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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February 13th, 2015

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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.

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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

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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

Blood. 2011;117:6963-70.
Biol Blood Marrow Transplant. 2014; http://dx.doi.org/10.1016/j.bbmt.2014.01.016 [Epub ahead of print].

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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

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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

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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

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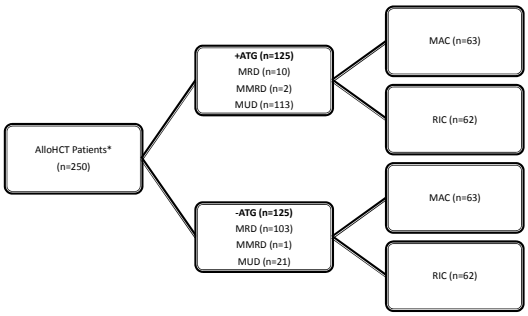
Results – Study Participants



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Results – Infection Rates

Mean Infection Count per Subject by ATG Group and Conditioning Regimen

	-ATG	*+ATG*	*p-value*
MAC	3.3	4.9	0.01
RIC	2.0	3.3	0.015
Total	2.7	4.1	0.0007

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

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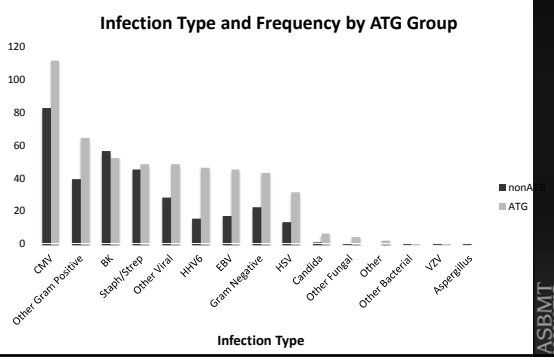
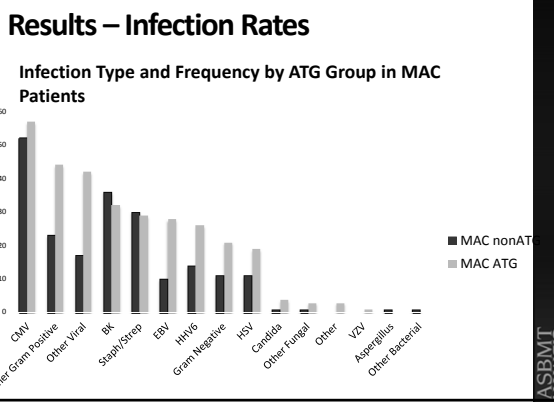
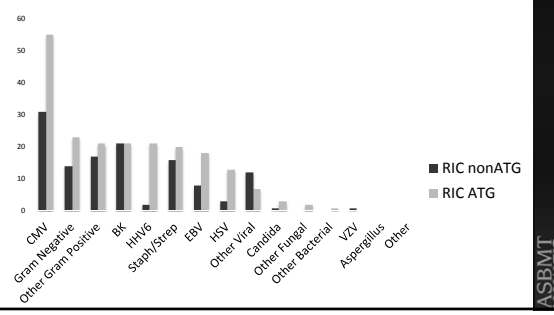
Results – Infection Rates



Results – Infection Rates



Results – Infection Rates



Results – Graft versus Host Disease

Incidence of any GVHD* by ATG Group and Conditioning Regimen

	-ATG	*+ATG*	*p-value*
MAC	46 (73%)	50 (79%)	0.658
RIC	40 (65%)	45 (73%)	0.82
Total	86 (68%)	95 (76%)	0.167

*occurrence of GVHD of any grade in any organ

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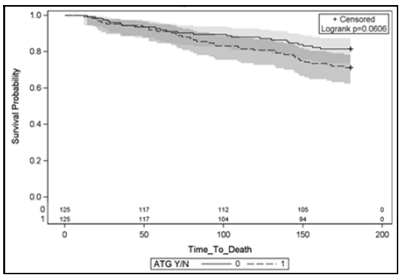
Results – Mortality

Mean Overall Survival by ATG Group



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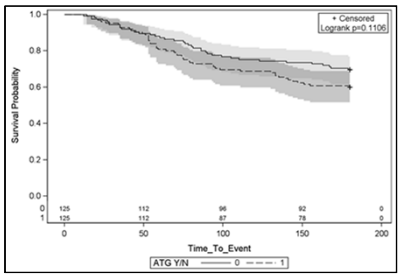
Results – Relapse or Death

Mean Relapse-Free Survival Time by ATG Group



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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

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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

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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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Acknowledgements

- Co-Investigators
  - Ryan Beechinor, PharmD; Rachel Lebovic, PharmD; Mary Roth, PharmD
- Physician Support
  - Katarzyna Jamieson, MD; Pearlie Chong, MD; Thomas Shea, MD
- Data Support
  - Andrew Sharf, Nicolas Ballarini, Ananta Bangdiwala
  - Anastasia Ivanova, PhD
- Mentorship
  - Kamakshi Rao, PharmD, BCOP, CPP, FASHP

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