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ORIGINAL COMMUNICATION

Infliximab biosimilar for treating neurosarcoidosis: tolerance and efficacy in a retrospective study including switch from the originator and initiation of treatment

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Abstract

Objectives Infliximab is increasingly used to treat neurosarcoidosis. We aimed to determine the efficacy and tolerance of an infliximab biosimilar for treating neurosarcoidosis.

Methods We conducted a retrospective single-center study to describe the efficacy, safety and immunogenicity of an infliximab biosimilar in neurosarcoidosis patients. We compared the survival time without relapse while receiving the biosimilar or previous originator-infliximab treatment.

Results Twenty patients with histologically documented neurosarcoidosis were treated with an infliximab biosimilar (initiation of treatment in 12 and switch from the originator drug in 8) between February 2016 and August 2018. All patients presenting with neurological involvement of one or more areas, including meningeal ($n=15$), cerebral ($n=10$), spinal cord ($n=9$), and/or cranial nerves ($n=5$); epilepsy ($n=3$); and/or intracranial hypertension ($n=3$) were enrolled. Eighteen patients received glucocorticoids during infliximab treatment, and 16 had methotrexate or azathioprine concomitant treatment. The median duration of follow-up was 25 months (19–28). Six patients relapsed during biosimilar treatment. Relapse rates and time-to-relapse did not differ between the infliximab originator previously received and biosimilar treatment groups ($p=0.40$ and 0.51, respectively). Nine patients experienced 11 adverse events with the infliximab biosimilar, including infections ($n=5$), urticaria ($n=4$), headache ($n=1$), and diarrhea ($n=1$). All side effects were grade 2 or less using the WHO classification.

Conclusions In this retrospective study, the infliximab biosimilar was efficacious and safe for treating neurosarcoidosis.

Keywords Neurosarcoidosis · Infliximab · Biosimilars

Introduction

Sarcoidosis is an inflammatory granulomatous disease of unknown cause that occurs in young adults [14]. Although the disease course is typically benign, neurological involvement may lead to significant disability. Thus, immunosuppressive drugs are often used to treat neurosarcoidosis in addition to glucocorticosteroids. Methotrexate (MTX), azathioprine (AZA) and mycophenolate mofetil (MMF) are usually used as first-line immunosuppressants. Infliximab, a chimeric IgG1 antibody approved for the treatment of Crohn's disease, ulcerative colitis, spondyloarthritis, rheumatoid arthritis, psoriatic arthritis, and chronic plaque psoriasis, has emerged as a therapeutic option, especially in refractory neurosarcoidosis [3, 5]. The patent for the infliximab originator expired in 2015 in Europe. Subsequently,

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several infliximab biosimilars have been approved by the European Medicines Agency. Randomized controlled trials were conducted in ankylosing spondylitis [11], rheumatoid arthritis [1], and, more recently, inflammatory bowel disease [8], either as the initial medication or as a switch from a reference product. According to the guidance for the regulatory approval of biosimilars, the extrapolation of the indication was given for all approved biosimilars [10]. However, due to the rarity of neurosarcoidosis, no randomized controlled trial was conducted for this condition. Concerns have been raised about extrapolating the efficacy and tolerance of biosimilars in these rare conditions.

In the Pitié-Salpêtrière Hospital, Assistance Publique-Hôpitaux de Paris, in February 2016, an infliximab biosimilar was recommended for all indications after informing the patient and obtaining medical approval depending on the patient condition. We report here a retrospective analysis of the efficacy, safety, and formation of anti-drug antibodies (ADAbs) in patients with neurosarcoidosis treated with the infliximab biosimilar.

Patients and methods

Patients and study design

Patients were selected from the local database and included if they fulfilled the following criteria: (1) definite or probable neurosarcoidosis [13] with histological documentation of noncaseating granuloma and exclusion of other causes of granulomatous diseases, and (2) receiving treatment with an infliximab biosimilar, either at initiation or as a switch from the originator. Cases of possible or suspected neurosarcoidosis were excluded. Patients were followed according to usual care, and the follow-up ended when the infliximab treatment was stopped or the end of the study was reached (August 2018).

Evaluation of safety and efficacy

The overall response to the infliximab biosimilar was evaluated after 6 months of treatment and at the end of follow-up. The complete and partial responses and progression criteria were described elsewhere [3]. The disease was considered "active" when the extra-pulmonary physician organ severity tool (ePOST) score was >0 in at least 1 organ [2]. A relapse was defined by an increase of at least 1 point in ePOST score. The baseline was considered the time of initiation of the biosimilar. The daily dose of corticosteroids was noted at baseline and at the end of treatment. During the study period, a steering committee was convened consisting of rheumatologists, pharmacists, and internal medicine practitioners who decided to switch to the infliximab originator in individual cases if they had concerns about safety or efficacy. For these patients, follow-up under the infliximab originator was also collected. All adverse events were noted during the study period. Relapse rate and time-to-relapse under the infliximab originator were extracted from medical records for the patients in the present study who previously received this treatment before switching ($n=8$). The patients were informed by their physician and gave written consent. The study was conducted in accordance with the principles of the Declaration of Helsinki. According to French law, the study was conducted under the MR-003 reference methodology edited by the "Commission Nationale Informatiques et Libertés".

Statistical analysis

Quantitative values are expressed as the median (range), and qualitative values are presented as numbers (percentages). Kaplan–Meier survival curves were constructed considering the time of infliximab (biosimilar or originator) initiation to relapse, progression, death or last follow-up. Comparisons between groups were performed with Fisher-exact tests, Mann–Whitney tests, or Wilcoxon tests as appropriate. All tests were two-sided, and a p value <0.05 was considered statistically significant. The analyses were carried out using GraphPad Prism V 6.0 (GraphPad software, La Jolla, CA, USA) and R version 3.4.2.

Results

Clinical characteristics

Twenty-two patients were screened, and 20 were included in the analysis (2 patients received only 1 perfusion of the infliximab biosimilar because the subsequent administrations were performed in other centers). The demographic and clinical characteristics of the 20 patients are detailed in Table 1. Briefly, 9 patients were female, and the median age at sarcoidosis diagnosis was 37 (interquartile range 31–45). The median duration of sarcoidosis before biosimilar-infliximab initiation was 12.5 months (range 1–132). The neurological localization of sarcoidosis consisted of meningeal involvement ($n=15$), cerebral involvement ($n=10$), myelitis ($n=9$), and/or cranial nerve involvement ($n=5$). Three patients had intracranial hypertension, 3 had epilepsy, and 2 had radiculopathy. Cerebro-spinal fluid (CSF) analyses showed elevated leucocyte counts in 11 patients. Before infliximab treatment, 15 patients had received at least one immunosuppressive drug, which was MTX in 11 cases, cyclophosphamide in 7 cases, AZA in 3 cases, and MMF in 2 cases. Two patients received treatment for tuberculosis before initiation of infliximab.

Table 1 Clinical characteristics of patients who received the infliximab biosimilar

Patient	Sex, age	Clinical manifestations	Follow-up	S/I	Outcomes[a]	Relapses[b]	Side effects	Prior treatment	Concomitant treatment[c]
#1	F, 41	T, J (M, C, R)	27	I	CR	0	Pulmonary infection	MTX, GC	MTX, GC (5)
#2	F, 37	T, E, S (M, Med)	24	S	PR	0	0	MTX, CYC, AZA, GC	MTX, GC (10)
#3	M, 31	T, E, (C, Med, E)	28	S	–	1 (5)	Infection Urticaria	GC	MTX, GC (7)
#4	M, 32	T, E, (M, ICH)	26	I	PR	0	Urticaria	MTX, GC	MTX, GC (5)
#5	F, 52	T, E, (M, C, Med)	28	S	–	1 (5)	Larva migrans	CYC, GC	MTX, GC(10)
#6	M, 41	T (M, Med, C)	28	S	CR	0	0	CYC, GC	MTX, GC(5)
#7	F, 50	T, S, (M, Med, CN, R, C)	25	S	CR	0	0	MTX, CYC, MMF, GC	MTX, GC(5)
#8	F, 42	T, (M)	27	S	PR	1 (9)	0	MTX, CYC, GC	MTX, GC (5)
#9	M, 29	T, O, (Med)	24	I	PR	0	0	MTX, GC	GC (5)
#10	F, 47	T, (M, CN, ICH)	24	I	PR	0	0	AZA, GC	GC (5)
#11	M, 52	T, (ICH, M)	27	I	PR	0	0	MTX, GC	MTX, GC (5)
#12	F, 49	T, (Med, CN)	28	S	–	0 (2)	Headache	GC	MTX, GC (5)
#13	M, 42	T, S, (C, E, M)	23	I	PR	0	Pulmonary infection	GC, MTX	MTX, GC (5)
#14	M, 32	T, H, (C, M, Med)	24	I	PR	0	0	GC, MTX, CYC, AZA, MMF	AZA, GC (5)
#15	F, 50	T, (M)	22	I	PR	0	Whitlow	GC	GC (10)
#16	F, 47	Hep, (M, C, Med, ICH)	22	I	PR	1 (3)	0	GC	MTX, GC (10)
#17	M, 43	T, E, B (CN, M, C)	19	I	PR	0	0	GC, MTX	MTX (0)
#18	M, 43	B, (C, E)	27	S	PR	1 (7)	Urticaria	GC, CYC	AZA, GC (5)
#19	M, 42	T, B, J, O, (M)	19	I	PR	1 (15)	Diarrhea, urticaria	GC, MTX, HCQ	MTX, HC (0)
#20	M, 50	T, O, (CN)	25	I	CR	0	0	GC	GC (5)

Follow-up in months

M male, *F* female, *T* thoracic, *O* ophthalmic, *E* ear-and-throat, *J* joints, *B* bones, *S* skin, *H* heart, *Hep* hepatic, *C* cerebral, *CN* cranial nerve, *M* meningeal, *Med* medullar, *ICH* intracranial hypertension, *R* radicular, *E* epilepsy, *GC* glucocorticoids, *MTX* methotrexate, *CYC* cyclophosphamide, *AZA* azathioprine, *MMF* mycophenolate mofetil, *HC* hydrocortisone, *HCQ* hydroxychloroquine, *CR* complete response, *PR* partial response, *S* switch, *I* initiation

[a]Outcomes at 6 months under infliximab biosimilar (patients #3, 5, and 12, who were switched to the originator during the first 6 months, were not evaluated in this column)

[b]Relapses occurring with infliximab biosimilar (time-to-relapse in months)

[c]Concomitant treatments (daily prednisone dosage at the end of follow-up; mg/day)

Treatment regimens and duration

Eight patients received the infliximab originator for a median time of 22.5 months (range 5–60) and then switched to infliximab biosimilar. Additionally, 12 patients received infliximab biosimilar at initiation. The clinical characteristics of the patients are detailed in Table 2 and did not differ between the two groups (initiations or switches).

All the patients received the infliximab biosimilar at a dose of 5 mg/kg. For the patients who were treated with the biosimilar at initiation of infliximab treatment, two infusions were given at an interval of 2 weeks and then at an interval of 4 weeks. For patients who were switched from the originator, the interval varied from 4 to 8 weeks and was not modified for at least the 6 first months of biosimilar treatment. At the time of biosimilar initiation, 12 patients had active disease, and the 8 patients who received the infliximab reference product before the study were all considered in partial or complete remission. Concomitant treatments during infliximab biosimilar treatment were glucocorticosteroids in 18 patients (2 patients had a contra-indication to steroids). Sixteen patients received another steroid-sparing, nonbiologic immunosuppressant treatment during the infliximab treatment: MTX was given to 14 patients, and AZA was given to 2 patients. The MTX

Table 2 Comparison of patients who received the infliximab biosimilar at initiation and those who were switched from the originator

	Switch ($n=8$)	Initiation ($n=12$)	p
Sex ratio (M/F)	3/5	8/4	0.36
Age at sarcoidosis diagnosis median (range)	36 (23–48)	38 (25–51)	0.87
Neurological involvement (n, %)			
Cerebral	5 (63%)	5 (42%)	0.51
Meningeal	5 (63%)	10 (83%)	0.65
Medullar	6 (75%)	3 (25%)	0.06
Cranial nerve	2 (25%)	3 (25%)	1.00
Intracranial hypertension	0 (0%)	3 (25%)	0.24
Radicular	0 (0%)	1 (8%)	1.00
Epilepsy	2 (25%)	1 (8%)	0.54
Concomitant treatment			
Steroids	8 (100%)	10 (83%)	0.42
Azathioprine	1 (13%)	1 (8%)	1.00
Methotrexate	7 (88%)	7 (58%)	0.32

M male, *F* female

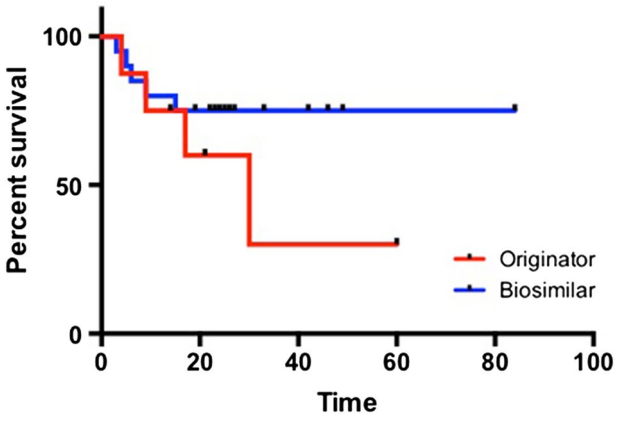

Fig. 1 Univariate cox-proportional hazard regression analysis of relapse-free survival of neurosarcoidosis patients under biosimilar or originator

dosage was 7.5 mg/week in 2 patients and 10 mg/week in 12 patients. AZA was given at a daily dose of 1 mg/kg/day.

Between the baseline and the end of the study, the median daily dose of steroids significantly decreased (daily dose was 11.5 mg at baseline and 5 mg at the end of follow-up, $p<0.0001$). The daily dose of steroids decreased both in patients who were treated at initiation ($p=0.002$) and in patients who were switched from the originator ($p=0.004$).

Outcomes

During the first 6 months of biosimilar treatment, three (2 switches and 1 initiation) patients relapsed or progressed, and one was switched back to the originator due to severe headache during the infusion (#12). Among the three patients who relapsed early during the first 6 months, one (#3) who was switched from the originator experienced progression of cerebral lesions on magnetic resonance imaging (MRI) 5 months after the switch. This adverse effect led to a switch back from the biosimilar to the infliximab originator. The MRI lesions did not improve after 6 months of infliximab originator. The second patient (#5), who was also switched from the originator, relapsed 5 months after the beginning of the biosimilar, with stable lesions on MRI but elevated CSF protein level and leucocyte count. The patient was switched back to the infliximab originator, with stable disease on MRI and an improvement in CSF leucocyte count. The third patient (#16), who was treated at infliximab initiation with the biosimilar, experienced progression of MRI lesions at M3. Because there was a questionable adhesion to oral glucocorticosteroid treatment, she was not switched to the originator. The biosimilar was pursued, and the clinical and radiological features improved within 6 months.

After 6 months of infliximab biosimilar treatment, all other patients ($n=17$) achieved partial or complete remission, and three had been switched back to the originator. During the following months, three additional patients (#8, 18, and 19) relapsed. Relapses were managed with an increase in daily steroid dose and methylprednisolone bolus ($n=1$) and/or a switch to the infliximab originator ($n=2$). Patient #8 improved on the originator, but the infusion interval was decreased. Patient #19, who also experienced urticarian lesions on the biosimilar, was switched to the originator but had an anaphylactic reaction to the originator, and treatment was definitively stopped.

Overall, the relapse rate (6/20 patients on biosimilar), as well as the time-to-relapse, did not differ between the infliximab originator and biosimilar treatments ($p=0.40$ and 0.51, respectively, Fig. 1).

The median follow-up duration was 25 months (range 19–28). Overall, 9 patients experienced 11 adverse events that were considered possibly related to infliximab biosimilar during treatment: 5 were infections (including 1 that led to hospitalization). Five patients had reactions to the infusion (4 urticaria and 1 headache). One patient had permanent diarrhea, with no explanation despite extensive check-up, including colonoscopy. The diarrhea disappeared when the infliximab treatment was stopped.

Overall, seven patients discontinued the infliximab biosimilar because of relapse ($n=6$) or adverse events ($n=1$). Among the six patients who relapsed, five subsequently received the infliximab originator. Four patients did not improve or relapsed with this switch to the originator, thus they were switched back to the biosimilar. Finally, at the end of follow-up, 3 patients had definitively stopped infliximab

treatment [1 because of anaphylaxis (#19) and 2 because they had stable disease], 2 were on the originator, and the remaining 15 were receiving the infliximab biosimilar.

ADAb levels were measured in 16 patients during biosimilar treatment after a median duration of 6 months (5–20) and were always negative.

Discussion

In this study that included 20 patients, we show that the infliximab biosimilar is a safe and efficacious treatment for neurosarcoidosis. We did not observe any difference in the relapse rate or time-to-relapse compared to the infliximab originator.

Biological therapies represent a large proportion of health care expenditures, and biosimilars should provide treatment options that help contain health care spending [4]. Biosimilars are products highly similar to authorized biologics and are supposed to have no clinically meaningful difference from the original product. Unlike generic drugs, biosimilars must be compared to the reference product in clinical studies before commercialization. In neurosarcoidosis, we and others demonstrated in retrospective series that infliximab is a valuable option for treating neurosarcoidosis [3, 5]. A recent study used an infliximab biosimilar in 29 patients with severe sarcoidosis, and showed a similar safety and efficacy profile as the originator [12, 15]. In this study, only eight patients had CNS sarcoidosis, and neurological outcomes were not specifically studied (3 patients out of 8 had a neurological functional response). Here, we demonstrated that efficacy, determined by the remission and relapse rates, was similar to that described in previous studies. Moreover, relapses rates were not different under the infliximab originator and biosimilar in eight patients who were previously treated with the originator.

In our study, eight patients were switched from the originator to the biosimilar. Biosimilar acceptability is a challenge for patients and clinical care teams [6]. Here, we demonstrate that, except for one patient who did not tolerate the treatment (headache), the switch was safely performed. Recent guidelines from rheumatologists stated that no switch to or among biosimilars should be initiated without the prior awareness of the patient and the treating healthcare provider [9]. In our study, we provided education to all patients, families, nurses, and medical teams and obtained a high degree of acceptability.

In our study, we observed several side effects during biosimilar treatment. Five patients experienced infections. This rate is similar to that reported in previous studies with infliximab originator [7]. We also observed four urticarial reactions. Three of them were managed with increasing premedication. For one patient, we had to switch to the originator because of an uncontrollable skin reaction, and this patient also had anaphylaxis with the infliximab originator.

This study has several limitations. The retrospective design did not allow us to obtain homogeneous data, in particular regarding steroid dosages, for all patients. However, due to the rarity of neurosarcoidosis, prospective studies are difficult to conduct. Moreover, ADAbs levels were not obtained for all patients.

Although infliximab is not an approved drug for treating neurosarcoidosis, switching to or initiating an infliximab biosimilar appears safe and efficacious in such patients. The infliximab biosimilar may represent an alternative to the originator in patients with severe or relapsing neurosarcoidosis. The practice of interchangeability is an important issue and data are very limited in the field of sarcoidosis. Even if our study is retrospective, we bring original data on the use of biosimilars in neurosarcoidosis. This study can also help fight the nocebo effect for patients, and negative physician perception of infliximab biosimilar for neurosarcoidosis.

Author contributions HJ, NB, PT, ZA, and FC-A designed the study. QR, CF, NB, AM, MH, JH, MM, and FC-A collected the data. QR and FCA conducted the statistical analysis. QR, PT, ZA, and FC-A analyzed and interpreted the data. MM centralized the dosages of anti-infliximab antibodies. QR, JH, ZA, and FC-A wrote the manuscript. All authors critically reviewed and approved the final version of the manuscript.

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Compliance with ethical standards

Conflicts of interest The authors declare they have no conflicts of interest to report.

Ethical approval The study was conducted according to the Declaration of Helsinki. Accorded to the French law (Loi Jardé 2012), a study that do not change the care of patients does not need to be submitted to a loca IRB.

Informed consent All the patients have been informed and signed written consent to participate.

References

1. Bae SC, Lee YH (2018) Comparative efficacy and safety of biosimilar-infliximab and originator-infliximab in combination with methotrexate in patients with active rheumatoid arthritis: a meta-analysis of randomized controlled trials. Int J Rheum Dis 21:922–929
2. Baughman RP, Drent M, Kavuru M, Judson MA, Costabel U, du Bois R, Albera C, Brutsche M, Davis G, Donohue JF, Muller-Quernheim J, Schlenker-Herceg R, Flavin S, Lo KH, Oemar B, Barnathan ES, Sarcoidosis I (2006) Infliximab therapy in patients with chronic sarcoidosis and pulmonary involvement. Am J Respir Crit Care Med 174:795–802

3. Cohen Aubart F, Bouvry D, Galanaud D, Dehais C, Mathey G, Psimaras D, Haroche J, Pottier C, Hie M, Mathian A, Devilliers H, Nunes H, Valeyre D, Amoura Z (2017) Long-term outcomes of refractory neurosarcoidosis treated with infliximab. J Neurol 264:891–897
4. Farhat F, Torres A, Park W, de Lima Lopes G, Mudad R, Ikpeazu C, Abi Aad S (2018) The concept of biosimilars: from characterization to evolution—a narrative review. Oncologist 23:346–352
5. Gelfand JM, Bradshaw MJ, Stern BJ, Clifford DB, Wang Y, Cho TA, Koth LL, Hauser SL, Dierkhising J, Vu N, Sriram S, Moses H, Bagnato F, Kaufmann JA, Ammah DJ, Yohannes TH, Hamblin MJ, Venna N, Green AJ, Pawate S (2017) Infliximab for the treatment of CNS sarcoidosis: a multi-institutional series. Neurology 89:2092–2100
6. Hakim A, Ross JS (2017) Obstacles to the adoption of biosimilars for chronic diseases. JAMA 317:2163–2164
7. Jamilloux Y, Cohen-Aubart F, Chapelon-Abric C, Maucort-Boulch D, Marquet A, Perard L, Bouillet L, Deroux A, Abad S, Bielefeld P, Bouvry D, Andre M, Noel N, Bienvenu B, Proux A, Vukusic S, Bodaghi B, Sarrot-Reynauld F, Iwaz J, Amoura Z, Broussolle C, Cacoub P, Saadoun D, Valeyre D, Seve P, Groupe Sarcoidose F (2017) Efficacy and safety of tumor necrosis factor antagonists in refractory sarcoidosis: a multicenter study of 132 patients. Semin Arthritis Rheum 47:288–294
8. Jorgensen KK, Olsen IC, Goll GL, Lorentzen M, Bolstad N, Haavardsholm EA, Lundin KEA, Mork C, Jahnsen J, Kvien TK, Nor-Switch Study Group (2017) Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. Lancet 389:2304–2316
9. Kay J, Schoels MM, Dorner T, Emery P, Kvien TK, Smolen JS, Breedveld FC, Task Force on the Use of Biosimilars to Treat Rheumatological Diseases (2018) Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases. Ann Rheum Dis 77:165–174
10. Lyman GH, Zon R, Harvey RD, Schilsky RL (2018) Rationale, opportunities, and reality of biosimilar medications. N Engl J Med 378:2036–2044
11. Park W, Hrycaj P, Jeka S, Kovalenko V, Lysenko G, Miranda P, Mikazane H, Gutierrez-Urena S, Lim M, Lee YA, Lee SJ, Kim H, Yoo DH, Braun J (2013) A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study. Ann Rheum Dis 72:1605–1612
12. Schimmelpennink MC, Vorselaars ADM, van Beek FT, Crommelin HA, Deneer VHM, Keijsers RGM, Veltkamp M (2018) Efficacy and safety of infliximab biosimilar Inflectra((R)) in severe sarcoidosis. Respir Med 138S:S7–S13
13. Stern BJ, Royal W III, Gelfand JM, Clifford DB, Tavee J, Pawate S, Berger JR, Aksamit AJ, Krumholz A, Pardo CA, Moller DR, Judson MA, Drent M, Baughman RP (2018) Definition and consensus diagnostic criteria for neurosarcoidosis: from the Neurosarcoidosis Consortium Consensus Group. JAMA Neurol 75:1546–1553
14. Valeyre D, Prasse A, Nunes H, Uzunhan Y, Brillet PY, Muller-Quernheim J (2014) Sarcoidosis. Lancet 383:1155–1167
15. Vorselaars AD, Crommelin HA, Deneer VH, Meek B, Claessen AM, Keijsers RG, van Moorsel CH, Grutters JC (2015) Effectiveness of infliximab in refractory FDG PET-positive sarcoidosis. Eur Respir J 46:175–185