memo (2009) Vol. 2: 103
DOI 10.1007/s12254-009-0116-8
Printed in Austria
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memo
magazine of european medical oncology

Chronic lymphocytic leukaemia

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Received 8 February 2009; accepted 3 March 2009

The dominating clinical presentations concerning CLL at this year's ASH meeting were given on the results of two large randomized phase III trials exploring the use of rituximab (R) in addition to fludarabine and cyclophosphamide (FC). The data of these trials as well as a phase II trial applying R-Bendamustin convincingly demonstrated the clinical benefit of chemoimmunotherapy in CLL, at least for the younger and physically fit patients without del17p.

Keywords: CLL, R-FC, standard therapy, Bendamustin, first line therapy, relapse therapy

Regarding CLL therapy the presentation of the CLL8 trial conducted by the German CLL Study Group was certainly a highlight [1]. In this multicentric phase III study, 817 previously untreated patients (median age 65 years) without significant comorbidities as assessed by the cumulative illness rating scale (CIRS < 6) were randomized to receive 6 cycles of FC (fludarabine 25 mg/m² iv in combination with cyclophosphamide 250 mg/m² over three days) with or without rituximab (R) 375 mg/m² on day 0 in cycle 1 and 500 mg/m² on day 1 in subsequent cycles. Concerning safety, no significant differences were found between both treatment arms with the exception of the incidence of °III/IV neutropaenia which occurred more often during treatment with FCR (33.7% vs 21%, $p < 0.0001$). However, this did not translate into a higher risk of infection. Concerning efficacy, the addition of rituximab resulted in significantly better overall response rate (ORR) than with FC alone (95% vs 88%, $p < 0.01$) as well as a significantly higher complete remission (CR) rate (45% vs 23%, $p < 0.01$). The progression-free survival (PFS) was also significantly longer in the FCR arm (43 months vs 32 months, $p < 0.00001$), whereas after a median follow-up of 25 months no impact on overall survival has been detectable. A detailed cytogenetic analysis of this trial was presented in a separate abstract [2]. Of note, patients with clinically often problematic del11q receiving FCR showed higher CR rates (61.5% vs 13.8%, $p < 0.001$) and also a longer PFS than those receiving FC. However, patients displaying del17p aberrations had no benefit by adding rituximab to the FC protocol. These data confirm the excellent efficacy of FCR in the first-line therapy of CLL for younger and physically fit patients without del17p.

In the REACH study the FCR regimen was also tested against FC as a second-line treatment [3]. In this multicentre phase III trial a total of 552 previously treated patients (median age 62 years; most patients had received alkylator-based first-line therapy) were randomized to receive either FC or FCR for a maximum of 6 cycles. In parallel to the CLL8 study the addition of rituximab was well tolerated and resulted in significantly higher OR (70% vs 58%; $p < 0.01$) and CR rates (24% vs 13%, $p < 0.001$). Again PFS was significantly longer in the FCR arm (30.6 months vs 20.6 months; $p = 0.0002$) whereas at a median follow-up of 25 months no differences have been detectable concerning overall survival. Although preliminary, cytogenetic data from this trial also suggests a particular benefit for patients with del11q, but not for patients with del17p. In conclusion, both trials showed that the concept of chemo-immunotherapy containing rituximab is a very effective strategy in B-CLL. In particular, patients with del11q may benefit from rituximab-based regimens such as FCR. However, for patients with del17p alemtuzumab-based therapy may be more effective [4].

Conflict of interest

The authors declare that there is no conflict of interest.

References

- [1] Hallek M, Fingerle-Rowson G, Fink AM, Busch R, et al. Chemoimmunotherapy with fludarabine (F), cyclophosphamide (C) and rituximab (R) versus fludarabine and cyclophosphamide (FC) improves response rates and progression-free survival of previously untreated patients with advanced chronic lymphocytic leukemia. *Blood*, 112: 11, 2008 (abstract #325).
- [2] Stilgenbauer S, Zenz T, Winkler D, Bühler A, et al. Genomic aberrations, VH mutation status and outcome after fludarabine and cyclophosphamide (FC) or FC plus rituximab (FCR) in the CLL8 trial. *Blood*, 112: 11, 2008 (abstract #781).
- [3] Robak T, Moiseev SI, Dmoszynska A, Solal-Célgny P, et al. Rituximab plus fludarabine and cyclophosphamide (R-FC) vs. FC alone in relapsed/refractory CLL: final results of REACH BO17072 trial. *Blood*, 112: 11, 2008 (late breaking abstract #1).
- [4] Stilgenbauer S, Zenz T, Winkler D, Bühler A, et al. Subcutaneous alemtuzumab (Campath) in fludarabine-refractory CLL: final results of the CLL2H trial of the GCLLSG and comprehensive analysis of prognostic markers. *Blood*, 112: 11, 2008 (abstract #329).

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