

A comparison of the incidence of hypertension in standard versus non-myeloablative stem cell transplant regimens in pediatric patients

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Acknowledgments

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Background

- ❖ The Bone Marrow Transplant Clinical Trials Network (BMT CTN) includes alemtuzumab (Campath®) as part of a non-myeloablative regimen
- ❖ Active trial (BMT CTN 0601)
- ❖ Alemtuzumab is included in a new pending pediatric trial for Stem Cell Transplantation (SCT) preparation

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Background

- ❖ Incidence of hypertension (HTN) with alemtuzumab in adults = 11% to 14%
- ❖ Adult dosing scheme = 4 to 12 weeks
- ❖ Pediatric dosing scheme = Test dose + 3 doses of alemtuzumab (4 days total)

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Introduction

- ❖ Anecdotal observations of patients with alemtuzumab treatment for Stem Cell Transplant (SCT) Preparation seem to have an association with higher rate of HTN
- ❖ Concomitant medications may affect rate of HTN with both regimens
- ❖ **Study Aim:**
 - ❖ Compare incidence of hypertension in patients that received alemtuzumab vs. those with standard stem cell preparation

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Study Objectives

❖ Primary Outcome

- ❖ Incidence of HTN in patients receiving alemtuzumab, fludarabine, and melphalan as preparative agents compared to standard regimen

❖ Secondary Outcome

- ❖ Timing of initiation of anti-hypertensive medication

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Research Design

- ❖ Retrospective chart review
 - ❖ Myeloablative preparative regimen
 - ❖ January 1, 2008 to December 31, 2008
 - ❖ Alemtuzumab preparative regimen
 - ❖ January 1, 2008 to December 31, 2009
- ❖ Institutional Review Board (IRB) approval prior to data collection

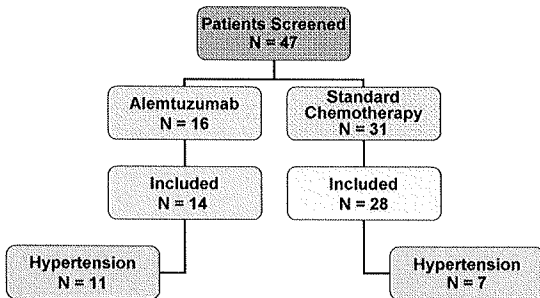
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Research Design

- | | |
|--|---|
| Inclusion Criteria <ul style="list-style-type: none"> ❖ Age 0-18 years at time of transplant ❖ Received alemtuzumab or standard preparatory regimen | Exclusion Criteria <ul style="list-style-type: none"> ❖ Prescribed medication for HTN prior to transplant |
|--|---|

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Study Population



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Data Elements

Hypertensive Patients

- | | |
|-------------|----------------------------------|
| ❖ Age | ❖ Diagnosis for SCT |
| ❖ Gender | ❖ Recorded BP* |
| ❖ Ethnicity | ❖ Co-Administered medications ** |

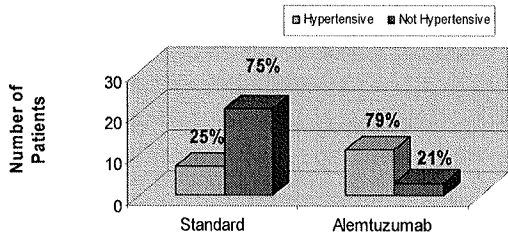
*BP recordings: Alemtuzumab - days -22,-18,-7,-1,7,14,21,28±7,60±7, and 90±7 Standard - days 0,7,14,21,28±7,60±7, and 90±7 only

**Co-Administered medications = Cyclosporine and/or Systemic steroids

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Results

Figure 1. Hypertension Among Alemtuzumab vs. Standard Group



P < 0.003

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Results

Table 1. Demographics for Hypertensive Patients

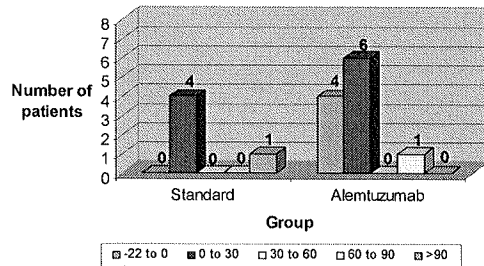
Variables	Alemtuzumab (n = 11)	Standard (n = 7)
Age (years)	8.08 ± 4.13 *	7.43 ± 6.05*
Gender		
Male	71 %	54 %
Female	29 %	46 %
Ethnicity		
African American	6 (55%)	4 (57%)
Asian	1 (9%)	0 (0%)
Hispanic	2 (18%)	0 (0%)
Caucasian	1 (9%)	3 (43%)
Other	1 (9%)	0 (0%)

*Mean ± Standard Deviation

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Results

Figure 2. Timing of Initiation of an Anti-Hypertensive Agent



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Discussion

- ❖ African Americans seem to have the highest incidence of alemtuzumab-induced HTN
- ❖ Majority of patients needed anti-hypertensive agents within the first 30 days
- ❖ Cyclosporine and steroids appear to contribute more to HTN with alemtuzumab vs. standard preparatory regimen

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Limitations

- ❖ Records had limited access
 - ❖ Paper vs. electronic charting
- ❖ Non-randomized
- ❖ Small sample size
- ❖ Study was not powered to detect significant results

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Conclusion

- ❖ Alemtuzumab-containing SCT preparative regimens may contribute to a higher incidence of HTN than standard regimens
- ❖ Alemtuzumab-induced HTN required treatment within 30 days of SCT preparatory initiation

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Future directions

- ❖ Consider a different agent than cyclosporine for GVHD prevention in patients receiving alemtuzumab for SCT preparation
- ❖ Identify modifiable risk factors to decrease incidence of HTN with Alemtuzumab prep

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Question:

- ❖ What other agents can be used for graft versus host disease aside from Cyclosporine?

ANSWER: Tacrolimus (Prograf®) or Mycophenolate Mofetil (CellCept®) or a short course of Methotrexate (3 doses every other day)

Questions

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References

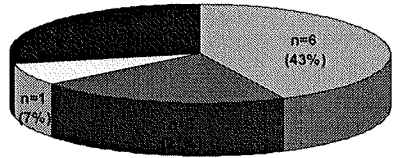
1. BMT CTN Protocol 0601 Unrelated Donor Hematopoietic Stem Cell Transplant for Children with severe Sickle Cell Disease using an Reduced Intensity Conditioning Regimen.
2. Kutkuhn B, Hollenbeck M, Heering P, et al: Development of insulin resistance and elevated blood pressure during therapy with cyclosporine A. *Blood Press* 1997; 6:13-17.
3. Hardin JG: Steroid-induced morbidity mimicking active systemic lupus erythematosus. *Ann Intern Med* 1973;78:558.
4. Campath [Package Insert]. Richmond, Ca.: Berlex Laboratories; 94804
5. Report of the Second Task Force on Blood Pressure Control in Children. *J Pediatrics* 1987;79:1.

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EXTRA INFORMATION

Alemtuzumab

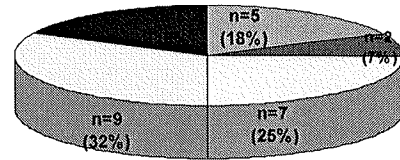
Diagnosis of Alemtuzumab Patients with HTN.



□ Sickle Cell ■ Thalassemia □ Aplastic Anemia □ SCID (0%) ■ Other

Standard Chemotherapy

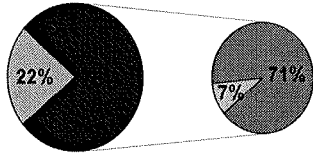
Diagnosis of Patients with HTN.



□ Leukemia ■ Lymphoma □ Neuroblastoma □ Brain Tumor ■ other

Co-administered medications (Alemtuzumab)

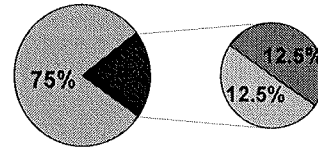
Hypertensive Patients that received Alemtuzumab and on Cyclosporine Only or Cyclosporine + Steroids



□ No ■ Yes □ Cyclosporine Only ■ Steroids + Cyclosporine

Co-administered medications (Standard Chemotherapy)

Hypertensive Patients that received Standard Chemotherapy and on Steroids Only or Both Cyclosporine and Steroids



□ No ■ Yes □ Steroids Only ■ Cyclosporine+Steroids