INTESINFIED B-LYMPHOCYTE DEPLETION WITHOUT IMMUNOSUPPRESSIVE MAINTENANCE TREATMENT AS A RESCUE THERAPY IN REFRACTORY LUPUS NEPHRITIS: A 4-YEAR OBSERVATION.

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BACKGROUND

B cells play a central role in systemic lupus erythematosus (SLE). Rituximab is expected to induce apoptosis of all the CD20-positive B cells. A proportion of patients are refractory or intolerant to standard immunosuppression. B-Lymphocytes depletion therapy still remains an attractive option, despite the disappointing results of RCTs in these selected cases.

PURPOSE

The present study focuses on the effects of an intensive course of therapy, using rituximab (4 plus 2 infusion protocol) in combination with two intravenous pulses of cyclophosphamide and three pulses of methylprednisolone and followed by a short course of prednisone, given prospectively to a selected cohort of severe SLE patients.

PATIENTS AND METHODS

Twelve SLE patients [10 female patients, mean age 43.8 yrs (29-54)] were enrolled in this study.

Clinical manifestations included:

- polyarthralgia and multiorgan involvement including class IV or V (ISN/RPS) glomerulonephritis (9 cases)
- skin lesions (9 cases, with necrotizing ulcers in 3),
- polyneuropathy (7cases, with CNS involvement in 2),
- lymphoadenopathy (6)
- polysierositis (5)

Protocol:

Rituximab 375 mg2 on days 1, 8,15 ,22, and 2 more doses after one and two months, associated with 2 IV administrations of 10 mg/kg of **cyclofosfamide** and 3 infusions of **methylprednisolone** (15 mg/kg) followed by oral prednisone
(0.8 mg/die, rapidly tapered to 5 mg/day in 10 weeks),
without further immunosuppressive maintenance therapy

Six patients have been treated with an intensive B-Lymphocytes depletion protocol for intolerance to conventional immunosuppressive therapy and the remaining **6** as a front line therapy.

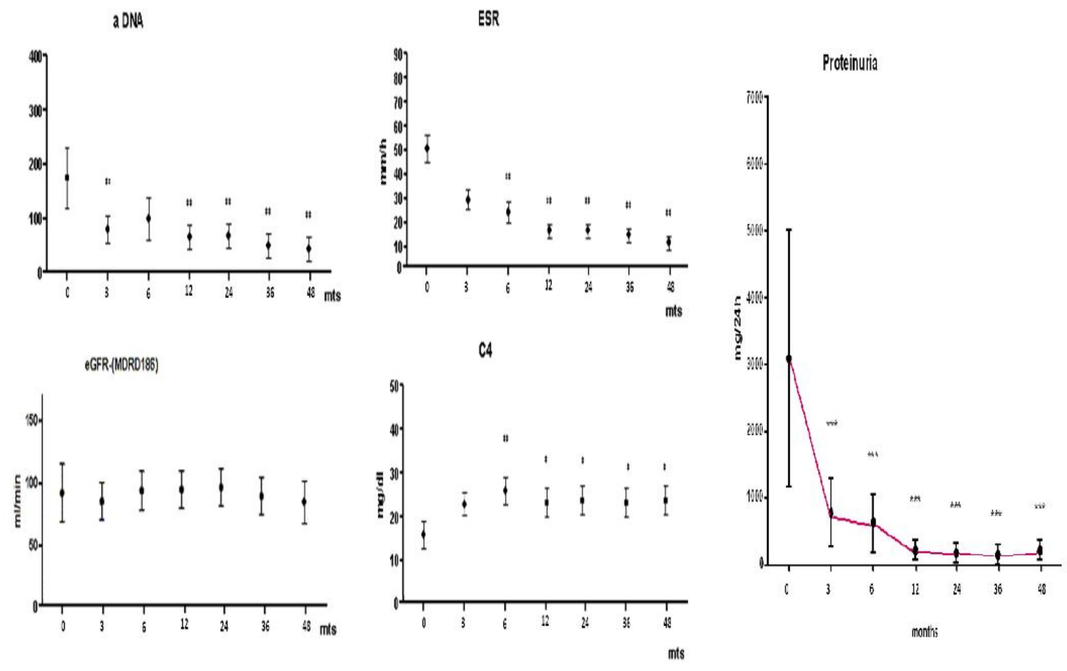
RESULTS

This protocol obtained a complete depletion of CD20+ B-lymphocytes for 12-18 months.

Patients had been followed-up for 48.9 (25-93) months.

ESR (baseline mean value: 54.2; 3 months: 33; end of follow-up: 14.9), anti-dsDNA antibodies (baseline: 192; 3 months:112; end of follow-up: 17) and proteinuria (baseline: 4.9 g/24 hours; 3 months:0.97; end of follow-up: 0.22) significantly declined ($p<0.05$), while C4 values (baseline 11 mg/dl) signifiicantly increased ($p<0.05$) after 3 months (22 mg/dl) and at the end of the follow-up (20 mg/dl).

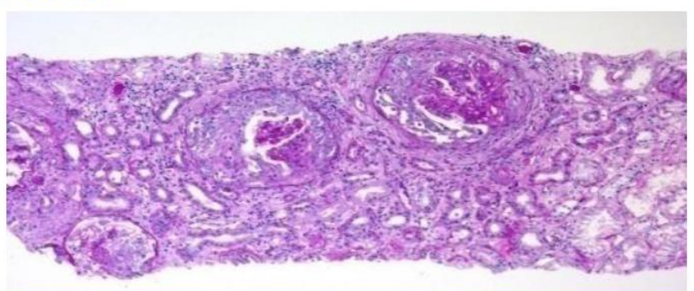
Three patients relapsed after 36,41 and 72 months respectively. They showed again a complete remission after retreatment over 13-48 months of observation.



CONCLUSIONS

These data confirm the opportunity to reconsider the regimens of B- Lymphocytes depletion in the treatment of the most severe forms of SLE despite the disappointing results of RCTs. A promising role of Rituximab in protocols of “intensified induction therapy” in selected patients for whom avoiding immunosuppressive maintenance therapy could be particularly appealing

Renal biopsy of patient # 3 who showed a class IV lupus nephritis with diffuse extracapillary proliferation (60 percent of florid crescents) and focal necrosis.



51ERA-EDTA
348--MP
K) Clinical Nephrology, primary and secondary glomerulonephritis.
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DOI: 10.3252/pso.eu.51era.2014
Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014