A Comparison of Outcomes of Two Preparative Regimens for Lymphoma Patients Receiving Autologous Hematopoietic Cell Transplant

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Disclosure

Disclosure statement: these individuals have the following to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation.

Presenter: LeAnne Kennedy

- Nothing to disclose

Co-Investigators: Rachel Filipek, David Hurd, Greg Russell

- Nothing to disclose

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Objective

Describe the tolerability and efficacy of Bu-Cy and CBV when used for autologous stem cell transplants in elderly patients

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Wake Forest Baptist Health

- Academic medical center
- Winston-Salem, NC
- 885 acute care beds
- 150 adult oncology beds
- 12 bed BMT unit

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Ideal Preparative Regimen

- Single vs. multiple drug regimen
- Minimize overlapping toxicities
  - Mucositis
  - Nausea, vomiting, diarrhea (N/V/D)
  - Febrile neutropenia (FN)
  - Organ dysfunction

Copelan EA. N Engl J Med. 2006;354:1813-26

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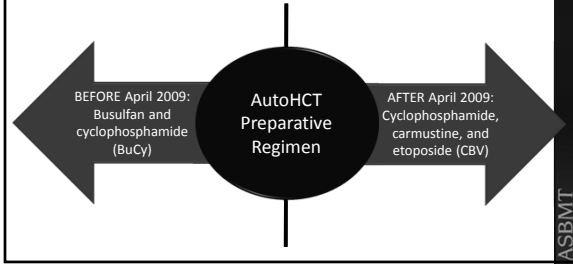
HCT at Wake Forest

- 100 HCT per year
  - 60% autologous
- All transplants occur inpatient



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Historical Comparison

Survival	BuCy	CBV
Overall survival (OS)	65%	66%
Progression-free survival (PFS)	52%	59%
Toxicity		
Mucositis	79-97%	63%
Gastrointestinal (GI)	43-100%	23-43%
Sinusoidal obstruction syndrome	8-12%	10%
Hepatic dysfunction	49%	9%
Renal dysfunction	21%	22-41%

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William BM et al. Clin Lymph Myel and Leuk. 2013;13(4):17-23.
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Hypothesis

Changing from Bu-Cy to CBV is better tolerated in elderly HCT patients without losing efficacy

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Study Objective

To compare the safety and efficacy of CBV versus BuCy as a preparative regimen for patients over the age of 60 who received an autoHCT

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Methods

- Study design
  - Single-center, retrospective chart review
- Patient selection
  - Computer-generated list of patients
    - Diagnosis of lymphoma
    - HCT between 01/2004 and 01/2014
- IRB-approved

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Outcomes

- Primary Endpoint
  - Incidence of grade 3 or 4 regimen-associated toxicities
- Secondary Endpoints
  - Overall survival (60 days and 3 years)
  - Relapse-free survival (60 days and 3 years)
  - Time to death
  - Time to relapse
  - Days to engraftment

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Subject Selection

Inclusion Criteria	Exclusion Criteria
• Diagnosis of lymphoma per lymph node biopsy • Received a HCT between 01/2004 and 01/2014	• Age < 60 years • Allogeneic HCT • Received any preparative regimen other than BuCy or CBV • No 60-day follow-up visit unless known mortality

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Statistical Analysis

- Descriptive statistics
- Fisher's Exact test
- Wilcoxon Rank-Sum test
- Chi-Square approximation of the log-rank test
- $\alpha < 0.05$

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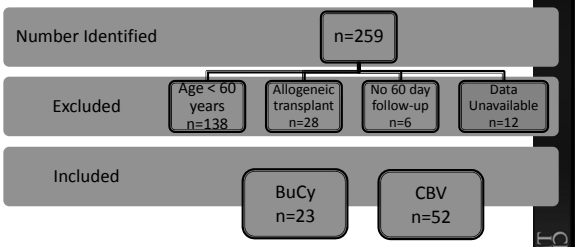
Study Enrollment



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Baseline Characteristics

	BuCy (n=23)	CBV (n=52)
Age (years), mean ± SD	68.3 ± 4.9	66.1 ± 4.4
Gender (male), %	57	65
Race (Caucasian), %	100	96
Type of lymphoma, n(%)		
Diffuse large B-cell	14 (61)	21 (40)
Mantle cell	1 (4)	12 (23)
T-cell	2 (9)	10 (19)
Follicular	3 (13)	7 (14)
Other	3 (13)	2 (4)
Time from diagnosis to HCT (months), mean ± SD	40 ± 32.1	32.5± 58.7

*No significant differences

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Primary Outcomes

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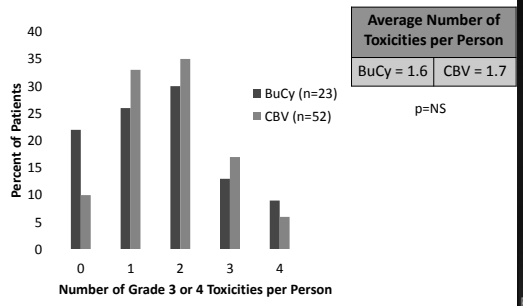
Grade 3 or 4 Regimen-Related Toxicities



Average Number of Toxicities per Person	
BuCy = 1.6	CBV = 1.7

p=NS

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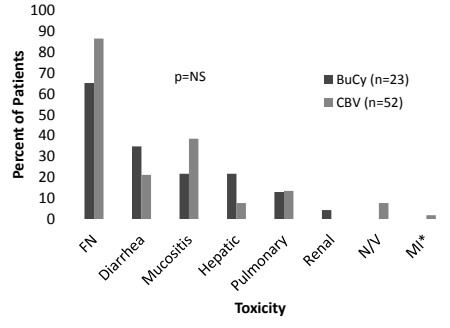
Individual Regimen Toxicities



*MI = myocardial infarction

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Secondary Outcomes

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Survival

Relapse-free Survival (% ± SE)			
	BuCy	CBV	P-value
60-Day (n=75)	86 ± 7	94 ± 3	0.29
3-Year (n=48)	31 ± 10	68 ± 7	0.063

Overall Survival (% ± SE)			
	BuCy	CBV	P-value
60-Day (n=75)	96 ± 4	94 ± 3	0.79
3-Year (n=48)	56 ± 11	60 ± 9	0.84

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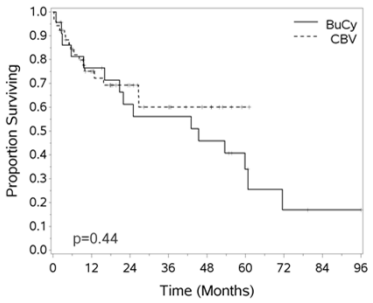
Overall Survival



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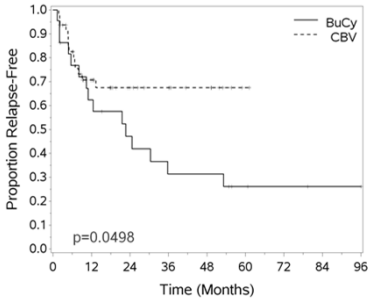
Relapse-Free Survival



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Other Outcomes

	BuCy (n=23)	CBV (n=52)
Time to ANC > 1,000 cells/mm^3 (days), mean	11.2	10.7
Time to platelets > 20,000 cells/mm^3 (days), mean	11	11.9

p=NS

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Summary

	Outcome	Significance
	Incidence of grade 3 or 4 regimen-related toxicity	NS
	60-Day survival	NS
☆	3-Year survival	NS – trend towards improved RFS with CBV
	Median survival duration	NS
☆	Median time to relapse	Favors CBV
	Time to engraftment	NS

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Conclusions

- Continue use of CBV as the primary preparative regimen for autoHCT at WFBH due to no difference identified in toxicities with potential relapse benefit
- Limitations
  - Retrospective design
  - Single-center
  - Limited number of patients who received BuCy
  - Patients who received BuCy were likely to have received HCT prior to 4/2009
  - Practice changes

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Audience Response

When comparing BuCy to CBV, which of the following is true in patients over 60 years of age?

A. BuCy had a higher incidence of grade 3-4 toxicities.
B. CBV had higher percentage of 60-day survival
C. CBV had a trend to improved relapse-free survival at 3 years
D. BuCy had a longer median time to relapse

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- Rachel Filipek, PharmD
- David Hurd, MD
- Gregory Russell, MS

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Length of Stay

Days, Mean ± SD	
BuCy	23.3 ± 3.8
CBV	20.4 ± 3.6

Day -9: Patients admitted to receive BuCy
Day -6: Patients admitted to receive CBV
Day 0: Stem cells infused
~Day +11: engraftment of WBC

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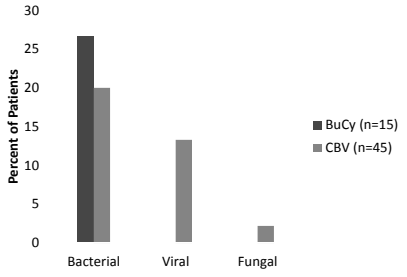
Culture Data



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CTCAE Criteria

	Grade 1	Grade 2	Grade 3	Grade 4
Mucositis	Erythema	Patchy ulcerations	Confluent ulcerations; bleeding with minor trauma	Tissue necrosis, spontaneous bleeding; life threatening
Nausea/ Vomiting	Loss of appetite; 1 episode vomiting	Decreased intake; dehydration; IV fluids <24 hours; 2-5 episodes vomiting	Inadequate intake; IV fluids, tube feeds, or TPN >24 hours; ≥ 6 episodes vomiting	Life threatening consequences
Diarrhea	Increase < 4 stools/day over baseline	Increase 4-6 stools/day over baseline; IV fluids <24 hours	Increase ≥ 7 stools per day over baseline; IV fluids >24 hours	Hemodynamic collapse
FN	-	-	Present	Life threatening (shock, hypotension, acidosis)

CTCAE Criteria

	Grade 1	Grade 2	Grade 3	Grade 4
Pulmonary	Asymptomatic	Symptomatic; not interfering with ADL	Symptomatic; interefere with ADL; O2 indicated	Life threatening; ventilator support
Renal	CRE > 1.5 x ULN	CRE 1.5-3 x ULN	CRE > 3-6 x ULN	CRE > 6 x ULN or chronic dialysis
Hepatic	AST > 2.5 x ULN ALT > 2.5 x ULN Bili > 1.5 x ULN Albumin > 3g/dL	AST > 2.5-5 x ULN ALT > 2.5-5 x ULN Bili > 1.5-3 x ULN Albumin 2-3g/dL	AST > 5-20 x ULN ALT > 5-20 x ULN Bili > 3-10 x ULN Albumin < 2g/dL	AST > 20 x ULN ALT > 20 x ULN Bili > 10 x ULN
MI	-	-	-	present