Costs and effectiveness of combination therapy with Bedaquiline and other anti-tuberculosis drugs in patients with multi- and extensively drug-resistant tuberculosis in Germany

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Background

Whereas normal, drug sensitive pulmonary tuberculosis can be treated and cured relatively simply by using two to four effective antibiotics over a period of 6 months, resistant strains of Mycobacterium tuberculosis are substantially more difficult to treat. Strains showing resistance to at least isoniazid and rifampicin, the two cornerstones of tuberculosis treatment, are defined as multi-drug resistant (MDR) by the WHO & FDA. [1]

Pulmonary, multidrug-resistant tuberculosis (MDR-TB) is designated an orphan disease in the EU, with approximately 60,000 newly incident patients per year in Germany. Depending on the individual patient’s resistance situation, regimens consisting of as many as 5 or more drugs with a treatment duration of up to 24 months are the current standard of care (SoC) for treatment of MDR-TB in Germany. [2]

Bedaquiline (BDQ), as one of the most recently approved new treatment options, is licensed for use as part of an appropriate combination regimen for pulmonary, multidrug resistant tuberculosis (MDR-TB) in adult patients when an effective treatment regimen of at least three antibiotics cannot otherwise be composed for reasons of resistance or tolerability.

The aim of this analysis is to evaluate the costs and effectiveness of adding BDQ for 24 weeks to a background regimen (BR) of the SoC in a German healthcare context.

Methods

• A cohort based Markov model was used to estimate the cost-effectiveness of bedaquiline plus background regimen (BDQ+BR) vs. BR alone for treatment of MDR- and XDR-TB (extensively drug resistant tuberculosis). The model structure is shown in figure 1.
• The model was adjusted for the German health care context and payer perspective.

Figure 1: Cyclic Markov model for MDR-TB; 1 month cycle length, adopted from [3]

- The effectiveness of treatment was evaluated in quality adjusted life years (QALY) and life years gained (LYG).
- Inputs into the model for clinical outcomes and dosages were derived from a randomised, placebo controlled Phase IIb trial of bedaquiline (TMC207-C208 Stage II) [4]. Rates for sputum culture converted (SCC) after 24 weeks were 79% for bedaquiline/BR and 58% for placebo/BR.
- Other model parameters - excluding utilities - were adopted from German data, or if not available from international literature after an extensive literature search and clinical opinions.
- Drug costs in 2014 Euros were taken from the German drug directory [6] always on the smallest price level unless specified otherwise.

Results

Base-case analysis shows that combination therapy (BDQ+BR) compared with BR alone for a cohort of 65 patients with MDR-TB and a 10 year time horizon results in
- slightly higher costs (incremental cost: 228.653 €)
- and better outcomes
  • 296.63 vs. 228.75 total QALYs
  • 367.81 vs. 299.71 total LYGs
  68,11 incremental LYGs

A discount rate of 3% was used according to DQWIG recommendations for the base case analysis.

• ICER: 3.369 €/QALY
• ICER: 3.357 €/LYG

Results were robust in multiple sensitivity analyses. Costs of bedaquiline, percentage of patients treated in hospital or community and disease relapse during treatment follow-up seem to have a major impact on costs per QALY [3] (Figure 3).

Base-case analysis for a cohort consisting of 10 patients with extensively drug resistant tuberculosis (XDR-TB) shows that combination therapy (BDQ+BR) compared with BR alone during a 10 year time horizon results in higher costs (incremental 311.167 €) and better outcomes (8,5 incremental QALYs and 8,9 incremental LYG).

• ICER: 19.218 €/QALY
• ICER: 18.367 €/LYG

Discussion

The results of our modelling approach imply that for Germany, adding bedaquiline to a background regimen (BR) proves as dominant treatment approach, being cost effective in most scenarios. There is a high probability of being cost-effective at two different threshold values.

In a patient cohort with only XDR-TB patients, results of our model show that BDQ+BR is still cost-effective, but to a lower extent than in the MDR-TB cohort. Most likely, this is due to the much smaller increment gained regarding treatment outcomes.

References

[4] Diel R. et al. (2011), Controlled Phase IIb trial of bedaquiline (TMC207-C208 Stage II) [4]. Rates for sputum culture converted (SCC) after 24 weeks were 79% for bedaquiline/BR and 58% for placebo/BR.
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In figure 4, the CE acceptability curve shows results of a probabilistic sensitivity analysis with a probability of an ICER below 31.000 €/QALY of 86%.

Adapting the British QALY threshold from the National Institute for Health and Clinical Excellence (NICE) of 20,000 £/QALY (25.300 €) [7], the probability of bedaquiline/BR being cost-effective is 82%. For a threshold of 50,000 £/QALY (63.400 €) [7], there is a 95 % probability of being cost-effective.

Figure 2: Incremental QALY
Figure 3: Cyclic Markov model for MDR-TB; 1 month cycle length, adopted from [3]
Figure 4: CE acceptability curve for BDQ/BR

Table 1: Model inputs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Weekly dose</th>
<th>Tablets/week</th>
<th>P of weeks</th>
<th>Cost per week [€]</th>
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<tbody>
<tr>
<td>Bedaquiline resistant patient</td>
<td>7x400 mg</td>
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<td>2</td>
<td>6931.6</td>
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<td>Bedaquiline/BR resistant patient</td>
<td>3x200 mg</td>
<td>6</td>
<td>22</td>
<td>1055.1</td>
</tr>
</tbody>
</table>

Figure 4: CE acceptability curve for BDQ/BR

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