COST-EFFECTIVENESS OF NIVOLUMAB FOR THE TREATMENT OF ADVANCED NON-SQUAMOUS NON-SMALL CELL LUNG CANCER (NSCLC) IN SAUDI ARABIA

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Introduction
- Lung cancers cause of significant morbidity and mortality worldwide.1
- Five-year survival of NSCLC is extremely poor for patients diagnosed with metastatic disease.2
- Nivolumab was approved as second line treatment in 2014 based on improved overall survival benefit against standard care chemotherapy.3

Objective
- Evaluate the cost-effectiveness of nivolumab for locally advanced or metastatic non-squamous NSCLC after prior chemotherapy from a Saudi Arabia healthcare payer perspective.

Methods
- Local model adaptation of a validated three health-states partitioned survival analysis model. Structure is described on Figure 1.
- Estimated QALYs and survival outcomes are described in Table 1.
- It is assumed all AEs are applied as a one-off cost in the first cycle of the analysis.
- Non-treatment specific utility values for PF and PD were used. Due to lack of local data, US specific utility weights and AEs disutility values from previous NICE submissions were applied.
- Progression free survival (PFS) was estimated using patient level data from Checkmate 057 trial by measuring PFS events as defined by RECIST 1.1 criteria.
- Proportion of patients occupying the progressive disease (PD) state was calculated as the proportion alive minus the proportion alive on progression free (PF) health state.
- Selection of parametric model for overall survival (OS) and PFS for nivolumab and docetaxel was based on the best fitting survival models by AIC and BIC statistics and clinical plausibility of the extrapolated survival.
- Inputs for the comparison to pemetrexed, erlotinib, gefitinib, and ramucirumab plus docetaxel were derived from indirect treatment comparisons.4
- A Saudi Arabian payer perspective was adopted, running the analysis with a 20 years time horizon, discount rate of 5.0% for costs and 3.5% for benefits.
- Mean body weight of 67 kg and a mean height of 165 cm were used.
- Disease management costs, drug administration, drug monitoring and adverse events (AE) management costs were estimated by conducting a Delphi exercise with 8 local medical oncologists to identify and estimate healthcare resource utilization. Local hospital tariffs were then applied to estimate the aggregated costs.
- All costs are expressed in 2016 Saudi Riyals (SAR)

Main assumptions validated with local experts for the base case
- Base case assumes a 2 year cap scenario on nivolumab’s duration of treatment based on clinical plausibility. It is assumed that this scenario doesn’t affect PFS or OS.
- It is assumed PFS and PD costs are applied as a constant cost.
- Non-treatment specific utility values for PF and PD were used. Due to lack of local data, US specific utility weights and AEs disutility values from previous NICE submissions were applied.
- It is assumed all AEs are applied as a one-off cost in the first cycle of the model with only grade 3-4 AEs included on the analysis.

Results
- Estimated QALYs and survival outcomes are described in Table 1.

Table 1. QALYs and survival outcomes

<table>
<thead>
<tr>
<th>Total QALYs</th>
<th>Total QALYs</th>
<th>Total LYs</th>
<th>Patients alive at 1 year (%)</th>
<th>Patients alive at 2 years (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab</td>
<td>1.57</td>
<td>2.25</td>
<td>48</td>
<td>29</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>0.76</td>
<td>1.04</td>
<td>41</td>
<td>13</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>0.73</td>
<td>0.95</td>
<td>37</td>
<td>10</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>0.84</td>
<td>1.11</td>
<td>44</td>
<td>15</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>0.63</td>
<td>0.82</td>
<td>30</td>
<td>6</td>
</tr>
<tr>
<td>Ramucirumab*</td>
<td>0.93</td>
<td>1.22</td>
<td>47</td>
<td>18</td>
</tr>
</tbody>
</table>

* Ramucirumab plus docetaxel

- Estimated costs and cost breakdown are described in Table 2.
- Treatment acquisition costs for nivolumab, pemetrexed and ramucirumab plus docetaxel represent 58%, 44% and 67% of total costs respectively.
- Disease management costs for docetaxel, erlotinib and gefitinib account for 45%, 47% and 58% of total costs respectively.

Table 2. Total costs and costs breakdown

<table>
<thead>
<tr>
<th>Total costs</th>
<th>Cost breakdown (SAR)</th>
<th>Disease</th>
<th>Trt acq</th>
<th>Trt admin</th>
<th>Trt mon</th>
<th>Subs. trt</th>
<th>AEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab</td>
<td>442,464</td>
<td>114,215</td>
<td>257,717</td>
<td>42,179</td>
<td>11,119</td>
<td>16,587</td>
<td>646</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>175,556</td>
<td>78,088</td>
<td>30,201</td>
<td>24,827</td>
<td>9,575</td>
<td>21,755</td>
<td>9,109</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>159,511</td>
<td>74,533</td>
<td>35,380</td>
<td>0</td>
<td>7,426</td>
<td>21,777</td>
<td>4,466</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>222,519</td>
<td>81,612</td>
<td>97,386</td>
<td>10,911</td>
<td>9,482</td>
<td>21,759</td>
<td>1,350</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>119,129</td>
<td>68,517</td>
<td>9,867</td>
<td>0</td>
<td>7,426</td>
<td>32,822</td>
<td>498</td>
</tr>
<tr>
<td>Ramucirumab*</td>
<td>492,174</td>
<td>82,537</td>
<td>331,466</td>
<td>43,023</td>
<td>12,564</td>
<td>21,636</td>
<td>947</td>
</tr>
</tbody>
</table>

* Ramucirumab plus docetaxel

- The incremental analysis of nivolumab against the selected comparators is described in Table 3. Nivolumab increases the QALYs and cost against all comparators in the range of 0.94 – 0.73 and 1.43 – 1.03 respectively.
- ICER on the deterministic analysis ranges from dominance over ramucirumab plus docetaxel to 344,492 SAR/QALY against gefitinib. ICER against docetaxel is estimated at 331,136 SAR/QALY.

Table 3. Incremental analysis of nivolumab against selected comparators

<table>
<thead>
<tr>
<th>Nivolumab vs.</th>
<th>Inc. costs (SAR)</th>
<th>Inc. LY</th>
<th>Inc. QALYs</th>
<th>Incremental cost per LYG (SAR)</th>
<th>Incremental cost per QALY (SAR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel</td>
<td>268,908</td>
<td>1.21</td>
<td>0.81</td>
<td>232,49</td>
<td>331,386</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>282,953</td>
<td>1.30</td>
<td>0.84</td>
<td>217,113</td>
<td>359,511</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>219,945</td>
<td>1.14</td>
<td>0.73</td>
<td>193,759</td>
<td>302,457</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>323,335</td>
<td>1.43</td>
<td>0.94</td>
<td>225,674</td>
<td>344,492</td>
</tr>
<tr>
<td>Ramucirumab*</td>
<td>492,709</td>
<td>1.03</td>
<td>0.64</td>
<td>48,148</td>
<td>77,429</td>
</tr>
</tbody>
</table>

* Ramucirumab plus docetaxel

- Deterministic and probabilistic sensitivity analysis for 5,000 iterations were performed. Uncertainty of the ICER appears to be driven by variation in treatment efficacy, resource utilization, body weight and utility weights.
- Cost-effectiveness acceptability curve is shown on Figure 2.

Figure 2. Cost-effectiveness acceptability curve

Conclusions
- Assuming a Saudi Arabia willingness-to-pay of SAR400,000 / QALY gained, nivolumab would be considered cost-effective against all of the comparators in the analysis.
- Given the improvement in clinical efficacy and a favorable ICER, nivolumab is a cost-effective second line treatment option for advance NSCLC from Saudi Arabia healthcare payer perspective.
- These results can assist third-party payers to allocate resources in a more cost-effective manner.

References
4. BMS data on file. 2015.

Acknowledgment
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