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Introduction

Recent data from phase III clinical trials showed that in previously untreated patients with indolent (low-grade) non-Hodgkin's lymphoma (iNHL) bendamustine plus rituximab (BR) resulted in superior progression-free survival (STiL NHL 1-2003) and non-inferior response rates (STiL NHL 1-2003, Rummel *et al.*, 2013 and BRIGHT, Flinn *et al.*, 2012) compared to R-CHOP. Since clinical trials are restricted to highly selected patients, we here investigated effectiveness of BR and R-CHOP in unselected patients treated in routine practice by German office-based haematologists.

Methods

The open, longitudinal, multicentre, clinical registry on lymphoid neoplasms (TLN Registry, ClinicalTrials.gov registry NCT00889798) prospectively collects data on the treatment of patients with lymphoid B-cell neoplasms as administered by a network of German office-based haematologists. Patients are followed for 5 years. A broad set of data regarding patient and tumour characteristics, comorbidities, all systemic treatments and response rates, progression-free survival and overall survival are recorded. Automated plausibility and completeness checks with subsequently generated queries by the electronic data capture system ensure data reliability. In addition, data managers regularly check for plausibility and issue queries. Since May 2009, 115 sites (currently 259 haematologists) have recruited a total of 3383 patients.

Results

BR is the most frequently used 1st-line regimen

947 patients with iNHL were recruited at the onset of their 1st-line therapy. The choice of therapy was at the discretion of the treating physician in accordance with the patient's informed consent. The most frequently used regimens were BR (n=640, 68%) and R-CHOP (n=145, 15%). Since 2009 BR has been used more frequently, while use of R-CHOP has decreased (Figure 2).

The following analysis is based on 785 patients with iNHL (53% follicular, 17% marginal zone (including MALT), 13% mantle cell lymphoma, 13% immunocytoma), treated with either BR or R-CHOP.

Patient characteristics differ between BR and R-CHOP

Overall, patients were median 69 years (yrs) old (range 24-93 yrs, mean 66 yrs), 52% were male, 53% had tumour stage IV (Ann Arbor), 24% presented with B symptoms, 24% with bulky disease, and 63% with at least one comorbidity.

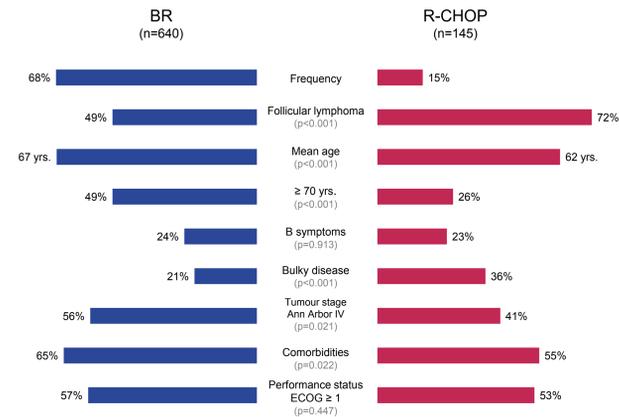


Figure 1: Patient characteristics in 1st-line treatment with BR or R-CHOP

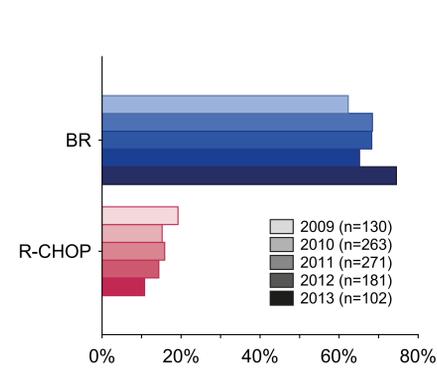


Figure 2: Frequency of 1st-line treatment with BR or R-CHOP over time

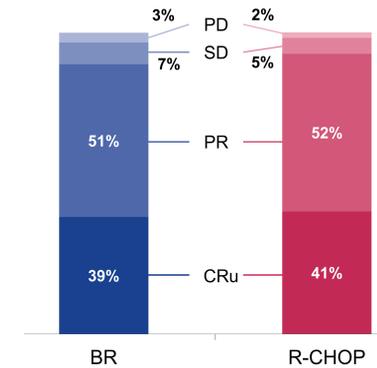


Figure 3: Best response in 1st-line treatment with BR or R-CHOP

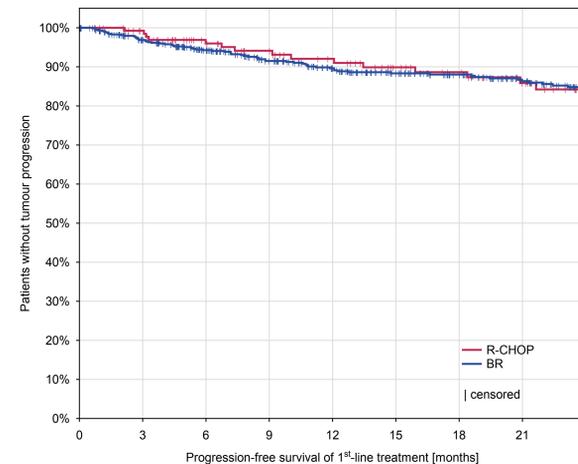


Figure 4: Progression-free survival (PFS) since start of 1st-line treatment with BR or R-CHOP

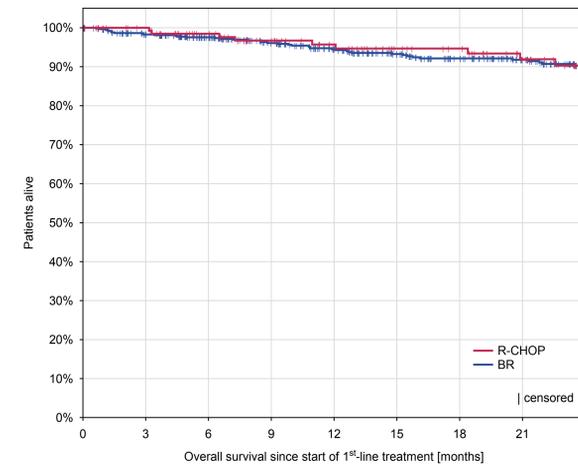


Figure 5: Overall survival (OS) since start of 1st-line treatment with BR or R-CHOP

Clinical and tumour characteristics differed between patients receiving BR or R-CHOP: Patients treated with BR were older (mean 67 vs. 62 yrs; p<0.001), presented more often with stage IV disease (56% vs. 41%; p=0.021) or comorbidities (65% vs. 55%; p=0.022), whereas patients treated with R-CHOP were more often diagnosed with follicular lymphoma (72% vs. 49%; p<0.001) and presented more frequently with bulky disease (36% vs. 21%; p<0.001) (Figure 1).

Objective response rate between BR and R-CHOP is similar

Objective response rate (ORR) as assessed by the local site was similar (p=0.817) between the two regimens: 90% of patients receiving BR (39% unconfirmed complete response (CRu)) and 93% receiving R-CHOP (41% CRu) responded to 1st-line therapy (Figure 3). On average patients received 5 cycles of BR or 6 cycles of R-CHOP, respectively. Both groups received a mean of 6 cycles rituximab.

In univariate analyses young age, male sex, follicular subtype and absence of comorbidities were significantly associated with an objective clinical response to the 1st-line regimen. In a multiple logistic regression analysis adjusted for type of 1st-line regimen (BR vs. R-CHOP) and age at the onset of therapy, the likelihood for response was lower for older patients (OR=0.97; p=0.015), while the type of 1st-line regimen had no effect (OR=1.28; p=0.537). At this point, the small number of non-responders (n=57) precluded analyses of more than two potential confounders.

Overall survival between BR and R-CHOP is similar

After a median follow-up of 22 months (maximum 51 months), 92% of patients receiving BR are alive (Figure 5), 89% are progression-free (Figure 4) and 8% received 2nd-line therapy. Of patients receiving R-CHOP, 91% are alive (Figure 5), 90% are progression-free (Figure 4) and 10% of patients received 2nd-line therapy. Overall, 5% of all patients have been lost to follow-up (Figure 4).

Conclusion

Our data show that previously untreated patients with iNHL receiving BR or R-CHOP in routine practice differ, with BR preferentially given to patients with a less favourable prognostic profile. Nevertheless, response rates to 1st-line treatment with BR or R-CHOP are similar. These results, from unselected patients treated in routine practice, favourably support response data from the clinical trials NHL 1- support response data from the NHL 1-2003 (StiL, Rummel *et al.*) and the BRIGHT (Flinn *et al.*, 2012) study.

In collaboration with:



Abbreviations:
BR: bendamustine + rituximab ± prednisone | R-CHOP: cyclophosphamide + doxorubicin + vincristine + prednisone + rituximab
CRu: unconfirmed complete response | PD: progressive disease | PR: partial response | ORR: overall response rate | PFS: progression-free survival | OS: overall survival | SD: stable disease

ECOG: Eastern Cooperative Oncology Group | iNHL: indolent (low-grade non-Hodgkin's lymphoma) | MALT: mucosa-associated lymphoid tissue | TLN: Tumour Registry on Lymphoid Neoplasms | yrs: years

References:
Rummel MJ, Niederle N, Maschmeyer G, Banat GA, von Grünhagen U, Losen C, u. a. Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial. *Lancet*. 2013; 381 (9873):1203–10.

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Disclosures:
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