Received: 19 October 2021 | Revised: 1 December 2021 | Accepted: 9 December 2021

DOI: 10.1002/ccr3.5233

CASE REPORT

Clinical Case Reports Open Access WILEY

Real-world evidence for subcutaneous infliximab (CT-P13 SC) treatment in patients with ankylosing spondylitis during the coronavirus disease (COVID-19) pandemic: A case series

Sooraj Vijayan[1] | **Kyungmin Hwangbo**[2] | **Nick Barkham**[1]

[1]Department of Rheumatology, New Cross Hospital, Royal Wolverhampton NHS Trust, Wolverhampton, UK

[2]Celltrion Healthcare Co., Ltd, Incheon, Korea

Correspondence
Nick Barkham, Department of Rheumatology, New Cross Hospital, Royal Wolverhampton NHS Trust, Wolverhampton Road, Heath Town, Wolverhampton WV10 0QP, UK.
Email: nick.barkham@nhs.net

Present address
Sooraj Vijayan, SUT Academy of Medical Sciences, Thiruvananthapuram, India

Funding information
The development of this case series article was funded by Celltrion Healthcare Co., Ltd (Incheon, Republic of Korea)

Abstract

The COVID-19 pandemic emphasized the utility of subcutaneous (SC) biologics for pressured healthcare systems. The first SC form of infliximab, CT-P13 SC, provided safe and effective treatment for ankylosing spondylitis in our case series, with increased convenience relative to intravenous treatment benefitting patients both during the pandemic and beyond.

KEYWORDS

ankylosing spondylitis, case report, case series, COVID-19, CT-P13, CT-P13 SC, infliximab, infliximab SC, infliximab subcutaneous, real-world evidence

1 | INTRODUCTION

Infliximab holds an important role in treatment guidelines for ankylosing spondylitis (AS).[1–3] The intravenously (IV) administered infliximab biosimilar CT-P13 IV received regulatory approval from the European Medicines Agency in 2013, followed by United States Food and Drug Administration approval in 2016, for the same indications as reference infliximab.[4–8] Subsequently, the first and only subcutaneous (SC) infliximab, CT-P13 SC, has been developed; this offers potential benefits for patients and healthcare systems.[9] Comparable safety and noninferiority of CT-P13 SC to CT-P13 IV in terms of efficacy and pharmacokinetics were demonstrated in clinical trials in patients with rheumatoid arthritis (RA)[10] and inflammatory bowel disease (IBD),[11] respectively. In July 2020, the marketing authorisation for CT-P13 SC was extended to all of the adult IV formulation indications, including AS.[12] This extension was approved based on extrapolation rather than clinical trial experience in each indication,

and to our knowledge, there are no published reports of CT-P13 SC treatment in patients with AS.

The coronavirus disease 2019 (COVID-19) pandemic has substantially impacted care and health behavior for patients with rheumatological conditions.[13–15] While moderate or high disease activity in patients with rheumatic diseases (including those with axial and peripheral spondyloarthritis) has been associated with an increased risk of COVID-19-related death,[16] biologic/tumor necrosis factor (TNF) inhibitor therapy has been associated with a reduced likelihood of hospitalization due to COVID-19.[17,18] This highlighted the importance of continuing treatment during the pandemic to maintain effective disease control. At The Royal Wolverhampton Hospitals National Health Service (NHS) Trust, rheumatic disease therapies have been maintained throughout the pandemic (in patients without COVID-19), as recommended by the European Alliance of Associations for Rheumatology.[19] In April 2020, National Institute for Health and Care Excellence (NICE) guidance recommended that patients with rheumatological autoimmune, inflammatory, and metabolic bone disorders who were receiving IV administered biologics should consider switching to an SC form of the same treatment or changing to a different SC administered biologic.[20] In this case series, 11 patients receiving CT-P13 IV treatment for AS switched to CT-P13 SC, helping to maximize patient and staff safety while optimizing healthcare system resource allocation.[20] This case series reports outcomes at up to 14.7 months of follow-up, providing a valuable perspective on CT-P13 SC therapy during the COVID-19 pandemic, offering insights into patient treatment decision-making and informing management approaches beyond the pandemic setting.

2 | CASE PRESENTATIONS

Eleven patients (seven male and four female) with diagnoses of AS were included in this case series (Table 1). Patient age ranged from 28–70 years. Patients were receiving CT-P13 for the treatment of AS at The Royal Wolverhampton Hospitals NHS Trust, UK, in April 2020. Following a telephone discussion with their consultant, patients agreed to switch from CT-P13 IV (5 mg/kg every 8 weeks) to CT-P13 SC (120 mg every 2 weeks) in line with NICE guidance for the COVID-19 pandemic.[20] Switching aimed to minimize hospital attendance, reducing the risk of exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and allowed hospital resources to be redeployed as needed. Patients received a visit from a homecare nurse for training on CT-P13 SC administration, followed by telephone appointments with a physician (typically 3 months after CT-P13 SC initiation and then every 6 months). A telephone helpline was available to address any problems raised by patients in the interim. Patients could switch back to CT-P13 IV at any time if desired; all patients were followed up until June 2021. Patients completed a Self-Injection Assessment Questionnaire (SIAQ) at the end of follow-up, using a method adapted from Keininger and Coteur.[21] Patients scored the following domains on a 10-point scale (0 worst; 10 best): feelings about self-injection, self-confidence, self-image, satisfaction with self-injection, pain and skin reactions during or after injection, and ease of use of the self-injection device.

A total of 195 doses of CT-P13 SC were administered, with a median of 26 doses per patient (Table 2). The total duration of follow-up while on CT-P13 SC was 94 months (median: 11).

2.1 | Patients who switched from CT-P13 IV to CT-P13 SC and continued CT-P13 SC treatment

Five patients switched from existing CT-P13 IV treatment to CT-P13 SC and were continuing CT-P13 SC at their last follow-up. Figure 1 shows the distribution of patients who decided to continue CT-P13 SC, by age, weight, and C-reactive protein (CRP) level.

Patient 1 was diagnosed with both AS and rheumatoid factor (RF)-positive RA before 2006 (Table 1). Syndesmophytes were identified on X-ray in 2015, and the patient had undergone spinal fixation surgery. He had received 13 years of prior infliximab treatment with concomitant methotrexate (MTX)—approximately 9 years of reference infliximab and 4 years of CT-P13 IV—but had not received any other prior biologic medications for his AS. Before switching to CT-P13 SC, he reported back pain, peripheral joint involvement, and iritis. While receiving CT-P13 SC, his CRP level remained consistent at 1.0–1.1 mg/L, and disease activity measures were maintained. The patient preferred to continue CT-P13 SC long term to save time and avoid travel to the hospital and payment of parking charges. He also noted that the time required for treatment was much shorter with CT-P13 SC, taking <2 min to administer compared with half a day for CT-P13 IV infusion.

Patient 2 had human leukocyte antigen (HLA)-B27-positive AS with sacroiliitis (Table 1). Prior to CT-P13 SC treatment, the patient reported iritis and upper back pain. She had received 8 years of prior infliximab treatment (approximately 4 years of reference infliximab and 4 years of CT-P13 IV) with concomitant MTX. The patient's CRP level remained consistent at 3 mg/L during CT-P13 SC treatment; disease activity was reasonably well

TABLE 1 Patient demographics, treatment history, and disease activity

Patient #	Sex	Age, years	Ethnicity	Occupation	Body weight, kg	Year of AS diagnosis	Prior treatment	Disease activity: Prior to CT-P13 SC (120 mg Q2W)	Disease activity: At follow-up	Safety
1	Male	68	White	–	93	1974 (RA diagnosed pre-2006)	Infliximab IV + MTX (15 mg PO weekly) CT-P13 IV + MTX (15 mg PO weekly)	Back pain, peripheral joint involvement, and iritis DAS28: 3.41 (May 2019) VAS spine: 3 (May 2019)	BASDAI: 3.2 (October 2020) VAS spine: 4 (October 2020) CRP: 1.0–1.1 mg/L (throughout CT-P13 SC treatment)	No side effects reported by patient
2	Female	59	White	Administrator	81	2002	Infliximab IV + MTX (15 mg PO weekly) CT-P13 IV + MTX (15 mg PO weekly)	Iritis and upper back pain BASDAI: 3 (June 2019); 1.76 (March 2020) VAS spine: 2 (June 2019)	BASDAI: 4 (August 2020) VAS spine: 3 (August 2020) CRP: 3 mg/L (throughout CT-P13 SC treatment)	Minor bruising at injection sites
3	Male	57	White	–	86	1992	Infliximab IV CT-P13 IV	BASDAI: 6.3 (May 2019) VAS spine: 7 (May 2019)	BASDAI: 5.2 (October 2020) VAS spine: 7 (October 2020); 5 (April 2021) CRP: 3 mg/L, 8 mg/L, 36 mg/L	No side effects reported by patient
4	Male	28	White	Tarmac layer	95	2017	Adalimumab (40 mg SC Q2W) Secukinumab CT-P13 IV	BASDAI: 7.8 (2017); 9.5 (December 2019) VAS spine: 9 (2017) Spinal pain: 10 (December 2019) CRP: 22 mg/L	BASDAI: 5 (August 2020) Spinal pain: 6 (August 2020) CRP: 37 mg/L	No side effects reported by patient
5	Female	30	White	Administrator and instructor	64	2017	Adalimumab (40 mg SC Q2W) CT-P13 IV	BASDAI: 6.67 (March 2020) VAS spine: 9 (March 2020)	CRP: <0.2 mg/L, 1 mg/L	Needle phobia
6	Male	60	White	Painter and decorator	98	2018	CT-P13 IV + MTX (15 mg PO weekly) + hydroxychloroquine (200 mg PO twice daily) + prednisolone (2.5 mg PO daily)	BASDAI: 4.6 (October 2019) VAS spine: 7 (October 2019) CRP: 1 mg/L	CRP: 2 mg/L	No side effects reported by patient

(Continues)

TABLE 1 (Continued)

Patient #	Sex	Age, years	Ethnicity	Occupation	Body weight, kg	Year of AS diagnosis	Prior treatment	Disease activity		Safety
								Prior to CT-P13 SC (120 mg Q2W)	At follow-up	
7	Male	48	White	Unemployed	92	1998	Secukinumab (150 mg SC weekly) Adalimumab (40 mg SC Q2W) Etanercept (50 mg SC weekly) CT-P13 IV	BASDAI: 7 (January 2020) VAS spine: 7 (January 2020) CRP: 2 mg/L	CRP: 4 mg/L	No side effects reported by patient
8	Male	37	White	Data analyst	106	1999	Infliximab IV CT-P13 IV	BASDAI: 0.3 (March 2020) VAS spine: 1 (March 2020)	CRP: 5 mg/L	No side effects reported by patient, and patient's Crohn's disease was not adversely affected
9	Female	36	White	Community medication provider	82	2011	Etanercept (50 mg SC weekly) Golimumab (50 mg SC Q4W) CT-P13 IV	BASDAI: 3 (April 2019) VAS spine: 2 (April 2019)	–	Localized injection-site reaction reported after first injection
10	Male	70	White	Retired	93	2009	Infliximab IV CT-P13 IV	Back pain, peripheral arthritis, and iritis DAS28: 1.67 (January 2020) VAS spine: 3 (January 2020)	CRP: <0.2–<1 mg/L	No side effects reported by patient
11	Female	63	White	–	68	2000	Sulfasalazine MTX Etanercept Adalimumab (40 mg SC Q2W) Infliximab IV CT-P13 IV	BASDAI: 6 (February 2020) VAS spine: 2 (February 2020)	CRP: 57 mg/L, 12 mg/L, 14 mg/L	No side effects reported by patient

Note: Infliximab IV and CT-P13 IV were administered at 5 mg/kg Q8W. The reference range for CRP was 0.0–0.5 mg/L for all patients. VAS spine scores were determined on a 10-cm scale.

Abbreviations: AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C-reactive protein; DAS28, Disease Activity Score in 28 joints; IV, intravenous; MTX, methotrexate; PO, per os; QnW, every *n* weeks; RA, rheumatoid arthritis; SC, subcutaneous; VAS, Visual Analog Scale.

TABLE 2 CT-P13 SC treatment characteristics

Patient	Body weight, kg	CT-P13 SC[a] doses received, *n*	Duration of follow-up on CT-P13 SC treatment, months[b]
1	93	26	13.09
2	81	26	13.73
3	86	26	13.16
4	95	26	14.73
5	64	26	13.09
6	98	4	1.54
7	92	10	4.16
8	106	10	3.42
9	82	1	0.50
10	93	12	5.64
11	68	28	10.77
Total number (median [range])	N/A	195 (26 [1–26])	93.84 (10.77 [0.50–14.73])

Abbreviations: N/A, not applicable; SC, subcutaneous.

[a]All patients were scheduled to administer 120 mg of CT-P13 SC every 2 weeks.

[b]Calculated from the date of CT-P13 SC initiation (where this differed from the date of prescription).

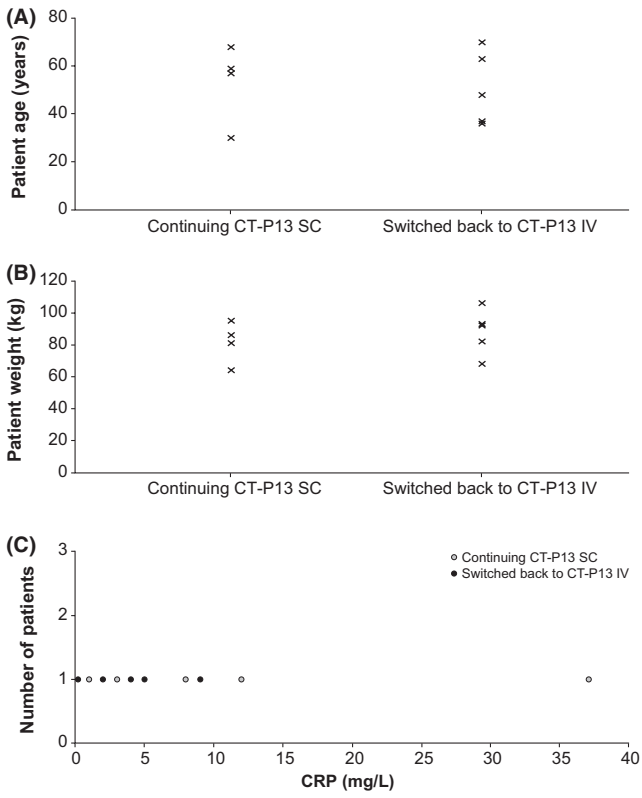

FIGURE 1 Distribution of patients deciding to continue CT-P13 SC or switch back to CT-P13 IV by (A) age, (B) weight, and (C) CRP level. CRP levels were obtained in June 2021 (end of follow-up) for those patients who continued CT-P13 SC; for those patients who decided not to continue with CT-P13 SC, CRP levels were obtained before they switched back to CT-P13 IV. CRP, C-reactive protein; IV, intravenous; SC, subcutaneous

maintained. The patient experienced minor bruising at injection sites but reported no other issues.

Patient 3 had AS with fused sacroiliac joints, significant spinal fusion, and no cervical spine movement prior to switching to CT-P13 SC (Table 1). The patient had received 15 years of prior infliximab treatment as monotherapy (approximately 11 years of reference infliximab and 4 years of CT-P13 IV). The symptomatic response to CT-P13 IV was suboptimal, although inflammatory markers were normal. While receiving CT-P13 SC, disease activity scores improved, although CRP levels increased.

Patient 4 had HLA-B27-positive AS diagnosed in 2017 (Table 1), following a history of back pain (since 2015), sacroiliac joint erosions on pelvis X-ray (2016), and sacroiliitis and thoracic spine marrow edema on magnetic resonance imaging (MRI) (2017). The patient had previously received adalimumab (discontinued because of lack of efficacy) and secukinumab (discontinued as no response was observed), before a treatment break when the patient was not in the UK. He received approximately 4 months of CT-P13 IV treatment before switching to CT-P13 SC. With CT-P13 SC, the patient's disease activity scores improved, although CRP levels increased. The patient reported problems with drug deliveries but decided to continue CT-P13 SC long term as treatment was convenient for his work schedule.

Patient 5 was diagnosed with HLA-B27-positive AS with a history of back pain and scalp psoriasis prior to CT-P13 SC treatment (Table 1). The patient had previously received adalimumab, which was discontinued because of local injection-site reactions (ISRs), before approximately

TABLE 3 Mean SIAQ domain scores

Patient	SIAQ domain mean scores[a]					
	Feelings about self-injection	Self-confidence	Self-image	Satisfaction with self-injection	Pain and skin reactions during or after injection	Ease of use of the self-injection device
Patients who decided to continue CT-P13 SC						
1	8	9	8	7	4	9
2	9	7	10	10	5	8
3	9	7	4	3	9	8
4	0	0	10	8	10	10
5	7	0	10	7	5	5
Mean (SD)	6.60 (3.38)	4.60 (3.83)	8.40 (2.33)	7.00 (2.28)	6.60 (2.42)	8.00 (1.67)
Patients who decided to switch back to CT-P13 IV						
6	8	9	7	7	10	9
7	8	10	1	9	10	10
8	10	10	7	9	8	8
9	1	1	10	1	0	9
10	9	10	10	4	7	10
11	10	10	10	8	9	10
Mean (SD)	7.67 (3.09)	8.33 (3.30)	7.50 (3.20)	6.33 (2.92)	7.33 (3.45)	9.33 (0.75)

Abbreviations: IV, intravenous; SC, subcutaneous; SD, standard deviation; SIAQ, Self-Injection Assessment Questionnaire.

[a]Scored on a 10-point scale from 0 (worst experience) to 10 (best experience).

2 years of CT-P13 IV monotherapy. During CT-P13 SC treatment, CRP levels were normal. The patient was needle phobic and expressed a desire to change to a treatment administered via a different route; however, the patient's friend assumed responsibility for administering the injections without any further issues.

Patients 1–5 completed the SIAQ at the end of the follow-up period (while remaining on CT-P13 SC). Mean scores were at least 6.60 for all domains other than self-confidence (Table 3). The lower mean self-confidence domain score (4.60) was skewed by two patients who scored 0; this may have been related to the needle phobia experienced by Patient 5 and generally low self-confidence affecting patients as a result of pandemic-related restrictions.

2.2 | Patients who switched from CT-P13 IV to CT-P13 SC, and decided to switch back to CT-P13 IV

Six patients in this case series switched from ongoing CT-P13 IV treatment to CT-P13 SC and later decided to switch back to CT-P13 IV. The distribution of patients who decided to switch back to CT-P13 IV, by age, weight, and CRP level, is shown in Figure 1.

Patient 6 was diagnosed with HLA-B27-positive AS and RF-positive RA (Table 1). He had received just over 1 year of prior CT-P13 IV treatment with concomitant MTX, hydroxychloroquine, and prednisolone. No clinical assessments were conducted during CT-P13 SC treatment; however, the patient reported that the treatment was less effective than CT-P13 IV. Prior to switching, the patient's CRP level was 1 mg/L; this was 2 mg/L during CT-P13 SC treatment and returned to 1 mg/L after the patient restarted CT-P13 IV.

Patient 7 had HLA-B27-positive AS with a fused dorsolumbar spine and uveitis (Table 1). He had previously received secukinumab (discontinued because of long-term failure of efficacy), adalimumab (discontinued because of anti-drug antibody formation), and etanercept (discontinued because of long-term failure of efficacy), before beginning CT-P13 IV in February 2020. No clinical assessments were conducted during CT-P13 SC treatment, but the patient reported that the therapy was less effective than CT-P13 IV. The patient's CRP level was 2 mg/L before switching to CT-P13 SC, 4 mg/L while receiving CT-P13 SC, and 8 mg/L after switching back to CT-P13 IV.

Patient 8 had AS and Crohn's disease (Table 1). The patient had received 17 years of prior infliximab treatment

(approximately 13 years of reference infliximab and 4 years of CT-P13 IV) as monotherapy. Initiation of CT-P13 SC was delayed because of late drug delivery due to the pandemic situation. No clinical assessments were conducted while the patient was receiving CT-P13 SC, but he reported that the therapy was less effective than CT-P13 IV. The CRP level while receiving CT-P13 SC was 5 mg/L; after the patient decided to switch back to CT-P13 IV, this was 7 mg/L.

Patient 9 had HLA-B27-positive AS with sacroiliitis, having reported back and hip pain at presentation (Table 1). She had received etanercept (discontinued because of ISR) and golimumab (discontinued because of ineffectiveness) before initiating CT-P13 IV. One hour following her first injection of CT-P13 SC, she experienced a localized ISR consisting of simple erythema of 2 cm in diameter. This resolved after 48 h without pain or itch, but as a consequence, the patient preferred to switch back to CT-P13 IV. After switching back to CT-P13 IV, her CRP level was 3 mg/L.

Patient 10 was diagnosed with both AS and seronegative RA in 2009, with the AS diagnosis following squaring of vertebrae, ankylosis, and Romanus lesions identified by MRI (Table 1). The patient had received 10 years of prior infliximab treatment as monotherapy (approximately 6 years of reference infliximab and 4 years of CT-P13 IV). Throughout CT-P13 SC treatment, CRP levels remained normal, but the patient decided to switch back to CT-P13 IV because of a perceived reduction in effectiveness. After switching back to CT-P13 IV, the CRP level was <0.2 mg/L.

Patient 11 had diagnoses of AS, uveitis, and Crohn's disease (Table 1). The patient had received etanercept and adalimumab prior to initiating infliximab and went on to receive 13 years of infliximab as monotherapy (approximately 9 years of reference infliximab and 4 years of CT-P13 IV). No clinical assessments were conducted during CT-P13 SC treatment, but the patient reported that the effect of the medication was not lasting 2 weeks. While receiving CT-P13 SC, the patient's CRP levels were 57 mg/L, 12 mg/L, and 14 mg/L. After switching back to CT-P13 IV, the CRP level was 20 mg/L.

Patients 6–11 completed the SIAQ at the end of the follow-up period (after they had switched back to CT-P13 IV). Mean scores were at least 7.33 for all domains other than satisfaction with self-injection, which was slightly lower at 6.33 (Table 3).

3 | DISCUSSION AND CONCLUSIONS

In our case series, of the 11 patients who switched from CT-P13 IV to CT-P13 SC, 5 (45.5%) decided to continue CT-P13 SC long term, while 6 (54.5%) decided to switch back to CT-P13 IV. Two of the patients who decided to continue CT-P13 SC long term noted increased convenience, with reduced time and travel requirements for treatment, as a reason for their choice. These findings are in keeping with those from a study of patient preferences in AS, in which patients receiving SC administered TNF inhibitors cited flexibility, convenience, and shortened administration time as benefits.[22] Similarly, the duration of infusion, need to travel, and appointment scheduling were the most frequent perceived disadvantages of IV therapy listed by patients with immune-mediated inflammatory diseases (IMIDs) receiving IV administered biologics.[23] In this case series, five of the six patients who decided to switch back to CT-P13 IV reported that CT-P13 SC was not as effective as CT-P13 IV. However, it is important to note that few clinical assessments were conducted in these patients because of the pandemic. Persistence with CT-P13 SC did not seem to be related to patient age, weight, or CRP level. Since decisions about whether to persist with CT-P13 SC treatment did not seem to correlate with objective findings in terms of CRP level, this suggests that factors including the nocebo effect might underpin subjective perceptions of reduced effectiveness in these patients.[24] Clinical trials evaluating CT-P13 SC in patients with RA and IBD found that efficacy was maintained following a switch from CT-P13 IV,[10,11] and this is supported by clinical experience in the IBD setting as patients have switched to CT-P13 SC during the pandemic.[25,26] In this case series, mean SIAQ scores for self-image and satisfaction with self-injection were higher for patients continuing CT-P13 SC compared with those who decided to switch back to CT-P13 IV. One of the patients in this case series, who ultimately decided to continue CT-P13 SC, reported needle phobia, requiring a friend to assume responsibility for administering the treatment. Dislikes of self-injection/needles or lack of comfort with self-injection was the most frequent reason given by patients with IMIDs who preferred IV over SC biologic therapy in a previous analysis,[23] indicating the potential influence of this concern on treatment decision-making. One patient highlighted problems or delays with receiving deliveries of CT-P13 SC, which may have adversely affected their treatment experience. Such issues are more likely to have been prevalent during the pandemic owing to the impact of staff shortages or redeployment; thus, any potential impact on CT-P13 SC-treated patients should be reduced in the future.

Although the number of patients included in this case series is limited, the safety profile of CT-P13 SC was consistent with data included within the EU product information,[4] with no new or unexpected safety findings. Two

patients experienced mild ISRs, consistent with those described in the EU product information.[4] The remaining patients did not report any adverse reactions. These safety findings are in keeping with reports for patients with IBD switching from IV to SC infliximab during the pandemic.[25–28] There were no reported cases of SARS-CoV-2 infection in our case series. Of the limited published data regarding SARS-CoV-2 infection in patients with AS or spondyloarthritis treated with TNF inhibitors, most reports found that the clinical course of COVID-19 was not severe in this population.[29–35] In addition, a survey found that TNF inhibitor treatment did not impact subjective scores ascribed by patients with spondyloarthritis to the severity of their COVID-19.[36]

Subcutaneous biologic therapy offers several potential benefits for healthcare systems and patients, including increased convenience and flexibility (including at-home administration) for patients, and reduced preparation, drug delivery time, and resource requirements for healthcare providers.[9] Indeed, benefits including enhanced control and improved convenience for patients, alongside reduced pressure on infusion units, have been reported in the IBD context as patients have switched from IV to SC infliximab treatment during the COVID-19 pandemic.[25,27,28] An analysis of 88 patients with IBD found that 85.2% of patients were happier receiving CT-P13 SC than infliximab IV, and 92.0% felt that CT-P13 SC was easy to use.[26] Given these potential benefits of CT-P13 SC, our findings suggest that it may be appropriate to offer patients currently receiving infliximab IV the opportunity to switch to CT-P13 SC; however, additional studies may be needed to confirm the efficacy and safety of making such a switch. In addition, it might be beneficial for patients with indications for infliximab therapy to initiate treatment with CT-P13 SC (after the required IV loading dose[4]).

Our results reflect 11 cases from a single center and, because of the low number of patients included, may not be fully generalizable to the wider AS patient population. However, since patients with AS are often of working age and may experience work instability as a result of the disease,[37] the benefit of increased convenience of CT-P13 SC treatment reported by some of the patients in this case series may be attractive to many individuals with AS, relative to the demands of frequent hospital visits for IV infusions. Our conclusions are limited by the observational nature of case reports, meaning that clinical and laboratory assessments were not collected consistently for all patients. Because of the pandemic situation, such assessments were made less regularly than usual, with reductions in both face-to-face and blood monitoring appointments further restricting data collection possibilities. However, an advantage of this management approach, offering patients a switch to CT-P13 SC, was the potential reduction in nosocomial exposure to SARS-CoV-2. Experience with online collection of outcome measures also suggests a model for patient management that is less dependent on face-to-face appointments and could be implemented post pandemic. Acknowledging the limitations of the case series, our findings make a valuable contribution to the available information about the efficacy and safety of CT-P13 SC in patients with AS. While these data were collected during the COVID-19 pandemic, we believe that our patient preference findings will be transferable to a post-pandemic setting.

In summary, our case series suggests that CT-P13 SC can provide safe and effective treatment for patients with AS. The convenience of CT-P13 SC may be a benefit for patients both during and beyond the COVID-19 pandemic.

ACKNOWLEDGEMENTS

Medical writing support, including development of a draft outline, and subsequent drafts in consultation with the authors, collating author comments, copyediting, fact checking, and referencing, was provided by Beatrice Tyrrell, DPhil, at Aspire Scientific Limited (Bollington, UK). Funding for medical writing support for this article was provided by Celltrion Healthcare Co., Ltd (Incheon, Republic of Korea).

CONFLICT OF INTEREST

Sooraj Vijayan has no potential conflicts of interest to declare. Kyungmin Hwangbo is an employee of Celltrion Healthcare Co., Ltd. Nick Barkham has received honoraria and speaker fees from Celltrion Healthcare.

AUTHOR CONTRIBUTIONS

Sooraj Vijayan and Nick Barkham collected data, contributed to analysis and interpretation, and drafted and critically revised the article. Kyungmin Hwangbo contributed to analysis and interpretation, and drafted and critically revised the article. All authors take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

CONSENT

The treatment described in this case series arose from a service development due to the COVID-19 pandemic and in response to NICE guidance, which is mandatory in the UK. Since the treatment was not part of a clinical trial, formal ethical submission was not required. All patients had a telephone call with their consultant to discuss the potential risks and benefits prior to the change of treatment and all agreed to it; approval was provided by the NHS Trust (treatment provider) and the Clinical Commissioning

Group (payer authority). The patients provided written informed consent for their cases to be included in this article.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

ORCID

Nick Barkham https://orcid.org/0000-0001-7754-6931

REFERENCES

1. van der Heijde D, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis*. 2017;76:978. doi:10.1136/annrheumdis-2016-210770
2. Hamilton L, Barkham N, Bhalla A, et al. BSR and BHPR guideline for the treatment of axial spondyloarthritis (including ankylosing spondylitis) with biologics. *Rheumatology*. 2017;56:313-316. doi:10.1093/rheumatology/kew223
3. National Institute for Health and Care Excellence Spondyloarthritis in over 16s: diagnosis and management. 2017. https://www.nice.org.uk/guidance/ng65/resources/spondyloarthritis-in-over-16s-diagnosis-and-management-pdf-1837575441349. Accessed November 17, 2021.
4. European Medicines Agency Remsima summary of product characteristics. 2021. https://www.ema.europa.eu/en/documents/product-information/remsima-epar-product-information_en.pdf. Accessed November 18, 2021.
5. European Medicines Agency Remicade summary of product characteristics. 2021. https://www.ema.europa.eu/en/documents/product-information/remicade-epar-product-information_en.pdf. Accessed November 18, 2021.
6. European Medicines Agency Inflectra summary of product characteristics. 2021. https://www.ema.europa.eu/en/documents/product-information/inflectra-epar-product-information_en.pdf. Accessed November 18, 2021.
7. US Food and Drug Administration Inflectra prescribing information. 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125544s018lbl.pdf. Accessed November 18, 2021.
8. US Food and Drug Administration Remicade prescribing information. 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103772s5401lbl.pdf. Accessed November 18, 2021.
9. Kim H, Alten R, Cummings F, et al. Innovative approaches to biologic development on the trail of CT-P13: biosimilars, value-added medicines, and biobetters. *mAbs*. 2021;13(1):1868078. doi:10.1080/19420862.2020.1868078
10. Westhovens R, Wiland P, Zawadzki M, et al. Efficacy, pharmacokinetics and safety of subcutaneous versus intravenous CT-P13 in rheumatoid arthritis: a randomized phase I/III trial. *Rheumatology*. 2021;60:2277-2287. doi:10.1093/rheumatology/keaa580
11. Schreiber S, Ben-Horin S, Leszczyszyn J, et al. Randomized controlled trial: subcutaneous versus intravenous infliximab CT-P13 maintenance in inflammatory bowel disease. *Gastroenterology*. 2021;160:2340-2353. doi:10.1053/j.gastro.2021.02.068
12. Biosimilar Development. European Commission grants marketing authorisation for world's first subcutaneous formulation of infliximab, Remsima SC, for an additional five indications including for use in inflammatory bowel disease and ankylosing spondylitis. 2020. https://www.biosimilardevelopment.com/doc/european-commission-grants-marketing-authorisation-for-world-s-first-subcutaneous-0001. Accessed November 17, 2021.
13. Ciurea A, Papagiannoulis E, Bürki K, et al. Impact of the COVID-19 pandemic on the disease course of patients with inflammatory rheumatic diseases: results from the Swiss Clinical Quality Management cohort. *Ann Rheum Dis*. 2021;80:238-241. doi:10.1136/annrheumdis-2020-218705
14. George MD, Venkatachalam S, Banerjee S, et al. Concerns, healthcare use, and treatment interruptions in patients with common autoimmune rheumatic diseases during the COVID-19 pandemic. *J Rheumatol*. 2021;48:603-607. doi:10.3899/jrheum.201017
15. Reuter K, Deodhar A, Makri S, Zimmer M, Berenbaum F, Nikiphorou E. The impact of the COVID-19 pandemic on people with rheumatic and musculoskeletal diseases: insights from patient-generated data on social media. *Rheumatology*. 2021;60:SI77-SI84. doi:10.1093/rheumatology/keab174
16. Strangfeld A, Schäfer M, Gianfrancesco MA, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2021;80:930-942. doi:10.1136/annrheumdis-2020-219498
17. Gianfrancesco M, Hyrich KL, Al-Adely S, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2020;79:859. doi:10.1136/annrheumdis-2020-217871
18. Annapureddy N, Nalleballe K, Onteddu SR, et al. Biologics in systemic autoimmune diseases during COVID-19 pandemic. *Clin Rheumatol*. 2020;39:3529-3531. doi:10.1007/s10067-020-05439-z
19. Landewé RBM, Machado PM, Kroon F, et al. EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2. *Ann Rheum Dis*. 2020;79:851. doi:10.1136/annrheumdis-2020-217877
20. National Institute for Health and Care Excellence COVID-19 rapid guideline: rheumatological autoimmune, inflammatory and metabolic bone disorders. 2020. https://www.nice.org.uk/guidance/ng167/resources/covid19-rapid-guideline-rheumatological-autoimmune-inflammatory-and-metabolic-bone-disorders-pdf-66141905788357. Accessed November 17, 2021.
21. Keininger D, Coteur G. Assessment of self-injection experience in patients with rheumatoid arthritis: psychometric validation of the Self-Injection Assessment Questionnaire (SIAQ). *Health Qual Life Outcomes*. 2011;9:2. doi:10.1186/1477-7525-9-2
22. Fajri DW, Brand CA, Dharmage SC, Martin BJ, Buchanan RRC, Schachna L. What factors determine patients' preference for tumour necrosis factor inhibitors in ankylosing spondylitis? *Clin Rheumatol*. 2009;28:599-602. doi:10.1007/s10067-009-1104-4
23. Bolge SC, Eldridge HM, Lofland JH, Ravin C, Hart PJ, Ingham MP. Patient experience with intravenous biologic therapies for ankylosing spondylitis, Crohn's disease, psoriatic arthritis, psoriasis, rheumatoid arthritis, and ulcerative colitis. *Patient Prefer Adherence*. 2017;11:661-669. doi:10.2147/PPA.S121032

24. Kristensen LE, Alten R, Puig L, et al. Non-pharmacological effects in switching medication: the nocebo effect in switching from originator to biosimilar agent. *BioDrugs*. 2018;32:397-404. doi:10.1007/s40259-018-0306-1
25. Argüelles-Arias F, Fernández Álvarez P, Castro Laria L, et al. Switch to infliximab subcutaneous during SARS-CoV-2 pandemic: preliminary results. *Rev Esp Enferm Dig*. 2021. doi:10.17235/reed.2021.8320/2021
26. Smith PJ, Storey D, Gregg B, et al. P496 Efficacy and safety of elective switching of inflammatory bowel disease patients from intravenous to subcutaneous infliximab (IFX): a multi-centre cohort study. *J Crohns Colitis*. 2021;15:S480-S481. doi:10.1093/ecco-jcc/jjab076.619
27. Verma AM, Patel A, Subramanian S, Smith PJ. From intravenous to subcutaneous infliximab in patients with inflammatory bowel disease: a pandemic-driven initiative. *Lancet Gastroenterol Hepatol*. 2021;6:88-89. doi:10.1016/s2468-1253(20)30392-7
28. McGoran J, Wilson A, McErlain S, et al. Initiation of subcutaneous infliximab (Remsima) therapy for the treatment of inflammatory bowel disease during the COVID-19 pandemic. *Frontline Gastroenterol*. 2021;13(1):89-90. doi:10.1136/flgastro-2020-101760
29. Lee JM, Lee SJ. Olfactory and gustatory dysfunction in a COVID-19 patient with ankylosing spondylitis treated with etanercept: case report. *J Korean Med Sci*. 2020;35:e201. doi:10.3346/jkms.2020.35.e201
30. Duret P-M, Sebbag E, Mallick A, Gravier S, Spielmann L, Messer L. Recovery from COVID-19 in a patient with spondyloarthritis treated with TNF-alpha inhibitor etanercept. *Ann Rheum Dis*. 2020;79:1251-1252. doi:10.1136/annrheumdis-2020-217362
31. Duret P-M, Spielmann L, Messer L. Rheumatic diseases and COVID-19: a cohort of 17 patients under DMARDs. Response to: 'Comment on: Recovery from COVID-19 in a patient with spondyloarthritis treated with TNF-alpha inhibitor etanercept. A report on a COVID-19 patient with psoriatic arthritis receiving ustekinumab' by Messina et al. *Ann Rheum Dis*. 2020;80:e80. doi:10.1136/annrheumdis-2020-218147
32. Brito CA, Paiva JG, Pimentel FN, Guimarães RS, Moreira MR. COVID-19 in patients with rheumatological diseases treated with anti-TNF. *Ann Rheum Dis*. 2021;80:e62. doi:10.1136/annrheumdis-2020-218171
33. Migkos MP, Kaltsonoudis E, Pelechas E, et al. Use of conventional synthetic and biologic disease-modifying anti-rheumatic drugs in patients with rheumatic diseases contracting COVID-19: a single-center experience. *Rheumatol Int*. 2021;41:903-909. doi:10.1007/s00296-021-04818-2
34. Hasseli R, Pfeil A, Hoyer BF, et al. Do patients with rheumatoid arthritis show a different course of COVID-19 compared to patients with spondyloarthritis? *Clin Exp Rheumatol*. 2021;39:639-647.
35. Şen N, Tezcan ME. Anti-tumor necrosis factor treatment in ankylosing spondylitis may not relate to poor prognosis in COVID-19. *Arch Rheumatol*. 2020;36:142-143. doi:10.46497/ArchRheumatol.2021.8228
36. Rosenbaum JT, Weisman MH, Shafer C, et al. Correspondence on 'Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry'. *Ann Rheum Dis*. 2021. doi:10.1136/annrheumdis-2021-220588
37. Gilworth G, Emery P, Barkham N, Smyth MG, Helliwell P, Tennant A. Reducing work disability in ankylosing spondylitis – development of a work instability scale for AS. *BMC Musculoskelet Dis*. 2009;10:68. doi:10.1186/1471-2474-10-68

How to cite this article: Vijayan S, Hwangbo K, Barkham N. Real-world evidence for subcutaneous infliximab (CT-P13 SC) treatment in patients with ankylosing spondylitis during the coronavirus disease (COVID-19) pandemic: A case series. *Clin Case Rep*. 2022;10:e05233. doi:10.1002/ccr3.5233