ORIGINAL INVESTIGATIONS

Comparative efficacy of tofacitinib and adalimumab in patients with psoriatic arthritis in real clinical practice. Data from the Russian nationwide register of patients with psoriatic arthritis

Loginova E.Yu.[1], Korotaeva T.V.[1], Gubar E.E.[1], Korsakova Yu.L.[1], Glukhova S.I.[1], Vasilenko E.A.[2], Vasilenko A.A.[3], Kuznetsova N.A.[4], Patrikeyeva I.M.[5], Nasonov E.L.[1,6]

[1]V.A. Nasonova Research Institute of Rheumatology, Moscow; [2]North-Western State Medical University named after I.I. Mechnikov, St. Petersburg; [3]Novgorod Regional Clinical Hospital, Veliky Novgorod; [4]City Clinical Hospital №40, Ekaterinbur; [5]Regional Clinical Hospital №1, Tyumen; [6]I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia (Sechenov University), Moscow

[1]34A, Kashirskoe Shosse, Moscow 115522, Russia; [2]41, Kirochnaya st., St. Petersburg 191015, Russia; [3]14, Pavla Levitta st., Veliky Novgorod 173008, Russia; [4]189, Volgogradskaya st., Ekaterinburg 620102, Russia; [5]55, Kotovskogo st., Tyumen 625023, Russia; [6]8, Trubetskaya St., Build. 2, Moscow 119991, Russia

Objective: *to compare the clinical efficacy in real clinical practice of the targeted synthetic disease-modifying antirheumatic drug (sDMARD) tofacitinib (TOFA) and the biologic DMARD (bDMARD), an inhibitor of tumor necrosis factor alpha (TNFα), adalimumab (ADA) in patients with psoriatic arthritis (PsA), included in the Russian nationwide register of patients with PsA.*

Patients and methods. *The study included 77 patients with PsA (43 men and 34 women) who met the CASPAR criteria and were observed in the Russian nationwide register. Patients were divided into two groups depending on the treatment. Group 1, in which oral TOFA was prescribed, 5 mg 2 times a day, included 41 patients: 24 (58.5%) men and 17 (41.5%) women, the median age was 41 [34; 50] years, the median duration of PsA was 72 [35; 120] months. Group 2, in which subcutaneous ADA was used, 40 mg every 2 weeks, included 36 patients: 19 (52.8%) men and 17 (47.2%) women, the median age was 44 [34; 51] years, the median duration of PsA was 59 [22; 102] months. Combination therapy, including methotrexate (MT), received 80.5% of patients in the TOFA group and 52.8% of patients in the ADA group.*

At the beginning of the study and every 6 months further, the activity and efficacy of PsA therapy were assessed in all patients according to DAPSA and criteria for minimal disease activity – MDA (number of painful joints ⩽1, number of swollen joints ⩽1, PASI ⩽1 or BSA ⩽3 , pain score ⩽15, patient's general assessment of disease activity ⩽20 mm on a visual analogue scale, HAQ ⩽0.5, enthesitis ⩽1), dynamics of BASDAI and BSA were also assessed. The number of patients who achieved remission (DAPSA ⩽4) or MDA (5 criteria out of 7) during therapy with TOFA and ADA was determined.

Results and discussion. *Before the start of the therapy in the 1st group, the median DAPSA was 44.2 [37.8; 55.3]: moderate PsA activity was in 5 (12.2%) patients, high in 36 (87.8%) patients. In group 2, the median DAPSA was 35.8 [21.1; 52]: low activity was detected in 3 (8.6%), moderate – in 11 (31.4%), high – in 21 (60%) patients (data from 35 patients was available). 6 months after the start of treatment in patients of the 1st and the 2nd group, there was a significant decrease in all indicators of PsA activity compared to the baseline. The median DAPSA was 11 [4.3; 17.3] and 9.1 [6; 19.6]; remissions according to DAPSA reached 11 (26.8%) and 6 (20.8%) patients, respectively, low activity – 15 (36.6%) and 13 (44.8%), MDA – 16 (40%) and 9 (30%). The number of patients with dactylitis in the 1st and in the 2nd group significantly decreased: from 22 (53.7%) to 5 (13.2%) and from 13 (36.1%) to 6 (20%), respectively. Median HAQ decreased from 1 [0.625; 1.5] to 0.5 [0; 0.875] and from 0.875 [0.5; 1.38] to 0.5 [0; 0.875]; median BASDAI – from 6 [4.2; 7] to 1.4 [0.6; 3.2] and from 4.4 [1.9; 5.8] to 3 [0.8; 4.5], respectively. In group 1, the number of patients with BSA> 3% decreased from 16 (39%) to 8 (26.7%; p<0.225), and in group 2, due to insufficient data (5 patients), we failed to evaluate BSA dynamics.*

Conclusion. *In real clinical practice TOFA and ADA both had comparable efficacy on all clinical manifestations of PsA: after 6 months of therapy, most patients with PsA achieved MDA, low disease activity and remission according to DAPSA and BASDAI.*

Key words: *psoriatic arthritis; tofacitinib; adalimumab; biologic disease-modifying antirheumatic drug; targeted synthetic disease-modifying antirheumatic drug; remission; minimal disease activity.*

Contact: *Elena Yurievna Loginiva;* ***eyloginova@mail.ru***

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Psoriatic arthritis (PsA) is a chronic immune-inflammatory disease characterized by the presence of peripheral arthritis, enthesitis, dactylitis, spondylitis, and psoriasis [1]. According to the 2019 EULAR (European League Against Rheumatism) recommendations, PsA therapy includes non-steroidal anti-inflammatory drugs (NSAIDs); synthetic basic anti-inflammatory drugs (sADDs) such as methotrexate (MT), sulfasalazine (SULF) and leflunomide (LEF); targeted synthetic basic anti-inflammatory drugs (TSHD), including the phosphodiesterase 4 inhibitor apremilast, the Janus kinase inhibitor (JAK) tofacitinib (TOFA); genetically engineered biological drugs (GIBD), such as inhibitors of tumor necrosis factor α (TNFα) and inhibitors of interleukins (IL) 12/23 and IL17 [2]. The appointment of certain groups of drugs depends on the dominant clinical phenotype of PsA (poly-, oligoarthritis, enthesitis, spondylitis, psoriasis) and its activity, the presence of unfavorable prognosis factors (polyarthritis, increased ESR / CRP, structural damage to joints, dactylitis, nail psoriasis) and clinically significant comorbid diseases (eg, uveitis, inflammatory bowel disease, cardiovascular disease) [2, 3].

For many years, TNF-alphas have been used in the therapy of PsA as effective and safe drugs. K. Murray et al. [4] noted a high level of remission (91.2%) in PsA patients after 12 years of treatment with adalimumab (ADA) and etanercept, which were used in the majority of patients (61%). Although TNF-α remains the "gold standard" of treatment for PsA, a number of issues have not yet been resolved, in particular, the problem of the "survival" of GIBD therapy. In a study by A. Haddad et al. [5] showed that ADA is one of the most frequently prescribed IFNO-α (29% of 2958 cases of GIBD prescribing), however, after 20 months, GIBD therapy is continued in 40% of patients, and after 5 years – only 20%. There was also a decrease in the effectiveness of the 2nd and subsequent lines of TNFα therapy, which is associated with various reasons, including immunogenicity [6]. Therefore, the search for new drugs (drugs), which would be comparable in effectiveness to the GIBD and would not induce a response production of neutralizing antibodies, is relevant for clinical practice.

Recently, the possibilities of PsA therapy have significantly expanded, including due to the emergence of a new class of oral drugs – JAK inhibitors. TOFA is the first representative of this class registered in the Russian Federation, which predominantly blocks the signaling pathways JAK3 and JAK1 with functional selectivity to JAK2 [7]. Inhibition of JAK leads to the suppression of the production of important cytokines involved in the pathogenesis of PsA, including TNFα, IL-17, IL-6, IL-23 [8, 9], which determines its clinical efficacy. The ability of TOFA to reduce the activity of arthritis, dactylitis, enthesitis and inhibit the progression of structural changes in the joints has been demonstrated in randomized placebo-controlled trials (RCTs) OPAL (Oral Psoriatic Arthritis triaL) Broaden and OPAL Beyond [10–12] and a number of observational studies [13]. In these studies, ADA was an active comparison drug, which made it possible to prove the comparable efficacy of ADA and TOFA in relation to all clinical domains of PsA. RFCIs for direct comparison of GIBD and TOFA have not yet been conducted.

In this regard, of interest is a comparative analysis of the effectiveness of TOFA and IFNO-α, in particular ADA, in real clinical practice, according to the data of the All-Russian register of patients with PsA.

The purpose of the study is Comparison of the clinical efficacy of tsBVP TOFA and GIBD ADA after 6 months of therapy in patients with active PsA in real clinical practice according to the data of the All-Russian register of patients with PsA.

Patients and methods. The study included 77 patients with PsA (43 men, 34 women) who met the CASPAR criteria (2006) and were observed in the All-Russian register of patients with PsA. The patients were divided into two groups depending on the therapy. Group 1, receiving TOFA 5 mg 2 times a day, included 41 patients: 24 (58.5%) men and 17 (41.5%) women, median age – 41 [34; 50] year, duration of PsA – 72 [35; 120] months. Group 2, in which ADA was prescribed at 40 mg / 2 weeks subcutaneously, included 36 patients: 19 (52.8%) men and 17 (47.2%) women, the median age was 44 [34; 51] years, the duration of PsA – 59 [22; 102] months. The patients were followed up for 24 weeks and received mainly combination therapy. In the TOFA MT group, 33 (80.5%) patients were taken at various doses (7.5–20 mg/week), SULF (2.0 g/day) – 4 (9.8%), LEF (20 mg/days) – 2 (4.9%). In the ADA group, 19 (52.8%) patients used MT therapy, SULF – 3 (8.3%), LEF – 1 (2.8%), and 13 (36.1%) patients did not receive DMARDs.

A standard rheumatological examination was performed before treatment and 24 weeks after starting therapy with TOFA or ADA. The number of painful joints (NPJ) out of 68, the number of swollen joints (NSJ) out of 66, the severity of pain in the joints and the activity of the disease in the opinion of the patient (OZP) and physician (OZV) were assessed using a visual analogue scale (VAS). Determined the number of fingers with dactylitis, as well as the number of inflamed enthesises using the Leeds Enthesitis Index (LEI). The functional health assessment questionnaire (HAQ) and the dermatology life quality index (DLQI) were assessed. Laboratory studies were carried out: general and biochemical blood tests to determine the level of glucose, bilirubin, aminotransferases, uric acid, creatinine, urea, total cholesterol and its fractions, CRP (in mg/l), hemoglobin, blood cell composition and ESR (in mm/h, according to Westergren).

The activity of peripheral arthritis was assessed by the DAPSA index (Disease Activity in Psoriatic Arthritis), the activity of spondylitis was assessed by the index BASDAI (Bath Ankylosing Spondylitis Disease Activity Index). DAPSA value >28 corresponded to high, 15–28 – moderate, 5–14 – low activity, 0–4 – remission. BASDAI i4 indicated high activity of spondylitis.

BSA (Body Surface Area, 0 to 100%) was used to determine the area of psoriatic skin lesions. For BSA >3%, the Psoriasis Area and Severity Index (PASI) was calculated. The presence or absence of nail psoriasis was noted.

To assess the effectiveness of therapy, the criteria of minimal disease activity were used – MAB (CHS ⩽1, NPV ⩽1, PASI ⩽1 or BSA ⩽3, pain ⩽15 mm, OZP ⩽20 mm, HAQ ⩽0.5, number of inflamed enthesis ⩽1) ... MAB was considered achieved if the patient had 5 out of 7 criteria. The number of patients who achieved remission/low PsA activity according to DAPSA, BASDAI was determined. For a general assessment of the effectiveness of therapy, we analyzed the individual dynamics of all parameters of PsA activity, the prevalence of psoriasis and the quality of life.

The main *criteria for* enrolling patients in the study were moderate or high inflammatory activity of PsA according to the DAPSA index and an insufficient response or poor tolerance to previous treatment with sADD, and/or tsBSA, and/ GIBD.

Table 1. Clinical and demographic characteristics of patients of the 1st and 2nd groups

Parameter	1st group (n = 41)	2nd group (n=36)	R
Age, years	41 [34; 50]	44 [34; 51]	0.674
Male gender, n (%)	24 (58.5)	19 (52.8)	0.611
BMI, kg / m ^{2}	27.4 [23.9; 32.6]	27.2 [24.2; 29.9]	0.99
Duration of psoriasis, months	192 [98; 312]	192 [58; 250]	0.317
Duration of PsA, months	72 [35; 120]	59 [22; 102]	0.313
NSJ of 66	11 [8; 16]	7 [3; 13]	0.021
NPJ from 68	19 [12; 24]	11 [5; 20]	0.0129
Pain according to VAS, mm	65 [50; 75]	70 [40; 74]	0.59
OZP	70 [50; 80]	60 [50; 70]	0.302
OZV	60 [50; 70]	65 [50; 75]	0.492
DAPSA	44.2 [37.8; 55.3]	35.8 [21.1; 52]	0.03
DAPSA, n (%): remission low activity moderate activity high activity	 0 0 5 (12.2) 36 (87.8)	 0 3 (8.6) 11 (31.4) 21 (60); n=35	0.0324
BASDAI	6 [4.2; 7]	4.4 [1.9; 5.8]	0.005
HAQ	1 [0.625; 1.5]	0.88 [0.5; 1.38]	0.301
The presence of enthesitis, n (%)	27 (65.9)	12 (44.4); n = 27	0.0794
LEI + PF	1 [0; 2]	1.5 [0.5; 2]	0.79
The presence of dactylitis, n (%)	22 (53.7)	13 (36.1)	0.123
CRP, mg/l	23.4 [5.6; 45]	18.6 [8; 23.2]	0.826
ESR, mm/h	28 [12; 52]	29.5 [20; 41.5]	0.547
BSA >3, n (%)	16 (39)	5 (35.7)	0.786
PASI	14.5 [7; 23.8]	0.7 [0; 13.8]	0.002
DLQI	5 [2; 12]	9 [4; 14]	0.278
Concomitant therapy: not carried out MT LEF SULF GK	 – 33 (80.5) 2 (4.9) 4 (9.8) –	 13 (36.1) 19 (52.8) 1 (2.8) 3 (8.3) 4 (11.1)	

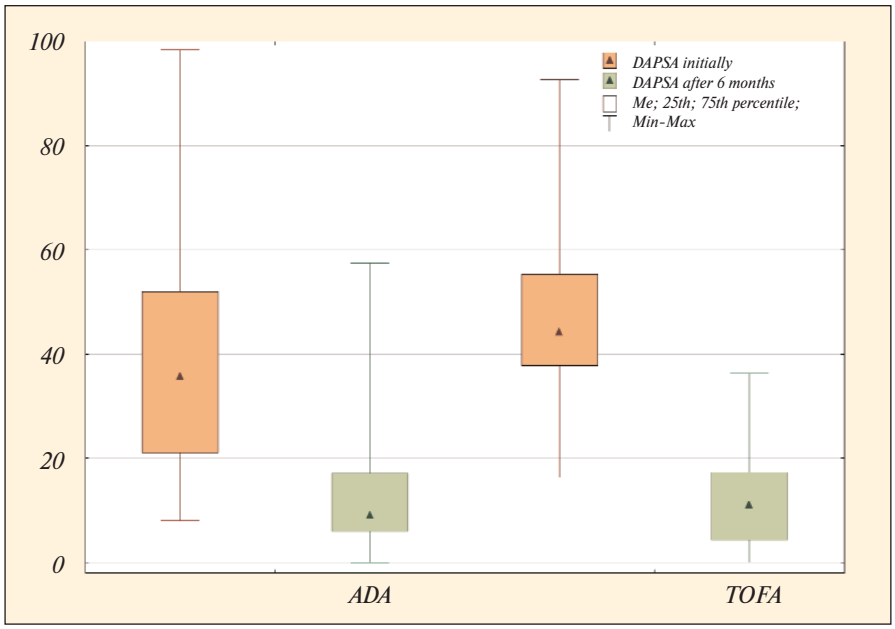
Note. Data are presented as Me [25th; 75th percentile], unless otherwise indicated (here and in Table 2). PF – plantar fascia; HA – glucocorticoids.

Patient groups practically did not differ in age, ratio of men and women, duration of PsA and psoriasis, body mass index (BMI), degree of functional impairment, presence of enthesitis and dactylitis. However, in the 1st group, the indicators of the activity of peripheral arthritis, spondylitis and psoriasis were significantly higher than in the 2nd group. So, at the time of inclusion in the study, the median of the DAPSA index in the 1st group was 44.2 [37.8; 55.3], while in 36 (87.8%) patients the disease activity according to DAPSA was high (DAPSA >28), and in 5 (12.2%) patients it was moderate (15 ⩽DAPSA ⩽28). In group 2, the median of the DAPSA index was initially 35.8 [21.1; 52] : high activity was noted in 21 (60%), moderate – in 11 (31.4%), low (5 ⩽DAPSA ⩽14) – in 3 (8.6%) patients (data from 35 patients are available). Group 1 showed high activity of spondylitis according to the BASDAI index (median 6 [4.2; 7]). In group 2, the activity of spondylitis was slightly lower – the median BASDAI was 4.4 [1.9; 5.8] (data of 30 patients are available). Both groups were characterized by the presence of moderate restrictions in the performance of daily activities, as evidenced by the value of the functional index HAQ, the median of which was 1 [0.625; 1.5] in the 1st group and 0.88 [0.5; 1.38] – in the 2nd group. More than a third of patients in groups TOFA and ADA (39 and 35.7%) experienced widespread psoriasis (BSA >3%), and the area of damage and its severity were used to lshimi in the 1st group: median PASI – 14, 5 [7; 23.8] and 0.7 [0; 13.8] (p=0.002) . General characteristics of PsA patients included in the study are presented in Table 1.

Table 2. Dynamics of clinical and laboratory parameters of PsA activity in patients of groups 1 and 2 after 24 weeks of treatment

Parameter	1st group (n = 41) initially	after 24 weeks	R	2nd group (n = 36) initially	after 24 weeks	R
Pain according to VAS, mm	65 (50–75)	17 (5–30)	0.001	70 (40–74)	28.5 (10–48)	0.001
NSJ of 66	11 [8; 16]	1 [0; 3]	0.001	7 [3; 13]	1 [0; 3]	0.001
NPJ from 68	19 [12; 24]	3 [0; 7]	0.001	11 [5; 20]	3 [1; 7]	0.001
OZP	70 [50; 80]	20 [10; 30]	0.001	60 [50; 70]	30 [10; 48]	0.001
OZV	60 [50; 70]	20 [10; 30]	0.001	65 [50; 75]	20 [10; 40]	0.001
DAPSA	44.2 [37.8; 55.3]	11.1 [4.3; 17.3]	0.001	35.8 [21.1; 52]	9.1 [6; 19.6]	0.001
DAPSA, n (%) remission low activity moderate activity high activity	 0 0 5 (12.2) 36 (87.8)	 11 (26.8) 15 (36.6) 13 (31.7) 2 (4.9)	0.001	 0 3 (8.6) 11 (31.4) 21 (60); n=35	 6 (20.8) 13 (44.8) 5 (17.2) 5 (17.2); n = 29	0.001
BASDAI	6 [4.2; 7]	1.4 [0.6; 3.2]	0.001	4.4 [1.9; 5.8]	3 [0.8; 4.5]	0.002
BASDAI ≥4	37 (90.2)	6 (14.6)	0.001	16 (53.3); n = 30	6 (26.1); n = 23	0.046
The presence of enthesitis, n (%)	27 (65.9)	12 (30.8)	0.002	12 (44.4); n = 27	4 (18.2); n=22	0.052
LEI and PF	1 [0; 3]	0 [0; 1.5]	0.001	1.5 [0.5; 2]	0 [0; 1]	0.059
The presence of dactylitis, nn (%)	22 (53.7)	5 (13.2)	0.001	13 (36.1)	6 (20); n=30	0.15
BSA >3, n (%)	16 (39)	8 (26.7); n=30	0.225	5 (35.7); n=14	5 (33.3); n=15	0.892
PASI	14.5 [7; 23.8]	5.6 [0; 10.4]	0.006	0.7 [0; 13.8]	0 [0; 0]	0.144
DLQI	5 [2; 12]	2 [0; 4]	0.001	9 [4; 14]	2 [0; 13]	0.221
HAQ	1 [0.625; 1.5]	0.5 [0; 0.875]	0.001	0.875 [0.5; 1.38]	0.5 [0; 0.875]	0.001
CRP, mg/l	21.3 [5.3; 31.3]	1.9 [0.8; 6.2]	0.001	14.6 [6; 34.2]	1.18 [0.2; 8.3]	0.001
ESR, mm/h	28 [12; 52]	10 [6; 16]	0.001	29.5 [20; 41.5]	16 [8; 20]	0.001

Statistical data processing was performed using the Statistica 10.0 software (StatSoft Inc., USA). Calculated mean values of



Comparative assessment of the effectiveness of TOFA and ADA according to the DAPSA activity index after 6 months of therapy

indicators (M) and standard deviation (SD), median (Me) [25th; 75th percentile], 95% confidence interval (CI), Min–Max . Comparison of the obtained quantitative data for subgroups was performed using Student's t-test, two-sided Z-test for comparison of proportions, Pearson χ^2 test and nonparametric Mann–Whitney and Wilcoxon tests. Differences were considered statistically significant at $p < 0.05$.

Results. 24 weeks after the start of treatment, both groups showed positive dynamics in almost all manifestations of PsA, including arthritis, spondylitis, dactylitis, enthesitis, and psoriasis; the main indicators of disease activity significantly decreased compared to baseline (Table 2).

By the 24th week of therapy in the 1st group, the number of patients with dactylitis significantly decreased: from 22 (53.7%) to 5 (13.2%; p=0.001), in contrast to the 2nd group, in which this the indicator decreased from 13 (36.1%) to 6 (20%) and the differences were insignificant (p=0.15). The number of patients with enthesitis decreased in both groups, but did not reach statistical significance (p=0.052): among those who took TOFA – from 27 (65.9%) to 12 (30.8%), among those who received ADA – from 12 (44, 4%) to 4 (18.2%) (in the 2nd group, data from 27 patients were available at baseline and 22 in dynamics).

The BASDAI median decreased from 6 [4.2; 7] to 1.4 [0.6; 3.2] in the 1st group and with 4.4 [1.9; 5.8] up to 3 [0.8; 4.5] in the 2nd. At the same time, the percentage of patients with high activity according to BASDAI i4 by the 24th week of therapy was slightly higher in the ADA group: 26.1% versus 14.6%. There was also a significant decrease in the level of CRP and ESR. Median HAQ decreased from 1 [0.625; 1.5] to 0.5 [0; 0.875] in the TOFA group and with 0.875 [0.5; 1.38] to 0.5 [0; 0.875] in the ADA group. The number of patients with BSA >3% decreased from 16 (39%) to 8 (26.7%) in group 1 (p=0.225; in group 2, due to the small amount of data, it was not possible to assess the dynamics of BSA, the differences are statistically insignificant (p=0.892).

By the 24th week of therapy, the median DAPSA significantly decreased as in the 1st group: from 44.2 [37.8; 55.3] to 11 [4.3; 17.3], and in the 2nd: from 35.8 [21.1; 52] to 9.1 [6; 19.6] (see figure). The difference in relative effect (decreased activity after 6 months compared to baseline) between groups 1 and 2 was 11.6 (95% CI 3.9–19.4).

Remissions according to DAPSA in groups 1 and 2 were achieved, respectively, by 11 (26.8%) and 6 (20.8%) patients, low activity – 15 (36.6%) and 13 (44.8%), MAB – 16 (40%) and 9 (30%), the differences are statistically insignificant (Table 3).

Table 3. Dynamics of PsA activity indices according to the DAPSA and MAB index by the 24th week of therapy in the 1st and 2nd groups

Parameter	1st group		2nd group			
	abs. (%)	n	abs. (%)	n	OR (CI 95%)	R
DAPSA: remission	11(26.8)	41	6 (20.8)	29	1.406 (0.453–4.366)	0.556
low activity	15 (36.6)	41	13 (44.8)	29	0.710 (0.269–1.872)	0.489
MAB reached	16 (40)	40	9 (30)	30	1.556 (0.569–4.249)	0.389

Note. OR – odds ratio.

Discussion. In recent years, the possibilities of PsA therapy have been rapidly expanding due to the introduction into practice of new classes of drugs, in particular, JAK inhibitors. The first among them was TOFA, which was first used to treat rheumatoid arthritis (RA) [14, 15] and relatively recently began to be used to treat PsA. It is believed that from the point of view of the immunopathogenesis of PsA and psoriasis, the inhibition of the biological effects of IL-23, IL-12, IL-17, IL-36, IL-18, and TNF-α, mediated through Jak1/Jak3-signaling pathways, is the most reasonable, which explains the clinical efficacy of TOFA against arthritis, dactylitis, enthesitis, and spondylitis. demonstrated both in the RPCI and in small observational studies [16, 17].

Phase III RCT results indicate the efficacy of TOFA against all major clinical manifestations of PsA in patients resistant to SDS. (OPAL Broaden) [10] and IFNOα (OPAL Beyond) [11], with a significant improvement in the quality of life [12]. Like IFNO-α ADA, TOFA has the ability to slow down the progression of structural changes in the joints in PsA [11, 18].

Direct comparisons of different drugs for PsA are rare. Currently, the results of two RCTs, SPIRIT H2H and EXEED, are available, in which a direct comparison of two GIBD with different mechanisms of action, IFNOα and ILI17, was carried out [19, 20]. There is evidence of the comparative efficacy of TNF-α etanercept and sBSAID MT (SEAM), as well as TNF-α golimumab and MT in early forms of PsA [21].

So far, only a network meta-analysis has been devoted to the comparison of TNF-α and TOFA, which shows that in relation to

the risk-benefit profile, GIBD of various classes are characterized by a greater effect and safety according to the ACR20 and PASI75 criteria during the induction period of PsA therapy (the first 12–16 weeks) compared with TSBVP TOPA and apremilast [22]. Meanwhile, the organization of such studies would be extremely important from a practical point of view.

The OPAL Broaden RCT [10] presents data on the comparable efficacy of TOFA and the most commonly used IFNO-α ADA, concerning all manifestations of PsA, including erosive changes in the joints. The study showed that, against the background of TOFA therapy at doses of 5 and 10 mg 2 times a day, an improvement in ACR20 was noted after 3 months in 50 and 61% of cases, respectively, compared with placebo (33%), and when using ADA 40 mg 1 time at 2 weeks – in 52% of cases. After 12 months, the frequency of ACR50 / ACR70 in the TOFA 5 and 10 mg / day and ADA groups was comparable (ACR50 – 45/48/41%, ACR70 – 23/31/39%, respectively). In terms of its effect on the main clinical manifestations of PsA (psoriasis, arthritis, dactylitis, enthesitis, and spondylitis) after 12 months of therapy, the effectiveness of TOFA was similar to that of IFNO-α ADA [10]. Simultaneously with a decrease in the number of affected joints, enthesitis and dactylitis, the fatigue of patients on the FACIT scale significantly decreased, the mental and physical components of the SF-36 questionnaire and the functional HAQ index improved. MAB after 3 months was achieved in 21 and 23% of patients in the TOFA 5 and 10 mg group and in 25% in the ADA group, and after 12 months in 34 and 40% and 41% of patients, respectively.

Similar results were obtained in our study based on data from the All-Russian register of patients with PsA, the purpose of which was to assess the achievement of remission or MAB during therapy. A comparative analysis of the clinical efficacy of tsBVP TOFA and GIBD ADA showed that after 6 months of therapy, both drugs significantly reduced the PsA activity: DAPSA remission in the TOFA and ADA groups was achieved in 26.8 and 20.8% of cases, low activity – in 36.6 and 44.8%, MAB – at 40 and 30%, respectively. In the TOFA group, significant dynamics of the psoriasis severity index (PASI) was revealed, which coincides with the data of clinical studies. At the same time, the differences in BSA dynamics in both groups were insignificant, which is due, on the one hand, to insufficient data in the ADA group, and, on the other hand, to the need to use a higher dose of TOFA (20 mg / day) in severe forms of psoriasis. There was also a comparable efficacy of TOFA and ADA in reducing the activity of spondylitis according to BASDAI. This fact seems to be extremely important in connection with the possibility of using JAK inhibitors for the treatment of axial spondyloarthritis and ankylosing spondylitis (AC).

Recently published results from a Phase III RCT the effectiveness of TOFA 10 mg / day in patients with AS [23]. Although similar studies have not been carried out with axial PsA, there are isolated observational studies that assessed the effectiveness of TOFA in patients with active sacroiliitis according to magnetic resonance imaging (MRI) in PsA [24]. All this significantly expands the profile of patients who can be prescribed this type of therapy.

Thus, TOFA and ADA had a comparable effect on all clinical manifestations of PsA: peripheral arthritis, spondylitis, enthesitis and dactylitis, improved the functional status and quality of life of patients.

The limitation of our study is the lack of data on the comparative safety of ADA and TOFA therapy in terms of both serious infections and malignancy, and an increased risk of thromboembolic complications characteristic of the entire class of JAK inhibitors. Currently, preliminary results of the ORAL Surveillance clinical study are being actively discussed regarding the safety of 5-year use of TOFA 5 and 10 mg twice daily and TNFα inhibitors (etanercept and ADA) in relation to the occurrence of cardiovascular events (CVS) in patients with RA. Comparative analysis of the outcomes of treatment with TOFA using both doses and TNFα inhibitors showed that in the group of TOFA at a dose of 10 mg 2 times a day, the risk of CVS was higher than in other groups. Moreover, RA patients were over 50 years of age and initially had at least one cardiovascular risk factor (smoking, arterial hypertension, dyslipidemia, diabetes mellitus, coronary heart disease, a history of myocardial infarction, etc.) [25]. It is believed that the risk of thrombus formation increases with the use of a dose of 20 mg / day TOFA, which is registered for the treatment of severe psoriasis [2 6]. In our study, 5 patients received this dose for 3 months due to widespread psoriasis, but these adverse reactions were not observed. Obviously, longer observation is required. Also, this fact should be taken into account when carrying out personalized therapy.

Conclusion. In real clinical practice, they showed comparable efficacy of TOFA and ADA in relation to all clinical manifestations of PsA: after 6 months of therapy, the achievement of MAB, low disease activity and remission according to DAPSA were noted in most patients with active PsA with insufficient response to previous therapy with DSA and/or GIBD. In addition to the efficacy and safety profile similar to that of GIBD, the advantages of TOFA are the lack of immunogenicity, tablet form, and simple storage conditions. Our results confirm the possibility of using TOFA on a par with GIBD in the treatment of patients with active PsA.

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Conflict of Interest Statement

The investigation has been conducted within scientific topic № АААА-А19-119021190147-6, 0514-2019-0009 «Pathogenetic features and personalized therapy of ankylosing spondylitis and psoriatic arthritis».

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Loginova E.Yu. https://orcid.org/0000-0001-6875-4552
Korotaeva T.V. https://orcid.org/0000-0003-0579-1131
Korsakova Yu.L. https://orcid.org/0000-0001-5968-2403
Gubar E.E. https://orcid.org/0000-0001-5015-7143
Glukhova S.I. https://orcid.org/000-0002-4285-0869
Vasilenko E.A. https://orcid.org/0000-0003-2153-5429
Vasilenko A.A. https://orcid.org/0000-0002-5486-2576
Patrikeeva I.M. https://orcid.org/0000-0003-0530-0080
Kuznetsova N.A. https://orcid.org/0000-0002-4972-7716
Nasonov E.L. https://orcid.org/0000-0002-1598-8360