Response to 1st-line treatment with BR or FCR in patients with chronic lymphocytic leukaemia
First outcome data from the German prospective TLN Registry

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Introduction

Fludarabine, cyclophosphamide, and rituximab (FCR) is currently considered the standard of care for medically fit patients with untreated chronic lymphocytic leukaemia (CLL). However, due to its significant haematological toxicity other, potentially less toxic regimens are currently under investigation. Results of the phase III trial CLL 10 of the German CLL-Study Group (GCLLSG) comparing FCR to bendamustine, rituximab (BR) are eagerly awaited.

Since clinical trials are restricted to highly selected patients, we here investigated effectiveness of BR and FCR in unselected patients with CLL treated in routine practice by German office-based haematologists.

Methods

The open, longitudinal, multicentre, clinical registry on lymphoid neoplasms (TLN Registry, ClinicalTrial.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 actively recruited a total of 3383 patients.

Results

BR is the most frequently used 1st-line regimen

620 patients with CLL 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=348, 56%) and FCR (n=137, 22%). Since 2009 BR has been used more frequently, while the use of FCR has decreased (Figure 2).

The following analysis includes 485 patients treated with either BR or FCR.

Patient characteristics differ between BR and FCR

Overall, patients were median 70 years (yrs) old (range 21-92 yrs, mean 68 yrs), 67% male, 42% had Binet stage C, 29% presented with B symptoms, 13% with bulky disease and 66% with at least one comorbidity.

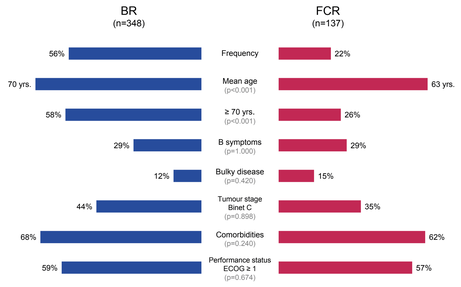

Figure 1: Patient characteristics in 1st-line treatment with BR or FCR

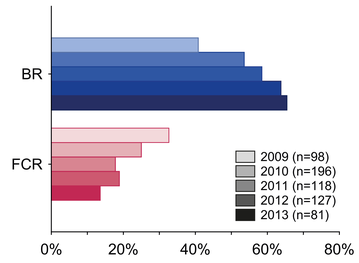

Figure 2: Frequency of 1st-line treatment with BR or FCR over time

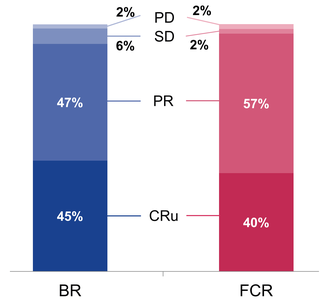

Figure 3: Best response in 1st-line treatment with BR or FCR

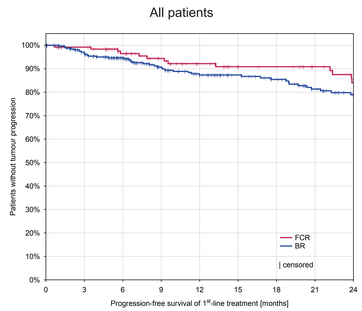

Figure 4a: Progression-free survival (PFS) since start of 1st-line treatment with BR or FCR

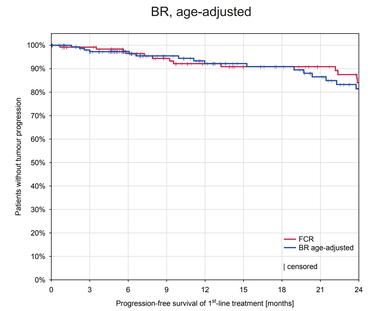

Figure 4b: Progression-free survival (PFS) since start of 1st-line treatment with BR (age-adjusted) or FCR

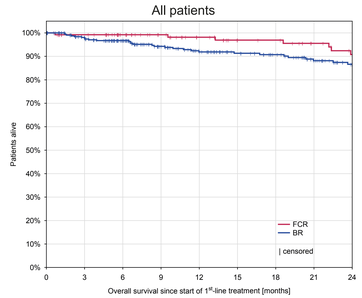

Figure 5a: Overall survival (OS) since start of 1st-line treatment with BR or FCR

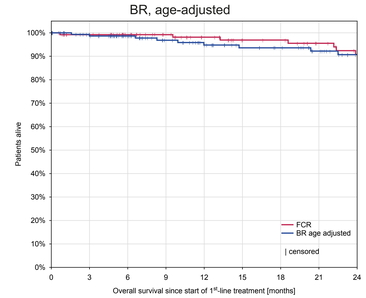

Figure 5b: Overall survival (OS) since start of 1st-line treatment with BR (age-adjusted) or FCR

Clinical and tumour characteristics differed between patients receiving BR or FCR: Patients treated with BR were older (mean 70 vs. 63 yrs; p<0.001) and presented more often with stage Binet C (44% vs. 35%) or comorbidities (68% vs. 62%) (Figure 1).

Objective response rate between BR and FCR is similar

Objective response rate (ORR) as assessed by the local site was similar (p=0.164): 92% of patients receiving BR and 97% receiving FCR responded to 1st-line therapy; the clinical (unconfirmed) complete remission rate (CRu) was reported to be 45% after BR and 40% after FCR, respectively (Figure 3). On average, patients received a mean of 5 cycles BR or FCR and rituximab.

In univariate analyses none of the parameters tested (type of 1st-line regimen, age, sex, B symptoms, bulky disease, tumour stage, comorbidities) had a significant impact on the response rate. Also, in a multivariate logistic regression model adjusted for the type of regimen (BR vs. FCR) and age neither factor had a significant impact on the response rate. At this point the small number of non-responders (n=24) precluded calculation of models adjusted for more than two parameters.

Overall survival between BR and FCR is similar

After a median observation time of 22 months (maximum 52 months), 89% of patients receiving BR are alive (Figure 5a), 84% are progression-free (Figure 4a) and 10% have received 2nd-line therapy. In patients receiving FCR 92% are alive (Figure 5a), 89% are progression-free (Figure 4a) and 8% have received 2nd-line therapy. Overall 5% of patients have been lost to follow-up.

Since age is a prognostic factor, overall survival was also analysed in age-adjusted groups receiving BR or FCR, respectively. 93% of patients receiving BR (mean age 63 yrs, n=169) and 92% of patients receiving FCR (mean age 63 yrs, n=137) are alive (Figure 5b).

Conclusion

Our data show that previously untreated patients with CLL receiving BR or FCR in routine practice differ, with BR preferentially given to older patients with comorbidities. Nevertheless, response rates to 1st-line treatment with BR or FCR are similar. BR is an effective and well tolerated treatment for elderly and medically less fit patients. BR may also present an alternative 1st-line treatment to medically fit patients with CLL.

In collaboration with:

AKS Arbeitskreis klinische Studien e.V.

Kompetenznetz Maligne Lymphome

Abrevations:
BR: bendamustine + rituximab ± prednisone | FCR: fludarabine + cyclophophamide + rituximab ± prednisone

CRu: unconfirmed complete response | PD: progressive disease | PR: partial response | ORR: overall response rate | PFS: progression-free survival | OS: overall survival | SD: stable disease

CLL: chronic lymphocytic leukaemia | ECOG: Eastern Cooperative Oncology Group | TLN: Tumour Registry on Lymphoid Neoplasms | yrs: years

ASH 2013 New Orleans
Publication Number 4181
Submission ID 57276

Disclosures:
Knauf: Mundipharma, Janssen, Roche Pharma: Consultancy, Honoraria.