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REVIEW

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How to stop radiographic progression. Reimbursement of secukinumab in the B.82 drug program

ABSTRACT

In the past, axial spondyloarthropathies (axSpA) were considered synonymous with ankylosing spondylitis (AS). However, there is a group of patients who present clinical features of axSpA but do not have radiographic changes. Advances in medicine, especially diagnostic imaging and genetics, have made it possible to diagnose the disease at this earlier stage. For this group of patients, the concept of non-radiographic axSpA has been introduced.

It is already known that for patients with non-radiographic axSpA, as for those with AS, it is crucial to diagnose as soon as possible and initiate effective treatment, which causes the relief of clinical symptoms, but also is to prevent the progression of radiological changes. The introduction of tumor necrosis factor--alpha (TNFα) inhibitors changed the course of the disease and the prognosis of patients with axSpA. However, drugs with other mechanisms of action are being sought. One of the new drugs is secukinumab, which blocks interleukin-17 (IL-17), which is important in the pathogenesis of SpA. It has been shown that the majority of patients with non-radiographic axSpA treated with secukinumab did not show radiological progression.

The role of IL-17 blockade in the therapy of axSpA seems to be more appreciated, which was reflected in the updated global guidelines. Until recently, in Poland, only two drugs with the same mechanism of action — TNFα blockade (certolizumab pegol and etanercept) were reimbursed for patients with non-radiographic axSpA. Fortunately, from July 1, 2022, patients with non-radiographic axSpA can also receive IL-17 inhibitors (ixekizumab and secukinumab) in the B.82 drug program.

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KEY WORDS: secukinumab, inflammatory spondyloarthropathies, non-radiographic form, interleukin-17

INTRODUCTION

Spondyloarthropathies (SpA) are a group of rheumatic diseases characterized by arthritis symptoms with the involvement of the spinal joints. SpA include disease entities of varying severity: ankylosing spondylitis (AS) and non-radiographic axial spondyloarthropathies (nr-axSpA), psoriatic arthritis (PsA), reactive arthritis, arthritis associated with inflammatory bowel diseases (Crohn's disease and ulcerative colitis) and undifferentiated SpA [1].

Despite the considerable variation in clinical signs between different SpA they all share a common pathomechanism of changes [1]. In the early days of research on the pathogenesis of SpA, a key role was attributed to Th1 lymphocytes and tumor necrosis factor alpha (TNFα). Subsequent years highlighted the importance of distinct pathways including interleukin-17 (IL-17). The group of cytokines that belong to the IL-17 family (designated by subsequent symbols IL-17A–IL-17F) was discovered relatively recently, i.e. in 1993. In SpA, IL-17A which is produced locally by sy-

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noviocytes (fibroblast-like synoviocytes — FLS and macrophage-like synoviocytes — MLS) and chondrocytes has a pathogenic effect. IL-17A stimulates the production of pro-inflammatory cytokines (e.g. IL-1β, IL-6, TNFα), inflammatory mediators (prostaglandins E2-PGE2) and angiogenic factors (vascular endothelial growth factor [VEGF]), thereby enhancing and maintaining the inflammatory response. Moreover, IL-17A induces the synthesis of extracellular matrix metalloproteinases (MMPs) by chondrocytes and increases the expression of receptor activator of nuclear factor κB ligand (RANKL), contributing to the destruction of articular cartilage and bone [2]. Receptors for IL-17 are widespread, hence IL-17 affects different cell types such as macrophages, neutrophils, keratinocytes, endothelial cells, fibroblasts, chondrocytes, osteoblasts and osteoclasts, which is reflected in a variety of signs and symptoms in the course of SpA, with involvement of multiple organs [3].

Due to their varied clinical presentation, SpA are often divided into two subgroups: peripheral form (in which peripheral joint symptoms predominate) and axial form (in which axial skeleton — the spine and sacroiliac joints — symptoms predominate). This division is clinically relevant due to therapeutic differences [1].

In this study, there will be a focus on axSpA and, in particular, on nr-axSpA and it will discuss new therapeutic options available from 1 July 2022 in Poland, under the B.82 drug program.

NON-RADIOGRAPHIC AXIAL SPONDYLOARTHROPATHIES

In the past, axSpA was considered synonymous with AS. However, it is now well known that this is not the case. There are often patients who have symptoms of inflammatory back pain and other clinical signs of axSpA but no radiographic changes, whereas the AS diagnosis based on the modified 1984 New York criteria requires, among other things, that the radiographic criterion is met. In other words, the diagnosis of AS requires noticeable changes in the sacroiliac joints on a conventional radiograph (X-ray): at least grade 2 changes if bilateral or grade 3–4 changes if unilateral [4]. However, medical advances, including diagnostic imaging, magnetic resonance imaging (MRI), genetic testing and the development of knowledge of human leukocyte antigen (HLA) genes, have made it possible to diagnose the disease at its earlier stage before advanced structural changes occur. The term „nr-axSpA" was introduced for this group of patients [5].

Non-radiographic axSpA is diagnosed in patients with typical signs and symptoms of AS, but without advanced radiographic changes in the sacroiliac joints. The diagnosis is made based on the presence of inflammatory changes on an MRI scan and/or by the presence of HLA-B27 antigen and the presence of other clinical and laboratory signs typical of SpA. Currently, the 2010 ASAS (ASsessment of Ankylosing Spondylitis) SpA classification criteria are widely used for the diagnosis of axSpA (Tab. 1) [6].

RISK OF PROGRESSION OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

It is not clear whether nr-axSpA represents an early stage of AS or is a separate disease entity with a more benign course [7]. It is estimated that approximately 10% of patients with nr-axSpA will develop full-blown AS during a 2-year follow-up period. However, at a 10-year follow-up, the rate is already around 40% [8]. It is not known what this percentage would look like at a follow-up of, for example, 30 years. It should be noted that the very concept of nr-axSpA is new and patient observations over many years are inadequate. In this case, much depends on the passage of time. We are therefore faced with uncertainty. It is possible that even without treatment, some patients with nr-axSpA will not develop full-blown AS after many years. However, expert opinions point to the need for the earliest possible treatment to prevent complications. This gives hope that with new therapies, the proportion of patients without disease progression will be even higher [7].

TREATMENT OF AXIAL SPONDYLOARTHROPATHIES

The current European recommendations for the treatment of axSpA (both AS and nr-axSpA — as the recommendations equate these two disease entities regarding therapy) were published jointly by ASAS and EULAR (European League Against Rheumatism) in 2016 and are based on the results of new clinical trials and expert opinions [9]. The US recommendations published in 2019 by the ACR (American College of Rheumatology) [10]

Table 1. SpA classification criteria according to the 2010 ASsessment in Ankylosing Spondylitis

axSpA (criteria can be applied to patients with back pain persisting ≥ 3 months and which occurred before 45 years of age) in the case when: 1) sacroiliitis is evidenced by an imaging examination (MRI or X-ray) and there is at least 1 (≥ 1) another sign of SpA or 2) HLA-B27 antigen and ≥ 2 other signs of SpA are present
SpA signs: — inflammatory back pain (IBP) — peripheral arthritis — enthesitis (within the heel) — uveitis — *dactylitis* — psoriasis — Crohn's disease or ulcerative colitis — good response to NSAIDs — SpA in family history — HLA-B27 antigen present — increased serum CRP levels

CRP — C-reactive protein; HLA — human leukocyte antigen; MRI — magnetic resonance imaging; NSAIDs — non-steroidal anti-inflammatory drugs; X-ray — radiographic imaging; SpA — spondyloarthropathies

remain generally in line with the European ones, with some differences due to advances in knowledge which will be discussed in the final section of this article.

In the therapy of axSpA, it is crucial to diagnose this disease as soon as possible and implement effective treatment that results in the resolution of complaints and clinical signs and prevents the progression of structural changes in the musculoskeletal system and the development of organ complications. The aim of the treatment is to achieve remission or low disease activity according to the "treat-to--target" strategy and then maintain this state, which often involves modification of treatment and engagement of multiple specialists during therapy. Interdisciplinary cooperation is essential, e.g. with a gastroenterologist (if inflammatory bowel disease accompanies the disease), an ophthalmologist (if uveitis is present), and a dermatologist (to confirm and treat psoriasis). Optimal management of SpA patients also needs non-pharmacological strategies such as patient education and regular physical activity. However, pharmacotherapy remains the cornerstone [11].

In both the European (ASAS-EULAR 2016) [9] and USA (ACR 2019) guidelines, the [10] first-line drugs for the treatment of axSpA remain non-steroidal anti-inflammatory drugs (NSAIDs) at the maximum recommended and tolerated dose — if there are certainly no contraindications to their use. Treatment with NSAIDs should include an assessment of risk factors for gastrointestinal, cardiovascular, and renal adverse effects. There was no significant advantage found for any NSAIDs. The maximum tolerated doses of NSAIDs should be used, however, the maximum doses should not be exceeded. Both the drug itself and its dose should be adjusted individually for each patient. Unfortunately, the use of NSAIDs alone does not significantly prevent radiographic progression. The efficacy of synthetic disease--modifying antirheumatic drugs (DMARDs) in the treatment of axSpA is extremely low and there are virtually no recommendations for their use, excluding patients with possible associated peripheral symptoms or other organ changes. A similar approach applies to glucocorticosteroids (GCs) that should not be used systemically but only topically when peripheral symptoms are predominant. Therefore, the only fully effective therapeutic options to achieve disease remission and halt radiographic progression are innovative therapies, including biologic DMARDs (bDMARDs) (TNFα and IL-17 inhibitors) and targeted-synthetic DMARDs (tsDMARDs) (Janus kinase [JAK] inhibitors). The possibility of using biologics in AS was a major breakthrough in the treatment of this group of patients, avoiding permanent structural changes to the axial skeleton [9, 10].

BIOLOGICS IN THE TREATMENT OF AXIAL SPONDYLOARTHROPATHIES

Failure of NSAIDs therapy in axSpA patients is an indication for the use of biologics. Failure of NSAIDs therapy is identified when at least 2 NSAIDs have been used for

at least 4 weeks and there is no clinical effect expressed by active disease according to a composite disease activity score, such as ASDAS (Ankylosing Spondylitis Disease Activity Score) of at least 2.1 or BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) of at least 4 [9].

According to the 2016 ASAS-EULAR guidelines, TNFα inhibitors are preferred as first-line biological therapy. This recommendation was based on currently available data indicating that treatment with TNFα inhibitors in this patient group reduces disease activity, pain, stiffness, as well as slightly improves overall functional and mental status. For the time being, it is difficult to assess the long-term effect of TNFα inhibitors on structural changes, although the first data seem to be promising. Five TNFα inhibitors can be used for treating axSpA: adalimumab, certolizumab pegol, etanercept, golimumab and infliximab. As with NSAIDs, global recommendations do not indicate an advantage for any particular originator drug or biosimilar [9, 10]. Their choice is thus an individual decision that is often taken depending on the presence of other organ changes [11].

If first-line TNFα inhibitor therapy fails, treatment with a second TNFα inhibitor or IL-17 inhibitor — secukinumab — should be considered. Authors of the recommendation note the lack of available studies on the efficacy and safety of treatment with TNFα inhibitors after the failure of therapy with secukinumab, however, they believe that such management may be warranted [9].

Subsequent, more recent recommendations no longer favor TNFα blockade so clearly. The role of IL-17 blockade appears to be increasingly recognized, as reflected in the subsequent 2019 ACR guidelines that consider IL-17 inhibitors to be equivalent to TNFα blockers [10]. Also, the new proposed 2022 ASAS-EULAR recommendations emphasize the importance of IL-17 blockade. In this year's EULAR 2022 Congress in Copenhagen, Dr. Sofia Ramiro from Leiden University Medical Centre presented a proposal for updated guidelines regarding the treatment of axSpA. Table 2 shows changes compared to previous (2016) recommendations [9].

The new proposed 2022 ASAS-EULAR guidelines put IL-17 inhibitors on a par with TNFα inhibitors, recommending both drugs as equivalent in biologic therapy — both in the first line and subsequent lines of treatment. TNFα inhibitors are still preferred for coexisting uveitis or inflammatory bowel disease, while IL-17 inhibitors are preferred for psoriatic skin lesions [9].

The growing importance of IL-17 inhibitors in the treatment of axSpA is based on new findings that prove treatment efficacy and inhibition of radiographic progression. The data come from, among others, the PREVENT study [12, 13].

PREVENT TRIAL

The PREVENT trial is the largest phase III trial (n = 555) conducted for a biologic drug that is used in the treatment of nr-axSpA [12, 14, 15]. The trial meets all the requirements for clinical trials, such as randomization, blinding and placebo control. In the above-mentioned trial, the effect of 150 mg dose of secukinumab every 4 weeks (with or without a loading dose) was assessed in patients with active nr-axSpA. Inclusion criteria included age ≥ 18 years, met classification criteria for axSpA according to the 2010 ASAS (inflammatory back pain for at least 6 months), presence of signs of inflammation (sacroiliitis on an MRI scan and/or elevated C-reactive protein [CRP] levels), disease activity based on a BASDAI parameter of ≥ 4 cm (0–10 cm) and backache measured on a visual analogue scale (VAS) of ≥ 40 mm (0–100 mm). The PREVENT trial included both patients who had not previously received biological drug therapy and patients with an inadequate response to previous treatment with a TNFα drug. Exclusion criteria for the PREVENT trial included active inflammation other than in SpA, and previous treatment with biologics other than anti-TNFα. Patients meeting the New York criteria that are necessary for the diagnosis of AS were not selected for the trial in question because, by design, the PREVENT trial was a study targeting the non-radiographic form. The assessment of treatment efficacy included evaluation according to recognized axSpA activity scales: changes in the BASDAI score and response according to the ASAS score and ASDAS-CRP score. The primary endpoint of the trial was ASAS40 response in patients not previously treated with other biologics. Moreover, in another trial that was presented at this year's EULAR [15], the progression of radiographic changes was assessed: the progression of radiographic changes on a conventional X-ray and the assessment of the reduction in mar-

Table 2. Treatment recommendations for axial spondyloarthropathies — the 2022 ASAS/EULAR proposal

Recommendations for the treatment of axSpA — the 2022 ASAS/EULAR proposal.	
1 ±	Treatment of axSpA patients should be personalised according to: — current disease symptoms (axial, peripheral and extra-articular symptoms); — patient characteristics, taking into account comorbidities and psychosocial factors.
2	Treatment monitoring should include clinical signs, laboratory tests and imaging examinations; all conducted by recognized methods that are appropriately selected for clinical signs. The frequency of monitoring should be determined individually according to symptoms, disease activity and type of therapy.
3	Treatment should be provided according to a predefined objective.
4 ±	Patients should be educated about the disease and encouraged to exercise regularly and quit smoking; physical therapy should be considered.
5 ±	Patients reporting pain and morning stiffness should take NSAIDs as first-line drugs up to maximum doses, bearing in mind the benefits and risks of their use. In patients who respond well to treatment with NSAIDs, ongoing treatment is preferred as long as it is necessary to control symptoms.
6	Analgesics, such as paracetamol and opioids, can be used for pain control in patients for whom previously recommended treatment is insufficient, contraindicated and/or poorly tolerated.
7	Local injections of GCs into inflamed areas may be considered. Long-term use of systemic GCs is not recommended.
8	Patients with axSpA and without peripheral lesions should usually not be treated with csDMARDs. Treatment with sulfasalazine may be considered in patients with peripheral joint involvement.
9 +	Treatment with iTNF, iIL-17 or iJAK should be considered in patients with persistently high disease activity despite conventional treatment. Currently, treatment with iTNF or iIL-17 is usually initiated.
10 &	In cases where recurrent uveitis or inflammatory bowel disease is identified, the use of monoclonal antibodies, iTNFs, is preferred. iIL-17 may be preferred in patients with extensive psoriasis.
11 &	The lack of response to the treatment should prompt reconsideration of the diagnosis and consideration of the presence of comorbidities.
12 +	If the first therapy with a given bDMARD or tsDMARD fails, a change to another bDMARD (iTNF or iIL-17) or iJAK should be considered.
13	If a patient is in long-term remission, a reduction in the dose of the used biologic may be considered.
14	Total hip arthroplasty should be considered in patients with pain that is refractory to conservative treatment or those with disability and radiographically evident structural changes, regardless of age. Corrective osteotomy of the spine may be considered in patients with severe, disabling deformity and should be performed in specialist centers.
15	If there is a significant change in the course of the disease, causes of the condition other than inflammation, such as a spinal fracture, should be considered and an appropriate evaluation, including imaging examinations, should be performed.

± minor modifications; + major, significant modifications; & — new recommendations relative to the 2016 ASAS/EULAR guidelines; axSpA — axial spondyloarthritis; DMARD — disease-modifying antirheumatic drug; iIL-17 — interleukin-17 inhibitor; iJAK — Janus kinase inhibitor; iTNF — TNFα inhibitor; NSAIDs — non-steroidal anti-inflammatory drugs

row oedema on an MRI scan of the sacroiliac joints. The safety analysis included all patients who received at least one dose of the tested molecule and included the recording of all adverse effects [12, 14, 15].

In conclusion, in all subsequent PREVENT trials, 150 mg of secukinumab every 4 weeks met the primary study objectives (ASAS40 response) at weeks 16, 52 and 104 of therapy in patients not previously treated with TNFα inhibitors. Secukinumab had a clinically significant and sustained (up to 2 years of follow-up) improvement in signs, symptoms, and objective inflammatory parameters in patients with nr-axSpA and those after the previous failure of TNFα therapy. Importantly, the vast majority of patients (88%) showed no progression of radiographic changes, and the use of secukinumab reduced the signs of marrow oedema on an MRI scan of the sacroiliac joints in most patients. At the same time, secukinumab was well tolerated and provided a high safety profile throughout follow-up [12, 14, 15].

These findings indicate that secukinumab is highly effective in nr-axSpA. Until recently, only two drugs with the same mechanism of action, i.e. TNFα blockade (certolizumab pegol and etanercept), were reimbursed in Poland. Fortunately, from 1 July 2022, nr-axSpA patients can also receive IL-17 inhibitors (ixekizumab and secukinumab) under the B.82 drug program [16].

B.82 DRUG PROGRAM

The B.82 drug program is intended for patients with active SpA and without radiographic changes typical of AS (ICD-10: M46.8). The following patients are selected for the drug program: (a) patients with inflammatory back pain, signs of sacroiliitis on an MRI scan but without conventional radiographic changes in the sacroiliac joints as observed on X-rays; (b) patients with the presence of HLA-B27 antigen and an established axSpA diagnosis according to ASAS; (c) patients with inflammation of the peripheral joints or enthesitis and a diagnosis of peripheral SpA based on the ASAS classification criteria for SpA; and with an active and severe form of the disease, which must be evidenced twice at an interval of at least 4 weeks, with no change in treatment during this period. The disease activity, depending on the form of the disease, is assessed according to recognized and special scales, taking into account the failure of other drugs previously used. For nr-axSpA, patients need to take two NSAIDs beforehand (4 weeks each) without a satisfactory treatment effect. Unsatisfactory effects of treatment include 1) BASDAI score ≥ 4 or ASDAS score ≥ 2.1 in double measurements at an interval of at least 4 weeks; 2) back pain of at least 4 as assessed by a VAS of 0 to 10 cm in double measurements at an interval of at least 4 weeks; 3) an overall assessment of disease status (disease activity, severity, further prognosis, and professional activity) greater than 5 on a VAS of 0 to 10 cm: a) this assessment should be performed by an attending physician and a second physician — an expert, a specialist in rheumatology, who is experienced in the treatment of inflammatory spondyloarthropathies with biologics; b) the expert opinion shall take into account clinical picture of the disease, risk factors for rapid progression of the disease, findings on acute-phase markers, results of imaging examinations, professional activity status, presence of organ complications including secondary amyloidosis, coexistence of enthesitis, ocular involvement with frequent exacerbations of uveitis, possibilities of alternative treatment options; c) assessment by an expert physician is conducted only once, after the second measurement of BASDAI or ASDAS scores. Importantly, in cases where patients are at risk of death or disability, they may be selected by the Coordinating Team for Biological Treatment in Rheumatic Diseases to receive biological treatment if some of the criteria described in the drug program are not met, in the case when the treatment is in line with current recommendations and medical knowledge. Therefore, biological treatment in line with global guidelines is worth considering in patients with nr-axSpA.

CONFLICT OF INTEREST

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References

1. Sieper J, Braun J, Dougados M, et al. Spondyloarthritis. Lancet. 2011; 377(9783): 2127–2137, doi: 10.1016/S0140-6736(11)60071-8, indexed in Pubmed: 21684383.
2. McGonagle DG, McInnes IB, Kirkham BW, et al. The role of IL-17A in axial spondyloarthritis and psoriatic arthritis: recent advances and controversies. Ann Rheum Dis. 2019; 78(9): 1167–1178, doi: 10.1136/annrheumdis-2019-215356, indexed in Pubmed: 31278139.
3. McGeachy MJ, Cua DJ, Gaffen SL. The IL-17 family of cytokines in health and disease. Immunity. 2019; 50(4): 892–906, doi: 10.1016/j.immuni.2019.03.021, indexed in Pubmed: 30995505.
4. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum. 1984; 27(4): 361–368, doi: 10.1002/art.1780270401, indexed in Pubmed: 6231933.
5. Rudwaleit M, van der Heijde D, Landewé R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis. 2009; 68(6): 777–783, doi: 10.1136/ard.2009.108233, indexed in Pubmed: 19297344.
6. Rudwaleit M. New approaches to diagnosis and classification of axial and peripheral spondyloarthritis. Curr Opin Rheumatol. 2010; 22(4): 375–380, doi: 10.1097/BOR.0b013e32833ac5cc, indexed in Pubmed: 20473175.
7. Ciurea A, Kissling S, Bürki K, et al. Current differentiation between radiographic and non-radiographic axial spondyloarthritis is of limited benefit for prediction of important clinical outcomes: data from a large, prospective, observational cohort. RMD Open. 2022; 8(1): e002067, doi: 10.1136/rmdopen-2021-002067, indexed in Pubmed: 35110365.
8. Protopopov M, Poddubnyy D. Radiographic progression in non-radiographic axial spondyloarthritis. Expert Rev Clin Immunol. 2018; 14(6): 525–533, doi: 10.1080/1744666X.2018.1477591, indexed in Pubmed: 29774755.

9. van der Heijde D, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017; 76(6): 978–991, doi: 10.1136/annrheumdis-2016-210770, indexed in Pubmed: 28087505.
10. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019; 71(10): 1599–1613, doi: 10.1002/art.41042, indexed in Pubmed: 31436036.
11. Regel A, Sepriano A, Baraliakos X, et al. Efficacy and safety of non-pharmacological and non-biological pharmacological treatment: a systematic literature review informing the 2016 update of the ASAS/EULAR recommendations for the management of axial spondyloarthritis. RMD Open. 2017; 3(1): e000397, doi: 10.1136/rmdopen-2016-000397, indexed in Pubmed: 28176966.
12. Deodhar A, Blanco R, Dokoupilová E, et al. Improvement of signs and symptoms of nonradiographic axial spondyloarthritis in patients treated with secukinumab: primary results of a randomized, placebo-controlled phase III study. Arthritis Rheumatol. 2021; 73(1): 110–120, doi: 10.1002/art.41477, indexed in Pubmed: 32770640.
13. Braun J, Blanco R, Marzo-Ortega H, et al. Secukinumab in non-radiographic axial spondyloarthritis: subgroup analysis based on key baseline characteristics from a randomized phase III study, PREVENT. Arthritis Res Ther. 2021; 23(1): 231, doi: 10.1186/s13075-021-02613-9, indexed in Pubmed: 34481517.
14. Poster #POS0900 presented at EULAR Congress 2021.
15. Poster #POS0299 presented at EULAR Congress 2022 Kopenhagen, 1-4 June 2022.
16. https://www.gov.pl/web/zdrowie/programy-lekowe (18.09.2022).