**FINAL RESULTS OF THE NCRI CLL210 TRIAL OF ALEMTUZUMAB, DEXAMETHASONE AND LENALIDOMIDE IN PATIENTS WITH HIGH-RISK CLL (ORIGINAL PROTOCOL)**

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**Background and aims:** High-risk (17p- and/or fludarabine-refractory) chronic lymphocytic leukaemia (CLL) presents a major therapeutic challenge. The Phase II NCRI CLL206 trial showed that alemtuzumab plus high-dose methylprednisolone was safe and effective in this setting, although the median progression-free survival (PFS) was only 11.8 months (J Clin Oncol 2012;30:1647-55). In an attempt to improve on these results, the NCRI CLL210 trial was developed to examine the safety and efficacy of alemtuzumab, dexamethasone and lenalidomide.

**Methods:** Patients with previously untreated 17p- CLL or CLL progressing within 12 months of FCR received dexamethasone (40 mg po day 1-4 of weeks 1,3,5,7,9,11,13,15), lenalidomide (5 mg od weeks 3-4 and 10 mg od weeks 5-24) and alemtuzumab (30 mg sc days 1,3,5 of weeks 7-22). Patients who achieved a complete response (CR) or partial response (PR) were allowed to proceed to allogeneic stem-cell transplantation if considered appropriate, or were randomised to lenalidomide maintenance (10 mg od until disease progression) versus no further treatment. Supportive medication consisted of allopurinol, G-CSF, co-trimoxazole, aciclovir, itraconazole, lansoprazole, alendronic acid, aspirin, plus immunoglobulin replacement therapy where appropriate. Written informed consent was obtained from all patients prior to entering the study. The primary endpoints were post-induction CR/CRi rate and progression-free rate after 2 years of maintenance therapy. Response data were assessed by an independent endpoint review committee using the 2008 NCI/IWCLL criteria.

**Results:** Sixteen patients out of the planned 85 were recruited from 7 UK sites during the first 7 months of recruitment before accrual was halted in September 2012 following the withdrawal of marketing authorisation for alemtuzumab. The protocol was subsequently amended to replace alemtuzumab with ofatumumab. This report describes the outcome of the initial cohort of alemtuzumab-treated patients (8 previously untreated and 8 FCR failures). Ten patients (62%) completed induction, whereas 6 (38%) stopped induction prematurely due to toxicity (3), disease progression (1), change in diagnosis (1) or death (1). Three patients (19%) proceeded to allogeneic stem-cell transplantation, 5 (31%) were randomised to lenalidomide maintenance (3) or no further treatment (2) and 2 (12%) withdrew from the randomised part of the trial despite completing induction successfully. The post-induction OR and CR/CRi rate among evaluable patients (11) was 91% and 18% respectively. The progression-free rate after 2 years of maintenance phase among evaluable patients (4) was 50% in both treatment arms. With a maximum follow-up period of 46 months, the median PFS for all 16 patients was 29.3 months. The median OS was not reached since there were only 4 deaths. Grade ≥3 toxicity occurred in 93% of patients and the treatment-related mortality was 6%.

**Conclusions:** Although the small sample size prevents definitive conclusions from being drawn, the results of this prematurely terminated study suggest that dexamethasone, lenalidomide and alemtuzumab is feasible to deliver in most patients with high-risk CLL and has an acceptable safety profile. The regimen also appears to be effective, with a high overall response rate and a median PFS somewhat longer than the 11.8 months that was observed with alemtuzumab plus methylprednisolone. We conclude that the efficacy of glucocorticoid/alemtuzumab in this setting may be enhanced by the addition of lenalidomide without incurring significant additional toxicity.

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