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► **To cite this version:**

Claudio Fozza, Antonio Galleu, Maria Grazia Careddu, Domenica Barbara Giannico, Silvana Bonfigli, et al.. Efficacy of rituximab in autoimmune hemolytic anemia associated with splenic marginal zone lymphoma. *Annals of Hematology*, 2009, 89 (1), pp.113-114. 10.1007/s00277-009-0782-y . hal-00535073

HAL Id: hal-00535073

<https://hal.science/hal-00535073>

Submitted on 11 Nov 2010

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Efficacy of rituximab in autoimmune hemolytic anemia associated with splenic marginal zone lymphoma

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Received: 17 June 2009 / Accepted: 20 June 2009 / Published online: 4 July 2009
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Dear Editor,

Autoimmune manifestations including autoimmune hemolytic anemia (AIHA) are often described in association with splenic marginal zone lymphoma (SMZL) [1]. Moreover, AIHA has been recently reported as a potential risk factor of poor outcome for SMZL patients [2]. Among the different available therapeutic options, rituximab monotherapy has been recently shown to be extremely effective in SMZL [3]. On the other hand, this monoclonal antibody plays a key role in the treatment of steroid-refractory AIHA [4]. More specifically, although rituximab has been recently included among the possible strategies to treat AIHA secondary to chronic lymphocytic leukemia [5], very few cases describing its use in the course of SMZL-related AIHA have been described so far [6]. In this paper, we report on a 67-year-old man who presented in September 2008 with fatigue, massive splenomegaly (with the spleen extending below the iliac crest), lymphocytosis (white blood cells, $42.4 \times 10^9/L$; lymphocytes, $36.8 \times 10^9/L$), and severe macrocytic anemia (hemoglobin, 5.9 g/L; mean corpuscular volume, 102 fl). Further laboratory tests showed: elevated lactate dehydrogenase (1,941 U/L) and total bilirubin (4.33 mg/dL); reduced haptoglobin (5 mg/dL); small IgM monoclonal component; and positive direct (C3d and IgG) and indirect Coombs' test. The platelet count was $170 \times 10^9/L$. Peripheral blood as well as bone marrow smears revealed the prevalence of medium-sized lymphoid cells without specific features, while their

immunophenotypic pattern was suggestive for SMZL, i.e., positive for CD19, CD20, CD22, CD11c, CD5 (reported in 20% of patients [7]), and kappa light chain with strong intensity and negative for CD10, CD23, CD25, and CD103. Total body computed tomography and abdomen ultrasound confirmed massive splenomegaly, showing also slight hepatomegaly and diffuse microlymphadenomegaly. The patient was initially started on 2 mg/kg methylprednisolone, but after 2 weeks, the hemoglobin level was only marginally improved. Therefore, a second-line treatment with weekly 375 mg/m^2 rituximab was started. The hemoglobin level increased to 10.8 g/dL 1 week after the first dose and normalized after the fourth dose. After six further monthly rituximab administrations, the patient is well, his hemoglobin level is above 13 g/dL, the white cell counts are normal, and the splenomegaly is markedly reduced (2 cm below the costal margin). The present case further suggests that rituximab represents an extremely valid therapeutic alternative in steroid-refractory AIHA associated with lymphoproliferative disorders other than chronic lymphocytic leukemia.

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