

Bendamustin-Rituximab Induction Followed by Observation or Rituximab Maintenance for Newly Diagnosed Patients with Waldenström's Macroglobulinemia:**Results From an ongoing Prospective, Randomized, Multicenter Study (StiL NHL 7-2008 –MAINTAIN-; ClinicalTrials.gov Identifier: NCT00877214)****Matthias J. Rummel, MD, Christian Lerchenmüller, MD, Richard Greil, MD, Martin Görner, Manfred Hensel, MD, Erik Engel, Ulrich Jaeger, MD, Friedhelm Breuer, Bernd Hertenstein, Otto Prummer, MD, PhD, Christian Buske, MD, Juergen Barth, Alexander C. Burchardt, MD and Wolfram Brugger****Background:**

Treatment for Waldenström's Macroglobulinemia (WM) typically consists of rituximab in combination with nucleoside analogs with or without alkylating agents or with cyclophosphamide-based therapies or cyclophosphamide and dexamethasone (1, 2). In addition, combination treatments including bortezomib, thalidomide, lenalidomide and bendamustine have been shown to have activity in WM.

Bendamustine has demonstrated durable responses in previously treated patients with WM both as monotherapy and in combination with rituximab (3).

In addition, a recent observational study suggests improved clinical outcomes following maintenance rituximab therapy in patients with WM who responded to induction treatment that consisted of a rituximab-containing regimen (4).

We initiated a multicenter, prospective, randomized phase III trial to investigate the impact of adding rituximab maintenance following B-R first-line induction. The trial includes patients with WM, marginal zone, small lymphocytic and mantle cell lymphomas (ClinicalTrials.gov Identifier: NCT00877214).

The trial is currently ongoing and we present first and preliminary results of the induction phase for patients with WM.

Methods:

Treatment consists of a maximum of 6 cycles of B-R (bendamustine 90 mg/m², rituximab 375 mg/m²) administered every 28 days plus 2 cycles of rituximab every 4 weeks.

Responding patients (≥ PR) are eligible for further treatment and are/will be randomized to observation or 2 years of rituximab maintenance every two months. The primary endpoint is PFS.

Results:

From April 2009 to July 2012, 57 centers included a total of 162 patients with newly diagnosed WM with a median age of 67 years (31% < 60 years, 69% > 60 years). At baseline/inclusion/screening, the following median values were recorded: β2-Microglobulin 3.3 mg/L, hemoglobin 10.1 g/dL, and IgM 2110 mg/dL (max. 13400 mg/dL).

The trial is currently ongoing, and we report results for 116 evaluable patients who have completed the induction phase (data cut-off Aug 2012): 43 women (37%) and 73 men (63%). 100 patients have responded to B-R leading to an overall response rate (ORR) of 86%. At the time of response evaluation, the median Hb was 12.6 g/dl and the median IgM was 380 mg/dl (Table 1).

No uncommon toxicities were observed during B-R induction.

To date, 90 patients have undergone randomization after completing the induction phase: 43 to observation and 47 to maintenance. Recruitment and randomization are ongoing. No results can be reported from the maintenance part of the trial.

Conclusion:

Initial results of our trial confirm that for patients with Waldenström's Macroglobulinemia, induction treatment with B-R is efficacious and has a manageable safety profile. The role of rituximab maintenance in this disease is under investigation.

References:

1. Gertz MA. Am J Hematol. 2012 May;87(5):503-10.
2. Treon SP. Blood. 2009 Sep 17;114(12):2375-85.
3. Treon SP, et al. Clin Lymphoma Myeloma Leuk. 2011 Feb;11(1):133-5
4. Treon S, et al. Br J Haematol 2011;154(3):357-62

Study details

Title	StiL Study NHL 7-2008: Prospective Randomized Multicenter Study in First-line Treatment of Advanced progredleNT Follicular And Other IndoleNt and Mantle Cell Lymphomas (MAINTAIN)
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ClinicalTrials.gov Identifier:	NCT00877214
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Study type	Multicenter, prospective, randomized, Phase III
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Treatment

Induction	Maximum of 6 cycles of B-R Bendamustine 90 mg/m ² Rituximab 375 mg/m ² administered every 28 days plus 2 cycles of rituximab every 4 weeks.
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Maintenance	Randomization to Observation or 2 years of rituximab maintenance, 375 mg/m ² , every two months
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Included Patients from 04/2008 to 8/2012	162 (recruitment ongoing)
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Evaluable patients	116 43 women [37%] 73 men [63%]
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Randomized patients (following completion of the induction phase)	90 43 observation 47 maintenance
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Values @ baseline/inclusion/screening

Median age	67 years 31% < 60 years 69% > 60 years
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β2-Microglobulin	3.3 mg/L
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Hemoglobin	10.1 g/dL
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IgM	2110 mg/dL (max. 13400 mg/dL)
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Values @ the time of response evaluation

Overall Response Rate	86 %
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Hemoglobin	12.6 g/dL
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IgM (median)	380 mg/dL
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Table 1: Overview of study details and preliminary results

