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Real-World Efficacy and Safety of Bendamustine With or Without Rituximab in Treatment-Naïve Older Patients With Chronic Lymphocytic Leukemia: Retrospective Analysis by Age Group From a German Registry

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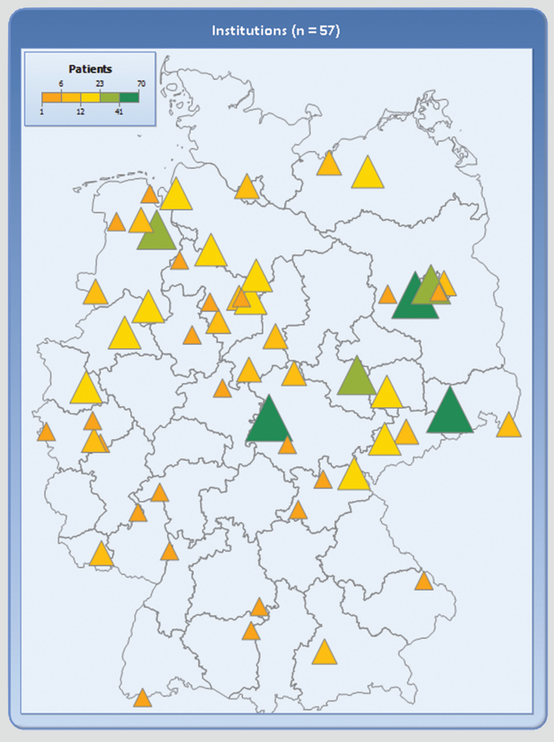
BACKGROUND

- Chronic lymphocytic leukemia (CLL) is the most common form of leukemia among adults in Western countries.[1] With a median age at diagnosis of 72 years, it primarily affects older adults.[1,2]
- Treatment of CLL in this age group remains a challenge as patients are at increased risk for adverse events (AEs) and frequently have comorbidities, both of which restrict treatment options.[1,3,4]
- Bendamustine, a unique alkylating agent with a multi-faceted mechanism of action, is an effective front-line therapy for CLL.[5,6]
- The cytotoxic activity of bendamustine against CLL-derived cell lines is synergized by rituximab, an anti-CD20 monoclonal antibody.[7]
- Large clinical studies have shown overall response rates (ORRs; complete response [CR] + partial response [PR]) of 68% (110/162) for bendamustine[5] and 88% (103/117) for bendamustine plus rituximab (BR)[7] in patients with previously untreated CLL (median age: 63 and 64 years, respectively). However, there are only a few published real-world data; separate recent chart reviews have supported effectiveness and tolerability of bendamustine alone and BR in previously untreated patients.
  - —A subanalysis of a chart review of 71 patients (median age: 72 years, range: 28–90 years) in Austria who received BR demonstrated an ORR of 86% (6/7).[8] A US chart review of 91 patients aged ≥70 years (median age at beginning of therapy: 75.4 and 74 years, respectively) showed ORRs of 50% (5/10) for bendamustine alone and 67% (4/6) for BR.[9]
- The National Comprehensive Cancer Network consensus guidelines recommend BR as a preferred chemoimmunotherapy regimen for older CLL patients or those with comorbidities; in younger patients, the guidelines list BR as a recommended regimen.[6]
- This retrospective analysis assessed real-world efficacy and safety of bendamustine monotherapy or BR in 3 age groups of treatment-naïve CLL patients from a large registry.

METHODS

- Records were obtained for all CLL patients from Projektgruppe Internistische Onkologie, the largest registry of treatment data from 57 private medical oncology practices in Germany (**Figure 1**). Data have been reanalyzed and this poster presents the latest findings.
- Patients received ≥3 cycles of first-line bendamustine monotherapy or BR from May 2008 to November 2011.
- Patients were divided into the following age/treatment groups: ≤60 years receiving BR ± prednisone [*≤60 BR*]; >60 to <70 years receiving bendamustine monotherapy [*60–70 B*] or BR ± prednisone [*60–70 BR*]; ≥70 years receiving bendamustine monotherapy [*≥70 B*] or BR ± prednisone [*≥70 BR*].
- The primary efficacy measure was ORR (CR plus PR); secondary efficacy measures included CR, PR, progression-free survival (PFS), and overall survival (OS).
- Safety measures included AEs and use of concomitant medications (eg, prophylactic antiemetics and antibiotics).
- Statistical analyses for continuous variables were reported as means, medians, standard deviations (SDs), and ranges. Categorical variables were reported using frequencies and proportions. Kaplan-Meier analysis was conducted for PFS and OS.

Figure 1. 57 Medical Oncology Practice Sites From Projektgruppe Internistische Onkologie



RESULTS

- Among 217 patients, ≥61% were male in each group (**Table 1**).
- At diagnosis, all patients had an Eastern Cooperative Oncology Group 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) (**Table 1**).

Table 1. Patient Demographics and Baseline Characteristics

Variable	*≤60 BR* n=24 (P, n=9)	*60–70 B* n=12	*60–70 BR* n=50 (P, n=10)	*≥70 B* n=36	*≥70 BR* n=95 (P, n=19)
Gender, n (%)					
Female	9 (38)	4 (33)	17 (34)	14 (39)	34 (36)
Male	15 (63)	8 (67)	33 (66)	22 (61)	61 (64)
Age at start of therapy, years, mean (SD)	53.1 (6.2)	65.9 (2.1)	65.7 (2.5)	76.9 (4.8)	75.5 (4.5)
Age at diagnosis, years, mean (SD)	50.3 (6.4)	62.6 (4.9)	63.2 (4.3)	74.5 (5.6)	72.5 (5.5)
RAI stage at diagnosis, n (%[a])					
0	2 (11)	1 (11)	9 (27)	2 (9)	7 (16)
I	9 (47)	3 (33)	8 (24)	11 (50)	22 (50)
II	7 (37)	3 (33)	12 (35)	6 (27)	10 (23)
III	1 (5)	0	5 (15)	2 (9)	2 (5)
IV	0	2 (22)	0	1 (5)	3 (7)
Binet stage at diagnosis, n (%)					
A	13 (54)	6 (50)	26 (52)	24 (67)	55 (58)
B	10 (42)	3 (25)	19 (38)	7 (19)	25 (26)
C	1 (4)	3 (25)	5 (10)	5 (14)	15 (16)

[a]Percentage of patients with RAI data.
B, bendamustine; *BR*, bendamustine+rituximab; P, prednisone; SD, standard deviation.

- The most common comorbidities at diagnosis (≥10.0% in any group) were primary hypertension (ranges in all groups: 14.8%–25.0%), chronic ischemic heart disease (12.5% in the *60–70 B* group and 10.1% in the *≥70 BR* group), other chronic obstructive pulmonary disease (12.5% in the *60–70 B* group), and unspecified diabetes mellitus (11.4% in the *≥70 B* group).

Effectiveness Measures

- Observed ORRs were >83% in all groups (**Table 2**); 5 patients in the *60–70 BR* group, 9 patients in the *≥70 BR* group, and 1 patient each in the *60–70 B* and *≥70 B* groups had stable disease; 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.

Table 2. Response Rate

Variable	*≤60 BR* n=24 (P, n=9)	*60–70 B* n=12	*60–70 BR* n=50 (P, n=10)	*≥70 B* n=36	*≥70 BR* n=95 (P, n=19)
ORR[a]	24 (100)	10 (83)	44 (88)	35 (97)	85 (89)
CR	14 (58)	4 (33)	22 (44)	7 (19)	35 (37)
PR	10 (42)	6 (50)	22 (44)	28 (78)	50 (53)
SD	0	1 (8)	5 (10)	1 (3)	9 (10)
PD	0	1 (8)	1 (2)	0	0
Not assessable	0	0	0	0	1 (1)

[a]ORR=complete response+partial response.
B, bendamustine; *BR*, bendamustine+rituximab; CR, complete response; ORR, overall response rate; P, prednisone; PD, progressive disease; PR, partial response; SD, stable disease.

- Median PFS (**Figure 2**) and OS (**Figure 3**) were reached in the *60–70 B* (PFS: 14.8 months, OS: 41.0 months) and *≥70 B* (PFS: 32.2 months, OS: 40.6 months) groups only.

Patterns of Treatment

- Mean dose per cycle ranged from 133.6 to 165.9 mg/m² for bendamustine and 392.1 to 412.1 mg/m² for rituximab, with mean treatment cycles (28 days/cycle) per group ranging from 5.1 to 5.9 (**Table 3**). Median follow-up was 3 years (range 1–5).

Table 3. Patterns of Care

Variable	*≤60 BR* n=24	*60–70 B* n=12	*60–70 BR* n=50	*≥70 B* n=36	*≥70 BR* n=95
Mean dose per cycle (SD)					
Bendamustine, mg/m²	154.0 (41.5)	153.7 (32.5)	165.9 (27.0)	133.6 (39.0)	147.7 (37.6)
Rituximab, mg/m²	412.1 (107.6)	NA	392.1 (100.4)	NA	402.5 (71.4)
Prednisone, mg	288.9 (77.4)	NA	234.5 (70.7)	NA	271.3 (72.0)
Mean cycles administered, n (SD)	5.5 (1.0)	5.9 (1.3)	5.5 (1.1)	5.1 (1.3)	5.4 (1.1)
Hospitalizations, patients (%)	3 (13)	2 (17)	6 (12)	5 (14)	14 (15)
Maximum cycle delay, patients (%)	1 (4)	1 (8)	0	4 (11)	1 (1)
1 week	0	0	0	2 (6)	0
2 weeks	0	1 (8)	0	1 (3)	0
>2 weeks	1 (4)	0	0	1 (3)	1 (1)
Dose reductions, patients (%)	9 (38)	2 (17)	9 (18)	12 (33)	30 (32)
Dose delays, patients (%)	1 (4)	1 (8)	0	4 (11)	1 (1)
Total of GCSF dispensed, n (%)	7 (3)	3 (3)	4 (1)	9 (4)	29 (4)

B, bendamustine; *BR*, bendamustine+rituximab; GCSF, granulocyte colony–stimulating factor; NA, not applicable; SD, standard deviation.

- A total of 30 patients were hospitalized (**Table 3**).
- During the chart-review period, antiemetics were commonly used (≥79% in any group), but granulocyte colony-stimulating factor was infrequently used (**Table 3**).

Tolerability

- 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 18%, respectively); however, dose delays were infrequent in all groups (**Table 3**).
- There were 28 deaths at the time of analysis.
- The most common (>20%) grade 3/4 hematologic AEs were febrile neutropenia in the *≤60 BR* and *≥70 BR* groups, leukopenia in all groups *except 60–70 B*, and thrombocytopenia in the *60–70 B* group only (**Table 4**).

Table 4. Patients With Grade 3/4 Adverse Events (≥2 Patients)

Variable	*≤60 BR* n=24	*60–70 B* n=12	*60–70 BR* n=50	*≥70 B* n=36	*≥70 BR* n=95
Hematologic					
Anemia	2 (8)	2 (17)	1 (2)	1 (3)	5 (5)
Febrile neutropenia	7 (29)	1 (8)	7 (14)	7 (19)	28 (29)
Leukopenia	7 (29)	0	10 (20)	8 (22)	25 (26)
Thrombocytopenia	0	3 (25)	3 (6)	1 (3)	12 (13)
Nonhematologic					
Fatigue	0	1 (8)	0	1 (3)	2 (2)
Infections and infestations (other, specify)	2 (8)	0	0	0	3 (3)

B, bendamustine; *BR*, bendamustine+rituximab.

- Rate of treatment discontinuation due to toxicity ranged from 6% in the *60–70 BR* group to 25% in the *60–70 B* group. (The leading reason for ending therapy was "planned.")
- Few patients were hospitalized (**Table 3**); the leading cause for hospitalization was nonhematologic AEs.

CONCLUSIONS

- In this retrospective, real-world chart review of older patients (age ≤60, 60–70, and ≥70 years) with previously untreated CLL, bendamustine alone or with rituximab provided meaningfully high response rates, with ORRs ≥83%.
- Median PFS and median OS were clinically meaningful, and were reached by 2 of the 5 groups (*60–70 B* and *≥70 B* groups).
- Bendamustine-based therapy also provided an adequate safety profile with low rates of dose delay in all patient age groups.
- These findings are similar to those reported in large clinical trials.

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Figure 2. Progression-Free Survival

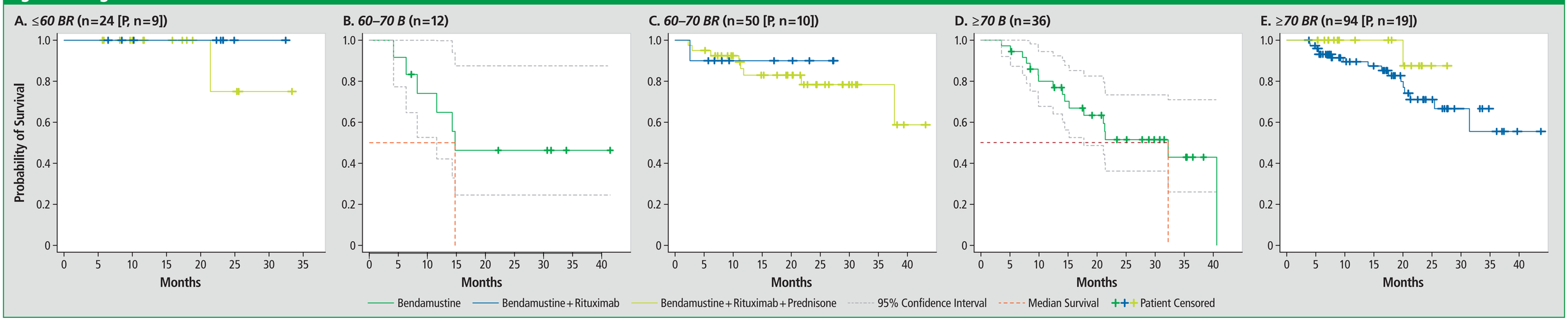
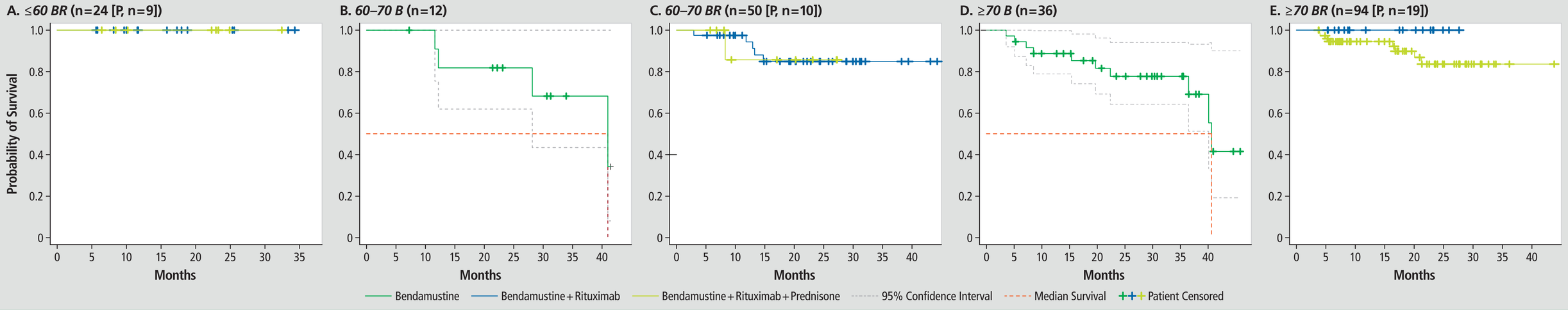


Figure 3. Overall Survival



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