**Tailoring B-cells depleting therapy in MS according to memory B-cells monitoring: a pilot study**

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**Background:** Phase II and III clinical trials revealed the potent suppressive activity on MRI activity and ARR of CD20 directed antibodies in MS. However, no studies to dissect the optimal infusion regimen (i.e.: the minimum drug dosage associated with maximum re-infusion interval that maintains maximum efficacy) have been performed. Infusion regimens with higher infusion intervals and lower drug dosage might maintain the same efficacy than current (fixed-dose) treatment schedule.
**Objective.** To evaluate rituximab (RTX) efficacy using a memory B-cell based reinfusion regimen, with a variable reinfusion cut-off, according to year of treatment. MS activity was assessed as clinical disease activity (annualized relapse rate – ARR) or MRI activity (new Gd+ enhancing lesion or new/enlarging T2 lesions).
**Methods** This is an observational, retrospective bicentric study including patients with MS treated with RTX in 2 Italian MS units. All patients were treated with rituximab induction (two-1g-infusion 15 day apart), followed by maintenance infusion at the dosage of 375 mg/m$^2$, according to memory B-cells repopulation. Predefined cut-off values for reinfusion (percentage of memory B cells among peripheral blood PBMC) were: 0.05% for the first two years of treatment, with subsequent doubling for each year of treatment (maximum cutoff at year 6 of 1.6%).
**Results** 101 patients were included in the analysis, 32 patients had a relapsing remitting phenotype, while 69 had a progressive phenotype (40 secondary progressive and 29 primary progressive).
Mean FU was 1.75 years (range 0.29-6.56).
ARR was 0.67 (95% Confidence Interval (CI): 0.53-0.85) in the year before RTX start and decreased to 0.02 (95%CI 0.004-0.04) during the whole FU.
Proportion of patient with MS activity (i.e.: relapse or MRI activity) was 74/101 (73.3%) in the year before RTX start and decreased to 11/71 (15.5%) and 1/27 (3.70%) in the two years after RTX initiation.
Annualized RTX infusion rate was 1.70 (95%CI:1.45-1.99), 1.41 (95%CI:1.09-1.80), 0.97 (95%CI:0.62-1.43) and 0.85 (95%CI:0.36-1.64) for the first four years after RTX initiation, respectively.
**Conclusions.** Results of this study show that memory B cells based RTX reinfusion protocol is able to reduce mean number of RTX reinfusion (and drug dosage) with persistent reduction of disease activity. A memory B cells threshold for disease activity recrudescence could be possibly identified with longer follow-up (and higher reinfusion cut-off).