RITUXIMAB AND SUBCUTANEOUS 2-CHLORO-2'-DEOXYADENOSINE (2-CDA) COMBINATION TREATMENT FOR PATIENTS WITH WALDENSTROM'S MACROGLOBULINEMIA (WM): CLINICAL AND BIOLOGICAL RESULTS OF A PHASE II MULTICENTER STUDY.

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Purpose: to assess the efficacy of 2-chlorodeoxyadenosine (2-CdA) given subcutaneously, in combination with Rituximab in the treatment of newly diagnosed/pretreated WM patients and to correlate the response to treatment with biological findings.

Patients and Methods: from December 2003 to February 2007, 29 patients were enrolled. Intended therapy consisted of a combination of Rituximab (375 mg/smq) on day one followed by 2-CdA 0.1 mg/kg (sc injection) for 5 consecutive days, administered monthly for 4 cycles. Anaemia (16pts), neurological symptoms (6pts), symptomatic cryoglobulinemia (4pts) and thrombocytopenia (3pts) represented the reasons for starting the treatment. The expression of Zap-70 and of 7 genes involved in 2-CdA metabolism as markers of response to the combination treatment was evaluated.

Results: with a median follow-up of 50 months the ORR rate observed was 89.6% with 7 CR, 16 PR and 3 MR without any difference between newly or pretreated patients (p=0.522). The therapy was well-tolerated except for transitory cardiac toxicity (2 pts) and intolerance to Rituximab (2 pts). No major infections were observed despite the lack of antimicrobial prophylaxis. No patients developed transformation to high-grade NHL nor myelodisplasia. Low expression levels of hCNT1 correlated with the failure to achieve a CR (p=0.024), while no association with Zap-70 expression was found.

Conclusion: the combination of Rituximab and subcutaneous 2-CdA is safe and effective in WM patients requiring treatment. The pharmacogenomic analysis associated with the study suggests hCNT1 might be beneficial in predicting clinical response to such a combination treatment.