Significance of Basiliximab Induction Therapy in Standard-Risk Renal Transplant in Tacrolimus Era: A Meta-Analysis

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• Acute rejection impairs graft survival
• Immunosuppressive protocols have been designed to overcome this challenge
• Basiliximab has been authorized as induction therapy since 2000
KDIGO Guidelines

1.2: We recommend including induction therapy with a biologic agent as part of the initial immunosuppressive regimen in KTRs. (1A)

1.2.1: We recommend that an IL2-RA be the first-line induction therapy. (1B)
Cyclosporine

Tacrolimus
Methodology

• We conducted a systematic review in PubMed, Medline, Embase and Cochrane databases to identify studies and research work that assessed effect of basiliximab on renal transplant outcomes.

• Standard risk for renal transplant was defined as:
  - Less than 2 DR mismatch
  - Panel reactive antibody (PRA) less than 20%
  - Recipients with no more than one previous transplant
<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Studies that compared basiliximab to placebo or no induction therapies</td>
<td>• Level 3-5 of evidence</td>
</tr>
<tr>
<td>• Standard risk population</td>
<td>• Studies that compared basiliximab to other depleting or non-depleting antibodies</td>
</tr>
<tr>
<td>• English language papers</td>
<td>• Cyclosporine-based immunotherapy</td>
</tr>
<tr>
<td></td>
<td>• High risk renal transplant recipients</td>
</tr>
<tr>
<td></td>
<td>• Follow-up period less than 1 year</td>
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<td>• Studies performed on animals</td>
</tr>
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<td></td>
<td>• Dual organ transplant</td>
</tr>
<tr>
<td></td>
<td>• Organ transplant other than the kidneys</td>
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</tbody>
</table>
Total of 470 papers from different databases

389 papers

10 papers

7 papers included for Meta-analysis

Excluded 81 repetitions

379 excluded:
- 271 unrelated
- 34 basiliximab versus ATG
- 26 Cyclosporine in he CNI
- 26 review articles
- 6 basilximab vs. daclizumab

3 papers excluded for short follow-up
<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Country</th>
<th>Journal</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wiland et al</td>
<td>Retrospective observational study</td>
<td>USA</td>
<td>Transplantation</td>
<td>2004</td>
</tr>
<tr>
<td>Gralla et al</td>
<td>Retrospective observational study</td>
<td>USA</td>
<td>Transplantation</td>
<td>2010</td>
</tr>
<tr>
<td>Sandes-Frietas et al</td>
<td>Retrospective observational study</td>
<td>Brazil</td>
<td>International nephrology</td>
<td>2013</td>
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<tr>
<td>Schwarz et al</td>
<td>Retrospective observational study</td>
<td>Austria</td>
<td>Transplantation proceedings</td>
<td>2015</td>
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<tr>
<td>Umber et al</td>
<td>Retrospective observational study</td>
<td>Italy</td>
<td>Journal of nephrology</td>
<td>2017</td>
</tr>
<tr>
<td>Martinez et al</td>
<td>Retrospective observational study</td>
<td>Spain</td>
<td>Transplantation proceedings</td>
<td>2009</td>
</tr>
<tr>
<td>Baek et al</td>
<td>Prospective study</td>
<td>Korea</td>
<td>Experimental transplantation</td>
<td>2016</td>
</tr>
<tr>
<td>Baseline characteristics</td>
<td>Basiliximab group (n=14974)</td>
<td>No basiliximab group (n=14667)</td>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-----------------------------</td>
<td>--------------------------------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Gender (male, %)</td>
<td>62.3%</td>
<td>62.9%</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Recipient age (years, mean)</td>
<td>48.65</td>
<td>47.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donor age (years, mean)</td>
<td>40.05</td>
<td>38.95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold ischemia time (hours, mean)</td>
<td>19.3</td>
<td>16.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of extended criteria donors</td>
<td>1347</td>
<td>1388</td>
<td>0.16</td>
<td></td>
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</table>
Acute rejection rate

<table>
<thead>
<tr>
<th>Study ID</th>
<th>RD (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>willand et al (2004)</td>
<td>-0.17 (-0.25, -0.10)</td>
<td>16.53</td>
</tr>
<tr>
<td>gralla et al (2010)</td>
<td>-0.01 (-0.02, -0.01)</td>
<td>24.88</td>
</tr>
<tr>
<td>sandes-frietas et al (2013)</td>
<td>0.01 (-0.08, 0.09)</td>
<td>15.36</td>
</tr>
<tr>
<td>schwartz et al (2015)</td>
<td>0.08 (-0.04, 0.20)</td>
<td>10.89</td>
</tr>
<tr>
<td>umber et al (2017)</td>
<td>-0.08 (-0.23, 0.08)</td>
<td>8.09</td>
</tr>
<tr>
<td>martinez et al (2009)</td>
<td>-0.07 (-0.25, 0.10)</td>
<td>6.84</td>
</tr>
<tr>
<td>baek et al (2016)</td>
<td>0.01 (-0.06, 0.08)</td>
<td>17.42</td>
</tr>
<tr>
<td>Overall</td>
<td>-0.03 (-0.09, 0.02)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
Graft survival

<table>
<thead>
<tr>
<th>Study ID</th>
<th>RD (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wiland et al (2004)</td>
<td>0(-0.05,0.06)</td>
</tr>
<tr>
<td>Gralla et al (2010)</td>
<td>0(-0.0,0.01)</td>
</tr>
<tr>
<td>Sandes-Frietas et al (2013)</td>
<td>-0.02(-0.11,0.6)</td>
</tr>
<tr>
<td>Umber et al (2017)</td>
<td>-0.07(-0.16,0.02)</td>
</tr>
<tr>
<td>Martinez et al (2009)</td>
<td>0.07(-0.07,0.20)</td>
</tr>
<tr>
<td>Baek et al (2016)</td>
<td>0(-0.04,0.04)</td>
</tr>
<tr>
<td>Overall</td>
<td>0(0,0.01)</td>
</tr>
<tr>
<td>(I-squared = 0.0%, p = 0.625)</td>
<td></td>
</tr>
</tbody>
</table>
# Patient survival

<table>
<thead>
<tr>
<th>Study ID</th>
<th>RD (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gralla et al (2010)</td>
<td>-0.03 (-0.03, -0.03)</td>
</tr>
<tr>
<td>Sandes-Frietas et al (2013)</td>
<td>0.01 (-0.05, 0.06)</td>
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<tr>
<td>Umber et al (2017)</td>
<td>0.02 (-0.04, 0.06)</td>
</tr>
<tr>
<td>Martinez et al (2009)</td>
<td>0.01 (-0.22, 0.13)</td>
</tr>
<tr>
<td>Baek et al (2016)</td>
<td>0.01 (-0.11, 0.13)</td>
</tr>
<tr>
<td>Overall</td>
<td>0 (-0.04, 0.04)</td>
</tr>
<tr>
<td></td>
<td>-0.01 (-0.04, 0.01)</td>
</tr>
</tbody>
</table>

(I-squared = 41.5%, p = 0.145)
Funnel plot with pseudo 95% confidence limits
Secondary results

• Change in creatinine

• NODAT

• CMV
Conclusions

• Basliximab induction therapy has no significant effect on acute rejection rate, patient or graft survival in standard-risk renal transplant recipients with tacrolimus-based maintenance immunotherapy.

• More randomised-controlled studies are needed to address these.
Acknowledgements

• Supervisors at Liverpool University
  Dr. Ahmed Halawa
  Dr. Ajay Sharma
  Dr. Atif Mohiuddin
  Dr. Mohsen El Kosi

• Library of Royal Wolverhampton hospitals
  Tina Dangerfield
  John Hudson
References


Thank you!