ORIGINAL INVESTIGATIONS

Efficacy and safety of 24-week therapy with a monoclonal antibody to TRBV9+ T lymphocytes (seniprutug) in patients with ankylosing spondylitis: real-world data

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In April 2024, the first biologic agent (seniprutug) selectively targeting CD8+ T lymphocytes bearing the TRBV9 segment was approved. This novel mechanism of action potentially affects the initial immunopathologic cascade in HLA-B27-associated ankylosing spondylitis (AS). During 2024, seniprutug therapy was initiated in 9 patients with AS in the European part of Russia.

Objective. *To evaluate the efficacy and safety of seniprutug in patients with AS at 12 and 24 weeks (3 and 6 months) in real-world clinical practice.*

Material and methods. *Nine patients with AS were included: 7 men (77.8%) and 2 women (22.2%); mean age 37.3±12.6 years. AS was diagnosed according to ASAS (2009) and the modified New York criteria (1984). Active sacroiliitis on magnetic resonance imaging (MRI) was present in 8 patients (88.9%); spondylitis in at least one spinal segment in 7 (77.8%), with bone-marrow edema (MRI-confirmed spondylitis) in 6 (66.7%). Baseline disease activity was high: Ankylosing Spondylitis Disease Activity Score (ASDAS) 3.83±0.53; Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 5.7±2.01; inflammatory markers were elevated: C-reactive protein (CRP) 49.6±36.7 mg/L (>5 mg/L in 8 patients) and erythrocyte sedimentation rate (ESR) 56.4±28.5 mm/h (>15 mm/h in all patients). Intravenous seniprutug infusions were administered at weeks 0 and 12. Complete 12- and 24-week follow-up data were available for all 9 patients by September 2025.*

Results and discussion. *At week 12, 8 from 9 patients reported subjective improvement. Mean activity scores decreased: ASDAS to 2.57±0.94 and BASDAI to 3.41±1.17. CRP and ESR declined to 26.79±46.35 mg/L and 25.7±29 mm/h, respectively; normalization of laboratory indices occurred in 55.6% of patients. Low disease activity by ASDAS and BASDAI was recorded in 33.3% and 77.8% of cases, respectively.*

At week 24, 8 of 9 patients (88.9%) achieved ASAS40 response; mean ASDAS was 1.59±0.21 and BASDAI 1.75±0.81. Mean reductions were ΔASDAS (weeks 0–24) 2.42±0.75 and ΔBASDAI (weeks 0–24) 4.24±2.0. In all patients completing follow-up, inflammatory markers markedly decreased (CRP 3.4±2.3 mg/L; ESR 11.6±7.2 mm/h). One non-responder was switched to an alternative biologic DMARD.

Conclusion. *This first real-world study demonstrates significant clinical and laboratory improvement in AS patients treated with seniprutug. The 24-week data support the potential of this approach to modulate the pathogenic cascade in HLA-B27-associated AS and justify further evaluation in larger cohorts.*

Keywords: *spondyloarthritis; ankylosing spondylitis; seniprutug; biologic agents; monoclonal antibody to TRBV9.*

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Ankylosing spondylitis (AS), or radiographic axial spondylitis, is a late stage of chronic inflammatory spondyloarthritis characterized by damage to the musculoskeletal system (sacroiliac joints, spine, peripheral joints and entheses), eyes (anterior uveitis), skin and subcutaneous tissues (psoriasis, psoriatic onychopathy), intestine (Crohn's disease and ulcerative colitis) [1].

AS is diagnosed in accordance with the Modified New York Criteria (1984). One of the key signs and classification criteria of spondyloarthritis is the presence of the HLA-B27 allele. HLA-B27 positivity may vary depending on the population. According to some data [2], the HLA-B27 allele is detected in approximately 85% of AS patients. The presence of this allele affects the age of onset of the disease, family predisposition and, in some cases, the phenotypic features of the disease course, such as the presence of certain manifestations, the rate of progression, etc. The results of the assessment of the Spanish registry of AS patients (REGISPONSER) showed that the disease onset was earlier and a family burden of the disease was higher in HLA-B27-positive patients than in HLA-B27-negative patients [3]. Some studies indicate a more aggressive course of AS de-

pending on the sex of both the patient and his/her parents with this diagnosis [4].

The first-line therapy for axial manifestations of spondyloarthritis typically involves non-steroidal anti-inflammatory drugs (NSAIDs). This group of drugs can be effective against pain and reduces the intensity of inflammation. However, their efficacy is often limited and the response to therapy may be insufficient. In such situations, it is necessary to additionally prescribe biological medicinal products, such as tumor necrosis factor α inhibitors, interleukin-17 inhibitors, and Janus kinase (JAK) inhibitors [5].

Notably, biological medicinal products do not provide disease control for all patients. More and more patients face the need to successively change several biological medicinal products with different mechanisms of action, which may be explained by the insufficient influence of drugs on all pathogenetic pathways [6]. This is why the development of drugs with alternative mechanisms of action is crucial. In rheumatology, there is a need to create drugs that could provide a more pronounced and sustainable effect, cause fewer adverse reactions (ARs) and ensure a higher rate of achieving minimal disease activity or remission. Another equally important aspect of therapy is not only achieving subjective improvement but also slowing down the structural progression of the disease.

To overcome the shortcomings of existing treatments, the development of a drug with a novel mechanism of action was initiated in Russia. This drug is targeting the TRBV9+ receptor segment of autoreactive CD8+ T cells, which may play an initiating role in the immunopathogenesis of spondyloarthritis. BCD-180 (international nonproprietary name: seniprutug) (Tribuvia®) is a humanized monoclonal antibody against the TRBV9 segment, which leads to the elimination of TRBV9 T cells, including autoreactive clones, through antibody-dependent cellular cytotoxicity [7]. According to the results of 36 and 48 weeks of the ELEFTA clinical study, the use of seniprutug resulted in a significant decrease in disease activity, a decrease in the level of laboratory markers of inflammation, an improvement in quality of life, spinal function, and, importantly, a decrease in the severity of objective signs of inflammation according to magnetic resonance imaging (MRI) in a significant proportion of patients. An important finding of the study is the favorable safety profile of the drug in patients with AS [7, 8].

Study aim: To evaluate the real-world efficacy and safety of seniprutug in patients with AS at 12 and 24 weeks (3 and 6 months).

Material and methods. From July to September 2024, 9 patients with AS were treated with seniprutug. AS was diagnosed according to the Modified New York Criteria (1984), all patients also met the ASAS (Assessment of SpondyloArthritis International Society, 2009) criteria. To assess the efficacy of therapy, standard indices of spondyloarthritis activity were used: ASDAS-CRP (Ankylosing Spondylitis Disease Activity Score with determination of CRP levels) and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index); moreover, the proportion of patients who achieved 20% and 40% improvement according to the ASAS criteria was assessed (ASAS20 and ASAS40, respectively) [9–11]. To determine the changes over time in achieving the target activity indicators, ASDAS was used, and low activity was determined as ASDAS-CRP <2.1. The severity of the inflammatory process was assessed using laboratory markers, including ESR and CRP, as well as by analyzing MRI images of the sacroiliac joints (SIJs) and the spine using the STIR and T1-SE (T1-weighted spin-echo) sequences. The safety of therapy was assessed by the frequency and profile of ARs.

Table 1. Clinical and demographic characteristics of patients with AS (n=9)

Parameter	Value
Men, n (%)	7 (77,8)
Age, years, M±SD	37,3±12,6
Disease duration, months, M±SD	106,2±108,6
History of axial, extra-axial and extra-articular manifestations, n (%):	
Sacroiliitis	9 (100)
Spondylitis affecting at least one part of the spine	7 (77,8)
Arthritis	9 (100)
Enthesitis	3 (33,3)
Uveitis	1 (11,1)

Table 2. Objective parameters of disease activity in patients with AS

Parameter	Value
CRP, mg/L, M±SD	49,6±36,7
CRP level >5 mg/L, n (%)	8 (88,9)
ESR, mm/h, M±SD	56,4±28,5
ESR >15 mm/h, n (%)	9 (100)
ASDAS-CRP, M±SD	3,83±0,53
BASDAI, M±SD	5,7±2,01
Active sacroiliitis, n (%)	8 (88,9)
Active spondylitis, n (%)	6 (66,7)

There were 7 (77.8 %) male and 2 (22.2 %) female patients, with an average age of 37.3±12.6 years. All patients were carriers of HLA-B27. Determination of HLA-B27 suballeles was not performed. None of the patients had previously received therapy with biological medicinal products or JAK inhibitors. Additional patient characteristics are presented in Table 1.

At baseline, all patients had high disease activity (ASDAS 3.83±0.53 on average; BASDAI 5.7±2.01) and increased inflammatory markers (CRP up to 49.6±36.7 mg/L on average; ESR up to 56.4±28.5 mm/h). Eight (88.9 %) patients had active sacroiliitis according to SIJ MRI, 6 (66.7 %) patients had signs of bone marrow edema in at least one segment of the spine (MRI-confirmed spondylitis). A more detailed description of the signs of AS activity is presented in Table 2.

Intravenous seniprutug infusions were administered at Weeks 0 and 12. At Week 0, a comprehensive examination of patients was

Table 3. Characteristics of activity indices at weeks 12 and 24 of therapy

Parameter	Week 12	Week 24
CRP, mg/L, M±SD	11,7±10,1	3,4±2,3
CRP >5 mg/L, n (%)	4 (44,4)	2 (25,0)
ESR, mm/h, M±SD	25,7±29,0	11,6±7,2
ESR >15 mm/h, n (%)	2 (22,2)	4 (50,0)
ASDAS-CPR, M±SD	2,57±0,94	1,59±0,21
BASDAI, M±SD	3,41±1,16	1,75±0,81
ΔASDAS, M±SD	1,25±1,12	2,42±0,75
ΔBASDAI, M±SD	2,29±1,81	4,24±2,0
ASAS20, n (%)	6 (66,7)	8 (88,9)**
ASAS40, n (%)	4 (44,4)	8 (88,9)**
Low disease activity (ASDAS-CRP <2.1), n (%)	3 (33,3)	8 (88,9)**
Achieving the target decrease in ASDAS-CRP by >1.1, n (%)*	6 (66,7)	6 (66,7)**

Note. * A decrease in ASDAS-CRP by ≥1.1 over the first 3 months and by ≥ 2.2 over 6 months; ** Calculation was based on the number of patients who received the first dose of the study drug.

performed to assess disease activity (ASDAS-CRP and BASDAI), laboratory markers (ESR and CRP), and MRI data of three segments of the spine and SIJs to detect structural changes and bone marrow edema. After a single standard premedication (according to the instructions for the medicinal product), seniprutug was infused at a dose of 3.5 mg/kg. At Week 12, activity indices (ASDAS-CRP and BASDAI), laboratory markers (ESR and CRP) were re-evaluated, followed by standard premedication and infusion of seniprutug at a dose of 7 mg/kg was performed. At Week 24, the activity indices (ASDAS-CRP and BASDAI) and laboratory activity markers (ESR and CRP) were determined. The safety assessment included evaluation of the frequency and profile of ARs, including serious ARs (SARs). Complete 12- and 24-week follow-up data were available for all 9 patients by September 2025.

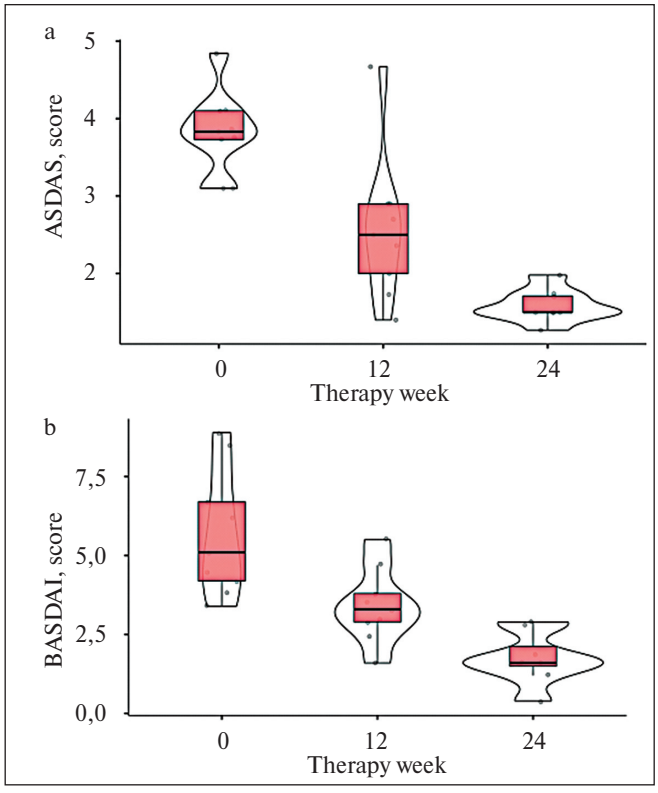

Fig. 1. *Dynamics of ASDAS (a) and BASDAI (b)*

Efficacy parameters at Week 12. In 8 patients receiving NSAIDs and disease-modifying anti-inflammatory drugs, which were initiated before the start of follow-up, a decrease in activity indicators was recorded 12 weeks after the start of therapy: ASDAS averaged 2.57±0.94 and BASDAI was 3.41±1.16 (Table 3, Fig. 1).

The proportion of patients who achieved an ASAS20 and ASAS40 response at Week 12 was 66.7% and 44.4 %, respectively, which indicates the clinical efficacy of seniprutug in most cases and is consistent with the results of the Phase II clinical study ELEFTA [7]. The majority of patients noted a significant improvement in clinical symptoms, manifested as a decrease in the intensity of pain, morning stiffness, and fatigue.

In addition to the subjective improvement, 7 of 9 patients showed positive changes in laboratory parameters (CRP and ESR), 1 patient had a decrease in ESR and normal CRP level. Normal CRP and ESR values were observed in 55.6% and 77.8% of cases, respectively.

By Week 12 of follow-up, 6 patients achieved the target decrease in ASDAS-CRP (on average by ≥1.1), other 2 patients had positive changes, which justified the continuation of therapy. One patient, due to the lack of treatment effect and the increase in clinical and laboratory activity indicators, was switched to therapy with another biological medicinal product. Further assessment of parameters was performed for 8 patients who continued therapy with seniprutug.

Efficacy parameters at Week 24. In 8 patients who continued therapy a further decrease in activity parameters was observed 24 weeks after the first infusion of seniprutug: ASDAS decreased to 1.59±0.21 on average and BASDAI decreased to 1.75±0.81 (see Fig. 1). All patients who continued treatment achieved an ASAS40 response. Mean reductions of ASDAS and BASDAI were 2.42±0.75 and 4.24±2.0, respectively. ASAS40 response at Week 24 was reported in 88.9 % of patients who started therapy.

By Week 24, all 8 patients achieved the target decrease in ASDAS-CRP activity (decrease by ≥1.1) and/or low ASDAS-CRP disease activity (<2.1; see Table 3).

When assessing the changes in clinical and laboratory activity parameters over time, we obtained results showing statistically significant differences in ASDAS (p=0.009), BASDAI (p=0.0028), CRP (p=0.039), and ESR (p=0.02) at Weeks 0 and 12.

Similarly, significant differences were identified for ASDAS (p<0.000001), BASDAI (p=0.0003), CRP (p=0.009), and ESR (p=0.003) at Weeks 0 and 24.

Improvements over time according to the SIJ and spine MRI. In a patient with a normal CRP level, MRI of all parts of the spine and SIJs was performed before the start of therapy to assess the presence of inflammatory changes typical for AS. Multiple sites of bone marrow edema in the SIJs (active sacroiliitis) and structural changes (erosion and adipose degeneration), which are typical for AS, were identified (Fig. 2). Multiple sites of bone marrow edema in three parts of the spine corresponding to manifestations of active spondylitis were also observed (Fig. 3).

After 24 weeks of therapy, the patient underwent repeated SIJ MRI, which showed positive changes (a decrease in bone marrow edema) (Fig. 4).

No infectious ARs were detected during the study, which is consistent with the concept of selective inhibition of the TRBV9+ CD8+ T cell subpopulation without significant suppression of the rest of the immune system.

Discussion. The obtained results on the use of seniprutug (Tribuvia®) demonstrate its high clinical efficacy in patients with AS in real-world practice. By Week 12 of treatment, a clinically significant improvement in disease activity (ASDAS-CRP and BASDAI), as well as a significant decrease in laboratory markers of inflammation was noted, which was accompanied by an improvement in well-being in the majority of patients. Achievement of ASAS20 and ASAS40 responses in 66.7% and 44.4 % of patients, respectively, is consistent with the results of the Phase II clinical study ELEFTA [7, 8] confirming the reproducibility of the previously obtained data in the AS population.

By Week 24 of therapy, an increase in the effect was noted: ASDAS and BASDAI values decreased more than 2-fold from the baseline, and the proportion of patients who achieved an ASAS40 response was 88.9 %. During the follow-up, the majority of patients had normal CRP and ESR levels. The treatment efficacy was confirmed by the regression of MRI signs of inflammatory activity (bone marrow edema). At the same time, 1 patient had no effect, which indicates the need for further evaluation of factors predicting response to seniprutug therapy, including genetic and immunological factors.

The use of seniprutug was accompanied mainly by mild and moderate ARs, the most common of which were infusion-related reactions after the first administration. No SARs were reported during the follow-up, suggesting a favorable short-term safety profile of the drug.

The obtained results are consistent with current views on the potentially key role of CD8+ T cells in the pathogenesis of HLA-B27-associated spondyloarthritis. Targeting a small population of TRBV9+ CD8+ T cells may represent a new therapeutic approach that can address the existing limitations of targeted therapy of spondyloarthritis focused primarily on inflammatory cytokines [12].

The presented results are the first in real-world practice. Further studies with a larger number of patients and a long-term follow-up period are needed to confirm these findings. Furthermore, the ability of seniprutug to influence structural disease progression is still unclear, which is of fundamental importance for long-term outcomes in patients with AS.

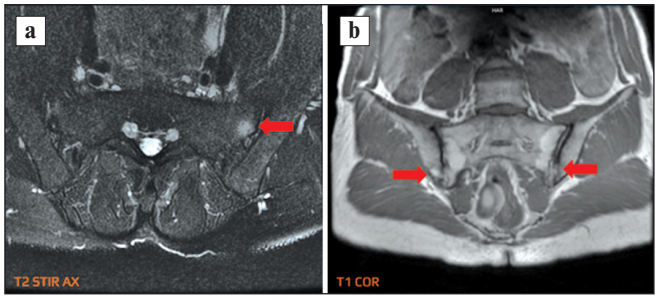

Fig. 2. *MRI of the sacroiliac joints (SIJs) using STIR (a) and T1-weighted sequences (b). Arrows indicate lesions: hyperintense area – bone marrow edema (a); erosions and fat metaplasia (b), typical for AS*

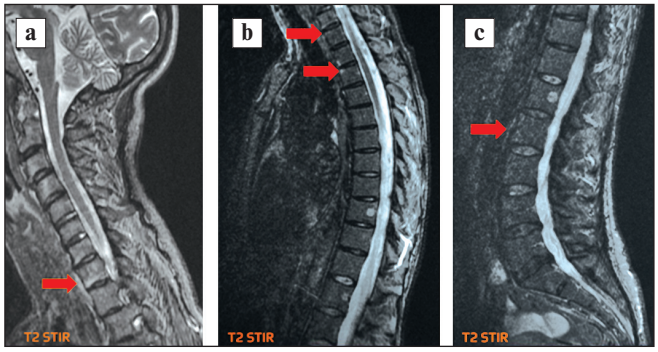

Fig. 3. *MRI of the cervical (a), thoracic (b), and lumbar (c) spine using STIR. Arrows show lesions: bone marrow edema – active spondylitis in all three spinal regions*

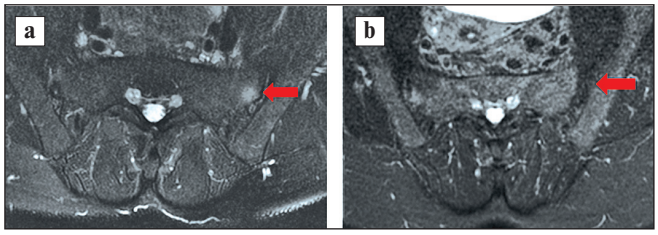

Fig. 4. *MRI of the SIJs using STIR before treatment (a) and after 24 weeks (b) of seniprutug therapy. Arrows indicate lesions: bone marrow edema – active left-sided sacroiliitis (a) and absence of pathologic changes (b)*

Conclusion. Treatment of HLA-B27-positive patients with AS with seniprutug (Tribuvia®) in real-world practice demonstrated a significant reduction in disease activity, positive changes in laboratory and instrumental parameters, and a favorable safety profile confirming the potential of the new mechanism of action and the need for further study of its long-term efficacy.

REFERENCES

1. Румянцева ДГ, Эрдес ШФ. Аксиальный спондилоартрит: современный взгляд на концепцию и эволюцию болезни. Современная ревматология. 2019;13(4):4-10.
Rumyantseva DG, Erdes ShF. Axial spondyloarthritis: a current look at the concept and evolution of the disease. *Sovremennaya Revmatologiya = Modern Rheumatology Journal*. 2019;13(4):4-10. (In Russ.).
doi: 10/14412/1996-7012-2019-4-4-10.
2. Braun J, Sieper J. Fifty years after the discovery of the association of HLA B27 with ankylosing spondylitis. *RMD Open*. 2023 Aug;9(3):e003102. doi: 10.1136/rmdopen-2023-003102.
3. Arevalo M, Gratacys Masmitja J, Moreno M, et al; REGISPONSER group. Influence of HLA-B27 on the Ankylosing Spondylitis phenotype: results from the REGISPONSER database. *Arthritis Res Ther*. 2018 Oct 3;20(1):221. doi: 10.1186/s13075-018-1724-7.
4. Van der Linden SM, Khan MA, Li Z, et al. Recurrence of axial spondyloarthritis among first-degree relatives in a prospective 35-year-followup family study. *RMD Open*. 2022;8: e002208. doi:10.1136/ rmdopen-2022-002208.
5. Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. *Ann Rheum Dis*. 2023 Jan;82(1):19-34. doi: 10.1136/ard-2022-223296.
6. Juanola X, Ramos MJM, Belzunegui JM, et al. Treatment Failure in Axial Spondyloarthritis: Insights for a Standardized Definition. *Adv Ther*. 2022 Apr;39(4):1490-1501. doi: 10.1007/s12325-022-02064-x.
7. Насонов ЕЛ, Мазуров ВИ, Лила АМ и др. Эффективность и безопасность препарата BCD-180, моноклонального антитела к TRBV9+ Т-лимфоцитам, у пациентов с активным рентгенологическим аксиальным спондилоартритом: результаты 36 недель рандомизированного двойного слепого плацебо-контролируемого клинического исследования фазы 2 ELEFTA. Научно-практическая ревматология. 2024;62(1):71-86.
Nasonov EL, Mazurov VI, Lila AM, et al. Effectiveness and safety of BCD-180, antiTRBV9+ T-lymphocytes monoclonal antibody in patients with active radiographic axial spondyloarthritis: 36-week results of doubleblind randomized placebo-controlled phase II clinical study ELEFTA. *Nauchno-Prakticheskaya Revmatologia*. 2024;62(1): 71-86. (In Russ.).
8. Мазуров ВИ, Лила АМ, Насонов ЕЛ и др. Эффективность и безопасность сенипрутуга при активном рентгенологическом аксиальном спондилоартрите и влияние коморбидности на достижение клинического эффекта: результаты 48 недель клинического исследования ELEFTA. Клиническая фармакология и терапия. 2025;34(1):20-32.
Mazurov VI, Lila AM, Nasonov EL, et al. The efficacy and safety of Seniprutug in active radiographic axial spondyloathritis and the impact of comorbidity on achieving the clinical effect: the results of 48 weeks of ELEFTA study. *Klinicheskaya farmakologiya i terapiya*. 2025;34(1):20-32. (In Russ.).
9. Machado P, Landewe R, Lie E, et al; Assessment of SpondyloArthritis international Society. Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores. *Ann Rheum Dis*. 2011 Jan;70(1):47-53. doi: 10.1136/ard.2010.138594.
10. Garrett S, Jenkinson T, Kennedy LG, et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol*. 1994 Dec;21(12):2286-91.
11. Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: A guide to assess spondyloarthritis. *Ann Rheum Dis*. 2009 Jun:68 Suppl 2:ii1-44. doi: 10.1136/ard.2008.104018.
12. Britanova OV, Lupyr KR, Staroverov DB, et al. Targeted depletion of TRBV9+ T cells as immunotherapy in a patient with ankylosing spondylitis. *Nat Med*. 2023 Nov;29(11): 2731-2736. doi: 10.1038/s41591-023-02613-z.

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