Health Economic Analysis of Rabbit Antithymocyte Globulin versus Basiliximab in Renal Transplantation – A German perspective

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Disclosures

Friedrich Thaiss

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• Advisory board member:
  - Novartis, Sanofi
Introduction

• Induction therapy is widely used after kidney transplantation to prevent organ rejection.

• While several options for induction therapy are available, limited health economic comparisons between treatments exist.

• The objective of this study was to conduct a health economic comparison between two agents approved for induction therapy in kidney transplantation: rabbit ATG (rATG, Thymoglobulin®) and basiliximab (Simulect®).

• This study combined clinical outcomes data from an available dataset¹ with resource utilization and cost estimates from several German hospitals to calculate a health-economic perspective for the German setting.

Brennan et al: A prospective, randomised, international trial

Patients at high risk for acute rejection or DGF

Deceased-donor kidney Tx

rATG: Total 7.5 mg/kg (intraoperative to Day 4)

Basiliximab 20 mg x 2 (Days 0 & 4)

CsA MMF Steroids

<table>
<thead>
<tr>
<th></th>
<th>rATG</th>
<th>Basiliximab</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DGF</strong></td>
<td>40.4%</td>
<td>44.5%</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Acute rejection</strong></td>
<td>15.6%</td>
<td>25.5%</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Antibody-treated acute rejection</strong></td>
<td>1.4%</td>
<td>8.0%</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>Graft loss</strong></td>
<td>9.2%</td>
<td>10.2%</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>4.3%</td>
<td>4.4%</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>85.8%</td>
<td>75.2%</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>CMV infection</strong></td>
<td>7.8%</td>
<td>17.5%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Methods

• Clinical events and outcomes occurring within 12 months of transplant were estimated using the original SAS Brennan database.

• Resource utilization and costs were supplemented with data from three German hospitals.

• Total treatment costs were estimated by multiplying resource utilization observations \( \times \) mean hospital-reported charges.

• Key inputs to the model included:
  - Drug costs, costs associated with avoidance of acute rejection, graft failure, use of dialysis, utility estimates, survival rates.

• Statistical approaches applied:
  - Demographic characteristics: Chi Square & Student’s t tests.
  - DGF, graft failure & death: Chi Square test.
  - Rejections & infections per patient: Wilcoxon rank sum test.
Methods

• A 4-state Markov model was used, with the following 3 cohorts:
  - Transplant patients receiving rATG
  - Transplant patients receiving basiliximab
  - Non-transplanted ESRD patients on dialysis

• In the model, patients are predicted to transition between 4 health states:
  - Never transplanted (0.68 utility)
  - Alive with functioning graft (0.84 utility)
  - Alive following graft failure (0.68 utility)
  - Deceased (0.0 utility)

• Estimates based on US Renal Data System data were used to model health state transitions

• Utility scores for calculating cost per quality-adjusted life year (cost/QALY) were obtained from the literature\(^1\)

• Costs and QALYs over the 10-year time horizon were estimated using the Markov model

\(^1\)Matas A. American Journal of Transplantation 2003; 4: 216–221
Model Schema with transition probabilities

Year 0
- Function
- Dialysis
- Deceased

Year 1
- Function
- Dialysis
- Deceased

Year 2
- Function
- Dialysis
- Deceased

Transition probabilities:
- Year 0 to Year 1: 0.9685 (Function to Function), 0.0205 (Function to Dialysis), 0.0110 (Function to Deceased)
- Year 1 to Year 2: 0.9685 (Function to Function), 0.8770 (Dialysis to Dialysis), 0.1230 (Dialysis to Deceased), 0.0110 (Deceased to Deceased)
Results: Costs within year 1 post-transplant

Total mean cost in year 1
- rATG = €48,412
- Basiliximab = €45,977

P<0.01

Wilcoxon Rank Sum test
Results: Patient health status to year 10

- Mortality is higher on dialysis than after transplant
- 10-year graft survival predicted to be ~2% higher with rATG versus basiliximab induction
Results: Cumulative incremental costs per patient @ 10 year time horizon

Cumulative treatment costs per patient:

- From the end of year 2, costs are projected to be lower in the rATG cohort, reaching €4,132 per patient savings by year 10.
- Cost savings over time for rATG vs basiliximab are driven by fewer patients returning to dialysis treatment (following graft rejection).
Results: Cumulative QALYs per patient @ 10-year time horizon

Difference in cumulative QALYs per patient rATG vs basiliximab

- rATG-treated patients are projected to enjoy a modest gain in total QALY benefit vs basiliximab, reaching 0.096 by year 10 per patient, for every 100 patients
  - 0.096 QALY benefits equates to more than a month in perfect health

- Compared with no treatment or dialysis, patients receiving either rATG or basiliximab accrue a substantial gain in quality-adjusted life years, equating to approximately 1.5 years in perfect health

<table>
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<tr>
<th></th>
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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<th>7</th>
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<tbody>
<tr>
<td>No Tx*</td>
<td>0.661</td>
<td>1.254</td>
<td>1.786</td>
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<tr>
<td>rATG</td>
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<td>2.245</td>
<td>2.882</td>
<td>3.471</td>
<td>4.014</td>
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<td>4.978</td>
<td>5.405</td>
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<td>Bas</td>
<td>0.802</td>
<td>1.542</td>
<td>2.224</td>
<td>2.852</td>
<td>3.431</td>
<td>3.965</td>
<td>4.457</td>
<td>4.910</td>
<td>5.327</td>
<td>5.711</td>
<td><strong>6.065</strong></td>
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</table>

*No transplant / dialysis
Results: Costs(€)/QALY, 10 year time horizon

Costs/QALYs per patient over 10 years

- Both rATG and basiliximab interventions are dominant to no transplant/dialysis, meaning they provide both greater clinical benefit (QALY gain) at a lower cost.

- Beginning end of year 2, rATG is dominant to basiliximab, by accruing greater clinical benefit (QALY gain) at lower cost.

- Dominance is the strongest interpretation of cost-effectiveness analysis, where greater clinical benefit is provided at lower cost.

<table>
<thead>
<tr>
<th>Year</th>
<th>No Tx*</th>
<th>rATG</th>
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<td>59,842</td>
<td>57,328</td>
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<td>21,380</td>
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<td>8</td>
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<td>19,871</td>
<td>20,865</td>
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<tr>
<td>9</td>
<td>91,284</td>
<td>19,470</td>
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<td>10</td>
<td>91,284</td>
<td>19,154</td>
<td>20,140</td>
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</table>

*No transplant/dialysis
Summary

• The purchase cost of rATG induction is €4,055 higher than basiliximab
  - Reduced costs associated with DGF, rejection, graft failure and return to dialysis substantially reduced this difference by year 1

• After 10 additional years, rATG is associated with an additional 0.096 QALYs vs basiliximab, and a €4,132 reduction in cost per patient for every 100 patients treated

• According to this model, the cost per QALY gained is €91,284, €25,142 and €26,268 for ESRD with no dialysis, transplant with rATG and transplant with basiliximab, respectively
Conclusion

- rATG provides more QALYs with lower long-term costs than basiliximab
  - The QALY advantage is evident within 1 year
  - Cost reduction occurs during year 2, and grows thereafter

- Health economic modeling, including cost/QALY analysis, is valuable to reflect the long-term cost and consequences – including the patient benefit – that may be achieved with different immunosuppressive agents

- Improved long-term clinical outcomes may facilitate delivery of more cost-effective care

- Because ESRD funding is in the public domain, it is appropriate for healthcare institutions and individual countries to investigate if policy and reimbursement changes might result in more cost-effective care
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