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Abstract 3922 Bendamustine in Chronic Lymphocytic Leukemia (CLL): Outcome According to Different Clinical and Biological Prognostic Factors in Everyday Practice

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Backgrounds

The therapeutic activity of Bendamustine ± Rituximab in CLL patients and, in particular, its effect in relationship to clinical and biologic prognostic factors has been analysed only in few studies.

Purpose

To evaluate in the contest of everyday practice the efficacy and safety of Bendamustine ± Rituximab in CLL patients according to different clinical and biological risk groups.

Patients and Methods

Nine hematological centers from the North-East of Italy reported retrospectively their experiences regarding the use of Bendamustine in CLL. Outcome and survival analyses were stratified according to the patients' clinical characteristics, previous treatments and cytogenetics. Response status and toxicity were assessed according to IWCLL (Hallek 2008) and to CTCAE V 4.0.

Results

Clinical data of 142 patients affected by CLL (median age 70 years, range 31-88; 92 males) treated with Bendamustine between January 2005 and June 2012, were analyzed. The investigated series included 39% go-go, 69% slow-go and 2% no-go patients (according to Eichhorst 2009); 11%, 46% and 43% of patients had Binet stage A, B and C, respectively. 19 slow-go patients (13%) were untreated; for the remaining patients, the median number of previous treatments was 2 (range 1-8); 60% of patients previously received a Fludarabine containing regimen; 11% of patients each had stable disease or no response to the last previous treatment. Cytogenetic data was available in 108 patients, being positive for 11q- and 17p- in 27% and 22%, respectively; 70% of patients had an unmutated IGHV status. Bendamustine was administered on day 1 and 2 for a median number of 4 cycles (range 1-6) every 28 days at a dosage of 60-70 mg/m^2 in 56% of patients and at 80-100 mg/m^2 in 44%; Bendamustine was combined with Rituximab in 84%. 132 patients were valuable for efficacy. Overall 69% responded to Bendamustine; Table 1 summarizes the efficacy results considering different clinical and biological risk groups. Higher response rates were observed among patients with early Binet stage, less number of previous treatments, non 17p- cytogenetic, and in those who received Bendamustine in combination with Rituximab. Median follow up was 9.5 months; overall 1 year estimated PFS and OS were 51%±5% and 76%±2%; significant better 1 year PFS was achieved in patients with previous response to Fludarabine containing regimen, £ 2 previous lines of therapy, absence of 17p-, mutated IGHV status, Rituximab combination. Grade 3-4 neutropenia, infectious complications, thrombocytopenia and anemia occurred in 40%, 13%, 11% and 12% of patients, respectively; extra-hematological toxicity was nearly absent. 37 patients died, 23 for causes strictly related to disease progression, 8 because of infections, 1 for colon carcinoma and 5 for other unrelated reasons.

Conclusions

Although the main clinical and biological prognostic factors which influence the response to Fludarabine containing regimens and, in particular, the presence of 17p- seem not to be overcome by Bendamustine therapy, this drug appeared an active and safe agent for the treatment of patients with CLL (including those with 11q-) in everyday practice, thus suggesting its role as an alternative therapeutic option particularly for "slow-go" patients. The addition of Rituximab to Bendamustine improves response rate and PFS.

Table 1

	Valuable patients	OR (%)		CR (%)	PR (%)	1 year estimated PFS	
All patients	132	91 (69)	/	20 (15)	71 (54)	51%±5%	/
Age </= 60 years	23	11 (48)	P=0.01	3 (13)	8 (35)	50%±10%	P=.68
Age > 60 years	109	80 (73)		17 (15)	63 (58)	51%±5%	
Go-go	53	39 (74)	P=0.08	9 (17)	30 (57)	61%±7%	P=0.002
Slow-go	77	52 (67)		11 (14)	41 (53)	46%±7%	
No-go	2	0		0	0	0%	
Binet stage A	12	11 (92)	P=0.001	1 (9)	10 (83)	75%±15%	P=0.004
stage B	49	42 (85)		11 (22)	31 (63)	59%±8%	
stage C	48	27 (56)		5 (10)	22 (46)	39%±8%	
</= 2 previous treatments	90	72 (80)	P<0.0001	17 (19)	55 (61)	67%±6%	P<.0001
> 2 previous treatments	42	19 (45)		3 (7)	16 (38)	16%±7%	
Fludarabine sensitive	65	41 (63)	P=0.67	7 (11)	34 (52)	56%±5%	P= .0003
Fludarabine refractory	11	7 (64)		1 (9)	6 (55)	9%±8%	
No 11q- or 17p-	52	42 (81)	P<0.0001	13 (25)	29 (56)	66%±9%	P<.0001
11q-	26	22 (85)		3 (12)	19 (73)	62%±10%	
17p-	24	6 (25)		0	6 (25)	20%±8%	
IGHV unmutated	53	34 (64)	P=0.41	8 (15)	26 (49)	43%±8%	P=.05
IGHV mutated	23	16 (69)		7 (30)	9 (39)	63%±11%	
Bendamustine monotherapy	24	11 (46)	P=0.006	1 (4)	10 (42)	29%±10%	P=0.009
Bendamustine + Rituximab	110	80 (72)		19 (17)	61 (55)	55%±6%	

Disclosures: Zaja: *Mundipharma:* Honoraria. **Fanin:** *Mundipharma:* Honoraria.