SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2025; 42 (4): 17246 DOI: 10.36141/svdld.v42i4.17246

Janus kinase inhibitors in pulmonary and extra-pulmonary sarcoidosis: A case series and a systematic review of the literature

Maxime Quaggetto[1], Thouraya Ben Salem[1], Julien Haroche[1], Julien Campagne[2], Quentin Moyon[1], Raphael Lhote[1], Zahir Amoura[1], Fleur Cohen Aubart[1]

[1] Sorbonne Université, Assistance Publique-Hôpitaux de Paris, Service de Médecine Interne 2, Centre National de Référence Maladies Systémiques Rares et Histiocytoses, Hôpital La Pitié-Salpêtrière, Paris, France; [2] Service de Médecine Interne, Hôpitaux UNEOS, Metz, France

Abstract. *Background and aim:* Sarcoidosis is an inflammatory granulomatous disease of unknown cause affecting the lungs and frequently extra-thoracic organs. Several immunosuppressive agents have been evaluated in patients refractory to steroids or as steroids-sparing treatments with low level of evidence and conflicting results. JAK inhibitors (JAKi) are novel immunosuppressive agents and recent reports suggested their potential to induce disease response. We report four new sarcoidosis cases treated with JAKi and present a systematic review of the literature. *Methods:* We describe four new cases and conducted a literature review using Pubmed, Medline, Embase and Cochrane Library. All English-language reports of sarcoidosis patients treated with JAKi published between January 2004 and 2024 were included. *Results:* We included 4 cases, as well as 45 cases from a systematic review of the literature, reported in 21 articles, leading to a cohort of 49 patients (female 53%, median [IQR 25-75] age 55 [43-60] years). Most cases had pulmonary and cutaneous sarcoidosis, while cardiac and neurological sarcoidosis were less frequent. Indication for JAKi were: steroid sparing agent (29%), refractory disease (22%), non-sarcoidosis indication (10%) and not specified (39%). Most patients received Tofacitinib 5 mg twice daily. Median corticosteroids dosage at treatment initiation was 15 [10-25] mg/day. After a median follow-up of 8 [6-12] months, complete response was achieved in 45% of cases and partial response in 49%, with few adverse events reported. Corticosteroids were discontinued in 11/23 (48%) and reduced in 6/23 (26%). *Conclusions:* JAK inhibitors appear to be a promising therapeutic option in sarcoidosis patients who are corticosteroid-dependent or refractory to conventional immunosuppressants. Prospective studies are now needed to confirm their efficacy and long-term safety.

Key words: sarcoidosis, janus kinase, review

Introduction

Sarcoidosis is an inflammatory granulomatous disease of unknown cause affecting the lungs in 90% of patients while extra-thoracic involvement is reported in 30-50% of cases(1). Sarcoidosis frequently results in disabling or life-threatening organ involvements requiring systemic treatment with oral corticosteroid being the current cornerstone treatment(2–4). However, this standard is increasingly being challenged by emerging corticosteroid-sparing strategies, particularly in thoracic forms(5). Nevertheless, corticosteroids remain the first-line therapy, especially in life-threatening or extra-thoracic manifestations. Even in such cases, they may be insufficient as monotherapy, and disease relapse is common during tapering(6,7). Several immunosuppressive agents have been evaluated in steroids refractory patients or as steroids-sparing treatments, mostly methotrexate, TNF-a inhibitors and cyclophosphamide with very low level of

Received: 9 June 2025
Accepted: 15 September 2025
Correspondence: Maxime Quaggetto, Service de Médecine Interne 2, Hôpital La Pitié-Salpêtrière, 47-83 Boulevard de l'hôpital, 75651 Paris CEDEX 13
E-mail: maxime.quaggetto@aphp.fr
ORCID: 0009-0004-9512-597X

evidence supporting their use(3,8–12). Other targeted therapies such as rituximab, ustekinumab and golimumab have been evaluated in small prospective studies with disappointing results(13–15). JAK inhibitors (JAKi) are immunosuppressive agents used in myeloproliferative disorders, rheumatoid arthritis, psoriasis arthritis, and ulcerative colitis(16). JAK-STAT pathway represents a promising target for sarcoidosis treatment. STAT1 is upregulated in sarcoidosis, and that STAT1 activation has been shown to correlate with disease severity(17). STAT3 was also identified as a key regulator of organ fibrosis in sarcoidosis(18). Some recent reports suggested JAKi could induce disease response(19). However, these data remain scarce, and need to be expanded. We wish to report on four sarcoidosis patients treated with JAKi jointly with a systematic review of cases from literature.

Patients and Methods

Patient selection

We retrospectively included all sarcoidosis patients treated with any JAK inhibitor between January 1st 2004 and May 30th 2023 at our center. As no formal registry exists for sarcoidosis or JAKi-treated patients, we performed a systematic search using keywords ("sarcoidosis" and the name of each JAKi molecule) in the electronic medical records. Only four patients were identified and included in the present analysis. Sarcoidosis was defined according to the ATS practice guideline: a clinic-radiological presentation consistent with sarcoidosis, histopathological support, and exclusion of other causes of granulomatous diseases or similar conditions(20).

Literature search

A literature search was conducted using PubMed, MEDLINE, EMBASE, and Cochrane Library, limited to the English language and to articles published between 2004 and 2024. Search was made with the key words "sarcoidosis" and "Janus kinase inhibitors" or any specific JAKi molecules ("tofacitinib", "baricitinib", "ruxolitinib", "deucravacitinib", "fedratinib", "peficitinib","upadacitinib", "ritlecitinib", "momelotinib", "pacritinib", "filgotinib", "decernotinib","abrocitinib").

Data collection

Demographic and clinical characteristics, previous treatments, JAKi treatment and outcomes were collected from medical records (case reports) or in the published articles (systematic review). Due to study heterogeneity and missing data, denominators indicate the number of available data points. Follow-up was defined as the time from JAKi prescription to the last available medical visit.

Efficacy and tolerance assessments

The response to JAKi was classified as complete, partial, or refractory according to clinician reported outcome. Response was defined as; complete: absence of signs or symptoms (clinical, laboratory, radiological and/or physiological parameters with exclusion of sequelae-related findings) with successful steroids withdrawal and without immunosuppressant introduction; partial: improvement of signs or symptoms with steroids < 10 mg/d (prednisone equivalent); refractory: new or worsening signs or symptoms and/or steroids increase and/or new immunosuppressant drug. Patients with no outcome assessment were reported as lost to follow-up.

Statistical analysis

Results for categorical variables were expressed as number (%) while those for continuous variables, expressed as mean ± standard deviation or median [interquartile range (IQR)]. Analyses were computed with R software 4.0.2 version (R project for Statistical Computing).

Ethical considerations

The database is registered at the "Commission Nationale de l'Informatique et des Libertés" (decision 2238959v0). The investigation conforms with the principles outlined in the Declaration of Helsinki. In accordance with the ethical standards of our hospital's institutional review board, the Committee for the Protection of Human Subjects, and French law, written informed consent was not needed for demographic, physiological and hospital-outcome data analyses because this observational study did not modify existing diagnostic or therapeutic strategies; however, patients were informed of their inclusion in the study.

Results

Case reports

The characteristics of the cases we report are shown in Table 1.

Patient #1: This 52-year-old man had a 16-year history of sarcoidosis with pulmonary, articular, and ocular involvement. Non-caseating granulomas were initially found on a salivary gland biopsy. Over the years, he received corticosteroids, hydroxychloroquine, methotrexate, azathioprine, mycophenolate mofetil, and leflunomide without sustained response. Infliximab was introduced due to persistent activity, then switched to adalimumab because of suspected TNF-inhibitor-induced lupus. Shortly after stopping adalimumab, he presented with cardiac involvement complicated by a resuscitated cardiac arrest. Given the severity of organ involvement, the limited therapeutic options, and prior intolerance to TNF inhibitors, tofacitinib 5 mg twice daily was initiated. He achieved complete clinical and radiological response within 6 months and remained relapse-free under tofacitinib, methotrexate, and low-dose prednisone after 29 months of follow up.

Patient #2: A 43-year-old man with a 15-year history of ocular sarcoidosis initially presented with right eye panuveitis, which led to irreversible blindness despite corticosteroid therapy. Years later, he developed neurosarcoidosis with leptomeningeal involvement on brain MRI. High-dose corticosteroids were reintroduced but caused a serous retinal detachment in the left eye, raising serious concern about the risk of bilateral blindness. Steroids were therefore discontinued. Infliximab was initiated as a corticosteroid -sparing strategy but induced a severe anaphylactic reaction. Tocilizumab led to a partial response, but relapse occurred despite treatment intensification.

Table 1. Demographic and Pre/Post-JAKi Treatment Sarcoidosis Related-Findings of Our Four Additional Case Reports

Cases	Gender	Age	Organ involved	Disease duration JAKi follow-up	Treatment	Previous treatments	Outcome
1	M	52	CS, M, J, E, L	16 y 29 m	TOFA 5mgx2/d MTX 10mg/w	GC, MTX, HCQ, AZA, MMF, IFN, ADA, LEF	Partial response: CS & M M3, GC maintained at 7.5 mg/d Normal 18-FDG-PET/CT at M8
2	M	43	LN, S, J, B, E, P, CNS	15 y 32 m	TOFA 5mgx2/d MTX 15mg/w	GC, MTX, IFN, HCQ, DOX, TOCI	Complete response: L, S & J M6 MTX 10 mg/w
3	F	38	LN, J	1 y 8 m	UPA 15 mgx1/d MTX 20mg/w	GC, MTX, TOCI	Complete response: J M8, Stable LN
4	M	56	LN, L, CNS	2.5 y 9 m	TOFA 5mgx2/d CERTO 400mgx2/m	GC, MTX, IFN, CP	Partial response: CNS M9, GC tapered at 5 mg/d

Abbreviations: ADA, adalimumab; AZA, azathioprine; B, bones; CERTO, certolizumab; CNS, central nervous system; CP, cyclophosphamide; CS, cardiac sarcoidosis; d, day; DOX, doxycycline; E, eyes; GC, glucocorticoids; HCQ, hydroxychloroquine; IFN, infliximab; J, joints; JAKi, Janus kinase inhibitor; LEF, leflunomide; L, lung; LN, lymph node; m, month; M, muscle; MMF, mycophenolate mofetil; MTX, methotrexate; P, parotids; S, skin; TOCI, tocilizumab; TOFA, tofacitinib; UPA, upadacitinib; w, week; y, year

Given the contraindications to corticosteroids and anti-TNF agents, and persistent neurologic and systemic disease, tofacitinib 5 mg twice daily was introduced in combination with methotrexate. The patient achieved complete and sustained response after 6 months, including resolution of neurological symptoms, maintained over 32 months of follow-up.

Patient #3: This 38-year-old woman had an 18-year history of sarcoidosis initially misdiagnosed as seronegative rheumatoid arthritis. She was treated with corticosteroids, methotrexate, and adalimumab for over a decade with good control. At age 30, she developed hidradenitis suppurativa (HS), which was managed with antibiotics. Adalimumab was discontinued due to secondary skin infections, and etanercept was introduced. Later, she developed systemic symptoms with polyarthritis and fever; a diagnosis of Still's disease was considered. After a new flare with systemic and articular symptoms, granulomatous involvement was confirmed on endobronchial biopsy. Tocilizumab was initiated but caused an urticarial rash with superinfections. Given the dual indication (sarcoidosis and HS) and the failure or intolerance to TNF and IL-6 inhibitors, upadacitinib 15 mg daily was started with methotrexate(21,22). The treatment led to sustained response of both articular and cutaneous symptoms after 8 months of treatment.

Patient #4: A 56-year-old man was diagnosed with sarcoidosis three years earlier based on cervical lymph node and nasal biopsies, with associated thoracic involvement. Initially untreated due to the absence of major organ dysfunction, he later developed neurological symptoms with altered mental status and inflammatory CSF findings. High-dose corticosteroids failed to induce improvement. Infliximab was attempted but immediately provoked anaphylaxis. Cyclophosphamide was administered over six months with partial benefit, but relapse occurred soon after treatment completion. Certolizumab was then introduced but did not control neurological symptoms. In light of the refractory, relapsing neurosarcoidosis and contraindications to other immunosuppressants, tofacitinib 5 mg twice daily was initiated as a compassionate treatment. The patient progressively improved, with cognitive and functional recovery, while corticosteroid tapering was made until 5 mg/day.

Literature review

Fourty-five patients from 21 studies were included (Figure 1)(19,23–42) and evaluated jointly with our 4 patients**.**

One case series involving 12 patients treated with tofacitinib was excluded due to insufficiently detailed case-level data(43). Patient's characteristics are described in Table 2.

Twenty-six women (53%) with a median age at treatment initiation of 55 [43-60] years and a median time from diagnosis to JAKi of 6 years [1.5-17]. All cases fulfilled ATS cases definition. Most frequent organ involvement were: lung 76%, skin 63%, extrapulmonary lymph nodes 35%, joint involvement 24% and kidney 14%(34). The median dosage of steroids associated tO JAKi at treatment start was 15 [10-25] mg/day. Most treatments used before JAKi (Table S1) were: glucocorticoids 80 %, methotrexate 67%, hydroxychloroquine 36%, infliximab 27%, adalimumab 14%, mycophenolate 14%, azathioprine 14%. JAKi type and regimens are shown in Table 3.

Main reasons for JAKi introduction were: not reported 39%, as corticosteroid sparing agent 29%, refractory diseases 22% and non-sarcoidosis indication 10%. After a median follow-up time of 8 [6-12] months, the rates of complete, partial response and evolving disease were: 45%, 49% and 4% respectively (Table 2). The median time from JAKi introduction to clinical response was 3 [1.5-5.75] months. Steroids could be withdrawn or tapered in 48% and 26% of cases while there were maintained unchanged or increase in 13% and 9% respectively (Table 2). No serious adverse event were reported (Table 3), and most frequent were infections 22%, mainly mild respiratory symptomatic infection including Sars-COV2 infection. Pediatric cases from literature with NOD2 mutation-proven Blau syndrome treated with JAKi are described apart in Table S3. All had complete response under treatment. Cases treated with topical JAKi are described in Table S4. All had at least partial response under treatment.

Discussion

Sarcoidosis is a rare disease associated with substantial morbidity and mortality(44–46). Corticosteroid, its cornerstone treatment, is associated with substantial toxicity. There is an unmet need for effective second-line treatments, either as steroid-sparing

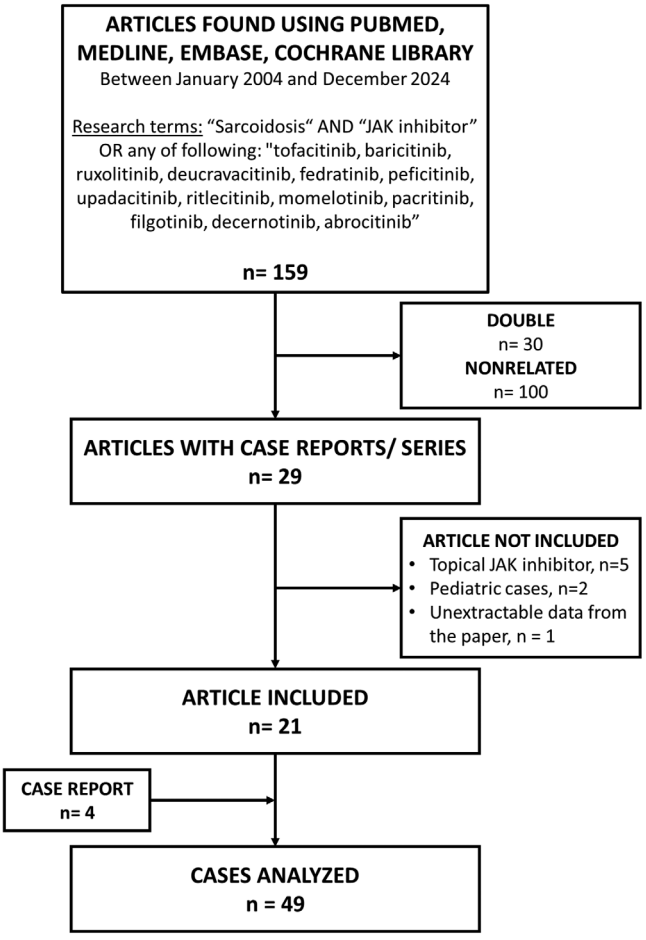

Figure 1. Systematic Review Of Literature Flow Chart. Literature review was made through Pubmed, Medline, Embase and Cochrane library, with the corresponding key words. A total of 49 articles were found. Selected articles concerned patients reports, retrospectives studies and prospective evaluations. *Abbreviation:* JAK, Janus kinase

agents or for refractory disease(7,47,8). We herein report early data suggesting JAKi might be effective in sarcoidosis with a good safety profile. Translational research data support the use of JAKi in sarcoidosis. STAT1 is upregulated in sarcoidosis(17). JAK-STAT pathway mediates several cytokines involved in the development and maintenance of granulomas, including interferon (IFN)-γ, IL-12, IL-18 and IL-10(48–50). Whole genome sequencing study reported the association of JAK2 variant and sarcoidosis(51). A large variety of cytokines have been implicated in the pathophysiology of sarcoidosis, and unlike single-target biologics, JAKi have a more pleiotropic anti-cytokine effect(8,15). Actual therapies used in sarcoidosis include Methotrexate, Azathioprine, Hydroxychloroquine and Anti-TNF agents. Methotrexate has shown efficacy as a steroid-sparing agent in prospective studies, and old series reported disease improvement among 66 % of the treated patients with multisystem sarcoidosis(52,53). Although methotrexate has traditionally been used as a second-line agent, the recent METHPRED study demonstrated its efficacy as a first-line monotherapy in pulmonary sarcoidosis(5). In contrast, patients treated with JAK inhibitors in our cohort had typically received multiple prior therapies—including methotrexate—and were refractory to conventional immunosuppressants(4). Azathioprine is reported as

Table 2. Characteristics, JAKi Treatment-Related Findings and Outcomes in the 49 Reported Sarcoidosis Cases

Variables	n=49
Demographic characteristics	
Woman	26/49 (53)
Age, years	55 [43-60]
Sarcoidosis-related findings	
Time since diagnosis, years	6 [1.5-17]
Lung involvement	37/49 (76)
Stage I	7/37
Stage II	13/37
Stage III	4/37
Stage IV	4/37
Unknown	9/37
Skin	31/49 (63)
Extra-pulmonary lymph nodes	17/49 (35)
Joint	12/49 (24)
ENT	8/49 (16)
Eye	8/49 (16)
Kidney	7/49 (14)
Spleen or hepatic	6/49 (12)
Brain	4/49 (8)
Heart	4/49 (8)
Muscle	2/49 (4)

Variables	n=49
Glucocorticoids at JAKi initiation	23/49 (48)
Median dose, mg/d	15 [10-25]
<5 mg/day	4/23 (17)
5-30 mg/day	17/23 (74)
>30 mg/day	2/23 (9)
Outcomes[1]	
Duration of follow-up, months	8 [6-12]
Time from JAKi introduction to clinical response, months	3 [1.5-5.75]
Complete response	22/49 (45)
Partial response	24/49 (49)
Evolving disease	2/42 (4)
Lost to follow up	1/42 (2)
Corticosteroid treatment modification	
None	3/23 (13)
Withdrawal	11/23 (48)
Tapering	6/23 (26)
Increase	2/23 (9)
Unknown	1/23 (4)

Abbreviations: CSAMI, Cutaneous Sarcoidosis Activity and Morphology Instrument; CT-SCAN, computed tomography; ENT, ear nose throat; GC, glucocorticoids; JAKi, Janus kinase inhibitor; PFT, pulmonary function test; SPECT-CT, Single photon emission computed tomography; 18-FGF-PET/CT, Fluorodeoxyglucose positron emission tomography. Continuous variables are expressed as median [interquartile range 25-75]; categorical variables are expressed as No. (%). [1]The evaluation of skin involvement was based upon: CSAMI score n=18/31 (58%) or physician reported outcome 13/31 (42%). Lung or extra-pulmonary involvement upon: SPECT-CT or ^{18}FDG-PET/CT n= 21/43 (49%), pulmonary function tests n=12/37 (32%), CT-scan 8/43 (19%) or chest X-ray alone 5/43 (12%).

having the same efficacy, as a sparring agent, with good reported outcome in about 70% of cases(47). Hydroxychloroquine was mainly assessed in cutaneous and ocular sarcoidosis, with good reported outcome for about 50 % to 70% of cases(54,55). Finally, anti-TNF are the recommended treatment in refractory disease, and reported an efficacy around 70% in multisystemic disease, with a lower outcome in pulmonary disease(56,57). Two studies reported a response rate superior to 90 % for Infliximab in multisystemic disease(11,58). Notably, complete response was reported in fewer than 20% of cases in a multicenter French study(59). In this study, a favorable outcome with JAKi was reported in more than 90% of patients, with a complete response achieved in nearly one out of two individuals.

JAKi are now approved in various immune-mediated diseases such as rheumatoid arthritis where JAKi are indicated as a second or third line therapy on top off methotrexate(60–65). They are also approved in spondylarthritis and psoriatic arthritis(66–69), and might be included in a near future in the therapeutic algorithm of alopecia Areata and inflammatory bowel diseases(70–72). Very few adverse events have been reported. Conversely to previous reports, and except for one pulmonary infection requiring hospitalization, no serious bacterial of viral infection occurred(36,73). Further, neither severe metabolic or thromboembolic events were reported while concerns have been raised in the literature(74–78). Given the retrospective nature of these studies and the short follow-up, these data should be interpreted with caution

Table 3. Reason for JAKi Introduction and Adverse Events in the 49 Reported Sarcoidosis Cases

Variables	n=49
Reason for JAKi introduction	
Not reported	19/49 (39)
As a corticosteroid sparing agent[1]	14/49 (29)
Refractory disease[2]	11/49 (22)
Non-sarcoidosis indication[3]	5/49 (10)
JAKi treatment	
Tofacitinib	41/49 (88)
Ruxolitinib	3/49 (7)
Baricitinib	2/49 (4)
Upadacitinib	2/49 (4)
Abrocitinib	1/49 (2)
Adverse events	
None	27/49 (55)
Infection[4]	11/49 (22)
Laboratory abnormalities[5]	3/49 (6)
Metabolic[6]	4/49 (8)

Abbreviations: JAKi, Janus kinase inhibitor. Categorical variables are expressed as No. (%).
[1]Corticodependent diseases n=9, corticosteroids contraindication n=5. [2]Frequent relapses n=6, compassionate treatment n=4, TNFα inhibitor-refractory disease n=1. [3]Associated autoimmune disease requiring treatment escalation n=3 (rheumatoid arthritis n=1, inflammatory bowel disease n =1, hidradenitis suppurativa n=1), Associated myeloproliferative syndrome requiring treatment escalation n=2. [4]Non-severe PCR-proven SARS-CoV2 infections n=5, bronchial infection n=4, acute sinusitis n=1 and urinary tract infection n=1. [5]Transient lymphocytopenia n=2, transient elevated liver function test n=1 [6]Hyperlipidemia n=1, weight gain n=2, nausea n=1.

but real-life experience of JAKi in other diseases has shown a fair safety profile(79,80). This study has several limitations. First, before JAKi initiation, 20% patients did not receive steroids as first line treatment. This might be explained by a high prevalence of lone sarcoidosis skin diseases(81). Second, as the median follow up is short, the long-term safety and efficacy in JAKi need to be evaluated. There was no relapse after 38 months of treatment in the case report with the longest follow up duration(32,35). Third, these data emerge from many proteiform retrospective studies, numerous case reports, and only two prospective studies, making the risk of publication bias substantial(19,33). Finally, we were unable to properly extract and analyze the data from one retrospective case series, but the results from the retrospective case series involving 12 patients treated with Tofacitinib are consistent with our findings, with 6 responders and 3 declared non responders to treatment(43). These results will need to be challenged in further prospective studies, as the current evidence is predominantly based on retrospective series and isolated case reports, which are inherently prone to publication bias—especially since non-responding cases are less likely to be published. This risk of bias is especially high, considering that numerous studies reported here include fewer than five cases. However, in the context of rare and heterogeneous diseases such as sarcoidosis—particularly in its extrapulmonary, refractory, or corticosteroid-intolerant forms—case reports often represent the only available published data. While we chose to include all published cases regardless of series size to provide a comprehensive overview, we fully acknowledge that the most reliable assessment of therapeutic efficacy should come from randomized controlled trials, followed by prospective series, then retrospective cohorts, and finally individual case reports. This hierarchy should be kept in mind when interpreting our findings. Fourth, while JAKi seems to be effective in controlling sarcoidosis and allowing steroids taper, it is unclear if it has a transient or a long-lasting effect after JAKi tapering or interruption. Fifth, data are lacking on long-term pulmonary function evolution under JAKi.

Conclusion

JAKi treatment seems to be a promising therapeutical class in sarcoidosis patients dependent or refractory to corticosteroids and conventional immunosuppressant. As many questions remain unanswered, further prospective studies now are needed to evaluate the efficacy of JAKi in sarcoidosis.

References

1. Valeyre D, Bernaudin JF, Jeny F, et al. Pulmonary sarcoidosis. Clin Chest Med. 2015;36(4):631–41. doi:10.1016/j.ccm.2015.08.006
2. Valeyre D, Prasse A, Nunes H, Uzunhan Y, Brillet PY, Müller-Quernheim J. Sarcoidosis. Lancet. 2014;383(9923):1155–67. doi:10.1016/S0140-6736(13)60680-7
3. Rahaghi FF, Baughman RP, Saketkoo LA, et al. Delphi consensus recommendations for a treatment algorithm in pulmonary sarcoidosis. Eur Respir Rev. 2020;29(155):190146. doi:10.1183/16000617.0146-2019

4. Baughman RP, Valeyre D, Korsten P, et al. ERS clinical practice guidelines on treatment of sarcoidosis. Eur Respir J. 2021;58(6):2004079. doi:10.1183/13993003.04079-2020
5. Kahlmann V, Janssen Bonás M, Moor CC, et al. First-Line Treatment of Pulmonary Sarcoidosis with Prednisone or Methotrexate. N Engl J Med. 2025 Jul 17;393(3):231-42. doi: 10.1056/NEJMoa2501443.
6. Judson MA. Causes of poor medication adherence in sarcoidosis. Chest. 2020;158(1):17–8. doi:10.1016/j.chest.2020.03.001
7. Khan NA, Donatelli CV, Tonelli AR, et al. Toxicity risk from glucocorticoids in sarcoidosis patients. Respir Med. 2017;132:9–14. doi:10.1016/j.rmed.2017.09.003
8. Baughman RP, Drent M, Kavuru M, et al. Infliximab therapy in patients with chronic sarcoidosis and pulmonary involvement. Am J Respir Crit Care Med. 2006;174(7):795–802. doi:10.1164/rccm.200603-402OC
9. Vorselaars ADM, Verwoerd A, van Moorsel CHM, Keijsers RGM, Rijkers GT, Grutters JC. Prediction of relapse after discontinuation of infliximab therapy in severe sarcoidosis. Eur Respir J. 2014;43(2):602–9. doi:10.1183/09031936.00055213
10. Cohen Aubart F, Bouvry D, Galanaud D, et al. Long-term outcomes of refractory neurosarcoidosis treated with infliximab. J Neurol. 2017;264(5):891–7. doi:10.1007/s00415-017-8444-9
11. Judson MA, Baughman RP, Costabel U, et al. Efficacy of infliximab in extrapulmonary sarcoidosis: results from a randomised trial. Eur Respir J. 2008;31(6):1189–96. doi:10.1183/09031936.00051907
12. Doty JD, Mazur JE, Judson MA. Treatment of corticosteroid-resistant neurosarcoidosis with a short-course cyclophosphamide regimen. Chest. 2003;124(5):2023–6. doi:10.1378/chest.124.5.2023
13. Lower EE, Baughman RP, Kaufman AH. Rituximab for refractory granulomatous eye disease. Clin Ophthalmol. 2012;6:1613-8. doi: 10.2147/OPTH.S35521.
14. Sweiss NJ, Lower EE, Mirsaeidi M, et al. Rituximab in the treatment of refractory pulmonary sarcoidosis. Eur Respir J. 2014;43(5):1525–8. doi:10.1183/09031936.00224513
15. Judson MA, Baughman RP, Costabel U, et al. Safety and efficacy of ustekinumab or golimumab in patients with chronic sarcoidosis. Eur Respir J. 2014;44(5):1296–307. doi:10.1183/09031936.00000914
16. Fragoulis GE, McInnes IB, Siebert S. JAK-inhibitors: new players in the field of immune-mediated diseases, beyond rheumatoid arthritis. Rheumatology (Oxford). 2019;58(Suppl 1):i43–i54. doi:10.1093/rheumatology/key276
17. Rosenbaum JT, Pasadhika S, Crouser ED, et al. Hypothesis: sarcoidosis is a STAT1-mediated disease. Clin Immunol. 2009;132(2):174–83. doi:10.1016/j.clim.2009.04.010
18. Celada LJ, Kropski JA, Herazo-Maya JD, et al. PD-1 up-regulation on CD4+ T cells promotes pulmonary fibrosis through STAT3-mediated IL-17A and TGF-β1 production. Sci Transl Med. 2018;10(460):eaar8356. doi:10.1126/scitranslmed.aar8356
19. Damsky W, Wang A, Kim DJ, et al. Inhibition of type 1 immunity with tofacitinib is associated with marked improvement in long-standing sarcoidosis. Nat Commun. 2022;13(1):3140. doi:10.1038/s41467-022-30615-x
20. Crouser ED, Maier LA, Wilson KC, et al. Diagnosis and detection of sarcoidosis: an official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med. 2020;201(8):e26–e51. doi:10.1164/rccm.202002-0251ST
21. Kozera E, Flora A, Frew JW. Real-world safety and clinical response of Janus kinase inhibitor upadacitinib in the treatment of hidradenitis suppurativa: a retrospective cohort study. J Am Acad Dermatol. 2022;87(6):1440–2. doi:10.1016/j.jaad.2022.07.047
22. Savage KT, Santillan MR, Flood KS, Charrow A, Porter ML, Kimball AB. Tofacitinib shows benefit in conjunction with other therapies in recalcitrant hidradenitis suppurativa patients. JAAD Case Rep. 2020;6(2):99–102. doi:10.1016/j.jdcr.2019.10.010
23. Rotenberg C, Besnard V, Brillet PY, Giraudier S, Nunes H, Valeyre D. Dramatic response of refractory sarcoidosis under ruxolitinib in a patient with associated JAK2-mutated polycythemia. Eur Respir J. 2018;52(6):1801482. doi:10.1183/13993003.01482-2018
24. Liu B, Yin H, Yang S, Lu L. Janus kinase inhibitor treatment improved both subcutaneous and pulmonary sarcoidosis in a patient with glaucoma. Clin Exp Dermatol. 2022 Oct;47(10):1868-70. doi: 10.1111/ced.15290
25. Levraut M, Martis N, Viau P, Suarez F, Queyrel V. Refractory sarcoidosis-like systemic granulomatosis responding to ruxolitinib. Ann Rheum Dis. 2019;78(11):1606–7. doi:10.1136/annrheumdis-2019-215387
26. Wei JJ, Kallenbach LR, Kreider M, Leung TH, Rosenbach M. Resolution of cutaneous sarcoidosis after Janus kinase inhibitor therapy for concomitant polycythemia vera. JAAD Case Rep. 2019;5(4):360–1. doi:10.1016/j.jdcr.2019.02.006
27. Sejournet L, Kodjikian L, Grange L, Grumet P, Jamilloux Y, Seve P. Resolution of ocular and mediastinal sarcoidosis after Janus kinase inhibitor therapy for concomitant rheumatoid arthritis. Clin Exp Rheumatol. 2021;39(1):225–6. doi:10.55563/clinexprheumatol/3gymd4
28. Scheinberg M, Maluf F, Wagner J. Steroid-resistant sarcoidosis treated with baricitinib. Ann Rheum Dis. 2020;79(9):1259–60. doi:10.1136/annrheumdis-2020-217271
29. Kerkemeyer KL, Meah N, Sinclair RD. Tofacitinib for cutaneous and pulmonary sarcoidosis: a case series. J Am Acad Dermatol. 2021;84(2):581–3. doi:10.1016/j.jaad.2020.10.016
30. Talty R, Damsky W, King B. Treatment of cutaneous sarcoidosis with tofacitinib: a case report and review of evidence for Janus kinase inhibition in sarcoidosis. JAAD Case Rep. 2021;16:62–64. doi:10.1016/j.jdcr.2021.08.012
31. Damsky W, Young BD, Sloan B, Miller EJ, Obando JA, King B. Treatment of multiorgan sarcoidosis with tofacitinib. ACR Open Rheumatol. 2020;2(2):106–9. doi:10.1002/acr2.11112
32. Damsky W, Thakral D, Emeagwali N, Galan A, King B. Tofacitinib treatment and molecular analysis of cutaneous sarcoidosis. N Engl J Med. 2018;379(26):2540–6. doi:10.1056/NEJMoa1805958
33. Friedman MA, Le B, Stevens J, et al. Tofacitinib as a steroid-sparing therapy in pulmonary sarcoidosis, an open-label prospective proof-of-concept study. Lung. 2021;199(2):147–53. doi:10.1007/s00408-021-00436-8
34. Collaborative group: MI(6) study group. Glucocorticoid sparing in sarcoidosis using the Janus kinase (JAK) inhibitor tofacitinib. Eur J Intern Med. 2022;98:119–21. doi:10.1016/j.ejim.2021.12.016
35. Damsky W, Thakral D, McGeary MK, Leventhal J, Galan A, King B. Janus kinase inhibition induces disease remission in cutaneous sarcoidosis and granuloma annulare. J Am Acad Dermatol. 2020;82(3):612–21. doi:10.1016/j.jaad.2019.05.098
36. Demir M, Kouranos V, Stoenchev K, et al. JAK-inhibitor Tofacitinib in Severe Laryngeal Sarcoidosis: A Case Report. Laryngoscope. 2025 Feb;135(2):829-832. doi: 10.1002/lary.31778.
37. Safadi M, Whittington K, Zahner S, Rubinstein I, Tsoukas M, Sweiss N. Recalcitrant cutaneous sarcoidosis treated with upadacitinib: case report. JAAD Case Rep. 2024;51:7–9. doi:10.1016/j.jdcr.2024.06.019
38. Farinha I, Ferreira PG. Salvage use of tofacitinib in sarcoidosis patient with refractory multiorgan involvement. Sarcoidosis Vasc Diffuse Lung Dis. 2024 Jun 28;41(2):e2024019. doi: 10.36141/svdld.v41i2.15655.
39. Russo G, Laffitte E. Successful Therapy of Severe and Refractory Cutaneous Sarcoidosis with Baricitinib. Acta Derm Venereol. 2024 Apr 2;104:adv39970. doi: 10.2340/actadv.v104.39970.
40. Yang Y, Yan J, Yang J, Wang P, Liu Y, Wang X. Janus kinase inhibitor abrocitinib as an off-label treatment for tattoo granuloma with uveitis (TAGU). Australas J Dermatol. 2024;65(3):297–9. doi:10.1111/ajd.14248

41. Ianhez M, Miot HA, Caetano LVN, De Paula HM, Freire GGS, Torres PPTS. Sarcoidosis and polymethyl methacrylate (PMMA) granulomas following COVID-19 vaccination (ChAdOx1): successful treatment with tofacitinib. Indian J Dermatol. 2024;69(4):328–32. doi:10.4103/ijd.ijd_56_24
42. Hindré R, Besnard V, Kort F, Nunes H, Valeyre D, Jeny F. Complete response to mTOR inhibitor following JAKi failure in severe pulmonary sarcoidosis. Pulmonology. 2024;30(6):639–41. doi:10.1016/j.pulmoe.2024.03.002
43. Leffers HCB, Baslund B, Lindhardsen J, Krintel SB, Graudal N. Abatacept and tofacitinib in refractory sarcoidosis: drug survival, safety, and treatment response. Clin Exp Rheumatol. 2024;42(11):2167–74. doi:10.55563/clinexprheumatol/mmzdlj
44. Jamilloux Y, Maucort-Boulch D, Kerever S, et al. Sarcoidosis-related mortality in France: a multiple-cause-of-death analysis. Eur Respir J. 2016;48(6):1700–9. doi:10.1183/13993003.00457-2016
45. Swigris JJ, Olson AL, Huie TJ, et al. Sarcoidosis-related mortality in the United States from 1988 to 2007. Am J Respir Crit Care Med. 2011;183(11):1524–30. doi:10.1164/rccm.201010-1679OC
46. Gerke AK, Judson MA, Cozier YC, Culver DA, Koth LL. Disease burden and variability in sarcoidosis. Ann Am Thorac Soc. 2017;14(Suppl 6):S421–S428. doi:10.1513/AnnalsATS.201707-564OT
47. Vorselaars ADM, Wuyts WA, Vorselaars VMM, et al. Methotrexate vs azathioprine in second-line therapy of sarcoidosis. Chest. 2013;144(3):805–12. doi:10.1378/chest.12-1728
48. Grunewald J, Grutters JC, Arkema EV, Saketkoo LA, Moller DR, Müller-Quernheim J. Sarcoidosis. Nat Rev Dis Primers. 2019;5(1):45. doi:10.1038/s41572-019-0096-x
49. Li H, Zhao X, Wang J, Zong M, Yang H. Bioinformatics analysis of gene expression profile data to screen key genes involved in pulmonary sarcoidosis. Gene. 2017;596:98–104. doi:10.1016/j.gene.2016.09.037
50. Zhou T, Zhang W, Sweiss NJ, et al. Peripheral blood gene expression as a novel genomic biomarker in complicated sarcoidosis. PLoS One. 2012;7(9):e44818. doi:10.1371/journal.pone.0044818
51. Fritz D, Ferwerda B, Brouwer MC, van de Beek D. Whole genome sequencing identifies variants associated with sarcoidosis in a family with a high prevalence of sarcoidosis. Clin Rheumatol. 2021;40(9):3735–43. doi:10.1007/s10067-021-05684-w
52. Baughman RP, Winget DB, Lower EE. Methotrexate is steroid sparing in acute sarcoidosis: results of a double blind, randomized trial. Sarcoidosis Vasc Diffuse Lung Dis. 2000 Mar;17(1):60-6. PMID: 10746262.
53. Lower EE, Baughman RP. Prolonged use of methotrexate for sarcoidosis. Arch Intern Med. 1995 Apr 24;155(8):846-51. PMID: 7717793.
54. Jones E, Callen JP. Hydroxychloroquine is effective therapy for control of cutaneous sarcoidal granulomas. J Am Acad Dermatol. 1990;23 (3 Pt 1):487–489. doi:10.1016/0190-9622(90)70246-e
55. Bert A, El Jammal T, Kodjikian L, Gerfaud-Valentin M, Jamilloux Y, Seve P. Hydroxychloroquine Therapy in Sarcoidosis-Associated Uveitis. Ocul Immunol Inflamm. 2024 Feb;32(2):154-60. doi: 10.1080/09273948.2023.2165952
56. Rezaee M, Zangiabadian M, Soheili A, et al. Role of anti-tumor necrosis factor-alpha agents in treatment of sarcoidosis: a meta-analysis. Eur J Intern Med. 2023;109:42–9. doi:10.1016/j.ejim.2022.12.003
57. Adler BL, Wang CJ, Bui TL, Schilperoort HM, Armstrong AW. Anti-tumor necrosis factor agents in sarcoidosis: a systematic review of efficacy and safety. Semin Arthritis Rheum. 2019;48(6):1093–104. doi:10.1016/j.semarthrit.2018.10.005
58. Saleh S, Ghodsian S, Yakimova V, Henderson J, Sharma OP. Effectiveness of infliximab in treating selected patients with sarcoidosis. Respir Med. 2006;100(11):2053–9. doi:10.1016/j.rmed.2006.02.017
59. Jamilloux Y, Cohen-Aubart F, Chapelon-Abric C, et al. Efficacy and safety of tumor necrosis factor antagonists in refractory sarcoidosis: a multicenter study of 132 patients. Semin Arthritis Rheum. 2017;47(2):288–94. doi:10.1016/j.semarthrit.2017.03.005
60. Burmester GR, Blanco R, Charles-Schoeman C, et al. Tofacitinib (CP-690,550) in combination with methotrexate in patients with active rheumatoid arthritis with an inadequate response to tumour necrosis factor inhibitors: a randomised phase 3 trial. Lancet. 2013;381(9865):451–60. doi:10.1016/S0140-6736(12)61424-X
61. Fleischmann R, Kremer J, Cush J, et al. Placebo-controlled trial of tofacitinib monotherapy in rheumatoid arthritis. N Engl J Med. 2012;367(6):495–507. doi:10.1056/NEJMoa1109071
62. van Vollenhoven RF, Fleischmann R, Cohen S, et al. Tofacitinib or adalimumab versus placebo in rheumatoid arthritis. N Engl J Med. 2012;367(6):508–19. doi:10.1056/NEJMoa1112072
63. Fleischmann R, Mysler E, Hall S, et al. Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomised controlled trial. Lancet. 2017;390(10093):457–68. doi:10.1016/S0140-6736(17)31618-5
64. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). 2021;73(7):924–39. doi:10.1002/acr.24596
65. Smolen JS, Landewé RBM, Bergstra SA, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. Ann Rheum Dis. 2023;82(1):3–18. doi:10.1136/ard-2022-223356
66. van der Heijde D, Song IH, Pangan AL, et al. Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis (SELECT-AXIS 1): a multicentre, randomised, double-blind, placebo-controlled, phase 2/3 trial. Lancet. 2019;394(10214):2108–17. doi:10.1016/S0140-6736(19)32534-6
67. Deodhar A, Sliwinska-Stanczyk P, Xu H, et al. Tofacitinib for the treatment of ankylosing spondylitis: a phase III, randomised, double-blind, placebo-controlled study. Ann Rheum Dis. 2021;80(8):1004–13. doi:10.1136/annrheumdis-2020-219601
68. McInnes IB, Anderson JK, Magrey M, et al. Trial of upadacitinib and adalimumab for psoriatic arthritis. N Engl J Med. 2021;384(13):1227–39. doi:10.1056/NEJMoa2022516
69. Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis. 2023;82(1):19–34. doi:10.1136/ard-2022-223296
70. King B, Ohyama M, Kwon O, et al. Two phase 3 trials of baricitinib for alopecia areata. N Engl J Med. 2022;386(18):1687–1699. doi:10.1056/NEJMoa2110343
71. Sandborn WJ, Ghosh S, Panes J, et al. Tofacitinib, an oral Janus kinase inhibitor, in active ulcerative colitis. N Engl J Med. 2012;367(7):616–64. doi:10.1056/NEJMoa1112168
72. Sandborn WJ, Su C, Sands BE, et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2017;376(18):1723–36. doi:10.1056/NEJMoa1606910
73. Kerschbaumer A, Smolen JS, Nash P, et al. Points to consider for the treatment of immune-mediated inflammatory diseases with Janus kinase inhibitors: a systematic literature research. RMD Open. 2020;6(3):e001374. doi:10.1136/rmdopen-2020-001374
74. Taylor PC, Weinblatt ME, Burmester GR, et al. Cardiovascular safety during treatment with baricitinib in rheumatoid arthritis. Arthritis Rheumatol. 2019;71(7):1042–55. doi:10.1002/art.40841
75. Hoisnard L, Pina Vegas L, Dray-Spira R, Weill A, Zureik M, Sbidian E. Risk of major adverse cardiovascular and venous thromboembolism events in patients with rheumatoid arthritis exposed to JAK inhibitors versus adalimumab: a nationwide cohort study. Ann Rheum Dis. 2022;annrheumdis-2022-222824. doi:10.1136/ard-2022-222824
76. Ytterberg SR, Bhatt DL, Mikuls TR, et al. Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. N Engl J Med. 2022;386(4):316–26. doi:10.1056/NEJMoa2109927

77. Charles-Schoeman C, Buch MH, Dougados M, et al. Risk of major adverse cardiovascular events with tofacitinib versus tumour necrosis factor inhibitors in patients with rheumatoid arthritis with or without a history of atherosclerotic cardiovascular disease: a post hoc analysis from ORAL Surveillance. Ann Rheum Dis. 2023;82(1):119–29. doi:10.1136/ard-2022-222259
78. Molander V, Bower H, Frisell T, Delcoigne B, Di Giuseppe D, Askling J. Venous thromboembolism with JAK inhibitors and other immune-modulatory drugs: a Swedish comparative safety study among patients with rheumatoid arthritis. Ann Rheum Dis. 2022;ard-2022-223050. doi:10.1136/ard-2022-223050
79. Wollenhaupt J, Lee EB, Curtis JR, et al. Safety and efficacy of tofacitinib for up to 9.5 years in the treatment of rheumatoid arthritis: final results of a global, open-label, long-term extension study. Arthritis Res Ther. 2019;21(1):89. doi:10.1186/s13075-019-1866-2
80. Harigai M. Growing evidence of the safety of JAK inhibitors in patients with rheumatoid arthritis. Rheumatology. 2019;58 (Suppl 1):i34–i42. doi:10.1093/rheumatology/key287
81. Paolino A, Galloway J, Birring S, et al. Clinical phenotypes and therapeutic responses in cutaneous-predominant sarcoidosis: 6-year experience in a tertiary referral service. Clin Exp Dermatol. 2021;46(6):1038–45. doi:10.1111/ced.14614
82. Álvarez-Reguera C, Prieto-Peña D, Herrero-Morant A, et al. Clinical and immunological study of tofacitinib and baricitinib in refractory Blau syndrome: case report and literature review. Ther Adv Musculoskelet Dis. 2022;14:1759720X221093211. doi:10.1177/1759720X221093211
83. Zhang S, Cai Z, Mo X, Zeng H. Tofacitinib effectiveness in Blau syndrome: a case series of Chinese paediatric patients. Pediatr Rheumatol Online J. 2021;19(1):160. doi:10.1186/s12969-021-00634-x
84. Singh K, Wang A, Heald P, et al. Treatment of angiolupoid sarcoidosis with tofacitinib ointment 2% and pulsed dye laser therapy. JAAD Case Rep. 2021;7:122–4. doi:10.1016/j.jdcr.2020.11.016
85. Alam M, Fang V, Rosenbach M. Treatment of cutaneous sarcoidosis with tofacitinib 2% ointment and extra virgin olive oil. JAAD Case Rep. 2021;9:1–3. doi:10.1016/j.jdcr.2020.12.021
86. Sauvageau AP, Oulee A, Huang YY, Patel RM, Hamp L. Cutaneous sarcoidosis mimicking pigmented purpuric dermatosis. J Cutan Pathol. 2022;cup.14326. doi:10.1111/cup.14326
87. Costanza MB, Reynolds KA, Mervak JE. Management of treatment-resistant angiolupoid sarcoidosis with adalimumab and tofacitinib 2% ointment. JAAD Case Rep. 2023;38:61–3. doi:10.1016/j.jdcr.2023.06.006
88. Smith JS, Woodbury MJ, Merola JF. Ruxolitinib cream for the treatment of cutaneous sarcoidosis. JAAD Case Rep. 2023;38:111–2. doi:10.1016/j.jdcr.2023.05.032

ANNEX

Table S1. Previous Treatments Received Before JAKi in the 49 Reported Sarcoidosis Cases

Variables	**n=49**
Oral corticosteroids	39/49 (80)
Methotrexate	33/49 (67)
Hydroxychloroquine	18/49 (36)
Infliximab	13/49 (27)
Topical corticosteroids	11/49 (22)
Mycophenolate mofetil	7/49 (14)
Adalimumab	7/49 (14)
Azathioprine	7/49 (14)
Minocycline/Doxycycline	4/49 (8)
Topical CNI	3/49 (6)
Leflunomide	3/49 (6)
Rituximab	3/49 (6)
Cyclophosphamide	2/49 (4)
Intravenous immunoglobulin	2/49 (4)
Tocilizumab	2/49 (4)
Apremilast	2/49 (4)
Tacrolimus	1/49 (2)
Ciclosporin	1/49 (2)
Thalidomide	1/49 (2)
Anakinra	1/49 (2)
Anti-tuberculosis therapy	1/49 (2)
Dapsone	1/49 (2)
Tildrakizumab	1/49 (2)

Abbreviations: CNI, calcineurin inhibitor; JAKi, Janus kinase inhibitor.
Categorical variables are expressed as No. (%).

Table S2. Characteristics, Previous Treatments, JAKi Treatment-Related Findings and Outcome of the 45 Sarcoidosis Cases Treated With JAKi Published to Date

Ref	Gender	Age	Organ involved	Disease duration Follow-up on JAKi	Treatment	Previous treatments	Outcome
(23)	F	59	S, ENT, L	18 y 12 m	RUXO 5mgx2/d	GC, MTX, HCQ, AZA, LEF, INF, ADA	Partial response: S & L M3, GC tapered at 8 mg/d
(34)	M	77	LN, L, K	Unknown 14 m	TOFA 10mgx2/d	GC, IgIV, CsA, RTX	Complete response: LN, L & K
(34)	F	43	LN, CS, CNS, J	Unknown 12 m	TOFA 5-10mgx2/d	GC, HCQ, MTX	Partial response: LN, CS, CNS, J, GC tapered at 5 mg/d
(34)	M	42	LN, M, K	Unknown 7 m	TOFA 5-10mgx2/d	GC, HCQ	Complete response: LN, M & K
(34)	M	20	LN, G, K	Unknown 8 m	TOFA 10mgx2/d	IFN	Complete response: LN, G, K
(34)	M	74	LN, L, K, Ca2+	Unknown 10 m	TOFA 5-10mgx2/d	None	Partial response: K, Ca2+ M10
(34)	M	67	LN, L, K	Unknown 4 m	TOFA 10mgx2/d	GC	Partial response: Ca2+, L, K M3, GC tapered at 10 mg/d
(34)	F	36	E, K	Unknown 8 m	TOFA 5mgx2/d	GC, MTX, MMF, IFN	Partial response: E, K, GC maintained at 5 mg/d
(19)	F	63	S, CS, L	6 y 6 m	TOFA 5mgx2/d	GC, MTX, IFN	Complete response: S M3, CS M6
(19)	F	55	S, E, ENT	6 y 6 m	TOFA 5mgx2/d	GC, MTX, HCQ	Partial response: S, E, ENT, GC withdrawn
(19)	M	50-59	S, Spl, ENT, L	5 y 12 m	TOFA 5-10mgx2/d	GC, MTX, HCQ	Complete response: S M8
(19)	M	50-59	S, ENT, L	16 y 6 m	TOFA 5mgx2/d	GC, MTX	Partial response: S M6, GC withdrawn
(19)	M	57	S, E, ENT, L	22 y 6 m	TOFA 5mgx2/d	GC, MTX	Partial response: S M6, GC withdrawn
(19)	F	50-59	S, ENT, L	27 y 6 m	TOFA 5mgx2/d	GC, MTX	Partial response: S, ENT, L M6, GC tapered at 8 mg/d
(19)	M	56	S, L	12 y 6 m	TOFA 5mgx2/d	GC, MTX, IFN	Complete response: S & L M6
(19)	M	55	S, L	6 y 6 m	TOFA 5mgx2/d	MTX, AZA	Partial response: Stable L M6, GC tapered
(19)	F	50-59	S	1 y 6 m	TOFA 5mgx2/d	GC, MTX	Complete response: S

(19)	M	50-59	S, L	31 y 6 m	TOFA 5mgx2/d	GC, MTX	Complete response: S
(32)	F	48	S, L	8 y 38 m	TOFA 5mgx2/d	MTX, HCQ, ADA, MIN, TACRO, APR	Complete response: S M10, stable L
(35)	M	34	S, L, Li, Spl	6 y 5 m	TOFA 5mgx2/d	GC, HCQ, ADA+MTX	Partial response: S M5, stable L
(35)	F	68	S, E	25 y 7 m	TOFA 5mgx2/d	Topical GC, Topical CNI, HCQ, MIN	Complete response: S, E M6
(24)	F	61	S, L	3 m 3 m	TOFA 5mgx2/d	None	Complete response: S, L M3
(25)	F	56	LN, L, Li, Spl, B, G, Ca2+	5 y 18 m	RUXO 10-15mgx2/d	GC, MTX, HCQ, AZA, INF, ADA, DOX, AT, MMF, CP, ANA	Complete response: LN, Li, Spl, B, G, Ca2 GC tapered
(26)	F	60	LN, S, L	8 y 9 m	RUXO 10mgx2/d	Intralesional steroid injections	Complete response: S M5 Partial response: L & LN M7
(27)	F	62	LN, E, ADA therapy induced disease	1 y 8 m	TOFA 5mgx2/d	ADA discontinuation, GC, MTX	Complete response: E & LN M8 Complete response of RA
(28)	F	35	LN, J	0,2 y 3 m	BARI 4mgx2/d	GC	Complete response: J & LN M3
(33)	M	37	L	4 y 16 m	TOFA 5mgx2/d	GC, MTX	L stable disease M16, GC withdrawn
(33)	M	35	L	2 y 1 m	TOFA 5mgx2/d	GC	Lost of follow-up
(33)	F	43	L	9 m 16 m	TOFA 5mgx2/d	GC	Partial response: L M12, GC withdrawn
(33)	M	39	S, J, L	5 y 12 m	TOFA 5mgx2/d	GC	Partial response: L M12, GC withdrawn
(33)	M	50	S, J, Spl, Ca2+, CNS, L	2 y 1 m	TOFA 5mgx2/d	MTX, MMF	Stable L Worsening of presumed peripheral sarcoid neuropathy
(29)	F	47	S, L	Unknown 9 m	TOFA 8mgx2/d	Topical GC, GC, PIM, ILKA, DAP	Partial response: S, stable L at M9
(29)	F	53	S, L	Unknown 8 m	TOFA 8mgx2/d	GC, ILKA, TILD	Complete response: S M8
(29)	F	75	S	Unknown 4 m	TOFA 2.5mgx1/d	Topical GC, GC, MTX, ILKA	Complete response: S M4

(continued)

Ref	Gender	Age	Organ involved	Disease duration Follow-up on JAKi	Treatment	Previous treatments	Outcome
(29)	F	49	S, L	Unknown 7 m	TOFA 2.5mgx1/d	GC, MTX, Topical CNI, ILKA, HCQ	Partial response: S
(29)	F	63	S	Unknown 4 m	TOFA 4mgx2/d	GC, HCQ, MMF, Topical TACRO	Partial response: S, GC withdrawn
(30)	F	65	S	11 y 6 m	TOFA 5mgx1-2/d	HCQ	Complete response: S M6 TOFA tapered at 5 mg/d
(31)	F	60	LN, S, B, L	21 y 9 m	TOFA 5-10mgx2/d	GC, MTX, MMF, IFN, RTX, IVIG	Complete response: S, L, LN & B M4
(39)	M	59	S, L	24 y 12 m	BARI 4mgx2/d	Topical GC, MTX	Complete response: S, L M12
(41)	F	59	S, L	0 y 12 m	TOFA 5mgx2/d	GC, HCQ	Complete response: S, L M11
(38)	M	44	CS, E, L, Li	7 y 11 m	TOFA 7.5mgx2/d	GC, MTX, AZA, LEF, INF	Complete response: CS, E, Li M11 and L on CT
(37)	M	56	S, J	30 y 18 m	UPA 15mgx1/d	Topical GC, GC, MTX, ADA, INF	Complete response: S, J M18
(40)	M	41	S, E	1 y 6 m	ABRO 100mgx1/J	GC	Partial response: S, E M6, GC withdrawn
(36)	F	57	S, J, ENT, L	19 y 24 m	TOFA 5mgx2/d	GC, MTX, AZA, HCQ, INF, MMF, RTX, THAL	Complete response :S, J, ENT M24 Partial L response, GC tapered 5 mg
(42)	F	53	S, Spl, Li, L	8 y 30 m	TOFA 5mgx2/d	GC, MTX, AZA, HCQ, ADA, INF	Initial Complete response M21 Relapse M30, Treatment with Sirolimus

Abbreviations: ADA, adalimumab; APR, apremilast; AT therapy, anti-tuberculosis therapy; AZA, azathioprine; B, bones; BARI, baricitinib; CNI, calcineurin inhibitor; CNS, central nervous system, CS, cardiac sarcoidosis; d, day; DAP, dapsone; DOX, doxycycline; E, eyes; CP, cyclophosphamide; CICLO, ciclosporine; ENT, ear nose throat; G, gastrointestinal, GC, glucocorticoids; HCQ, hydroxychloroquine; INF, infliximab; IVIG, intravenous immunoglobulin; J, joints; JAKi, Janus kinase inhibitor; L, lung LEF, leflunomide; Li, liver; LN, lymph node; m, month; M, muscle; MIN, minocycline; MMF, mycophenolate mofetil; MTX, methotrexate; P, parotids; PFT, pulmonary function test; PIM, pimecrolimus, RA, rheumatoid arthritis; Ref, reference; RTX, rituximab; RUXO, ruxolitinib; S, skin; Spl, spleen; TACRO, tacrolimus; THAL, thalidomide; TILD, tildrakizumab; TOCI, Tocilizumab; TOFA tofacitinib; y, year

Table S3. Characteristics, Previous Treatments, JAKi Treatment-Related Findings and Outcome of the 4 Blau Syndrome Cases Treated with JAKi Published to Date

Ref	Gender	Age	Organ involved	Disease duration JAKi follow-up	Treatment	Previous treatments	Outcome
(82)	F	25	S, E, J	2.5 y 21 m	TOFA 5mgx2/d then BARI 4mg/d	MTX, ETN, ANA, ADA	Lymphopenia under TOFA Complete Response: S, E, J M2 with BARI
(83)	M	3	J	3 y 12 m	TOFA 1.6mg/d	NSAID, MTX, GC, TOCI, ETN	Complete Response: J M12
(83)	M	9	J	7 y 12 m	TOFA 2.5mg/d	NSAID, ETN, MTX, TOCI	Complete Response: J M12
(83)	M	2	S, J	2.5 y 4 m	TOFA 2.5mg/d	NSAID, MTX, GC, TOCI, ETN	Complete Response: S, J M4

Abbreviations: ANA; anakinra; ADA, adalimumab; BARI, baricitinib; d, day; DOX, Doxycycline; E, eyes; ETN, etanercept; GC, glucocorticoids; J, joints; JAKi, Janus kinase inhibitor; L, lung; LN, lymph node; m, month; M, muscle; MTX, methotrexate; NSAID; non-steroidal anti-inflammatory drugs; Ref, reference; S, skin; TOCI, tocilizumab; TOFA, tofacitinib; w, week; y, year

Table S4. Characteristics, Previous Treatments, JAKi Treatment-Related Findings and Outcome of the 6 Cutaneous Sarcoidosis Cases Treated With Topical JAKi Published to Date

Ref	Gender	Age	Organ involved	Disease duration JAKi follow-up	Treatment	Previous treatment	Outcome
(84)	F	50	S, L	5 y 2.5 m	Topical 2% TOFAx2/d	Topical GC, Topical CNI, DOX, MTX,	Partial response: S M2
(85)	M	46	S, LN, L	9 y 5 m	Topical 2% TOFAx2/d	Topical GC, Topical CNI, Topical ATRA, ADAP, HCQ, DOX	Partial response: S M5
(86)	F	26	S, M	Unknown 6 m	Topical 2% TOFAx2/d	AZA, GC	Partial response: S M6
(86)	F	26	S, M	1 y 6 m	Topical 2% TOFAx2/d	AZA, GOL	Partial response: S M6
(87)	F	44	S, LN	1 y 6m	Topical 2% TOFAx2/d and ADA	Topical GC, DOX, MTX, HCQ, ADA	Partial response: S M6
(88)	F	66	S, CS, L	Unknown Unknown	Topical 1.5% RUXOx2/d	Topical GC, MTX, INF	Complete response: S M2

Abbreviations: ADA, adalimumab; ADAP, adapalene; ATRA, tretinoin; AZA, azathioprine; CNI, calcineurin inhibitor; d, day; DOX, doxycycline; GC, glucocorticoids; GOL, golimumab; HCQ, hydroxychloroquine; JAKi, Janus kinase inhibitor; L, lung; LN, lymph node; m, month; M, muscle; MTX, methotrexate; Ref, reference; S, skin; TOFA, tofacitinib; RUXO, ruxolitinib; y, year.