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LETTER TO THE EDITOR

Successful treatment with a rituximab-based regimen of a splenic marginal zone lymphoma with villous lymphocytes in a very frail patient on maintenance dialysis

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To The Editor,

The treatment approach to non Hodgkin lymphoma (NHL) in patients with renal failure is a challenging concern. The case of a dialysed patient, suffering from a splenic marginal zone lymphoma (SMZL) with villous lymphocytes, who received rituximab associated with chlorambucil as first-line treatment is here described.

A 70-year-old woman was admitted to the hospital in July 2007 because of massive splenomegaly, lymphocytosis, moderate anaemia and severe thrombocytopenia. A comprehensive work up, including a body CT scan, was performed. Extensive spleen enlargement and deep abdominal adenomegalies but not enlarged nodes suitable for an excision biopsy were found. According to morphological features and immunophenotype (CD19, CD79a, CD22, CD20, CD45, CD79b, CD52, FMC7 and lambda positive B-cells), a diagnosis of SMZL was made. The past medical history was notably remarkable. Indeed, she was affected by long-lasting hypertension and diabetes mellitus complicated by chronic ischaemic miocardiopathy, advanced retinopathy, distal leg ulcers, peripheral neuropathy and end-stage renal failure for which the patient had been on dialysis from 3 years before. A comprehensive laboratory evaluation revealed no abnormalities other than those related to the renal failure; in particular, HCV infection as potential underlying cause of the SMZL was ruled out. Indeed, HCV-Ab was negative and the serum concentration of liver enzymes was into normal values. Moreover, no signs of associated autoimmune disease were present. Given the relevant burden of her comorbidities, the patient was unsuitable for a standard chemotherapy. Therefore, she was scheduled to receive rituximab (375 mg/m^2, day 1) in combination with chlorambucil (6 mg/m^2, days 1–10) for six cycles. Each course was administered every 28 days. In order to prevent tumour lysis syndrome (TLS) and hyperkalemia, dialysis was performed daily for 3 days after the first rituximab administration and then on regular basis. Mild infusion-related side effects (fever and chills) occurred during the first two administration of rituximab and were successfully managed with metylprednisolone and chlorpheniramine given intravenously. We observed no clinical and no laboratory TLS-related features and, in general, no major adverse events occurred. Rituximab-based treatment resulted in disappearance of splenomegaly and normalisation of absolute lymphocyte counts after the fourth of the six courses administered. Thus, after eight months from the start of treatment, the patient is well and is regularly followed up. SMZL with villous lymphocytes is an indolent lymphoma, presenting with massive splenomegaly, generally associated with leukaemic dissemination. In patients requiring therapy, splenectomy is the treatment of choice [1]. Very favourable results with rituximab in the management of SMZL, which is characterised by a high expression of cellular CD20 antigen, has been reported [2], for which in frail patients it could be considered as a substitute or alternative to splenectomy [3]. Very few data concerning the NHL management in patients on maintenance dialysis have provided so far [4–6]. Pharmacokinetic studies on rituximab in patients with end-stage renal disease demonstrated that this agent is not eliminated by dialysis [6]. Chlorambucil is almost all metabolised by

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the liver and its pharmacokinetic is not influenced by renal impairment. Therefore, these agents, given alone or in combination, could be the ideal drugs of choice in this difficult to treat group of NHL patients with renal insufficiency. Although chlorambucil, given as single agent, does not confer durable remissions to NHL patients, its combination with rituximab provided favourable results in the setting of indolent lymphomas [7–10].

The optimum dose of chlorambucil to administer in combination with rituximab has not been defined and different dosing schedules have been reported [7, 9, 10]. In the setting of indolent lymphomas, 6 mg/m^2/day of this agent was given for six consecutive weeks in combination with a standard 4-weekly rituximab administration schedule as induction treatment [10].

In order to avoid severe toxicities in a very frail patient, basing on our judgement and clinical experience, we adopted a less intensive regimen using a lower dose of chlorambucil than those previously reported [7, 9, 10]. No remarkable toxicities were observed in our experience and no complications requiring hospital admissions occurred. Although the efficacy of the treatment approach adopted by us needs to be ascertained by longer patient's follow-up and by prospective controlled studies, in our experience rituximab in combination with chlorambucil, given according to a relatively low intensive schedule, proved to be a safe and effective measure and can be considered to be a feasible option as first-line treatment for CD20 positive B-cell malignancies in dialysis-dependent patients.

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