

# Bendamustine, Bortezomib and Rituximab in Patients with Relapsed/Refractory Indolent and Mantle-Cell Non-Hodgkin Lymphoma

Friedberg JW et al.

*Proc ASH 2009;Abstract 924.*

# Introduction

- > Bendamustine (B) is approved for the treatment of relapsed/refractory indolent non-Hodgkin's lymphoma.
- > Phase II trials of bendamustine and rituximab (R) demonstrated tolerability and high response rates in indolent and mantle-cell lymphomas (*JCO* 2008;26:4473, *JCO* 2005;23:3383).
- > Bortezomib (V) has significant single-agent activity in indolent and mantle-cell lymphoma (MCL) (*Clin Cancer Res* 2010;16(2):719; *J Clin Oncol* 2005;23(4):676).
- > Current study objective:
  - Evaluate the activity and tolerability of combined bendamustine/rituximab and bortezomib in patients with relapsed/refractory indolent B-cell or mantle-cell lymphomas.

# Phase II Trial Schema

## Eligibility (N = 31)

Relapsed or refractory  
indolent or mantle-cell  
NHL

No prior ASCT or radio-  
immunotherapy within  
4 months

B 90 mg/m<sup>2</sup> (d1, 4)

R 375 mg/m<sup>2</sup> (d1)

V 1.3 mg/m<sup>2</sup>

(d1, 4, 8, 11)

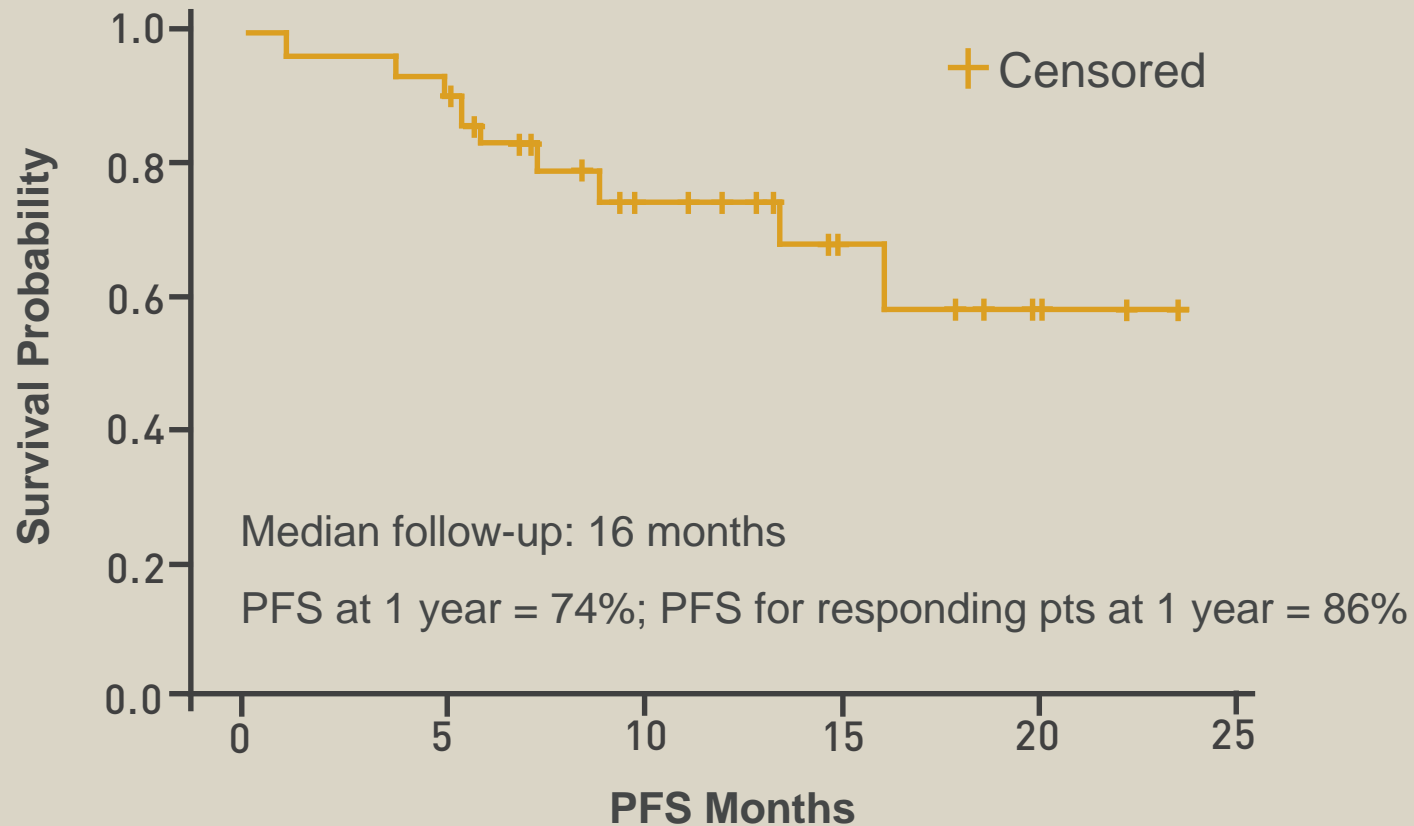
q28 days x 6

# Best Response

<b>Response Rate</b>	<b>N = 29*</b>
Overall response rate (ORR)	79%
Complete response	51%
Partial response	28%
Stable disease	10%
<b>Response by Histology</b>	
Follicular NHL (n = 16)	85%
Mantle cell (n = 7)	71%

\* One patient was not evaluable for response; one patient was not eligible.

# Progression-Free Survival (PFS)



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# Adverse Events (n = 30)

Select Adverse Events	Grade 3 (%)	Grade 4 (%)
Neutropenia	12	3
Thrombocytopenia	15	—
Varicella-zoster virus reactivation	6	—
Peripheral neuropathy	14	3
Fatigue	7	—
Nausea	3	—
Diarrhea	3	—

Grade 5 adverse events: One patient died of sepsis. Alopecia was not observed.

# Conclusions

- > VBR is highly active (ORR = 79%) and more toxic than BR.
  - Prophylaxis against varicella zoster reactivation is indicated with this regimen.
- > There is no association between prior R sensitivity and response to VBR (data not shown).
- > Ongoing correlative studies are being conducted to determine predictors of toxicity and response.

# Faculty Comments

**DR FOSS:** VBR in this setting is an interesting combination, but a randomized trial comparing it to BR is necessary before one can conclude that VBR is superior. The usefulness of this regimen to the practicing physician is for relapsed MCL, for which the goal is to achieve a CR to salvage therapy so that a patient can then receive an autotransplant. The study also demonstrated a good response rate with reasonable toxicity.

**DR FISHER:** This Phase II study demonstrated that VBR is tolerable with a good ORR. Interestingly, responses were higher in the follicular histology and toxicity was manageable. Thus, it will be explored in untreated FL as an alternative to established regimens. Evaluation will continue for patients with MCL, with some variation in schedule and dosing.



# Phase II Trial of Bortezomib/ Lenalidomide for Relapsed/ Refractory MCL (CALGB 50501): Results of a Planned Interim Analysis

Morrison VA et al.

*Proc ASCO 2010;Abstract 8106.*

# Introduction

- > Patients with mantle-cell lymphoma (MCL) typically experience relapse despite high response rates to initial treatment.
- > Treatments (tx) such as stem cell transplant (SCT) are not curative and many patients are not eligible for SCT because of age or comorbid conditions.
- > As single-agent therapies, thalidomide (an immunomodulatory agent in the same therapeutic class as lenalidomide) and bortezomib are both active against MCL.
- > Current study objective:
  - The purpose of the CALGB-50501 study was to evaluate the use of bortezomib (V) and lenalidomide (LEN) in patients with relapsed or refractory MCL.

# Methods

Accrual: 54 (Open)

## Eligibility

Histologically documented MCL  
Measurable disease  
≥1 prior tx  
No prior radioimmunotherapy  
ECOG PS 0-2  
No ≥Grade 3 peripheral neuropathy

## Induction

LEN (20 mg, qd, d1-14)  
V (1.3 mg/m<sup>2</sup>, d1, 4, 8, 11)

CR/PR at  
6 mos

Yes

## Maintenance

LEN (15 mg, qd, d1-14)  
V (1.3 mg/m<sup>2</sup>, d1, 8)

Sept 2009 protocol dose-reduction schedules for V and LEN with neuropathy and myelosuppression, respectively; CR = complete response; PR = partial response

# Methods

- > Primary endpoint
  - Overall response rate
- > Secondary endpoints
  - Time to disease progression
  - Disease-free/overall survival
  - Correlating changes in activated NK/T-cells and plasma cytokines with response
- > Study began in November 2007
- > Interim analysis planned after 19 patients
- > 10 or more responses required to reopen study (achieved)
- > As of December 2, 2009, 38 patients were accrued
- > Interim toxicity available for 31 patients

# Grade 3/4 Adverse Events

Toxicity	N = 31
Anemia	3%
Leukopenia	3%
Thrombocytopenia	32%
Fatigue/aesthenia	19%
Dyspnea	16%

Morrison VA et al. *Proc ASCO 2010*;Abstract 8106.

## Grade 3/4 Adverse Events (continued)

Toxicity	N = 31
Infection	6%
Motor neuropathy	13%
Sensory neuropathy	3%
Hypotension	13%

Morrison VA et al. *Proc ASCO* 2010;Abstract 8106.

# Conclusions

- > Therapy was fairly well tolerated.
- > Most common Grade 3/4 toxicities:
  - Thrombocytopenia (32%)
  - Fatigue/aesthenia (19%)
  - Dyspnea (16%)
- > Interim data suggest that the combination of lenalidomide and bortezomib has an acceptable toxicity profile in patients with MCL.

# Faculty Comments

**DR VOSE:** The study is evaluating the combination of bortezomib and lenalidomide in relapsed/refractory mantle-cell lymphoma.

The planned interim analysis showed acceptable efficacy to continue further enrollment. The regimen was fairly well tolerated with minimal toxicity.