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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

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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} for whom treatment options are often restricted due to comorbidities and greater risk for adverse events (AEs).1,3,4
- Bendamustine, a unique alkylating agent, is effective front-line therapy for CLL.^{5,6}
- —Large clinical studies have shown overall response rates (ORRs; complete response [CR] plus partial response [PR]) of 68% (110/162) for bendamustine⁵ and 88% (103/117) for bendamustine with rituximab (BR)⁷ in patients with previously untreated CLL (median age, 63 and 64 years, respectively).
- Although there are few published real-world data, separate recent chart reviews support the effectiveness and tolerability of bendamustine alone and BR in previously untreated patients ≥70 years of age.8,9
- This retrospective analysis assessed real-world efficacy and safety of bendamustine alone and BR in 3 age groups of treatment-naïve patients with CLL from Projektgruppe Internistische Onkologie, the largest registry of treatment data from private medical oncology practices in Germany.

METHODS

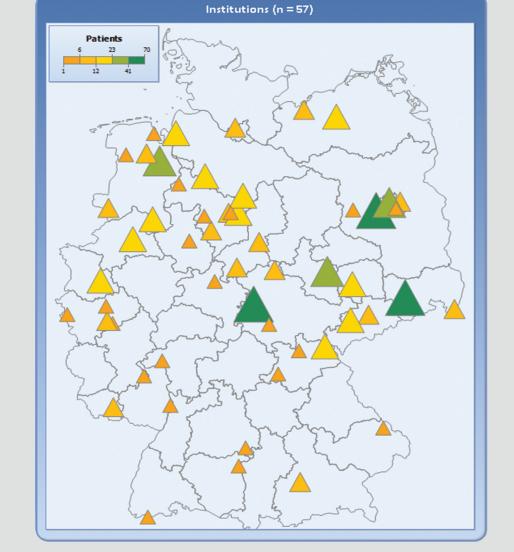
- Records were obtained for all patients with CLL treated from May 2008 to July 2011 in a registry from 57 German oncology practices (Figure 1). Data have been reanalyzed and this poster presents the latest findings.
- Patients received ≥3 cycles of first-line bendamustine monotherapy or BR.
- Patients were divided into the following age/treatment groups: —≤60 years of age; BR±prednisone (P) [≤60 BR];
- —>60 to <70 years of age; bendamustine monotherapy [60–70 B];
- ->60 to <70 years of age; BR±P [60–70 BR];

-≥70 years of age; BR±P [≥70 BR].

(PFS), and overall survival (OS).

- -≥70 years of age; bendamustine monotherapy [≥70 B];
- The primary efficacy measure was ORR (CR plus PR); secondary efficacy measures included CR, PR, progression-free survival
- Safety measures included AEs and use of concomitant medications (eg, prophylactic antiemetics such as 5-HT3 antagonists).
- 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. Medical Oncology Practice Sites from Projektgruppe Internistische Onkologie



RESULTS

 A total of 217 patients with CLL from the registry (≥61% male in each group) were included in the analysis (**Table 1**).

Variable	≤60BR n=24 (P, n=9)	60-70B n=12	60-70BR n=50 (P, n=10)	≥70 <i>B</i> n=36	≥70BR 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, years, mean (SD)					
At diagnosis	50.3 (6)	62.6 (5)	63.2 (4)	74.5 (6)	72.5 (6)
Start of therapy	53.1 (6)		` '	76.9 (5)	
Rai stage at diagnosis, n (%)					
0	2 (8)	1 (8)	9 (18)	2 (6)	7 (7)
1	9 (38)	3 (25)	8 (16)	11 (31)	
I	7 (29)	3 (25)	12 (24)	6 (17)	10 (11)
III	1 (4)	0	5 (10)	2 (6)	2 (2)
IV	0	2 (17)	0	1 (3)	3 (3)
Missing	5 (21)	3 (25)	16 (32)	14 (39)	51 (54)
Binet stage at diagnosis, n (%	5)				
A	13 (54)	6 (50)	26 (52)	24 (67)	55 (58)
В	10 (42)	3 (25)	19 (38)	7 (19)	25 (26)
C	1 (4)	3 (25)	5 (10)	5 (14)	15 (16)

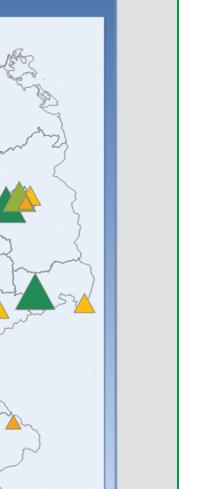
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Bendamustine is FDA-approved for adults with chronic lymphocytic leukemia or indolent B-cell non-Hodgkin's lymphoma that has progressed during or within 6 months of treatment with rituximab or a rituximab-containing regimen.

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- B, bendamustine; BR, bendamustine plus rituximab; CR, complete response; ORR, overall response rate; P, prednisone; PD, progressive disease; PR, partial response; SD, stable disease.
- PFS and OS data by age and treatment group are presented in **Figures 2** and **3**.
- Median PES and OS were reached in the 60–70 B (PES, 14.8) months; OS, 41.0 months) and \geq 70 B (PFS, 32.5 months; OS, 40.1 months) groups only (Figure 2, B and D; Figure 3, B and D).

Patterns of Treatment

dispensed, n (%)

5-HT3 antagonists

Dopamine antagonists

 Median number of treatment cycles (28 days/cycle) was 6 (ranges, from 3–6 to 3–8) in all groups except for the \geq 70 B group in which it was 5.5 (range, 3–8) (**Table 3**).

Table 3. Patterns of Treatment 60–70BR Dose per cycle, mean (SD) 165.9 (27.0)392.1 Rituximab, mg/m 234.5 Prednisone, mg (70.7)Cycles administered, n,

0	2 (6)	0	
0	1 (3)	0	
0	1 (3)	1 (1)	
(12)	5 (14)	14 (15)	•

7(3) 3(3) 4(1) 9(4) 29(4)

• 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),

Effectiveness Measures

 Observed ORRs were high (≥83%) in all age/treatment groups (Table 2).

and unspecified diabetes mellitus (11.4% in the \geq 70 B group).

Table 2. Response Rates					
Variable, n (%)	≤60 <i>BR</i> n=24 (P, n=9)	60–70B n=12	60-70BR n=50 (P, n=10)	≥ <i>70B</i> n=36	≥70BR n=95 (P, n=19)
ORRª CR PR	24 (100) 14 (58) 10 (42)	10 (83) 4 (33) 6 (50)	44 (88) 22 (44) 22 (44)	35 (97) 7 (19) 28 (78)	85 (89) 35 (37) 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)

- Median follow-up was 3 years (range, 1–5).

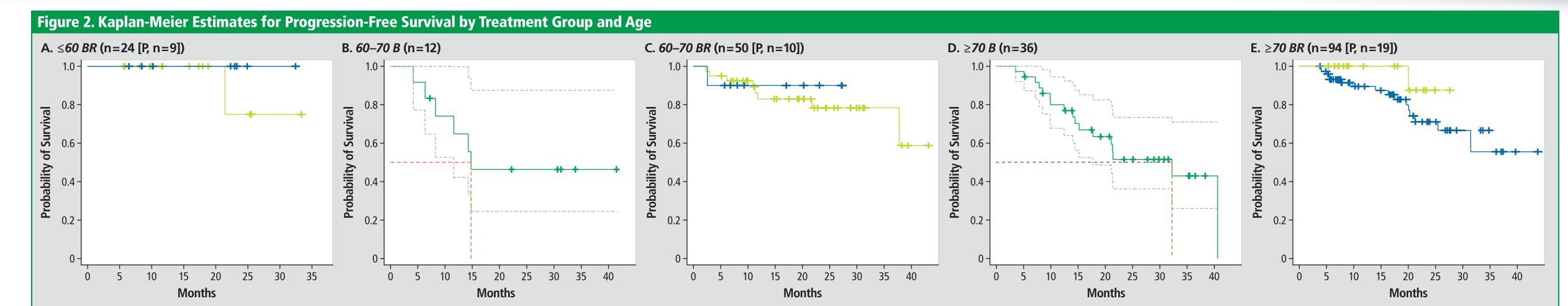
n=24 *60-70B* n=50 ≥*70B* n=95 (P, n=9) n=12 (P, n=10) n=36 (P, n=19)133.6 147.7 (39.0) (37.6) NA NA 271.3 6 (3–6) 6 (4–8) 6 (3–6) 5.5 (3–8) 6 (3–8) 2 (17) 9 (18) 24 (67) 30 (32) Dose delays, patients, n (%) 1 (4) 1 (8) 0 4 (11) 1 (1) Maximum duration of delay, >2 weeks Hospitalizations, patients, n (%) 3 (13) 2 (17) Concomitant medications

B, bendamustine; BR, bendamustine plus rituximab; GCSF, granulocyte colony-stimulating factor; NA, not applicable; P, prednisone; SD, standard deviation.

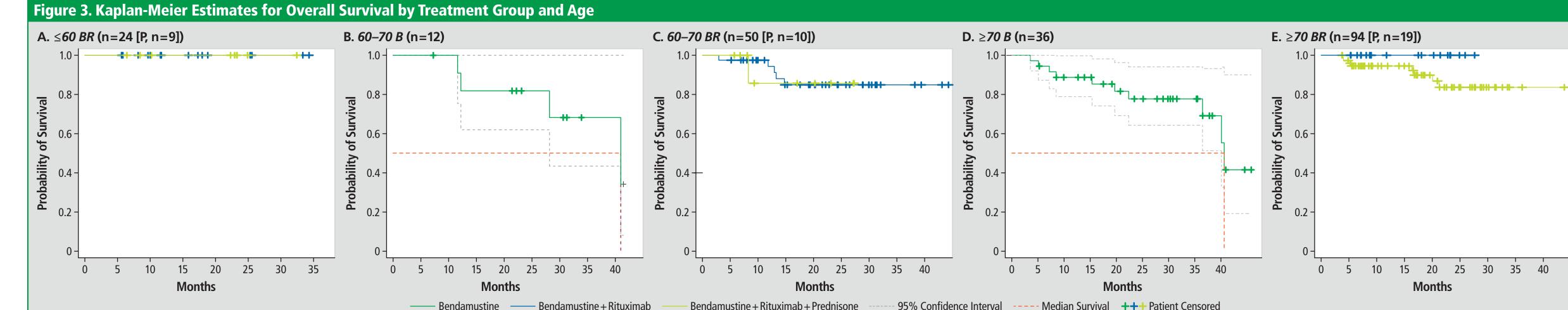
73 (31) 51 (57) 143 (39) 121 (53) 326 (40)

54 (23) 20 (22) 103 (28) 44 (19) 162 (20)

38 (16) 4 (4) 71 (19) 0 136 (17)



B, bendamustine; BR, bendamustine plus rituximab; P, prednisone.



B. bendamustine; BR, bendamustine plus rituximab; P, prednisone.

- 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 in those groups.
- During the chart-review period, 5-HT3 antagonists, dopamine antagonists, and antihistamines were commonly used, but granulocyte colony-stimulating factor was infrequently used (**Table 3**).

Tolerability

- The most common (>20%) grade 3/4 hematologic AEs were febrile neutropenia and leukopenia (**Table 4**).
- The most common grade 3/4 nonhematologic AEs included fatigue and infections/infestations (**Table 4**).
- Rate of treatment discontinuation due to toxicity ranged from 6.0% in the 60-70 BR group to 25.0% in the 60-70 B group.
- A total of 30 patients were hospitalized (**Table 3**) for a total of 33 events.

Table 4. Grade 3/4 Adverse Events (≥2 Patients) by Age and Treatment

Variable, n (%)	≤60BR n=24 (P, n=9)	60–70 <i>B</i> n=12	60-70BR n=50 (P, n=10)	≥ <i>70B</i> n=36	≥70BR n=95 (P, n=19)	
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	2 (8)	Ò	0	Ò	3 (3)	

B, bendamustine; BR, bendamustine plus rituximab; P, prednisone.

— Nineteen hospitalizations were attributed to nonhematologic events, 6 to hematologic, and 8 to other causes.

There were 28 deaths at the time of analysis.

CONCLUSIONS

- This retrospective, real-world chart review of patients with previously untreated CLL demonstrated that bendamustine monotherapy or BR is safe and effective in older patients (≥70 years of age).
- —Response rates were similar to those seen in younger patients, with ORRs of 89%–97% in patients ≥70 years of age compared with ORRs of 83%-100% in patients <70 years of age.
- —An acceptable safety profile was seen across age/treatment groups.
- A pattern of increase in AEs with age was not observed, although the number of participants in some age/treatment groups was too small in relation to others for definitive comparison.
- Low rates of dose delay were seen in all patient age groups, although dose reductions were often required, particularly in patients ≥70 years of age receiving bendamustine monotherapy.
- Promising survival rates were seen; at a median follow-up of 3 years, median PFS and OS were reached by Kaplan-Meier analysis in 2 of 5 groups (the 60-70 B [14.8 and 41.0 months, respectively] and ≥70 B groups [32.5 and 40.1 months]) and not yet reached in the other groups at the time of analysis.
- These findings are similar to those reported in large clinical trials.

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