

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 **high efficacy of anti-CD20 antibodies on MRI parameters** in MS.
- There is some evidence about the **putative role of memory B cells (CD19+ CD27+)** in disease activity.
- However, **no studies have investigated the optimal infusion regimen as yet** (i.e.: the minimum drug dosage associated with maximum re-infusion interval that maintains maximum efficacy)

Methods:

- This is an **observational study** including patients with **MS treated with rituximab (RTX)** in 2 Italian MS centers.
- Patients were retreated with RTX according to peripheral blood memory B cells re-appearance** (cut-off value 0.05% of PBMC in the first 2 years, 0-1% in the third year, with subsequent doubling every year)

Results:

- 101 patients were included** in the study, 98 patients were then included in the analysis.
- The **median follow up was 1.9 (range 0.5-6.8) years**.
- ARR was 0.42** (95% Confidence Interval (CI): 0.34-0.52) in the **2-year before RTX start**, it **increased to 0.67** (95% CI 0.52-0.85) in the **year before RTX start** and **decreased to 0.01** (95%CI 0.002-0.04) during the **2 years after RTX initiation** ($p < 0.0001$) (Fig. 1).
- Annualized RTX infusion rate was 1.65** (95% CI: 1.40-1.93) in the **first year after RTX initiation**, it **decreased to 1.31** (95% CI 1.01-1.65) in the **second year after RTX start** and **decreased to 0.94** (95%CI 0.61-1.38) during the **third year after RTX start** (Fig.2).
- Proportion of **patient with MS activity** (i.e.: relapse or MRI activity) was **74/101 (73.27%)** in the year before RTX start and **decreased to 3/98 (3.06%), 1/98 (1.02%) and 1/98 (1.02%)** in the **6-month, 1-year and 2-year after RTX initiation**.

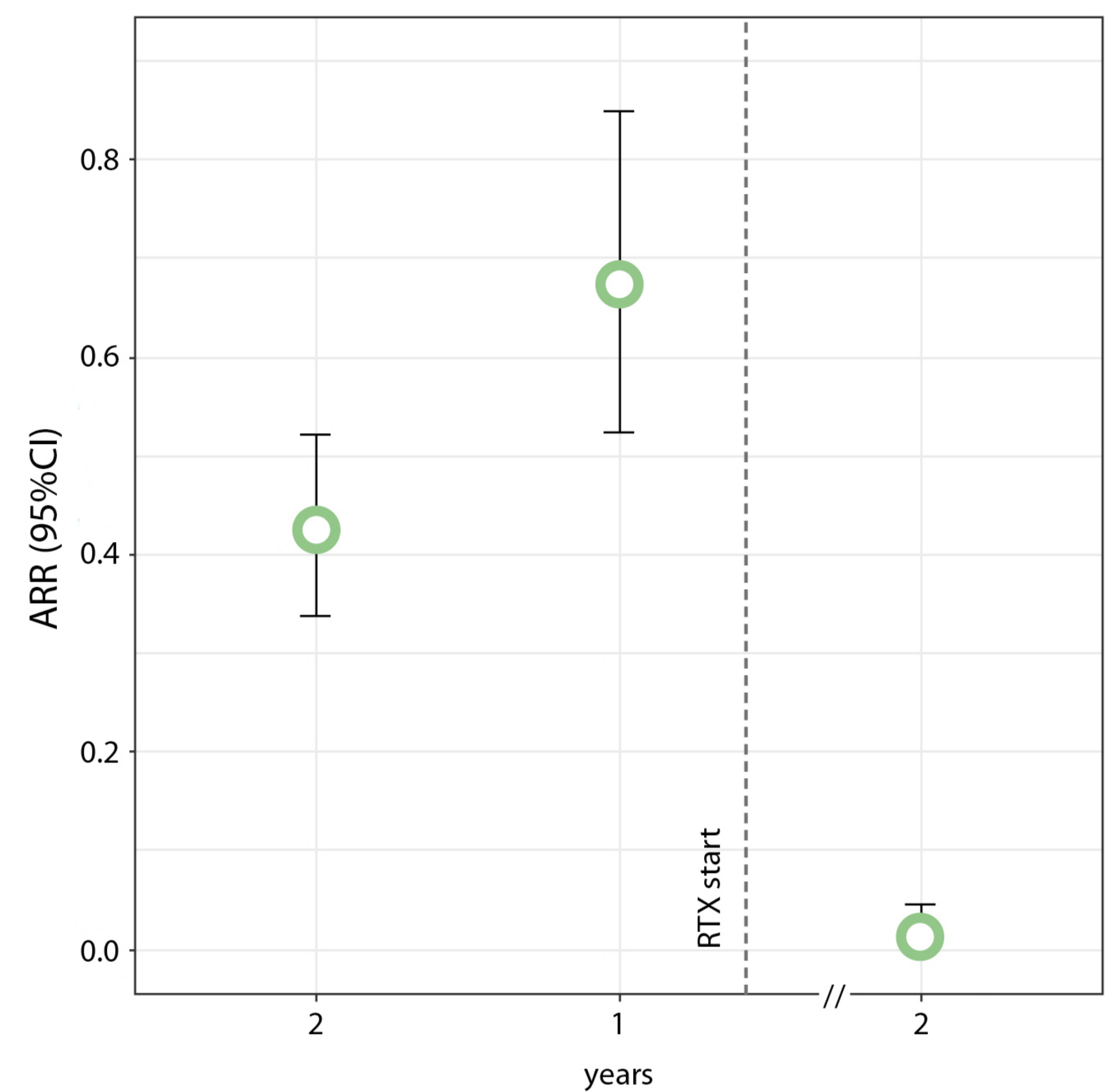


Fig.1
Annualized relapse rate (ARR):
ARR was 0.42 in the 2-year before RTX start, 0.67 in the year before RTX start and decreased to 0.01 during the 2 years after RTX initiation.

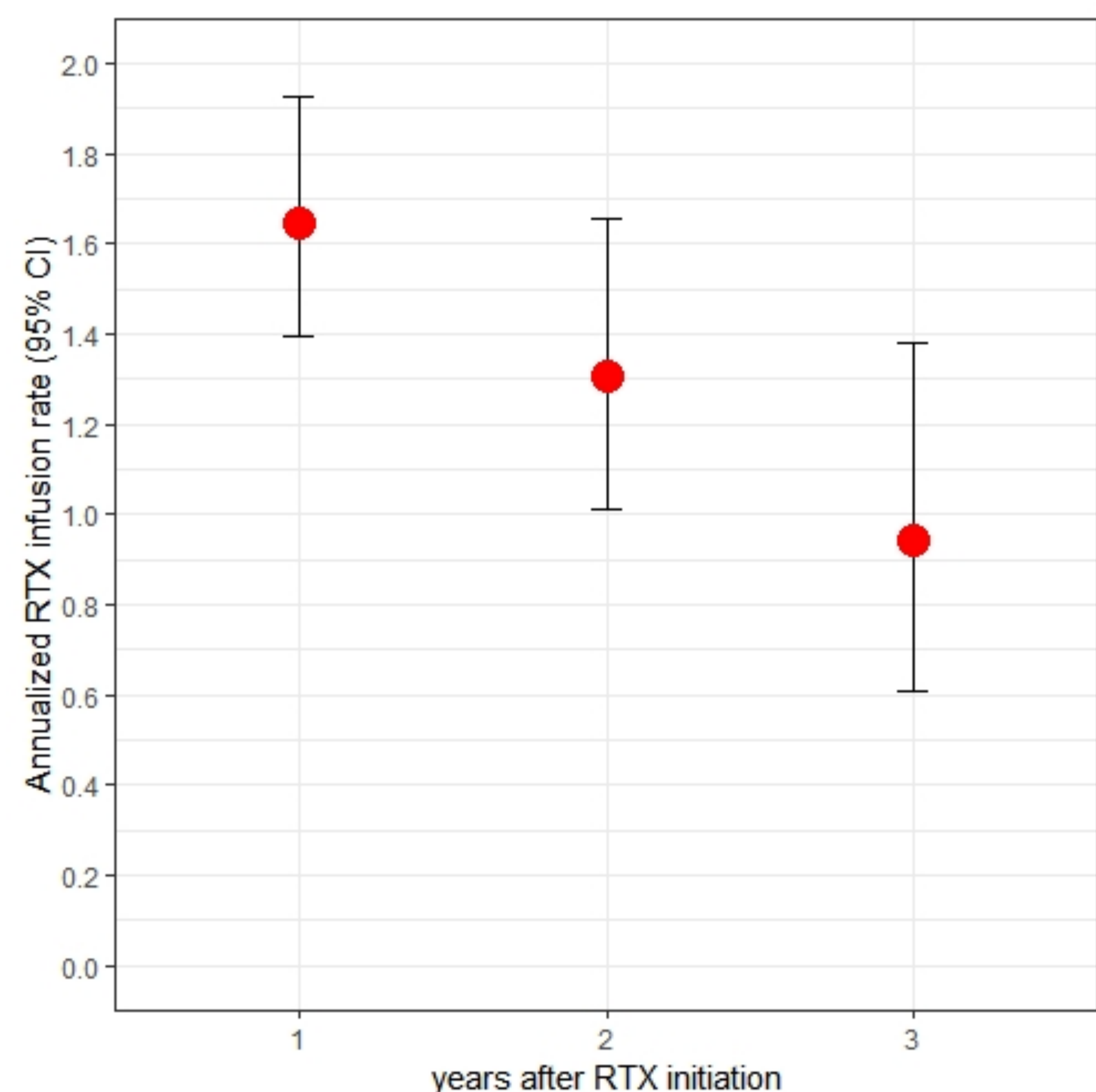


Fig.2
Annualized rituximab infusion rate (ARIR):
ARIR was 1.65 in the first year after RTX initiation, 1.31 (95% CI 1.01-1.65) in the second year after RTX start and 0.94 (95%CI 0.61-1.38) during the third year after RTX start

Discussion:

- Memory B cells number-based RTX reinfusion protocol is able to reduce mean number of RTX reinfusion (and drug dosage) with persistent reduction of disease activity.**
 - A longer follow-up might lead to the identification of a **memory B cells number threshold** to prompt reinfusion and prevent disease activity recrudescence