The Cost-Effectiveness and Value of Information Associated with Biologic Drugs for the Treatment of Psoriatic Arthritis

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BACKGROUND
Recent clinical trials indicate that new biologic drugs combine efficacy with low toxicity for the treatment of PsA patients. Anti-TNFα drugs – etanercept (Enbrel®), infliximab (Remicade®) and adalimumab are all parameterized and distinct from R.A.

However, their acquisition costs are substantially higher than standard therapy with DMARDs and evidence on the maintenance of benefits in the long term is very limited. A synthesis of all available evidence was required.

AIM
To estimate the cost-effectiveness of new biologics for the treatment of active PsA in patients with inadequate response to DMARDs, characterize decision uncertainty and identify research priorities which can inform decisions towards their future use.

METHODS
A probabilistic decision analytic model was constructed to compare the 3 main alternatives (etanercept, infliximab, palliative care) in the context of their licensed indications. The model is a cohort model which takes the form of a recursive decision tree (Fig.1).

Fig.1: Simplified model structure

Evidence synthesis
We combine both initial 3 months response to treatment (PsARC criteria) and disease activity (HAQ) as efficacy outcomes.

• Progressive disability – modelled as underlying HAQ natural progression (A).
• Quality of life and costs as a function of disability (HAQ scores).

The limited trial evidence was combined using Bayesian methods of multiple parameter synthesis1, which enable the indirect comparison of all 3 treatment options and the combination of the main outcome measures, whilst maintaining their correlation structure.

Table 1: Treatment comparisons forming the chain of evidence

<table>
<thead>
<tr>
<th>Trials</th>
<th>Treatment option</th>
<th>Etanercept</th>
<th>Placebo</th>
<th>Infliximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mease et al. 1999</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Mease et al. 2004</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

The evidence synthesis consists of two random baseline, fixed treatment effects meta-analyses that estimated:

• Treatment response rates.
• Mean HAQ change from baseline conditional on PsARC response.

Mean HAQ change is adjusted by placebo effect (Fig.2). We also add the HAQ increment for treatment non-responders.

Fig.2: Placebo effect adjustment

Treatment: 1 - N = P_c X N + δ_{rebound} - P_i X e^{δ_{rebound}}

Annual withdrawal rates were modelled based on observational evidence. Given the lack of evidence on the rebound effect after treatment failure we present 3 alternative scenarios (Fig.3).

Fig.3: Alternative rebound scenarios

The ICER for Etanercept is £26K per QALY gained for the base-case scenario (S1), which increases to £30K if rebound after treatment failure is equal to natural progression (S2). Infliximab shows a very high ICER that ranges between £165K to £440K. Alternative treatment assumptions have an impact on expected cost-effectiveness.

Expected Value of Perfect Information (EVPPI)

\[ EVPI = E_p \times \text{NB}(j) - \text{max}(E_p \times \text{NB}(j)) \]

Expected NB with perfect information

Population EVPPI places an upper bound on the value of further research for the population of current and future UK PsA patients.

Population \[ EVPI = EVPI_j = \sum j = 0 \]

The value of information reaches a maximum when the threshold is equal to the expected ICER of the technology (Fig.5).

Fig.4: CEAC - Base case

The Cost effectiveness results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean costs</th>
<th>Mean QALYs</th>
<th>ICER</th>
<th>Probability cost-effective at:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S1) Rebound effective</td>
<td>£154,111</td>
<td>4.024</td>
<td>£440,982</td>
<td>a 0 0 0</td>
</tr>
<tr>
<td>(S2) Rebound to natural progression</td>
<td>£64,633</td>
<td>0.5</td>
<td>£64,633</td>
<td>a 0 0 0</td>
</tr>
<tr>
<td>(S3) Rebound palliative care</td>
<td>£3,541,163</td>
<td>0.6</td>
<td>£3,541,163</td>
<td>a 0 0 0</td>
</tr>
</tbody>
</table>

Table 2: Cost effectiveness results

The Cost of further research should not exceed the population EVPI to make it potentially worthwhile. Population EVPPI for parameters can help prioritise research focusing on those parameters where the value of information and so the return of research to society is higher.

Fig.6: Population EVPPI - Base case

CONCLUSIONS
Bayesian methods of evidence synthesis can enable the comparison of technologies that have not been directly compared in clinical trial evidence. Policy decisions should benefit from an analytic framework which can structure the decision problem so that all evidence can be combined, all uncertainty surrounding the decision incorporated and evidence of parameters can be updated as evidence accumulates. This project is an example of how Bayesian evidence synthesis and value of information analysis can conform such analytic framework, producing results that are a powerful aid for decision-making, consistent with both the objectives and budget constraints of health care provision.

References:

Table 3: Population EVPPI for all scenarios

<table>
<thead>
<tr>
<th>Value of information for threshold at:</th>
<th>£0</th>
<th>£5,000,000</th>
<th>£10,000,000</th>
<th>£15,000,000</th>
<th>£20,000,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>£3,541,163</td>
<td>£3,541,163</td>
<td>£3,541,163</td>
<td>£3,541,163</td>
<td></td>
</tr>
<tr>
<td>S2</td>
<td>£440,982</td>
<td>£440,982</td>
<td>£440,982</td>
<td>£440,982</td>
<td></td>
</tr>
<tr>
<td>S3</td>
<td>£12,584</td>
<td>£12,584</td>
<td>£12,584</td>
<td>£12,584</td>
<td></td>
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</table>

Table 4: Population EVPPI - Base case

<table>
<thead>
<tr>
<th>Parameters</th>
<th>£ (milk)</th>
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</thead>
<tbody>
<tr>
<td>Short-term effectiveness</td>
<td>£3,336,125</td>
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<tr>
<td>Mortality rate</td>
<td>0.997</td>
</tr>
<tr>
<td>Costs (mTAR)</td>
<td>£4,202,464</td>
</tr>
<tr>
<td>Utilities (HS)</td>
<td>£11,923,298</td>
</tr>
</tbody>
</table>

Note: Threshold equal to ICER etanercept (S6): £500,100,000

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