNivoIpi (REF. 14; NCT02496208) | I Previously treated disease No comparator | RP2D and safety and tolerability of combination regimens | Total RCC cohort:  
- ORR: 54%  
- mPFS: 18.4 months  
Cabozantinib dose reduced 40 mg daily |

CR, complete response; DLT, dose-limiting toxicity; IRC, independent review committee; IRR, incidence rate ratio; ITT, intention-to-treat; mOS, median overall survival; mPFS, median progression-free survival; MTD, maximum tolerated dose; NR, not reached; PFS, progression-free survival; PR, partial response; ORR, objective response rate; OS, overall survival; PD-L1+, PD-L1 positive; RP2D, recommended phase II dose. *Experimental arm versus control arm.

**Supplementary references**


