A randomized phase II study with ilixadencel, a cell-based immune primer, plus sunitinib versus sunitinib alone in synchronous metastatic renal cell carcinoma

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Disclaimer

• Consulting or Advisory role
  Pfizer
  Bristol-Myers Squibb

• Honoraria
  Pfizer
  Bristol-Myers Squibb
  Ipsen
Ilixadencel: donor-derived inflammatory DCs

1. **Healthy donor leukapheresis**
   - GM-CSF
   - IL-4
   - TLR3 ligand
   - TLR7/8 ligand
   - IFN-γ

2. **Ilixadencel**
   - Allogeneic inflammatory DCs
   - Cryopreserved up to 4 years
   - Intratumoral administration in primary tumor or metastasis
   - Ultrasound or CT guided

3. **Recruitment and activation**
   - Chemokines: CCL3-5, CXCL9-10
   - Cytokines: IL-12, TNF-α, IL-1β
   - Patient NK cells
   - Patient bystander DCs
   - IFN-γ production
   - Cross-presentation of tumor antigens to CD8+ T cells

4. **Results**
   - Tumor cell killing
   - Cross-presentation of tumor antigens to CD8+ T cells
Phase II MERECA study: design and timelines

• Randomized exploratory phase II study
• Synchronous metastatic RCC in 1st line, stratified for IMDC (Heng) poor-intermediate risk
• 8 European countries and United States; FPI April 2015, LPLV June 2019

n=56

n=30

n=25

n=45

2:1 randomization

nephrectomy

control – no injections

< 8 weeks

6 weeks

Baseline imaging

sunitinib

survival follow-up

2 weeks

sunitinib

tumor response scans

Baseline imaging
Phase II MERECA study: endpoints

Primary:
• OS from randomization overall and by risk group
• 18-month survival

Secondary:
• Safety
• PFS from start of sunitinib
• Proportion of Objective Response Rate (ORR) from start of sunitinib treatment and duration of response in each subgroup
# Phase II MERECA study: patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Ilixadencel-sunitinib</th>
<th>Sunitinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age median (range)</td>
<td>62 (41-76)</td>
<td>64 (49-86)</td>
</tr>
<tr>
<td>Male sex no. (%)</td>
<td>45 (78%)</td>
<td>21 (70%)</td>
</tr>
<tr>
<td>IMDC intermediate risk no. (%)</td>
<td>41 (71%)</td>
<td>22 (73%)</td>
</tr>
<tr>
<td>IMDC poor risk no. (%)</td>
<td>17 (29%)</td>
<td>8 (27%)</td>
</tr>
<tr>
<td>Sarcomatoid features no. (%)</td>
<td>13 (22%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Sweden</td>
<td>19 (32.8%)</td>
<td>12 (40.0%)</td>
</tr>
<tr>
<td>Rest of Europe</td>
<td>38 (65.5%)</td>
<td>17 (56.6%)</td>
</tr>
<tr>
<td>USA</td>
<td>1 (1.7%)</td>
<td>1 (3.3%)</td>
</tr>
</tbody>
</table>
Overall Survival by Kaplan-Meier probability curve

- **18-months OS rate similar**
  - 63% for ilixadencel-sunitinib
  - 66% for sunitinib

- **Median OS not mature**

- **Progression-Free Survival**
  - 11.8 mo. ilixadencel-sunitinib
  - 11.1 mo. for sunitinib

- **Patients alive/censored**
  - 54% (n=30) ilixadencel-sunitinib
  - 37% (n=11) sunitinib

Censored patients in follow-up who were alive at last contact
Overall Survival by risk group

IMDC Intermediate risk

Median OS not mature

IMDC Poor risk

Median OS
- 10.6 mo. for ilixadencel-sunitinib
- 9.3 mo. for sunitinib
## Tumor response (according to RECIST 1.1 by independent blinded review)

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<tbody>
<tr>
<td><strong>ORR</strong> (Best Overall Response)</td>
<td>44% (n=20/45)</td>
<td>48% (n=12/25)</td>
</tr>
<tr>
<td>- Complete Response</td>
<td>11%* (n=5/45)</td>
<td>4.0% (n=1/25)</td>
</tr>
<tr>
<td>- Partial Response</td>
<td>33% (n=15/45)</td>
<td>44% (n=11/25)</td>
</tr>
<tr>
<td><strong>Confirmed ORR</strong></td>
<td>42% (n=19/45)</td>
<td>24% (n=6/25)</td>
</tr>
<tr>
<td>- Complete Response</td>
<td>6.7% (n=3/45)</td>
<td>0% (n=0/25)</td>
</tr>
<tr>
<td>- Partial Response</td>
<td>36% (n=16/45)</td>
<td>24% (n=6/25)</td>
</tr>
</tbody>
</table>

* Two patients had CR as best response at last available CT scan (at 10 mo. and 18 mo. respectively)

- Median duration of response was 7.1 mo (ilixadencel-sunitinib) vs 2.9 mo (sunitinib)
- Sarcomatoid features were not associated with ORR to ilixadencel-sunitib
Phase II MERECA study: safety and tolerability

- Safety profile of combination treatment similar to sunitinib alone
- Most common ilixadencel-related AE was pyrexia
- No signs of induced autoimmunity; 57% (n=32) of patients treated with ilixadencel developed de novo ilixadencel-specific alloantibodies
Phase II MERECA study: Conclusions

• Feasibility and safety of ilixadencel-sunitinib in synchronously metastatic RCC confirmed

• No difference in 18 mo. OS or in PFS

• OS data immature – follow-up ongoing

• Late separation of survival curves may indicate OS signal and warrants further follow-up

• Higher rate of confirmed PR and CR in ilixadencel-sunitinib arm vs. sunitinib alone

• All 5 CR in ilixadencel arm were alive after a minimal FU of 33 months
Acknowledgements

• The patients and their families
• Co-investigators and research nurses

Sponsor

Immunicum AB (publ)