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CLL/SLL

Bendamustine-rituximab as a front line therapy in CLL patients: a retrospective study report

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This article was written by Massimo Gentile from the UOC Ematologia, Ospendale Annunziata in Italy along with co-authors from various other centers; and published in the European Journal of Cancer in June 2016. The article describes clinical data results from a retrospective, multicenter study in a cohort of patients (n=279) with progressive Chronic Lymphocytic Leukemia (CLL) from 33 centers (29 Italian, 3 Israeli and 1 German) across Europe. Patients were administered at least 1 cycle of bendamustine–rituximab (BR) as front line therapy during the period 2008–2014. The primary and secondary objectives of the study were to determine safety and efficacy of BR as frontline therapy and to establish the progression free survival (PFS) and overall survival (OS) respectively. These objectives were evaluated on the intention to treat (ITT) population which included all patients receiving at least 1 cycle of BR. Other biological parameters on overall response rate [ORR, complete response (CR), partial response (PR)] were also assessed and recorded according to the CLL (IWCLL) 2008 criteria.

The key findings of the study were as follows:

- The majority of the patients were males (62.4%, n=174); with a median age of 70 years (range, 43–86 years). One hundred and fifty-seven patients (52%) were 70 years of age or older and 35.8% of patients were found to have Binet stage C. Forty-two patients (15.2%) were found to be unfit (CIRS score ≥7) and 140 (50.2%) were reported with CrCl ≤70ml/min
- Fluorescent in situ hybridization (FISH) analysis was reported for 192 cases; their results showed that 21 (10.9%) had a deletion of 11q and 18 (9.4%) had a deletion of 17p. Sixty-one patients (31.6%) were CD38 positive and 57 (46.3%) showed an unmutated immunoglobulin heavy-chain variable-region (IGHV). The low numbers of patients with del11q and mutated IGHV, as well as the high rate of cases with del17p positive, probably reflected the fact that the available biological data was incomplete due to the retrospective nature of the study
- The ORR in the ITT population was 86.4% (n=241), CR rate was 28% (n=78) and PR rate was 58.4% (n=163); 22 patients (7.9%) had a stable disease and 5 (1.8%) were found to progress
- Patients with a deletion of 17p were reported to have a lower rate of ORR (66.7%) than those with other FISH anomalies (not statistically significant)
- The two year PFS for the entire cohort was shown to be 69.9%; with a median PFS of 40 months
- Only CIRS ≥7, IGHV unmutated status, del17p and BR dose intensity <80% were shown to be independently associated with a shorter PFS
- The most common SAEs of CTC grade III or IV were hematologic toxicities: neutropenia, thrombocytopenia, and anemia were observed in 72 (25.9%), 43 (15.4%) and 42 (15.1%) patients respectively
- Ten patients (3.6%) were reported dead during the treatment; 5 patients died due to therapy related infections, 3 patients due to disease progression, 1 patient due to fulminant hepatitis and 1 patient due to cardiac failure unrelated

to therapy. Twenty four patients (8.6%) had severe infections (20 of grades III and IV of grade IV); the most common infections were found reported to be pneumonia and febrile neutropenia.

Conclusions

Although the combination of fludarabine, cyclophosphamide and rituximab (FCR) represents the gold standard front line therapy for young and fit patients with CLL; BR has shown to be a suitable alternative especially for elderly and fit patients. The results of this retrospective study are also in good agreement with the results obtained in three other prospective primary studies [GCLLSG phase II and II trials and the MABLE trial (NCT01056510)]. BR has shown to achieve similar outcome end-points in previously untreated CLL patients outside of controlled clinical trials.

The full article can be found here

Combination of bendamustine and rituximab as frontline therapy for patients with chronic lymphocytic leukaemia: multicenter, retrospective clinical practice experience with 279 cases outside of controlled clinical trials

Abstract

Recently, encouraging results in terms of safety and efficacy have been obtained using bendamustine-rituximab (BR) in untreated chronic lymphocytic leukaemia (CLL) patients enrolled in a phase II study. Here, we report a retrospective international multicentre study of CLL patients treated with BR as front-line therapy. The cohort included 279 patients with progressive CLL from 33 centers (29 Italian, 3 Israeli and 1 German) who received at least 1 cycle of BR as first-line treatment during the 2008-2014 period. The primary objective of this study was to evaluate the efficacy and safety of BR administered as front-line therapy, outside of controlled clinical trials. Median age was 70 years (range, 43e86 years); 62.4% were males and 35.8% had Binet stage C. Forty-two patients (15.2%) were unfit (cumulative illness rating scale [CIRS] score _7), and 140 (50.2%) had creatinine clearance _70 ml/min. Fluorescent in situ hybridisation analysis, available for 192 cases, showed that 21 (10.9%) had del11q and 18 (9.4%) del17p. The overall response rate (ORR) was 86.4%, with a complete remission rate of 28%. Patients with del17p had an ORR of 66.7%. After median follow-up of 24 months, the 2-year progression-free survival (PFS) was 69.9%; CIRS _7, immunoglobulin heavy-chain variable-region (IGHV) unmutated status, del17p and BR dose intensity <80% were independently associated with shorter PFS. Grade III or IV neutropenia, thrombocytopenia, and anaemia were observed in 25.9%, 15.4%, and 15.1% of patients, respectively. Twenty-four patients (8.6%) had severe infections. BR is also an effective and safe regimen for untreated CLL patients, outside of controlled clinical trials.

Reference:

1. Gentile M. *et al.*, Combination of bendamustine and rituximab as frontline therapy for patients with chronic lymphocytic leukaemia: multicenter, retrospective clinical practice experience with 279 cases outside of controlled clinical trials. Eur J Cancer. 2016 Jun; 60:154-65. doi: 10.1016/j.ejca.2016.03.069. Epub 2016 Apr 27.