Evaluation of the Impact of Anti-Thymocyte Globulin (ATG) on Post-Hematopoietic Stem Cell Transplant (HCT) Outcomes in Patients Undergoing Allogeneic HCT

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Disclosure

• I, nor any of the other contributors to this project, have any actual or potential conflicts of interest in relation to this project and presentation.

Objectives

• Describe the rationale behind the use of ATG in alloHCT

• Explain the impact of ATG on infectious complications of alloHCT

• Describe the impact of ATG on other alloHCT outcomes including relapse and GVHD
Background

• Several studies have demonstrated the positive effects of ATG on chronic graft-versus-host disease (cGVHD) when used prior to alloHCT

• There are mixed results on the impact on overall survival and relapse rates with the use of ATG
  • Recent data has shown that ATG use in the reduced intensity conditioning (RIC) setting is associated with decreased overall survival
  — Increased infection rates may be a potential cause for this mortality difference

Background

• University of North Carolina Hospitals (UNCH) performs 180-200 HCTs annually
  • ~40% are alloHCTs
  • ~60% of alloHCTs are from matched unrelated donors (MUD) or mismatched related donors (MMRD)
    — UNCH protocols utilize ATG for all MUD and MMRD transplants for GVHD prophylaxis
    — Conditioning regimens for MUD and MMRD:
      • Busulfan-fludarabine (Bu-Flu)
      • Recent increase in use of busulfan-cyclophosphamide (Bu-Cy) and total body irradiation (TBI) in myeloablative conditioning (MAC) setting

Objectives

• To test the hypothesis that the addition of ATG to alloHCT myeloablative conditioning (MAC) and reduced intensity conditioning (RIC) regimens, when compared to non-ATG regimens, results in a significant difference in:
  • Primary endpoint:
    — Incidence of infections
  • Secondary endpoints:
    — Incidence and severity of acute graft-versus-host disease (aGVHD)
    — Relapse
    — Mortality
Methods

- Retrospective cohort study of adult alloHCT patients at UNCH from 2006-2013 through day +180
  - 125 +ATG, 125 –ATG
  - Inclusion criteria:
    - MRD, MUD, and MMRD alloHCT patients who underwent a MAC or RIC transplant
    - Age ≥ 18 years
  - Exclusion criteria:
    - Active infection at the time of transplant
    - Transplant source other than peripheral blood or bone marrow
    - Patients receiving haploidentical transplants
    - Patients enrolled in clinical trials involving ATG
    - Patients with multiple transplants

Results – Study Participants

AlloHCT Patients*
(n=250)

+ATG
(n=125)

MRD (n=10)
MMRD (n=2)
MUD (n=113)
MAC (n=63)
RIC (n=62)

–ATG
(n=125)

MRD (n=103)
MMRD (n=1)
MUD (n=21)
MAC (n=63)
RIC (n=62)

Results – Infection Rates

Mean Infection Count per Subject by ATG Group and Conditioning Regimen

<table>
<thead>
<tr>
<th></th>
<th>+ATG</th>
<th>-ATG</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>MAC</td>
<td>3.3</td>
<td>4.9</td>
<td>0.01</td>
</tr>
<tr>
<td>RIC</td>
<td>2.0</td>
<td>3.3</td>
<td>0.015</td>
</tr>
<tr>
<td>Total</td>
<td>2.7</td>
<td>4.1</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

- Factors other than ATG use with significant impact on infection incidence in multivariate analysis:
  - Conditioning regimen (p=0.0034)
  - Increasing age (p=0.0129)
Results – Infection Rates

Infection Type and Frequency by ATG Group

Results – Infection Rates

Infection Type and Frequency by ATG Group in MAC Patients

Results – Infection Rates

Infection Type and Frequency by ATG Group in RIC Patients
Results – Graft versus Host Disease

Incidence of any GVHD* by ATG Group and Conditioning Regimen

<table>
<thead>
<tr>
<th></th>
<th>-ATG</th>
<th>+ATG</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>MAC</td>
<td>46 (73%)</td>
<td>50 (79%)</td>
<td>0.658</td>
</tr>
<tr>
<td>RIC</td>
<td>40 (65%)</td>
<td>45 (73%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Total</td>
<td>86 (68%)</td>
<td>95 (76%)</td>
<td>0.167</td>
</tr>
</tbody>
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*occurrence of GVHD of any grade in any organ

Results – Mortality

Mean Overall Survival by ATG Group

Results – Relapse or Death

Mean Relapse-Free Survival Time by ATG Group
Audience Response Question

• Incidence of what type of infection was most significantly impacted by ATG use?
  
  A) Gram positive
  B) Gram negative
  C) Viral
  D) Fungal

Limitations

• Data collection limited to day +180

• Difficult to detect true differences in GVHD rates as per protocol at UNCH most higher risk patients (MUD, MMRD) receive ATG

• Infection data limited to culture-documented infections

Conclusions and Future Directions

• ATG use is associated with increased infection rates in alloHCT patients, with greater impact in the RIC setting
  
  • Greatest increase is seen in rate of viral infections (CMV, HSV, HHV-6)

• ATG use does not appear to be associated with an increase in mortality in the first 180 days post-HCT

• In the future, we plan to further examine outcomes related to increased infection rates and assessing all outcomes beyond day +180
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