Response to: 'Could abatacept directly target expanded plasmablasts in IgG4-related disease?' by Alegria *et al*

We thank Alegria *et al*¹ for their response to our letter.² IgG4-related disease (IgG4-RD) is a chronic fibroinflammatory disorder that can involve various organs, but its origin remains unknown.³ Although elevated levels of circulating plasmablasts are observed in the active phase of IgG4-RD,^{4,5} the pathogenesis cannot be fully explained by plasmablasts alone. In our report,² we described a patient treated with abatacept who presented with complete depletion of circulating CD19⁺ cells at the secondary failure of rituximab. Because the serum levels of IgG4 decreased suddenly, the circulating plasmablasts and tissue resident plasma cells might also have decreased (figure 1). Despite this condition, the patient relapsed. It is important to identify the mechanism of the secondary failure of rituximab in this patient, and we consider that T cells play an important role in the pathogenesis of IgG4-RD.

As previously described, we did not know the specific reason why abatacept was effective in this patient because there was no expression of CD28 in the biopsy specimens. It is possible that follicular helper T cells are decreased by abatacept.² Alternatively, abatacept may make dendritic cells and macrophages secrete indoleamine 2,3-deoxygenase, which can inhibit the proliferation of T cells.⁶ As Alegria *et al* noted, there is of course the possibility that abatacept affects both CD19⁺ B cells and CD19⁺CD38^{high} plasmablasts. It was recently reported that abatacept is effective for systemic lupus erythematosus (SLE).⁷ Elevated levels of plasmablasts, which have a population, that is, different from IgG4-RD, are observed in SLE.⁸ Understanding how abatacept works in SLE may be a reference for understanding why it was effective in this patient.

This patient has now successfully completed a 17th administration of abatacept without any adverse effects, and her condition is very good. Although her serum levels of IgG4 initially continued to decline, they have recently remained around 200 mg/dL. We consider that maintenance treatment is needed even when administering abatacept.

It is important to both identify the reasons for the efficacy of abatacept in IgG4-RD and verify the clinical efficacy of abatacept in IgG4-RD.

Figure 1 Clinical course of a patient treated with abatacept. Complete depletion of circulating CD19⁺ cells was observed at the secondary failure of rituximab. No relapse has been observed after switching from rituximab to abatacept. ABT, abatacept; RTX, rituximab.

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