Successful treatment with baricitinib of refractory arthritis in a patient with severe diffuse cutaneous systemic sclerosis-rheumatoid arthritis overlap syndrome

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Commonly, during the disease course of systemic sclerosis (SSc) up to 60% of patients may develop musculoskeletal symptoms (1, 2). Joint involvement in SSc is predictive of worsening of the modified Rodnan skin score (mRSS) and of the overall disease progression (3). Data from the EUSTAR registry showed that tocilizumab (TCZ) and abatacept (ABA) were effective and well tolerated in patients with SSc-polyarthritis (4, 5). Poly-autoimmunity is common in SSc and the overlap with RA may be present in some patients making diagnosis and subsequent management even more difficult (6). Here, we report the case of a patient with SSc-RA overlap syndrome presenting with refractory arthritis successfully treated with baricitinib.

A 48-year-old man presented in 2015 with Raynaud's phenomenon, severe skin sclerosis (mRSS at 31/51) and multiple synovitis. Anti-Scl-70 was strongly positive, anti-cyclic citrullinated peptide antibody was 164UI/mL (normal value <17UI/mL) and rheumatoid factor was 67UI/mL (normal value <14UI/mL). X-rays revealed no periarticular erosions but multiple proximal interphalangeal joint space narrowing. High-resolution computed tomography showed minimal interstitial lung disease. A diagnosis of SSc-RA overlap syndrome was made. Prednisone 10mg once a day and MTX 20mg once a week were prescribed but were ineffective on both skin sclerosis and synovitis. Rituximab (RTX) was then prescribed but was stopped after 2 cycles owing to primary failure. Intravenous TCZ was prescribed with some improvement in joint symptoms. No effect on skin disease was observed. However, TCZ was eventually discontinued after 6 months because of secondary failure and persistent elevated liver transaminase levels. Then, ABA 125mg weekly was started with a moderate articular response after 3 months. ABA was discontinued after 12 months because of secondary failure demonstrated by a plateau of the mean DAS28-CRP response around 4 points. No effect on skin disease (mRSS at 30/51) was observed. Therefore, baricitinib 4mg once a day was started. After 2 months, his articular symptoms began to improve and disease activity was significantly reduced (DAS28-CRP: 2.81). The response was maintained at subsequent 6, 12 and 18-month's follow-up visits (DAS28-CRP 2.46 at last follow-up). CRP levels decreased from 40mg/L to 8mg/L (normal value <5mg/L). CRP levels decreased from 40mg/L to 8mg/L (normal value <5mg/L). Figure 1 reveals a striking dissociation between joint and skin involvement (mRSS 28/51) responses on baricitinib therapy.

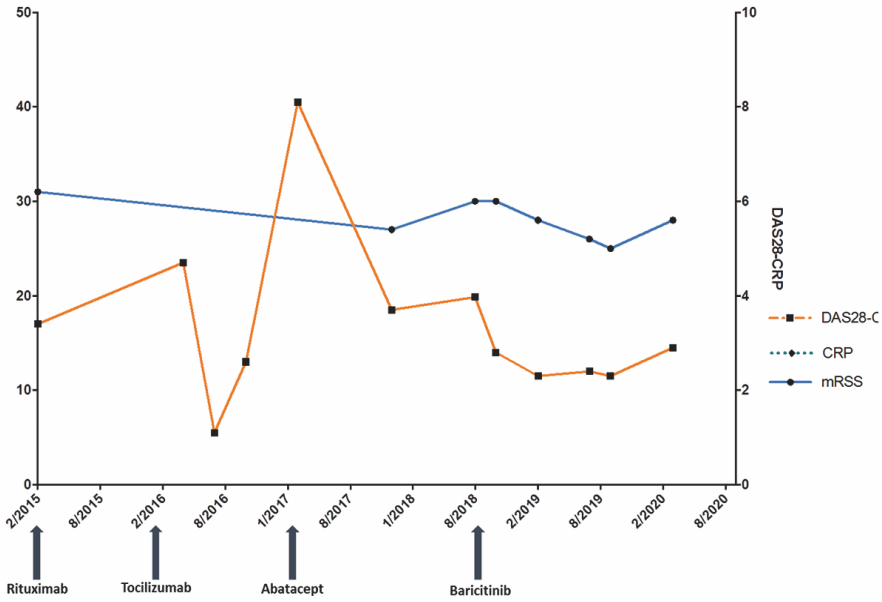

Fig. 1. Clinical course from diagnosis to last follow-up visit.

To our knowledge, this is the first reported case of a patient with severe diffuse cutaneous SSc-RA overlap with severe arthritis refractory to multiple targeted immunosuppressants successfully treated with baricitinib. Fujita *et al*. reported the case of a 71-year-old patient with limited cutaneous SSc-RA refractory to TCZ and adalimumab who responded to baricitinib. Interestingly, an improvement in mRSS was observed (8 points to 2 points after 24 weeks) but it must be highlighted that the patient had limited skin disease (7). Conversely, our patient had severe skin disease and although the outcomes were favourable for joint manifestations no skin improvement was observed.

Baricitinib is a reversible Janus Kinase (JAK) inhibitor that has been approved for the treatment of RA. JAK-2 is activated in SSc in a TGFβ-dependent manner and mediates the stimulatory effects of TGFβ on fibroblasts (8). Recently, a phase 1/2 double-blind, randomised placebo-controlled trial, tested tofacitinib, another JAK inhibitor, in patients with recent SSc with active skin disease (9). Despite a good safety profile there was no significant improvement of clinical outcome measures.

This observation points out how joint involvement can represent a major therapeutic challenge in SSc. JAK-inhibitors may be considered in SSc patients with difficult-to-treat arthritis despite the use of other synthetic or targeted immunosuppressants. Furthermore, this observation also highlights how current effective therapeutic options are very scarce in SSc patients with severe skin involvement.

Written informed consent was obtained from the patient and Ethics board approval was received (Comité de Protection des Personnes CPP Ile de France III, no. 2008-A00624-51).

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Competing interests: none declared.

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