Dear Editor,

We read with interest the recent article by Wang and Liu [1], describing their experience with rituximab (RTX) in 6 systemic lupus erythematosus (SLE)-associated antiphospholipid syndrome (APS) patients. These data support the idea that, in line with previous sporadic cases reported in literature, RTX at different regimens is able to reduce thrombotic recurrences and to improve SLE activity, with an overall good safety profile. Moreover, they confirm the disappearance/decrease of titer of antiphospholipid antibodies after RTX [1].

Here we report our monocentric experience of seven patients treated with repeated courses of RTX at standard regimen (Table). Our data confirm in part those of Wang, but there are also some concerns. Among 455 patients of our Lupus Clinic, we retrieved 69 SLE-associated APS cases. Eight patients were treated with RTX, while seven of them with repeated standard low-dose infusions (the patient treated only once was excluded from this case series).

In our experience, RTX reduced the incidence of thrombotic relapses in almost all patients (median follow-up = 36 months, range: 12–48) (Table). Indeed, 6/7 patients had APS clinical remission (i.e., no thrombotic events) after RTX (Fig. A). Only one patient (ID 4) relapsed after 6 months of treatment and his clinical...
course was catastrophic, with several thrombotic episodes despite adequate anticoagulation and repeated cycles of RTX (Table). Interestingly, he was the only patient in whom the indication for RTX treatment was recurrent thrombosis despite good anticoagulation and good control of SLE activity. In line with the literature [1], RTX was able to reduce SLE activity in our patients: the median SLEDAI before RTX was 10 (range: 4–14) and after 6 months, from the last treatment, was 4 (range: 2–6; Fig. B).

Regarding the treatment-related toxicity, only one patient developed pneumonia 2 months after RTX treatment and promptly responded to antibiotic therapy. The same patient underwent other three retreatments with RTX at low dose, without any other complication. Treatment-related hematologic toxicity was almost absent and all patients presented a reduction of B-lymphocytes, without appreciable clinical symptoms.

In our cohort, the indication for the first RTX treatment was APS activity only for one patient (ID 4), while in the remaining patients the indication was SLE activity. These data are quite different from those reported by Wang, who described that almost all the patients had recurrent thrombotic events despite adequate anticoagulation, thus requiring RTX treatment. The data of the literature are poor and conflicting, since 5/10 patients required RTX for SLE activity, and the others for recurrent thrombotic events [1].

Unlike the Wang cohort, all the patients followed at our dedicated center were treated with a standardized protocol: induction treatment with RTX 1000 mg twice/2 weeks apart, and maintenance with low dose of RTX (500 mg). A similar infusion scheme has been already successfully proposed in Granulomatosis with Polyangitiis, showing a low rate of relapses [2]. A limitation of our work is the variable time interval between the retreatments; indeed, 5/7 patients were retreated after 6 months from the induction infusion, while two patients (IDs 1 and 6) were retreated, respectively, at 18 and 36 months. Only two patients were retreated at 12 months (IDs 1 and 4), while the others received a second RTX retreatment after 18 months (ID 3), 30 months (ID 5), 36 months (ID 1), and 42 months (ID 6) (Table).

Finally, we did not observe a disappearance of lupus anticoagulant and/or modifications of the titer of anticardiolipin antibodies, differently from what reported by Wang and Liu [1].

RTX is emerging as a potential weapon in primary APS [3] and, despite the failure of the registrative trials, it is a good option in clinical practice for SLE patients who are refractory or intolerant to conventional therapies [4]. Despite this, poor data are available on the correct usage and the potential usefulness of RTX in secondary forms of APS, associated with SLE. This kind of patients often needs a combination of immunosuppressive and anticoagulant treatments for the control of both the conditions, and RTX could be an important alternative in resistant or active patients. Also in our case series (the largest reported in literature), RTX has confirmed its efficacy in preventing recurrent thrombosis in SLE-associated APS patients. However, unlike Wang’s report, we have treated our patients for their SLE activity, and not for the recurrence of the thrombotic events; interestingly, we have successfully applied a standard protocol with repeated low doses of RTX for the retreatments, with a persistent clinical response, and a good safety profile.

More prospective data with largest cohort of patients are necessary to establish the right indication and the better regimen of RTX treatment.
References


