Long-term efficacy of sarilumab on the progression of interstitial lung disease in rheumatoid arthritis: the KEIO-RA cohort and literature review

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Abstract

Objective

To clarify the impact of sarilumab (SAR) on the progression of interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA).

Methods

We conducted a retrospective review of all consecutive RA patients from the KEIO-RA cohort who visited our institution between 2018 and 2024 and received SAR treatment. Patients were followed for 24 months from the initiation of SAR. The primary outcome was the rate of progression of ILD as assessed by high-resolution computed tomography (HRCT). We also conducted a literature review regarding the efficacy of SAR on RA-ILD in PubMed, Web of Science, and Scopus databases.

Results

Among 123 cases, 21 (17.1%) had ILD. The median age at SAR initiation was 56 years, and 71.4% were female. Except for 6 cases, SAR was administered as monotherapy via subcutaneous injection at 200 mg every two weeks. During SAR treatment, 18 cases (85.7%) exhibited stable HRCT findings, coupled with improvements in arthritis. Two cases with NSIP and OP patterns demonstrated improvements in both HRCT findings and arthritis post-SAR treatment. One case experienced an exacerbation of ILD at 18 months, with worsening arthritis observed prior to the deterioration of ILD. Serum KL-6 levels also improved or remained stable after SAR initiation, except in one case of ILD exacerbation. There were no adverse events, including serious infections, during the observation period. Additionally, our literature review identified a case of RA-ILD treated with SAR and achieved remission of arthritis and ILD.

Conclusion

In our study, SAR exhibited encouraging efficacy in stabilising RA-ILD in most cases.

Key words

rheumatoid arthritis, interstitial lung disease, sarilumab, interleukin-6 inhibitor, biologics

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Introduction

Interstitial lung disease (ILD) is a prevalent and serious complication of rheumatoid arthritis (RA), affecting approximately 10% to 20% of RA patients (1, 2). The clinical course of RA-ILD varies widely, with factors such as older age, male sex, smoking history, a usual interstitial pneumonia (UIP) pattern of ILD, higher arthritis activity, Krebs von den Lungen-6 (KL-6) elevation, or positive rheumatoid factor (RF)/ anti-cyclic citrullinated peptide (anti-CCP) antibody identified as predictors of RA-ILD progression (3, 4).

To prevent the progression of RA-ILD, achieving remission of arthritis is paramount because uncontrolled disease activity poses a risk for ILD progression (4). However, RA-ILD patients often present challenges in treatment, as these individuals are typically older and may have impaired renal function, which limits the use of methotrexate (MTX), the anchor drug for RA. Consequently, the limited application of MTX reduces the efficacy of biological disease-modifying anti-rheumatic drugs (bDMARDs), notably tumour necrosis factor (TNF) inhibitors (5). On the other hand, interleukin-6 (IL-6) inhibitors have evidence of efficacy in controlling arthritis as monotherapy without concomitant MTX, compared with TNF inhibitors, thereby offering a potential treatment option for RA-ILD patients (6, 7).

Sarilumab (SAR) is a human monoclonal antibody targeting the IL-6 receptor, approved for the treatment of RA, effectively disrupting the IL-6 signalling pathway (8). Although SAR is a potential treatment option for patients with RA-ILD, there is currently a lack of data regarding its impact on the progression of ILD. Therefore, this study aimed to clarify the impact of SAR on the progression of ILD in patients with RA.

Materials and methods

Patients and data collection

We retrospectively reviewed all consecutive patients with RA from the KEIO-RA cohort who were treated with SAR at Keio University Hospital between February 2018 and March 2024. RA was diagnosed according to the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) RA classification criteria (9). The treatment of RA was conducted using medications approved by the pharmaceuticals and medical devices agency in Japan. Difficult-to-treat (D2T) RA was defined based on the EULAR definition (10). All patients received a subcutaneous dose of 200 mg of SAR every two weeks. Patients were followed up for 24 months from the initial SAR administration. For cases where SAR was discontinued before 24 months, the last observation carried forward methodology was applied. This study received approval from the Ethics Committee of Keio University School of Medicine (approval no. 20130506). All investigations were conducted in accordance with the principles outlined in the Declaration of Helsinki. Written informed consent was waived in accordance with Japanese regulations.

ILD assessment

All patients underwent chest radiography prior to initiating SAR, with chest high-resolution computed tomography (HRCT) performed if ILD was suspected. The evaluation of ILD on chest HRCT was performed by clinical radiologists' reports and rheumatologists with over ten years of experience in the field. ILD patterns were categorised using criteria outlined in the American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias (11). The extent of ILD was evaluated by HRCT score based on Goh's algorithm, assessing airspace consolidation, ground-glass attenuation, and interlobular septal thickening and/or reticular opacity at five zones: (1) origin of great vessels, (2) main carina, (3) pulmonary venous confluence, (4) halfway between the third and fifth section, and (5) immediately above the diaphragm (12). Acute exacerbation of RA-ILD was defined when all of the following criteria were met: confirmed diagnosis of RA-ILD; unexplained worsening or sudden onset of dyspnea within 30 days; new bilateral ground-glass opacities and/or consolidation superimposed on reticu-

Table I. Clinical characteristics of patients with RA-ILD at start of sarilumab treatment.

Characteristics	n=21
Age, median [IQR] (years)	56 [44-64.5]
Female (n, %)	15 (71.4)
Disease duration, median [IQR] (months)	16 [9-24.5]
Smoking (n, %)	8 (38.1)
RF positive (n, %)	19 (90.4)
Anti-CCP positive (n, %)	18 (85.7)
D2T RA (n, %)	13 (61.9)
Laboratory test, median [IQR]	
CRP (mg/dL)	0.27 [0.03-2.83]
ESR (mm/h)	30 [8.75-53.25]
MMP-3 (ng/mL)	145.9 [79.4-247.8]
KL-6 (U/mL)	490.5 [344.8-682.3]
eGFR (ml/min/1.73m^2)	67 [53.5-83]
eGFR <60 (n, %)	7 (33.3)
DAS28-ESR	4.44 [2.96-5.4]
CDAI	15.4 [9.7-27.4]
HAQ	1.4 [0.8-1.8]
Type of ILD (n, %)	
NSIP	14 (66.7)
UIP	6 (28.6)
OP	1 (4.7)
HRCT score, % [IQR]	7 [4-11]
Current treatment (n, %)	
Prednisolone	10 (47.6)
Methotrexate	3 (14.3)
Other csDMARDs	3 (14.3)
Prior csDMARD use (n, %)	13 (61.9)
Prior bDMARD use (n, %)	21 (100)
TNF inhibitors	13 (61.9)
Tocilizumab	17 (80.9)
Abatacept	2 (9.5)
JAK inhibitors	1 (4.7)

ILD: interstitial lung disease, Anti-CCP: anti-cyclic citrullinated peptide antibody, RF: rheumatoid factor, CRP: C-reactive protein, ESR: erythrocyte sedimentation rates, D2T RA: difficult-to-treat rheumatoid arthritis, MMP-3: matrix metalloproteinase-3, KL-6: Krebs von den Lungen-6, eGFR: estimated glomerular filtration rate, DAS28: disease activity score in 28 joints, CDAI: the Clinical Disease Activity Index, HAQ: the Health Assessment Questionnaire Disability Index, NSIP: nonspecific interstitial pneumonia, UIP: usual interstitial pneumonia, OP: organising pneumonia, HRCT: high-resolution computed tomography, csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs, bDMARDs: biological disease-modifying anti-rheumatic drugs, TNF: tumour necrosis factor, JAK: Janus kinase. Smoking included past or current habit.

lar or honeycomb patterns observed on HRCT; absence of pulmonary infection confirmed by culture and serological tests; and exclusion of other identifiable causes of lung injury (13). Chest HRCT was evaluated annually as a standard practice, and the progression of ILD on HRCT was defined as the worsening of HRCT scores. The primary outcome was the rate of progression of ILD, as assessed by HRCT. A sub-analysis was conducted on the changes in KL-6 levels before and after SAR treatment.

Clinical assessment

Demographic and clinical data were obtained from patients' medical records, including age, sex, disease duration, smoking history, treatment history, laboratory data, and RA disease activity. Chronic kidney disease was defined as an eGFR less than 60 mL/min/1.73m^2. RA disease activity was evaluated according to the Clinical Disease Activity Index (CDAI) (14) and the Disease Activity Score in 28 joints using erythrocyte sedimentation rate (DAS28-ESR) (15). The Health Assessment Questionnaire Disability Index (HAQ) score (16) was assessed as a measure of functional outcome. We collected these data at the time of SAR initiation, 24 months after SAR initiation, or at the time of SAR discontinuation. As a secondary outcome, the change in RA disease activity, as assessed by DAS28-ESR, CDAI, and HAQ scores following SAR treatment, were assessed. We defined non-responders to SAR as patients who discontinued SAR due to uncontrolled disease activity or failed to achieve remission or low disease activity at 24 months following SAR initiation.

Statistical analysis

Continuous variables are shown as the median with the interquartile range (IQR) and categorical data are presented as percentages. Categorical data or continuous variables were compared between the two groups using Fisher's exact test or the Mann-Whitney U-test, respectively. Receiver operating characteristic (ROC) analysis was used to determine cut-off values. We analysed the retention rates of SAR using Kaplan-Meier curves. All statistical analyses were performed with JMP software 17 (SAS Institute Inc., Cary, NC, USA).

Search strategy

For the literature review on the efficacy of SAR in RA-ILD, we conducted a search of the PubMed, Web of Science, and Scopus databases using keywords 'sarilumab' AND 'interstitial lung disease' AND 'rheumatoid arthritis' on 13 October 2024 with guidelines for writing a narrative review (17).

Results

Patient characteristics

Of the 123 patients who began SAR for RA treatment, 60 showed no abnormal shadow on chest radiographs, and the remaining 63 underwent HRCT. As a result, 21 patients with RA-ILD were identified. There were no cases of newly developed ILD following the initiation of SAR treatment.

The clinical characteristics of 21 patients with RA-ILD at the initiation of SAR are shown in Table I. The median age was 56 years, and 71.4% were female. The majority of cases were positive for RF or anti-CCP antibody (RF, 90.4%; anti-CCP, 85.7%). Chronic kidney disease was found in 33% of cases, and the median eGFR value was 67 ml/min/1.73m^2. Thirteen cases (61.9%) had been treated with conventional synthetic DMARDs but had an inadequate response. Additionally, all 21 patients had inadequate response to prior bDMARDs, of whom 13 (61.9%)

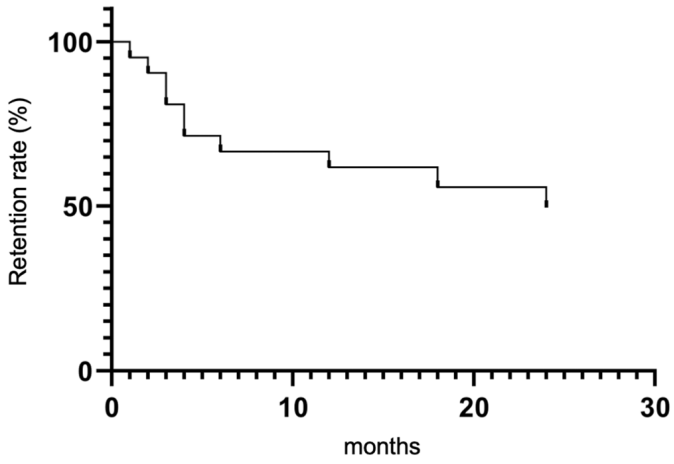

Fig. 1. Kaplan-Meier curves of sarilumab retention rate.

had been treated with more than two b-DMARDs without achieving sufficient response, and were classified as D2T RA. Of note, 17 patients had a history of tocilizumab use. The median values of CDAI and DAS28-ESR were 15.4 and 4.4, respectively. The median HAQ score was 1.5. Regarding the patterns of ILD on HRCT, 14 patients (66.7%) had non-specific interstitial pneumonia (NSIP) pattern, 6 (28.6%) had UIP pattern, and 1 (4.7%) had organising pneumonia (OP) pattern. At the time of SAR initiation, 7 patients (33.3%) exhibited worsening of ILD compared to one year prior to starting SAR, and the median HRCT score was 7. Fifteen patients were treated with SAR monotherapy, while MTX was concurrently used in 3 patients, and other conventional synthetic DMARDs were used in 3 patients. Despite all cases being refractory to prior bDMARDs and the majority being D2T RA, the SAR retention rate was 67% at 6 months and 52.3% at 24 months (Fig. 1). The most common reason for discontinuation was lack of efficacy (9 out of 10 patients: 90%). No patient had an infection that resulted in discontinuation of SAR.

Clinical course of ILD after SAR treatment

Regarding the clinical course of ILD, all cases except one remained stable without respiratory symptoms caused by RA-ILD during SAR treatment. One patient experienced an acute exacerbation of ILD 18 months after initiating SAR treatment, with an increase in the HRCT score from 4 to 35 (Fig. 2a). In this case, uncontrolled arthritis activity preceded with an increase in CDAI score from 9.8 to 18.1, followed by acute exacerbation of ILD. On the other hand, two patients showed improvements in HRCT findings and arthritis activity following SAR treatment. One patient, who had an NSIP pattern, experienced a reduction in the HRCT score from 7 to 3.3, while the other patient, with an OP pattern, experienced a reduction from 3 to 1 (Fig. 2b, c). The remaining 18 patients, including 6 with gradually progressive ILD courses prior to SAR initiation, showed stable HRCT images and consistent HRCT scores throughout SAR

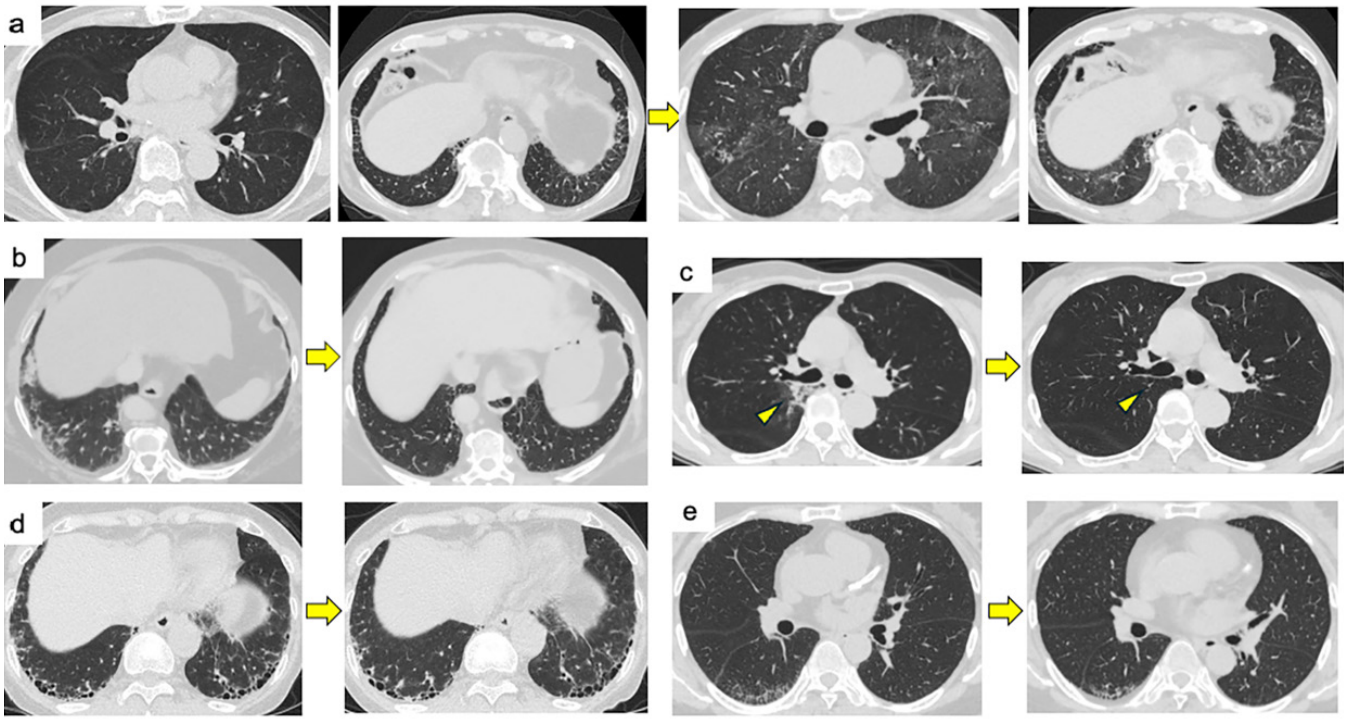

Fig. 2. HRCT findings of ILD in patients with RA-ILD after initiation of sarilumab.
One patient experienced an acute exacerbation of RA-ILD at 18 months of treatment (**a**), whereas one patient with NSIP (**b**) and one patient with OP (**c**) showed improvement of ILD (arrowhead). The remaining 18 patients remained stable on HRCT, and two typical cases with UIP (**d**) and NSIP (**e**) are presented.

treatment (Fig. 2d, e). Collectively, SAR treatment resulted in either improvement or stability of ILD in 20 out of 21 patients (95%) (Fig. 3a). Serum KL-6 levels also improved or remained stable during SAR treatment, except in the case of acute ILD exacerbation (Fig. 3b). In the patient who experienced acute exacerbation of RA-ILD, we successfully managed to induce remission with high-dose prednisolone as adjunctive therapy.

Clinical course of arthritis after SAR treatment

Throughout the observation period, DAS28-ESR, CDAI, and HAQ scores showed improvements following SAR initiation in all patients (median values: DAS28-ESR, 4.46 *vs*. 2.41; CDAI, 15 *vs*. 7.7; HAQ, 1.4 *vs*. 1.1), except for one patient who experienced an acute exacerbation of ILD following uncontrolled arthritis activity.

Comparison of the characteristics of SAR responder vs. non-responder

We compared the characteristics of responders and non-responders to SAR. Of the 21 patients, 11 were responders and 10 were non-responders. The clinical characteristics of both groups are summarised in Table II. Age, sex distribution, smoking history, RF and anti-CCP antibody positivity, CRP, ESR, KL-6, DAS28-ESR, CDAI, HAQ, and ILD subtypes were similar between the two groups. However, non-responders exhibited significantly higher levels of anti-CCP antibody titre compared to responders (329.5 *vs*. 20.4 U/mL; p=0.03), and there was a tendency for lower prevalence of prior TCZ treatment among responders. ROC curve analyses of anti-CCP antibody titre levels identified anti-CCP antibody titres >206 U/mL as a significant indicative level to distinguish the non-responder from the responder (sensitivity 70%, specificity 82%, AUC 0.78)

Results of the literature review

We initially identified 1 article in PubMed, 3 articles in Web of Science, and 26 articles in Scopus, and ultimately, one case report was selected (18). The flow chart of our literature search is illustrated in Figure 4. The selected case involved a 75-year-old male with RA-ILD of the UIP pattern. His RA disease activity, with a DAS28-CRP score of 6.71, could not be controlled with hydroxychloroquine 400 mg/day and methylprednisolone 4 mg/day. HRCT and pulmonary function tests revealed ILD progression over the two years following diagnosis, despite treatment with nintedanib 200 mg/day. After SAR initiation, he achieved RA remission with a DAS28-CRP score of 2.11, and his ILD remained stable without any adverse events for six months (18).

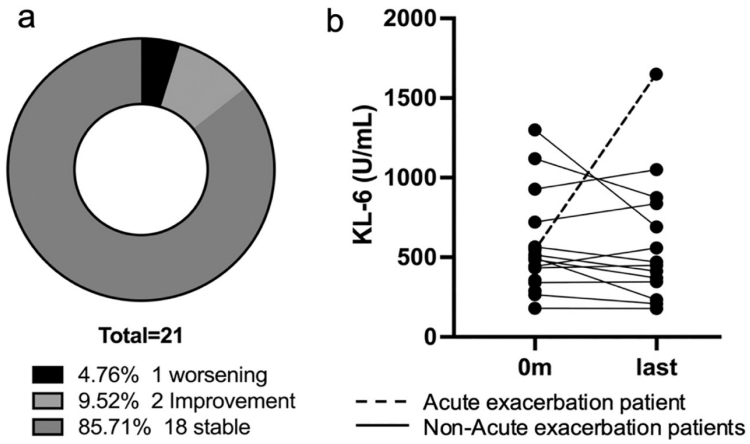

Fig. 3. Outcome of RA-ILD after initiation of sarilumab.
A: The pie chart illustrates the rate of progression of RA-ILD assessed by HRCT after sarilumab treatment; **b**: Changes of KL-6 after sarilumab treatment. Dashed line shows the change in a patient with acute exacerbation of ILD.

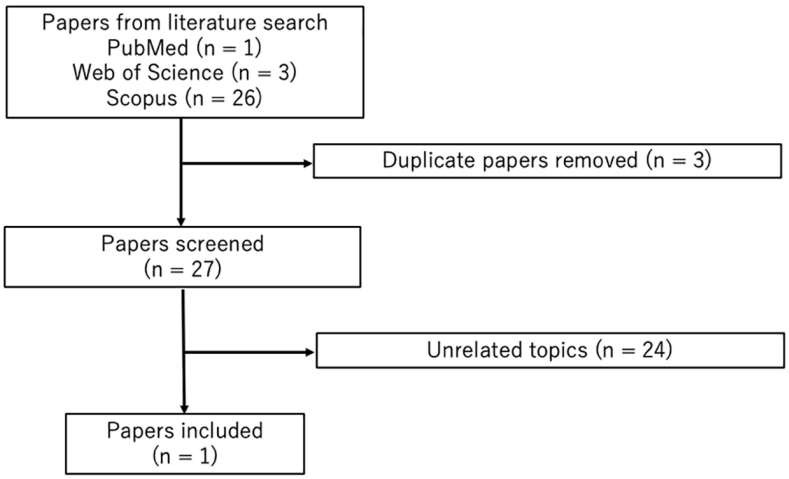

Fig. 4. Flowchart of our literature search.

Discussion

In this study, we found that SAR treatment led to stability or improvement of ILD in 20 out of 21 cases (95%), along with improvements in arthritis activity. These results and literature review suggest that SAR is a potential treatment option for patients with RA-ILD and exhibits encouraging efficacy in stabilising RA-ILD. Our study also suggested that anti-CCP antibody titre levels below 206 U/mL were characteristics of SAR responders in RA-ILD patients, offering insights into tailor-made treatment approaches for RA-ILD.

The efficacy of SAR for RA has been validated in several double-blind phase III trials (19, 20). However, these trials lacked specific data on RA-ILD patients, leaving a gap in understanding the effectiveness of SAR in this subgroup. Our study contributes by demonstrating the efficacy of SAR in ILD stabilisation and arthritis activ-

Table II. Clinical characteristics of responders *vs*. non-responders to sarilumab.

Characteristics	Responders (n=11)	Non-responders (n=10)	*p*-value
Age, median [IQR] (years)	71 [66-76]	76 [70.8-79.5]	0.17
Female (n, %)	7 (63.6)	8 (80)	0.64
Smoking (n, %)	4 (36.4)	4 (40)	1.00
RF positive (n, %)	9 (81.8)	10 (100)	0.48
RF titre (U/mL)	71 [38-169]	104 [35.3-377.5]	0.29
Anti-CCP positive (n, %)	9 (81.8)	9 (90)	1.00
Anti-CCP titre (U/mL)	20.4 [8.4-154]	329.5 [35.6-520.5]	0.03*
D2T RA (n, %)	7 (63.6)	8 (80)	0.64
Laboratory test, median [IQR]			
CRP (mg/dL)	0.27 [0.03-1.9]	0.29 [0.03-4.5]	0.97
ESR (mm/h)	37 [10.5-50]	29 [8-68]	0.89
MMP-3 (ng/mL)	128.1 [74.8-232.8]	149.6 [83.3-276.1]	0.62
KL-6 (U/mL)	504.5 [325-876.3]	490.5 [344.8-515.5]	0.67
DAS28-ESR	4.32 [2.55-4.91]	4.93 [4.25-6.46]	0.11
CDAI	11.2 [8.6-21.2]	17.4 [12.8-37.9]	0.14
HAQ	1.4 [0.8-1.6]	1.6 [0.6-2]	0.39
Type of ILD (n, %)			
NSIP	7 (63.6)	7 (70)	1.00
UIP	3 (27.3)	3 (30)	1.00
OP	1 (9.1)	0 (0)	1.00
HRCT score, % [IQR]	7 [3-11]	7 [4.8-15]	0.65
Current treatment (n, %)			
Prednisolone	5 (45.5)	5 (50)	1.00
Methotrexate	2 (18.2)	1 (10)	1.00
Prior bDMARD use (n, %)			
TNF inhibitors	6 (54.6)	7 (70)	0.66
Tocilizumab	7 (63.6)	10 (100)	0.09
Abatacept	1 (9.1)	1 (10)	1.00
JAK inhibitors	1 (9.1)	0 (0)	1.00

ILD: interstitial lung disease, Anti-CCP: anti-cyclic citrullinated peptide antibody, RF: rheumatoid factor, CRP: C-reactive protein, ESR: erythrocyte sedimentation rates, D2T RA: difficult-to-treat rheumatoid arthritis, MMP-3: matrix metalloproteinase-3, KL-6: Krebs von den Lungen-6, DAS28: disease activity score in 28 joints, CDAI: the Clinical Disease Activity Index, HAQ: the Health Assessment Questionnaire Disability Index, NSIP: non-specific interstitial pneumonia, UIP: usual interstitial pneumonia, OP: organising pneumonia, HRCT: high-resolution computed tomography, bDMARDs: biological disease-modifying anti-rheumatic drugs, TNF: tumour necrosis factor, JAK: Janus kinase. Smoking included past or current habit.

ity improvement. Moreover, despite all patients in this study being refractory to one or more prior bDMARDs, SAR achieved a 24-month drug retention rate of 52.3%, closely aligning with findings from previous studies on bDMARDs in RA-ILD patients (21). Thus, this retention rate is noteworthy, especially considering that over half of the cases involved D2T RA in the present study.

In the treatment of RA-ILD, beyond efficacy, safety is a crucial consideration when selecting therapies. Especially in elderly patients with concomitant lung complications, immunosuppressive therapies pose an increased risk of serious infections, including pneumocystis pneumonia (22, 23). Although safety data from previous clinical trials of SAR reveal that serious infections did not increase compared to other bDMARDs, these studies did not report treatment-emergent adverse events associated with RA-ILD (24), and evidence on the safety of SAR in RA-ILD patients remains limited. Our study showed no serious SAR-related adverse events, including infections, during the observation period, suggesting the safety of SAR for RA-ILD. However, careful observation during therapy is necessary for this high-risk population.

Although significant progress has been made in understanding the pathogenesis of RA and advancing its treatment over the past decade (25), there is currently no established treatment strategy for RA-ILD. A recent prospective observational study found that non-TNF inhibitors (such as abatacept, tocilizumab, and rituximab) reduced the risk of ILD progression compared to TNF inhibitors (26). Retrospective studies examining tocilizumab in RA-ILD patients have shown stable HRCT findings in most cases (4, 27). Given that SAR has a similar mechanism of action to tocilizumab, it was hypothesised that SAR could also be safely used in RA-ILD patients. Our study demonstrated that ILD did not progress during the observation period, even in cases with a gradually progressive course prior to SAR initiation, except in one case with poorly controlled arthritis. Furthermore, the IL-6 pathway has been reported to play a role in the development of ILD. Upregulated IL-6 and soluble IL-6 receptor produced by lung macrophages enhance fibroblast proliferation and extracellular matrix protein production (28, 29). This supports the potential efficacy of anti-IL-6 receptor inhibitors, including SAR, in preventing lung fibrosis progression.

Uncontrolled arthritis disease activity has been reported as a risk for ILD progression (30). RA with high disease activity exhibits elevated levels of soluble IL-2Rα, primarily produced by activated T cells, which is also increased in RA-ILD, suggesting that high RA disease activity has an impact on RA-ILD progression (31). Furthermore, some retrospective studies revealed that ILD progression occurred mainly in patients with poorly controlled arthritis (4, 27). In our report, the exceptional one case of acute ILD exacerbation was also associated with preceding uncontrolled arthritis activity. This case was a D2T RA for whom etanercept, certolizumab pegol, and tocilizumab had failed to control arthritis activity, and had experienced acute ILD exacerbation twice before SAR initiation when arthritis disease activity worsened with increases in the CDAI score from 0 to 9.6 and 2.3 to 9.8, respectively. After remission induction therapy with high-dose prednisolone, this patient is now being treated with peficitinib, resulting in stable arthritis and ILD. Notably, six other cases in our study and one case from the literature, which had gradually progressive ILD courses prior to SAR initiation, were successfully treated with SAR, leading to remission of arthritis and prevention of ILD progression.

Considering that maintaining RA disease activity in remission is crucial for

both joint prognosis and ILD stabilisation, it is essential to elucidate the characteristics of responders to SAR. A previous *post hoc* analysis of four phase 3 SAR trials demonstrated that anti-CCP antibody positivity and CRP levels higher than 1.23 mg/dL were predictors of response to SAR (32). Although no significant difference in these factors was observed in our study, possibly due to differences in patient population or small sample size, our study found that elevated levels of anti-CCP antibody titre were characteristic of non-responders to SAR. Although the report on the relationships of anti-CCP antibody titres and treatment response to bDMARDs was limited (33), *in vitro* studies have revealed that anti-CCP antibodies have pathogenic effects on the inflammatory response and bone erosion in RA (34). Furthermore, it has been reported that anti-CCP antibody levels are significantly higher in RA-ILD patients compared to those without ILD (35), likely due to local production in the affected lungs, which contributes to lung fibrosis (1). Since IL-6 inhibition has a limited effect on anti-CCP antibody production (36), it is plausible to hypothesise that RA-ILD patients with high anti-CCP antibody levels may show a poor response to SAR. Further accumulation of cases and validation studies are warranted.

RA-ILD is recognised as a risk factor for D2T RA (37), presenting a significant challenge for clinicians to achieve arthritis remission, which holds critical importance not only for joint prognosis but also for ILD management, as described above. Several studies have highlighted the comparable efficacy of SAR in both bDMARD-naive cases and individuals resistant to multiple bDMARDs, including tocilizumab (38, 39). Hence, SAR emerges as a promising therapeutic option for patients with RA-ILD, even in challenging clinical scenarios such as D2T RA.

Our study has several limitations. Firstly, its retrospective and single-centre design led to a small sample size. Secondly, the limited use of pulmonary function tests in our cohort hindered the assessment of changes in lung function. Thirdly, there is no control group comparing the efficacy and safety of SAR in RA-ILD. Fourthly, the prevalence of the NSIP pattern in this study was higher than in the general RA-ILD population, where the UIP pattern accounts for over half of RA-ILD cases (40). This may be due to the small sample size and retrospective nature of the study. The characteristics of this cohort, primarily consisting of D2T RA cases, may also contribute to the discrepancy in prevalence. Despite these limitations, our study represents the first exploration of efficacy and safety of SAR in patients with RA-ILD, highlighting its potential as a therapeutic option in this challenging patient population. Further validation through prospective randomised controlled trials of SAR for RA-ILD is necessary in the future.

In conclusion, SAR demonstrated efficacy in stabilising ILD in patients with RA. SAR may be a potential treatment option for RA-ILD.

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