PHARMACOECONOMIC ANALYSIS OF THE USE OF EVEROLIMUS COMPARED TO AXITINIB IN SECOND LINE THERAPY OF PATIENTS WITH METASTATIC RENAL CELL CARCINOMA

Kolbin A ¹, Frolov M ², Kurylev A ¹, Balykina Y ³, Proskurin M ³
Renal cell cancer (RCC) – kidney cancer from the renal parenchima cells

RCC is 90% of all kidney carcinomas

Clear cell hystotype is 80-85% of all RCCs

Metastatic RCC (mRCC) – the stage of the disease when the distant metastasis present

In the treatment of mRCC targeted antiangiogenic drugs play an essential role:

- VEGFR tyrosine kinase inhibitors (sorafenib, sunitinib, pazopanib, axitinib)
- VEGF monoclonal antibodies (bevacizumab)
- mTOR inhibitors (everolimus, temsirolimus).

Everolimus and axitinib are second line therapy drugs in case of progression after first line anti-VEGF/VEGFR therapy in accordance with the RCC management guidelines (NCCN, ESMO, RUSSCO)
The aim of the study was to conduct a health economic evaluation of using everolimus and axitinib in patients with metastatic renal cell carcinoma (mRCC).
For the calculation of the efficacy data of clinical trials (n = 4) were used:

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Study</th>
<th>(N of patients), old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anklesaria B., et al.</td>
<td>Open – control – prospective study</td>
<td>(n=352), 20-54</td>
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<tr>
<td></td>
<td>(1999)</td>
<td></td>
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<tr>
<td>Dennerstein L., et al.</td>
<td>A double blind crossover trial</td>
<td>(n=23), 18-45</td>
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<td></td>
<td>(1985)</td>
<td></td>
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<tr>
<td>Haspels A.A., et al.</td>
<td>A double-blind, placebo-controlled, multi-center study</td>
<td>(n=130), 18 -40</td>
</tr>
<tr>
<td>(1981)</td>
<td></td>
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</tbody>
</table>
METHODS

- CEA, BIA were performed
- The mathematical Markov model was built with the two arms for second line therapy: everolimus and axitinib
- The model was constructed as following each branch of the decision tree were analyzed cost and efficacy of a group of 100 patients and per patient
- Direct medical costs included: cost of drug, cost of ADR correction, palliative care costs, laboratory tests and diagnostics costs
- Efficiency was estimated on the basis of clinical trials (efficacy) – LY and PFSM
- The cost-effectiveness ratio (CER) and incremental cost-effectiveness ratio (ICERs) were calculated
- ICER/LY results were evaluated against cost-effectiveness threshold in Russia
- PSA was used in order to check the robustness of the model results to the uncertainty of input parameters
mRCC patient progressed after first line sunitinib therapy

**DECISION TREE**

- **M**
  - Everolimus (10 mg/day)
    - Survived or progression free
    - Not survived or progressed
  - Axitinib (14 mg/day)
    - Survived or progression free
    - Not survived or progressed
METHODS

- The study was done from the State Healthcare System perspective. CEA, BIA were performed.
- The mathematical Markov model was built with two arms for second-line therapy: everolimus and axitinib.
- The model was constructed as following each branch of the decision tree was analyzed in terms of costs and efficacy of a group of 100 patients and per pt.
- Direct medical costs included: cost of drug, cost of ADR correction, palliative care costs, laboratory tests and diagnostics costs.
- Efficiency was estimated on the basis of clinical trials (efficacy) – LY and PFSM.
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- ICER/LY results were evaluated against cost-effectiveness threshold in Russia.
- PSA was used in order to check the robustness of the model results to the uncertainty of input parameters.
Patients with mRCC progressed after first-line sunitinib therapy and treating with everolimus or axitinib as the second line

- No progression

- Palliative care
Direct costs structure

<table>
<thead>
<tr>
<th></th>
<th>Everolimus</th>
<th>Axitinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palliative care</td>
<td>640 850</td>
<td>382 223</td>
</tr>
<tr>
<td>ADRs</td>
<td>148 172</td>
<td>132 494</td>
</tr>
<tr>
<td>2nd line therapy</td>
<td>897 441</td>
<td>1 768 521</td>
</tr>
</tbody>
</table>
Direct costs structure

### Costs shares

<table>
<thead>
<tr>
<th></th>
<th>Everolimus</th>
<th>Axitinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palliative care</td>
<td>38%</td>
<td>17%</td>
</tr>
<tr>
<td>ADRs</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>2nd line therapy</td>
<td>53%</td>
<td>77%</td>
</tr>
</tbody>
</table>
CEA results

OS (life-years)

TOTAL costs, RUR

CER – circle diameter

Everolimus

Axitinib
CEA results

PFS (months)

TOTAL costs, RUR

CER – circle diameter

- Everolimus
- Axitinib

- 5,20
- 5,15
- 5,10
- 5,05
- 5,00
- 4,95
- 4,90
- 4,85
- 4,80
- 4,75
- 4,70

- 1 600 000
- 1 800 000
- 2 000 000
- 2 200 000
- 2 400 000

- 4,70
- 4,75
- 4,80
- 4,85
- 4,90
- 4,95
- 5,00
- 5,05
- 5,10
- 5,15
- 5,20
BIA results

- Total number of RCC patients in Russia is 19 102.
- The number of patients with mRCC (metastatic renal cell carcinoma) is 3 285.

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Total number of patients</th>
<th>Cost per patient</th>
<th>Total cost per patient population</th>
<th>Cost difference, RUR</th>
<th>No. of additional patients treated with everolimus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everolimus</td>
<td>3 285</td>
<td>1 686 463</td>
<td>5 540 032 345</td>
<td>1 960 401 550</td>
<td>1 162</td>
</tr>
<tr>
<td>Axitinib</td>
<td>2 283 237</td>
<td>7 500 433 890</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Conclusion

Everolimus therapy in patients with mRCC progressed after first-line sunitinib is associated with longer OS (Overall survival life-years).

Total costs for Everolimus are lower comparing to axitinib.

Everolimus dominates axitinib.

The positive budget impact is seen for everolimus therapy.
List of References


