



at admission. After the discontinuation of glucocorticoids within 1 week, we initiated the treatment of telitacicept (160 mg every week hypodermic injection) for 60 weeks due to his unwillingness to use long-term systemic glucocorticoid therapy. His symptoms were gradually relieved after the initiation of treatments. IgG4-RD RI decreased from 12 to 1 at week 60 (figure 1A). The levels of IgG4, IgE, IgG and IgM decreased and serum complement C3, C4, creatinine and eGFR returned to normal during the treatment of telitacicept (figure 1A). MRI detections showed a gradual and persistent reduction in the sizes of the involved salivary glands (returned to normal size at week 60) and the renal cortex lesions (almost diminished) during the 60 weeks' treatment with telitacicept (figure 1B and online supplemental figure S1).

Besides the aforementioned case, based on the criteria listed in online supplemental table S1, we recruited additional nine IgG4-RD cases (eight belonged to the 'Mikulicz and Systemic' group and one belonged to the 'Head and Neck-Limited' group,<sup>5</sup> online supplemental table S2) and treated with the same therapeutic strategy to examine the remission rate after telitacicept treatment. No severe adverse event was observed, however, injection site reactions (redness or mass formation), which were mild and controllable, were observed in 80% of the patients (figure 1C). Similar high ratio of injection site reactions of telitacicept administration could also be observed in clinical trials for other diseases.<sup>6</sup> Trend analyses showed significant decreases in IgG4-RD RI, serum IgM, IgE and CD19<sup>+</sup>CD24<sup>+</sup>CD38<sup>hi</sup> plasmablast levels during the 24 weeks of follow-up (figure 1D, online supplemental figure S2), while no statistical significances were observed in ESR, complement C3 and C4, total IgG and its subclasses (online supplemental figure S3). However, there were four patients without response to telitacicept (improvement of IgG4-RI less than 2) during the 24 weeks of follow-up, resulting in a partial remission rate of 60% to telitacicept. Principal component analysis based on the baseline laboratory data distinguished the responsive and nonresponsive patients well on the first principal component (contributing rate: 56.97 %) (figure 1E). Analyses to the baseline data indicated that ESR, serum IgG4, IgG and plasmablast ratio contributed substantially to the status of 'remission', while total T, CD4<sup>+</sup> T, CD8<sup>+</sup> T and B cell counts contributed to the status of 'non-remission' (figure 1F and online supplemental table S3). This result suggested that patients with therapeutic response to telitacicept had relatively higher levels of serum immunoglobulin and plasmablast at baseline, while non-remission patients had relatively higher counts of lymphocytes.

To the best of our knowledge, this is the first study reporting the therapeutic potential of BLyS/APRIL-targeting biologics in IgG4-RD. Patients with IgG4-RD patients have limited treatment options, especially for those who were unable or unwilling to use long-term glucocorticoid therapy due to various conditions. Here, we reported a 60% partial remission rate at week 24, a duration widely adopted for the observation of IgG4-RD remission<sup>7</sup> under the treatment of telitacicept, which showed potential effects on reducing lesion size, relieving symptoms and improving laboratory parameters in patients with IgG4-RD, especially in those who had high levels of ESR, IgG4, IgG and plasmablasts. Although future larger sample size studies are required to optimise the dosage and duration, this study may provide an important basis for developing a treatment strategy for IgG4-RD patients who are not suitable for glucocorticoid therapy.

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