<table>
<thead>
<tr>
<th>IMDC score</th>
<th>RMH score</th>
<th>MDACC score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>Poor prognostic factor</td>
<td>Factor</td>
</tr>
<tr>
<td>HGB</td>
<td>&lt; LLN</td>
<td>Albumin</td>
</tr>
<tr>
<td>Plts</td>
<td>&gt; ULN</td>
<td>LDH</td>
</tr>
<tr>
<td>ANC</td>
<td>&gt; ULN</td>
<td>Metastatic sites</td>
</tr>
<tr>
<td>KPS</td>
<td>&lt; 80%</td>
<td>-</td>
</tr>
<tr>
<td>Corrected calcium</td>
<td>&gt; ULN</td>
<td>-</td>
</tr>
<tr>
<td>Dx to systemic tx</td>
<td>&lt; 1 year</td>
<td>-</td>
</tr>
</tbody>
</table>

**IMDC risk group definitions**
- Favorable: 0 factors
- Intermediate: 1-2 factors
- Poor: ≥ 3 factors

**Supplemental Table 1:** Definitions of the IMDC, RMH, and MDACC prognostic scores

**Supplemental Table 1 Legend:** HGB = hemoglobin, LLN = lower limit of normal, g = grams, dL = deciliter, Plts = platelets, ULN = upper limit of normal, LDH = lactate dehydrogenase, ANC = absolute neutrophil count, ECOG = Eastern Cooperative Oncology Group, PS = performance status, KPS = Karnofsky performance status, Dx = diagnosis, tx = treatment
### Mechanism of action

- Anti-CSF1R + PD-1 checkpoint inhibitor
- Arginase inhibitor
- BET inhibitor
- CCR-4 inhibitor
- Coenzyme Q10 + gemcitabine
- CTLA-4 inhibitor + TLR9 agonist
- Exportin inhibitor + PD-1 checkpoint inhibitor
- EZH2 inhibitor + CTLA-4 checkpoint inhibitor
- Glutaminase inhibitor
- Glutaminase inhibitor + mTOR inhibitor
- Glutaminase inhibitor + multi-target angiogenesis TKI
- Glutaminase inhibitor + PARP inhibitor
- Glutaminase inhibitor + PD-1 checkpoint inhibitor
- ICOS monoclonal antibody
- IDO-1 inhibitor + JAK inhibitor
- MDM2 inhibitor
- mTOR inhibitor + carboplatin + paclitaxel
- Multi-target angiogenesis TKI
- Multi-target TKI + mTOR inhibitor
- Nanoparticle drug conjugate + VEGF targeted therapy
- PARP inhibitor
- PARP inhibitor + ATM inhibitor + cisplatin
- PD-1 checkpoint inhibitor
- PD-1 checkpoint inhibitor + CTLA-4 checkpoint inhibitor
- PD-1 checkpoint inhibitor + cyclophosphamide
- PD-1 checkpoint inhibitor + enterococcus
- PD-1 checkpoint inhibitor + LAG-3 checkpoint inhibitor
- PD-L1 checkpoint inhibitor + 4-1BB agonist + OX40 inhibitor
- Pegylated IL-10 + PD-1 checkpoint inhibitor
- PI3K inhibitor
- Proteasome inhibitor + VEGF targeted therapy
- Proteasome inhibitor + HDAC inhibitor
- STING pathway agonist

**Supplemental Table 2:** Mechanisms of action of agents in phase 1 trials enrolling patients in the present study

**Supplemental Table 2 Legend:** TKI = tyrosine kinase inhibitor
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Treatment(s)</th>
<th>OS</th>
<th>PFS</th>
<th>ORR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ko, et al</td>
<td>IMDC, second-line</td>
<td>VEGF or mTOR inhibitor</td>
<td>12.5 m</td>
<td>3.9 m</td>
<td>N/A</td>
</tr>
<tr>
<td>Wells, et al</td>
<td>IMDC, third-line</td>
<td>VEGF or mTOR inhibitor</td>
<td>12.4 m</td>
<td>3.9 m</td>
<td>10.4%</td>
</tr>
<tr>
<td>METEOR</td>
<td>mccRCC after ≥ 1 prior VEGF TT</td>
<td>Cabozantinib vs. everolimus</td>
<td>21.4 vs. 16.5 m</td>
<td>7.4 vs. 3.9 m</td>
<td>17% vs. 3%</td>
</tr>
<tr>
<td>CheckMate</td>
<td>mccRCC after 1-3 prior lines</td>
<td>Nivolumab vs. everolimus</td>
<td>25.0 vs. 19.6 m</td>
<td>4.6 vs. 4.4 m</td>
<td>25% vs. 5%</td>
</tr>
<tr>
<td>Hahn, et al</td>
<td>MDACC, median third-line*</td>
<td>Phase 1 clinical trial</td>
<td>31.2 m</td>
<td>5.9 m</td>
<td>22%</td>
</tr>
</tbody>
</table>

**Supplemental Table 3**: Clinical outcomes for second-line or later treatment of metastatic renal cell carcinoma from select population-based studies and clinical trials.  
**Supplemental Table 3 Legend**: OS = overall survival, PFS = progression-free survival, ORR = objective response rate, IMDC = International Metastatic RCC Database Consortium, VEGF = vascular endothelial growth factor, mTOR = mammalian target of Rapamycin, * = median third-line, but range from 0-9 prior lines of treatment.