An unfavourable outcome following switching intravenous abatacept and tocilizumab to subcutaneous forms during the COVID-19 pandemic

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Key Message – Unfavourable outcomes in rheumatoid arthritis following switching from intravenous to subcutaneous biologics during the pandemic.

Dear Editor,

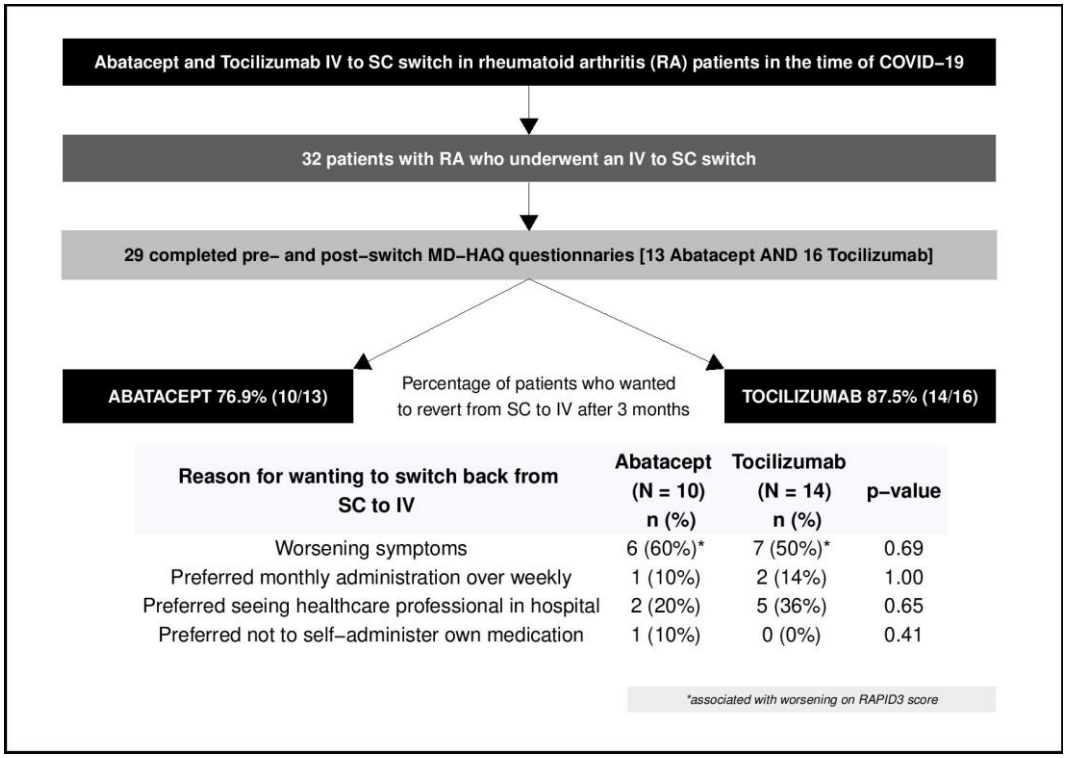
The COVID-19 pandemic has seen profound adaptations made to rheumatology practice. National Institute for Health and Care Excellence (NICE) published COVID-19 rapid guidelines proposing that clinicians should consider switching intravenous (IV) biologic disease-modifying anti-rheumatic drugs (bDMARDs) to subcutaneous (SC) forms to minimise face-to-face contact in a hospital setting.

We identified 250 patients on IV abatacept or tocilizumab with rheumatoid arthritis (RA) at our hospital. Patients were considered for switching to SC injection if they had stable disease, receiving a standard dose, had not had the equivalent drug administered subcutaneously previously, and had no changes to their DMARD in the last 3 months. Some patients did not agree to switch; reasons included not wanting to self-administer injections and not being able to have blood monitoring locally. Adopting a joint decision-making approach between doctor and patient, only 32 patients were switched to the SC formulation.

In line with the British Society of Rheumatology's published guidance, 24 of the 32 patients who switched were shielding because of their co-morbidities or concurrent immunosuppressant use and the other 8 patients were self-isolating at their discretion. None of our patients had COVID-19 symptoms at the time of data collection. Between February and March 2020, 14 patients on abatacept were switched from 4-weekly IV infusion to weekly SC injection whilst 18 patients on tocilizumab were switched from 4-weekly IV infusion to weekly SC injection. Patient-reported outcome measures (PROMs) were recorded directly before, and three months after the switch using Multi-Dimensional Health Assessment Questionnaire (MD-HAQ). These responses were used to calculate RAPID3 scores (1), a quantitative measure accounting for patients' functional ability, pain, and global wellbeing. We also explored whether patients wanted to revert to the IV form and their reasoning behind this decision.

29 of the 32 patients (90.6%) who switched completed our questionnaire. 85% (11/13) of abatacept patients and 88% (14/16) of tocilizumab patients were in clinical remission or experiencing low disease activity as assessed by DAS28-ESR prior to switching from IV to SC. Overall, 77% (10/13) of abatacept and 88% (14/16) of tocilizumab patients indicated a desire to revert to IV administration 3 months after switching to SC injections (Figure 1). 60% (6/10) of abatacept patients who wanted to return to the IV formulation described worsening joint pain, stiffness, and swelling since the switch to SC, particularly in the days immediately prior to their weekly injection. These worsening symptoms were demonstrated by the increasing total scores of RAPID3 (11.08 to 15.43, p=0.01), along with functional ability (3.63 to 4.63, p=0.04), pain (4.55 to 6.05, p=0.04) and global wellbeing (0.90 to 4.75, p= 0.01) where higher values indicate worsening patient function (Supplementary Figure S1). Similarly, half of the patients (7/14) who desired to revert to IV tocilizumab cited worsening of symptoms, evidenced by the increase in total RAPID3 scores (8.66 to 11.8, p=0.01), functional ability (2.99 to 3.51, p=0.02), and global wellbeing (2.61 to 3.71, p=0.02).

Fig. 1 Details of patients who wanted to revert to i.v.from s.c. administration.



Reason for wanting to switch back from SC to IV	Abatacept (N = 10) n (%)	Tocilizumab (N = 14) n (%)	p–value
Worsening symptoms	6 (60%)*	7 (50%)*	0.69
Preferred monthly administration over weekly	1 (10%)	2 (14%)	1.00
Preferred seeing healthcare professional in hospital	2 (20%)	5 (36%)	0.65
Preferred not to self–administer own medication	1 (10%)	0 (0%)	0.41

*associated with worsening on RAPID3 score

The effectiveness of SC compared to IV bDMARDs has been investigated previously. A 2018 study of 3,448 RA patients from eight European registries involving IV to SC switches, concluded that SC tocilizumab is an acceptable alternative to IV tocilizumab. No details about the cause of switching were provided (2). A 2011 double-blind study of 1,457 RA patients demonstrated equivalent efficacy between IV and SC abatacept for RA (3). However, a small real-world study of abatacept IV to SC switchers reported that 22.9% switched back to IV over a 6-month period due to worsening of symptoms (4).

In our study, 29.2% (7/24) who wanted to revert to IV medication did so because they preferred the 4-weekly face-to-face visits with a healthcare provider, reinforcing the role of the therapeutic relationship in determining patient satisfaction. A 2017 study of 405 patients on IV bDMARDs outlined the patient-reported advantages of IV administration; including the visit acting as an additional physical assessment and staff being able to monitor for side-effects and provide emotional support (5). Only half of patients considered their administration method to have resulted from joint decision-making between patient and doctor, with 35.3% stating this decision was made solely by their doctor (5).

The majority of patients in our small study who went through IV to SC switch preferred to return to the IV formulation. Those who preferred to return to IV administration did so because of worsening of their symptoms (reflected by total, and all components of RAPID3). It is tempting to speculate that a reduction in face-to-face interactions with healthcare professionals may have influenced the worsening disease activity as assessed by PROMs. Taken together, our results suggest switching from IV to SC abatacept or tocilizumab should not be mandatory and perhaps not even advisable for future pandemics and may only have a limited impact if adopting a joint decision-based approach due a low percentage of patients agreeing to switch formulation.

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