Abstract Submission Deadline: August 14, 2012
Character limit (excluding spaces, title, author info, and figures): 3800. Current (excluding spaces): 3581.

Real-World Efficacy and Safety of Bendamustine with or without Rituximab in Treatment-Naïve Patients with Chronic Lymphocytic Leukemia: Retrospective Analysis of a German Registry

G. Günther,[1] S. Bartels[2], H.W. Tessen,[3] J.A. Sterchele[4]

[1]Medizinisches Versorgungszentrum für Blut- und Krebserkrankungen, Potsdam, Germany
[1]rgb Onkologisches Management GmbH, Sarstedt, Germany
[2]Private Practice, Goslar, Germany
[4]Teva Pharmaceutical Industries Ltd., Frazer, Pennsylvania, USA

Key words: Bendamustine, Rituximab, Chronic Lymphocytic Leukemia

642. CLL: Therapy, excluding Transplantation

Background
Bendamustine, a unique alkylating agent with a multifaceted mechanism of action is effective front-line therapy for chronic lymphocytic leukemia (CLL). In vitro studies showing that cytotoxic activity of bendamustine against CLL-derived cell lines is synergized by rituximab, an anti-CD20 monoclonal antibody, have led to investigation of combination bendamustine plus rituximab (BR) as first-line therapy and treatment of relapsed disease. This retrospective analysis assessed real-world efficacy and safety of bendamustine alone and combined with rituximab in treatment-naïve CLL patients from Projektgruppe Internistische Onkologie, the largest registry of treatment data from private medical oncology practices in Germany.

Methods
Records were obtained for all CLL patients in a registry from 57 German oncology practices from May 2008 to July 2011. Patients who received ≥3 cycles of first-line bendamustine monotherapy or BR were divided into the following age/treatment groups: ≤60 years treated with BR ± prednisone (P) [*≤60 BR*]; >60 to <70 years treated with bendamustine monotherapy [*60-70 B*]; >60 to <70 years treated with BR ± P [*60-70 BR*]; ≥70 years treated with bendamustine monotherapy [*≥70 B*]; and ≥70 years treated with BR ± P [*≥70 BR*].

The primary efficacy measure was ORR (complete response [CR] plus partial response [PR]); secondary efficacy measures included CR, PR, progression-free survival (PFS), and overall survival (OS). Adverse events (AEs) were assessed.

Results

A total 217 patients (≥61.1% male in each group) were included in the analysis (Table). At diagnosis, all patients had an ECOG score of 0-2; most had RAI stage 0-II (16 had stage III/IV) and Binet stage A or B (29 had stage C). Mean number of treatment cycles (28 days/cycle) per group ranged from 5.1 to 5.9. Mean dose per cycle ranged from 133.6 to 165.9 mg/m^2 for bendamustine and 391.1 to 412.1 mg/m^2 for rituximab in those groups (Table). Median follow-up was 3 years (range 1-5).

Observed ORRs were >83% in all groups (Table); 1 patient each in the *60-70 B* and *60-70 BR* groups had progressive disease, and 1 in the *≥70 BR* group was not assessable. By Kaplan-Meier analysis, median PFS and OS have been reached in the *60-70 B* (PFS: 14.8 months, OS: 41.0 months) and *≥70 B* (PFS: 32.5 months, OS: 40.1 months) groups only. PFS results are shown in the Figure.

There were 26 deaths at the time of analysis. The most common grade 3/4 hematologic AEs were febrile neutropenia (n=28) in the *≥70 BR* group, leukopenia (n=15) in the *≤60 BR* group, and leukopenia (n=25) in the *≥70 BR* group. Depression was the most common grade 3/4 nonhematologic AE, affecting all patients in the *≤60 BR* and *60-70 B* groups, 48/50 patients in the *60-70 BR* group, 35/36 in the *≥70 B,* and 94/95 in the *≥70 BR*. Other common grade 3/4 nonhematologic AEs included fatigue (2 patients in *≥70 BR* and 1 patient each in *60-70 B* and *≥70 B*) and infections/infestations (2 patients in *≤60 BR* and 3 in *≥70 BR)*. Thirty patients were hospitalized (Table). Dose reductions were most frequent in the *≥70 B* group (67%) and least in the *60-70 B* and *60-70 BR* groups (17% and 12.0%, respectively) (Table). Dose delays occurred for 1 patient each in the *≤60 BR, 60-70 B,* and *≥70 BR* groups and 4 patients in the *≥70 B* group.

Conclusions

Data from this real-world chart review indicate that bendamustine alone or with rituximab provides high response rates and an acceptable safety profile with low rates of dose delay in all patient age groups (≤60, 60-70, and ≥70) with previously untreated CLL. These findings are similar to those reported in large clinical trials.

Support: Teva Pharmaceutical Industries Ltd.

Table

	<60 BR n=24	*60-70 B* n=12	*60-70 BR* n=50	*>70 B* n=36	*>70 BR* n=95
Mean (SD) age					
At diagnosis	50.3 (6.4)	62.6 (4.9)	63.2 (4.3)	74.5 (5.6)	72.5 (5.5)
Start of therapy	53.1 (6.2)	65.9 (2.1)	65.7 (2.5)	76.9 (4.8)	75.5 (4.5)
Mean dose (mg/m^2) per cycle					
Bendamustine	154.0 (41.5)	153.7 (32.5)	165.9 (27.0)	133.6 (39.0)	147.7 (37.6)
Rituximab	412.1 (107.6)	NA	392.1 (100.4)	NA	402.5 (71.4)
Response					
ORR %	100	83	88	97	90
CR	58	33	44	19	37
PR	42	50	44	78	53
Hospitalizations, patients (%)	3 (13)	2 (17)	6 (12)	5 (14)	14 (15)
Dose reductions, patients (%)	9 (38)	2 (17)	9 (18)	24 (67)	30 (32)
Dose delays, patients (%)	1 (4)	1 (8)	0	4 (11)	1 (1)

Figure: Kaplan-Meier estimates for PFS