Bendamustine Retreatment of CLL in the Outpatient Setting – High Activity and Tolerability

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Background

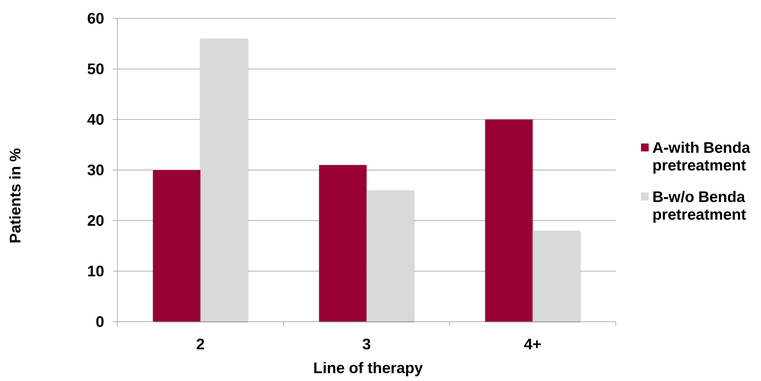
Several studies have proven that Bendamustine is a highly active drug in the therapy of CLL (1,2). Nevertheless, only few data exist about the real-life use and efficacy of Bendamustine therapies in the non-trial setting. The project group of internal oncology (PIO/Germany) therefore implemented a registry for routine use of Bendamustine in patients with CLL (3). Since 2008 a total of 614 patients have been registered, out of which 494 have been thoroughly documented. To evaluate whether a retreatment with Bendamustine in relapsed CLL is still active and well tolerable we present comparative data on therapies in patients with (group A) or without (group B) Bendamustine pretreatment.

Methods

232 documented patients from 67 office based sites in Germany were retrospectively appointed to one of two groups. The relapsed patients were treated in the time period from May 2008 till September 2010:

	Group A (with Benda pretreatment)	Group B (without Benda pretreatment)
n	87	145
Gender m/f	57/30	88/57
Median age (range)	74 (51-86)	72 (45-93)
Ratio B/B+Rituximab in %	54/46	51/49
ECOG 0/1/2 in %	13/63/**24**	21/64/**15**
Binet A/B/C in %	3/**53/44**	4/**45/51**

Patient characteristics - Distribution by line of therapy



Bendamustine treatment : Number of cycles and dose intensity

	Median no of cycles	Number of cycles	Median Benda dose intensity*
with Benda (n=87)	5	376	150,2 mg/m^2
w/o Benda (n=145)	6	654	154,5 mg/m^2

*Bendamustine was administered according to standard proven clinical trials regimens (1+2d q4w).

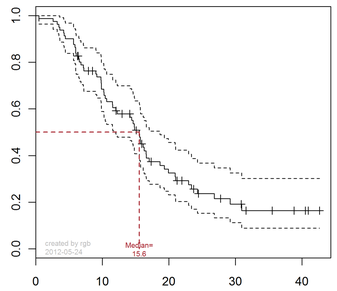
Results - Activity

In the group with Bendamustine pretreatment the ORR was 80% and the median PFS lasted 15.6 months. In the patients without prior Bendamustine treatment the ORR was 84% and the median PFS lasted 20.8 months.

Progression free survival – PFS

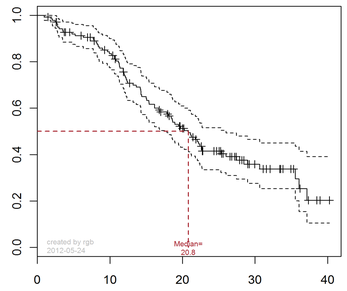
With Benda pretreatment (n=81*)

median=15.6 months



Without Benda pretreatment (n=141*)

median=20.8 months

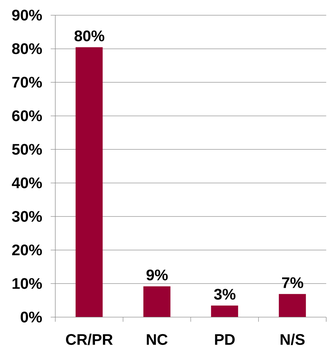


*Patients with unconfirmed outcome excluded from PFS calculation

Overall response rate – ORR

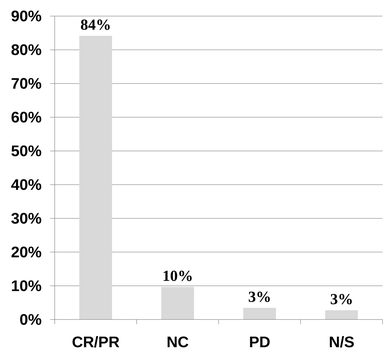
With Benda pretreatment (n=87)

ORR = 80%



Without Benda pretreatment (n=145)

ORR = 84%



CR/PR, complete/partial response; NC, no change; PD, progress in disease; N/S not specified

Results - Tolerability

The grade 3/4 toxicities were mostly hematologic and comparable in both groups. Similar grade 3/4 toxicities were observed for neutropenia (about 25% of the patients), thrombocytopenia (16%).

Hematological toxicities – Grade 3/4

	with Benda pretreatment		without Benda pretreatment	
	Number of cycles	%	Number of cycles	%
Anemia	17	5%	17	3%
Thrombocytopenia	23	6%	46	7%
Leucopenia	44	12%	82	13%
Neutropenia	55	15%	75	11%
Total cycles	376	100%	655	100%

Non hematological toxicities were neglectable in both groups with about 12% NCI/CTC grade 3 toxicities and no grade 4 toxicities. Infection rate was about 5%.

Conclusion

- **Bendamustine is broadly used in the routine treatment of CLL.**
- **Bendamustine-therapies show impressive high activity and tolerability, even in an advanced-line context with prior exposure to Bendamustine.**
- **The treatment results are comparable to results of clinical trials and underline the quality and feasibility of Bendamustine in the outpatient treatment.**
- **The patients from this registry adequately reflects the treatment reality in the outpatient setting as the patients are older with more comorbidities, ECOG is worse and the Binet stages are more advanced.**
- **Nevertheless, it is to note that this is a registry and that both groups therefore are not composed of randomized patient-populations. (e.g ECOG, patients in lines and ratio of rituximab combinations).**

Entrance of the IMET, the institute where Bendamustine was synthesized first (4). Today it is the Hans-Knöll-Institute / Jena, Germany.
Fresco is showing a hero (drug) fighting against a dragon (disease).

References

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2. Fischer et al. J Clin Oncol. 2011;29(26):3559-3556
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4. Ozegowski W et al. J Prakt Chem. 1963;20:178–86

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Georg Guenther - Consultant or Advisory Role – Mundipharma; Honoraria - Mundipharma
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