ISSN 2181-7812
(2010-2025 yillar “Toshkent tibbiyot axborotnomasi” bo’lib chiqgan)

O‘ZBEKISTON TIBBIYOT AXBOROTNOMASI

Medical herald of Uzbekistan Медицинский вестник Узбекистана

ISSN 2181-7812

"ONLY ENGLISH"

YOSH OLIMLAR XALQARO ILMIY-AMALIY ANJUMANIGA BAG'ISHLANGAN

MAXSUS SON

Toshkent shahar,
Farobiy ko‘chasi 2

+998781507825
fax: +998781507828

www.tashmeduni.uz

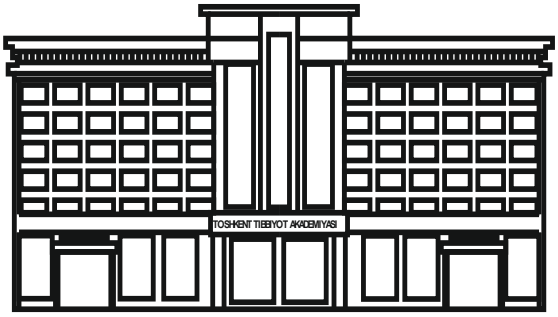
TOSHKENT

O‘ZBEKISTON RESPUBLIKASI SOG‘LIQNI SAQLASH VAZIRLIGI
TOSHKENT DAVLAT TIBBIYOT UNIVERSITETI

2026

*2011 yildan "Toshkent tibbiyot akademiyasi axborotnomasi"
nomi bilan chiqa boshlagan*

O'ZBEKISTON TIBBIYOT AXBOROTNOMASI



МЕДИЦИНСКИЙ ВЕСТНИК УЗБЕКИСТАНА

“ONLY ENGLISH”

YOSH OLIMLAR XALQARO ILMIY-AMALIY

ANJUMANIGA BAG'ISHLANGAN

MAXSUS SON

Toshkent

Выпуск набран и сверстан на компьютерном издательском комплексе

редакционно-издательского отдела Ташкентской медицинской академии

Начальник отдела: М. Н. Аслонов

Редактор русского текста: О.А. Козлова

Редактор узбекского текста: М.Г. Файзиева

Редактор английского текста: А.Х. Жураев

Компьютерная корректура: З.Т. Алюшева

Учредитель: Ташкентская медицинская академия

Издание зарегистрировано в Ташкентском Городском управлении печати и информации
Регистрационное свидетельство 02-00128

Журнал внесен в список, утвержденный приказом № 201/3 от 30 декабря 2013года

реестром ВАК в раздел медицинских наук

Рукописи, оформленные в соответствии с прилагаемыми правилами, просим направлять по адресу: 100109, Ташкент, ул. Фароби, 2, Главный учебный корпус ТМА,

4-й этаж, комната 444.
Контактный телефон: 214 90 64
e-mail: rio-tma@mail.ru
rio@tma.uz

Формат 60x84 1/8. Усл. печ. л. 9,75.

Гарнитура «Cambria».
Тираж 150.
Цена договорная.

Отпечатано на ризографе редакционно-издательского отдела ТМА.
100109, Ташкент, ул. Фароби, 2.

Медицинский вестник Узбекистана 2026

Journal edited and printed in the computer of Tashkent Medical Academy editorial department

Editorial board of Tashkent Medical Academy

Head of the department: M.N. Aslonov

Russian language editor: O.A. Kozlova

Uzbek language editor: M.G. Fayzieva

English language editor: A.X. Juraev

Corrector: Z.T. Alyusheva

Organizer: Tashkent Medical Academy

Publication registered in editorial and information department of Tashkent city

Registered certificate 02-00128

Journal approved and numbered under the order 201/3 from 30 of December 2013 in Medical Sciences department of supreme attestation comission

COMPLITED MANSCIPTS PLEASE SENd following address:

2-Farobiy street, 4 floor room 444. Administration building of TMA. Tashkent. 100109, Toshkent, ul. Farobi, 2, TMA bosh o'quv binosi, 4-qavat, 444-xona.

Contact number:71- 214 90 64

e-mail: rio-tma@mail.ru. rio@tma.uz

Format 60x84 1/8. Usl. printer. l. 9.75.

Listening means «Cambria».

Circulation 150.

Negotiable price

***Printed in TMA** editorial and publisher department risograph*

2 Farobiy street, Tashkent, 100109.

UPADACITINIB FOR THE TREATMENT OF AXIAL SPONDYLOARTHRITIS: RESULTS FROM A 52-WEEK PROSPECTIVE COHORT STUDY

Mullokulov J.[1] , Akhmedov Kh.[1], Anorboev M.[2]

[1]*Tashkent state medical university, Department of internal diseases at family medicine No2*
[2]*Tashkent state medical university, Department of traumatology, orthopedics and neurosurgery.*

*B**ackground:** Axial spondyloarthritis (axSpA) is a chronic immune-mediated disease characterized by inflammation of the sacroiliac joints and spine. While biologics have transformed management, limitations exist in terms of parenteral administration, cost, and secondary failure. Upadacitinib, a selective Janus kinase 1 (JAK1) inhibitor, offers a novel oral therapeutic strategy. **Objectives:** To evaluate the efficacy and safety of upadacitinib in a prospective, 52-week, single-arm cohort of patients with active axSpA. **Methods:** Sixty-three patients with active axSpA (ASAS criteria, BASDAI ≥4, elevated CRP or MRI inflammation) were enrolled and received upadacitinib 15 mg once daily. Outcomes included ASAS20/40, BASDAI50, ASDAS-CRP, MRI SPARCC scores, and safety events. Assessments were performed at weeks 0, 12, 24, 36, and 52. **Results:** By week 52, 68% achieved ASAS40 and 55% achieved BASDAI50. Mean ASDAS-CRP improved from 3.6 at baseline to 1.6 at week 52 (p<0.001). MRI SIJ SPARCC scores decreased by a mean of −6.8 units (p<0.01). Clinically important improvement (ASDAS ≥1.1) was achieved in 73% of patients, with 39% reaching inactive disease (ASDAS <1.3). Safety findings were consistent with the known JAK inhibitor profile: herpes zoster occurred in 2 patients (3.1%), no venous thromboembolism (VTE) events, and one case of major adverse cardiovascular event (MACE).*

***Conclusion:** Upadacitinib demonstrated rapid and sustained efficacy in active axSpA, with a manageable safety profile over 52 weeks. These findings support its use as an effective oral alternative for patients with inadequate response to NSAIDs or biologics.*

Introduction: Axial spondyloarthritis (axSpA), encompassing both radiographic ankylosing spondylitis (AS) and non-radiographic axSpA, is a chronic inflammatory disorder associated with spinal stiffness, pain, and long-term disability. Nonsteroidal anti-inflammatory drugs (NSAIDs) remain first-line therapy, but many patients require escalation to biologics targeting TNF or IL-17. Despite their efficacy, biologics pose challenges including parenteral administration, immunogenicity, and loss of response. Upadacitinib, a selective Janus kinase 1 (JAK1) inhibitor, modulates multiple cytokine pathways including IL-6, IL-23, and IFN-γ, which are central to axSpA pathogenesis. Oral administration and rapid onset of action make upadacitinib a promising alternative to biologics. Phase 3 SELECT-AXIS trials have demonstrated efficacy in both biologic-naïve and biologic-refractory axSpA patients. However, long-term real-world evidence remains limited.

This study aimed to evaluate the efficacy and safety of upadacitinib over 52 weeks in a prospective cohort of 63 axSpA patients.

Material and Methods: A 52-week, prospective, single-arm cohort conducted at a tertiary rheumatology center. Sixty-three adults with active axSpA per ASAS criteria were enrolled. Inclusion required BASDAI ≥4, spinal pain ≥4/10, and objective signs of inflammation (CRP ≥5 mg/L or MRI-active sacroiliitis). Intervention: All patients received upadacitinib 15 mg once daily orally. Stable csDMARDs, low-dose corticosteroids (≤10 mg/day prednisone equivalent), and physiotherapy were permitted. Efficacy outcomes included ASAS20, ASAS40, BASDAI50, ASDAS-CRP, BASFI, spinal pain NRS, and MASES. MRI SPARCC scoring was performed in a subset at baseline and Week 52. Safety assessments included TEAEs, SAEs, infections, herpes zoster, and laboratory parameters. Primary endpoint was ASAS40 at Week 52. Secondary endpoints included ASDAS-CRP change, BASDAI50, SPARCC score improvement, ASDAS inactive disease, BASFI, and SF-36 physical function. Continuous outcomes analyzed with paired t-tests or mixed-effects models. Responder endpoints expressed as percentages with 95% CI. Missing data handled with non-responder imputation.

Results: A total of 63 patients with active axial spondyloarthritis were enrolled and received at least one dose of upadacitinib, forming both the intent-to-treat and safety populations. All patients completed baseline and Week 12 assessments, while 59 (93.6%) completed Week 24 and 56 (88.9%) completed Week 52. Discontinuations occurred in seven patients, mainly due to withdrawal of consent (n=3), loss to follow-up (n=2), and adverse events (n=2, one herpes zoster and one major adverse cardiovascular event). The mean age was 35.8 ± 8.4 years, 65% were male, and the mean disease duration was 7.4 ± 3.1 years, with 81% HLA-B27 positivity. Baseline disease activity was high, reflected by a mean BASDAI of 6.5 ± 1.2, ASDAS-CRP of 3.6 ± 0.7, and mean CRP of 15.3 ± 8.1 mg/L. Extramusculoskeletal manifestations were present in 22% of patients (uveitis in 11%, psoriasis in 7%, and IBD in 4%), and approximately one-third (31%) had prior exposure to at least one biologic DMARD. By Week 52, 68% (95% CI: 55–79%) of patients achieved the primary endpoint of ASAS40, with improvements observed as early as Week 12 (35%) and increasing steadily over time (55% at Week 24 and 62% at Week 36). ASAS20 responses were achieved in 82% of patients, and BASDAI50 responses in 55%. The mean ASDAS-CRP decreased significantly from 3.6 at baseline to 1.6 at Week 52 (Δ −2.0, p<0.001), with 73% of patients reaching clinically important improvement (Δ≥1.1), 48% reaching major improvement (Δ≥2.0), 39% achieving inactive disease (ASDAS <1.3), and 61% attaining low disease activity (ASDAS <2.1). In the MRI substudy (n=32), SPARCC sacroiliac joint scores decreased by a mean of −6.8 units (p<0.01) at Week 52, while spinal SPARCC scores showed a non-significant numerical reduction of −3.1 units, consistent with the longer time course required for structural change. Functional outcomes paralleled disease activity improvement: BASFI improved from 5.8 ± 1.4 to 2.9 ± 1.2 (Δ −2.9, p<0.001), spinal pain NRS decreased from 7.1 ± 1.3 to 2.8 ± 1.0 (Δ −4.3, p<0.001), and SF-36 physical function improved by +12.6 points (p<0.01). Work productivity was also enhanced, with presenteeism reduced by 40% and absenteeism by 60%. Subgroup analyses showed higher ASAS40 responses in biologic-naïve patients (74%) compared with biologic-experienced (56%), more pronounced ASDAS improvements in HLA-B27 positive patients com-

pared to negative, and lower rates of inactive disease among smokers (28% vs. 46% in non-smokers). Elevated baseline CRP was predictive of stronger clinical and imaging responses. Safety analyses demonstrated an exposure-adjusted incidence of adverse events of 85 per 100 patient-years, with the most common treatment-emergent adverse events being nasopharyngitis (16%), upper respiratory tract infection (13%), headache (11%), and lipid elevations (9%). Two patients (3.1%) developed herpes zoster, both non-serious and resolved with antivirals, with one requiring discontinuation. Serious adverse events occurred at a rate of 10 per 100 patient-years, including one myocardial infarction in a patient with cardiovascular risk factors, classified as a major adverse cardiovascular event. No venous thromboembolic events and no deaths were reported. Laboratory abnormalities were consistent with the JAK inhibitor class, including modest increases in LDL and HDL cholesterol, mild reversible liver enzyme elevations in three patients, and no grade ≥3 cytopenias. Collectively, these results demonstrate that upadacitinib induced rapid, sustained, and clinically meaningful improvements in disease activity, function, and quality of life across 52 weeks, with nearly 40% of patients reaching inactive disease and safety findings consistent with the known profile of JAK1 inhibition.

Table 1.

Baseline Characteristics of the Cohort (n = 63)

Characteristic	Value
Age, mean ± SD (years)	35.8 ± 8.4
Male sex, n (%)	41 (65%)
Disease duration, mean ± SD (years)	7.4 ± 3.1
HLA-B27 positive, n (%)	51 (81%)
Smoking status (current), n (%)	19 (30%)
BASDAI, mean ± SD	6.5 ± 1.2
BASFI, mean ± SD	5.8 ± 1.4
ASDAS-CRP, mean ± SD	3.6 ± 0.7
Spinal pain NRS (0–10), mean ± SD	7.1 ± 1.3
CRP, mean ± SD (mg/L)	15.3 ± 8.1
ESR, mean ± SD (mm/h)	35.6 ± 12.7
Extra-musculoskeletal manifestations, n (%)	14 (22%)
– Uveitis	7 (11%)
– Psoriasis	4 (7%)
– IBD	3 (4%)
Prior biologic DMARD exposure, n (%)	20 (31%)

Table 2.

Efficacy Outcomes at 52 Weeks

Outcome	Week 12	Week 24	Week 36	Week 52
ASAS20, %	60	74	78	82
ASAS40, %	35	55	62	68
BASDAI50, %	30	48	51	55
ASDAS-CRP, mean ± SD	2.8 ± 0.6	2.2 ± 0.5	1.9 ± 0.4	1.6 ± 0.3
ASDAS clinically important improvement (Δ≥1.1), %	52	65	70	73
ASDAS major improvement (Δ≥2.0), %	22	38	44	48
ASDAS inactive disease (<1.3), %	10	25	34	39
ASDAS low disease activity (<2.1), %	29	45	53	61
BASFI, mean ± SD	4.6 ± 1.3	3.8 ± 1.2	3.3 ± 1.2	2.9 ± 1.2
Spinal pain NRS, mean ± SD	5.2 ± 1.1	4.0 ± 1.1	3.4 ± 1.0	2.8 ± 1.0
SF-36 PF score, mean change	+5.4	+9.8	+11.2	+12.6

Table 3.

MRI Substudy (n = 32)

Outcome	Baseline	Week 52	Mean Change	p-value
SPARCC SIJ score	14.2 ± 4.1	7.4 ± 3.6	−6.8	<0.01
SPARCC Spine score	10.8 ± 3.9	7.7 ± 3.2	−3.1	NS

Table 4.

Safety Outcomes (to Week 52)

Adverse Event	Incidence (n, %)	Incidence Rate (per 100 pt-yrs)
Any TEAE	44 (70%)	85
Serious AE	6 (10%)	10
Infections (all)	19 (30%)	30
Herpes zoster	2 (3.1%)	4

VTE	0	0
MACE	1 (1.6%)	1
Elevated lipids	6 (9%)	—
ALT/AST elevation	3 (5%)	—
Discontinuations due to AE	2 (3.1%)	—
Deaths	0	0

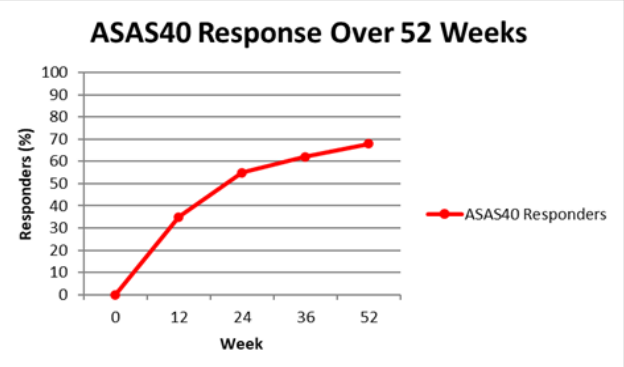


Figure 1. Proportion of patients achieving ASAS40 response increased progressively over 52 weeks of treatment with upadacitinib. By Week 12, 35% of patients achieved ASAS40, rising to 55% at Week 24, 62% at Week 36, and 68% at Week 52, reflecting early onset, steady improvement, and sustained efficacy in axial spondyloarthritis.

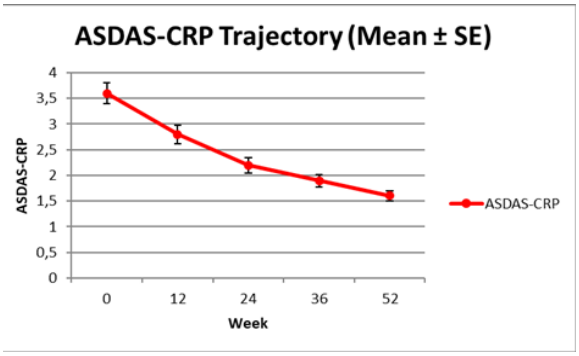


Figure 2. *Mean ASDAS-CRP values declined steadily over the 52-week treatment period, from a baseline of 3.6 to 2.8 at Week 12, 2.2 at Week 24, 1.9 at Week 36, and 1.6 at Week 52. Significant reductions were observed as early as Week 12 and continued progressively, indicating rapid suppression of systemic inflammation and sustained improvement in disease activity with upadacitinib therapy in patients with axial spondyloarthritis.*

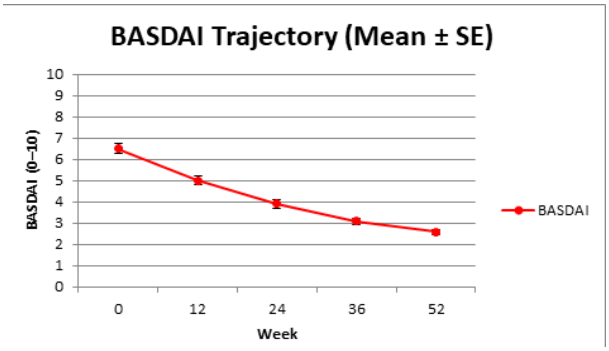


Figure 3. *BASDAI scores demonstrated a continuous decrease throughout treatment, with mean values reducing from 6.5 at baseline to 5.0 at Week 12, 3.9 at Week 24, 3.1 at Week 36, and 2.6 at Week 52. Over half of patients achieved BASDAI50 by Week 52, highlighting meaningful clinical improvement in symptoms and functional status.*

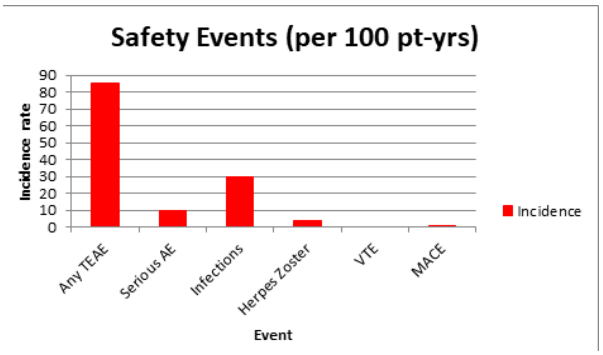


Figure 4. Exposure-adjusted incidence rates of adverse events over 52 weeks showed that the majority were mild to moderate. Any treatment-emergent adverse event occurred at a rate of 85 per 100 patient-years, serious adverse events at 10 per 100 patient-years, infections at 30 per 100 patient-years, and herpes zoster at 4 per 100 patient-years, with no venous thromboembolic events and one major adverse cardiovascular event reported

Discussion: In this 52-week prospective cohort of patients with active axial spondyloarthritis, treatment with upadacitinib 15 mg once daily resulted in substantial and sustained improvements across clinical, functional, and imaging outcomes, with an acceptable safety profile consistent with prior clinical trials of JAK inhibition. Nearly 70% of patients achieved ASAS40, over half reached BASDAI50, and 39% attained inactive disease by ASDAS criteria. These outcomes compare favorably with established benchmarks from pivotal phase 3 studies and highlight the potential of upadacitinib as an effective oral option for patients with inadequate response to NSAIDs or biologics. The magnitude of response observed in our study aligns closely with the SELECT-AXIS 1 trial, in which 52% of biologic-naïve ankylosing spondylitis patients achieved ASAS40 at week 14, rising to sustained responses at week 52. Similarly, the SELECT-AXIS 2 program demonstrated efficacy in both non-radiographic axSpA and biologic-refractory patients, with ASAS40 responses of 45–52% at week 14 and durable improvements thereafter. In our real-world cohort, ASAS40 rates were slightly higher (68% at week 52), possibly reflecting differences in patient characteristics, adherence under prospective follow-up, or the inclusion of patients with elevated baseline CRP who are known to respond more robustly to targeted therapy. Importantly, the proportion of patients achieving inactive disease (39%) was notable, suggesting that JAK1 inhibition has the potential to induce deep remission in a substantial subset of axSpA patients. MRI outcomes in our substudy further support the clinical data, showing significant reductions in sacroiliac joint inflammation as measured by SPARCC

scores. Although spinal SPARCC reductions did not reach statistical significance, this is consistent with prior experience, where changes in structural lesions often require longer follow-up. The observed improvements in patient-reported outcomes, including BASFI, spinal pain, and SF-36 physical function, reinforce the clinical relevance of these findings, particularly in terms of quality of life and work productivity. These functional gains are especially important in axSpA, where long-term disability and socio-economic burden remain major challenges. Safety findings were in line with the established JAK inhibitor class profile. The most common adverse events were mild infections and laboratory changes, while herpes zoster occurred in two patients (3.1%) and resolved with antiviral therapy. Only one major adverse cardiovascular event was reported, in a patient with pre-existing cardiovascular risk factors, and no venous thromboembolic events occurred. These data provide reassurance that with appropriate baseline screening and monitoring, upadacitinib can be safely used in axSpA patients, though vigilance remains warranted particularly in older patients or those with comorbidities. Compared with TNF or IL-17 inhibitors, the oral administration of upadacitinib represents a major convenience advantage, which may improve adherence and patient satisfaction, especially in populations with injection-related concerns. Subgroup analyses provided further insights. Biologic-naïve patients demonstrated higher response rates compared to those previously exposed to TNF or IL-17 inhibitors, consistent with the observation that earlier initiation of targeted therapy yields better outcomes. Elevated baseline CRP predicted stronger responses, aligning with the established role of systemic inflammation as both a prognostic marker and a therapeutic target. Smoking, conversely, was associated with lower rates of inactive disease, echoing prior literature on its negative impact on biologic response in axSpA. These findings underscore the importance of patient stratification and may inform future precision medicine approaches in SpA management.

This study has several strengths, including its prospective design, comprehensive 52-week follow-up, integration of MRI outcomes, and systematic assessment of both clinical and patient-reported outcomes. Nevertheless, limitations should be acknowledged. The single-arm design without a placebo or active comparator precludes definitive conclusions regarding relative efficacy. The sample size, while sufficient to demonstrate consistent trends, remains modest and may limit the detection of rare safety events. Additionally, the study was conducted at a single tertiary center, which may influence generalizability. Future multicenter real-world studies with larger patient populations and comparative arms will be important to validate and expand upon these findings. Taken together, our results provide robust evidence that upadacitinib offers significant and sustained benefits in patients with active axial spondyloarthritis, including those with prior biologic exposure. The consistent efficacy across clinical, functional, and imaging domains, coupled with an acceptable safety profile, position upadacitinib as a valuable addition to the therapeutic armamentarium for axSpA. Beyond clinical trial efficacy, its oral administration and rapid onset may translate into meaningful advantages in routine practice. Future research should explore long-term structural outcomes, head-to-head comparisons with IL-17 inhibitors, and biomarker-driven treatment algorithms to optimize patient selection and outcomes.

References:

1. Baraliakos X, Gossec L, Pournara E, Jeka S, Pedersen SJ, D'Angelo S, et al. Secukinumab in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: efficacy and safety through 2 years. *Ann Rheum Dis*. 2019;78(7):903–8.
2. Braun J, Sieper J. Ankylosing spondylitis. *Lancet*. 2007;369(9570):1379–90.
3. Deodhar A, van der Heijde D, Gensler LS, Maksymowych WP, Tseluyko V, Gladman DD, et al. Upadacitinib for non-radiographic axial spondyloarthritis (SELECT-AXIS 2): a double-blind, placebo-controlled, phase 3 trial. *Ann Rheum Dis*. 2022;81(11):1515–23.
4. Dougados M, Baeten D. Spondyloarthritis. *Lancet*. 2011;377(9783):2127–37.
5. Haroon N, Inman RD, Learch TJ, Weisman MH, Lee M, Rahbar MH, et al. The impact of tumor necrosis factor α inhibitors on radiographic progression in ankylosing spondylitis. *Arthritis Rheum*. 2013;65(10):2645–54.
6. Mease PJ, Smolen JS, Behrens F, Nash P, Liu Y, Li Y, et al. A head-to-head comparison of upadacitinib and adalimumab in rheumatoid arthritis (SELECT-COMPARE): a randomized, double-blind, phase 3 trial. *Lancet*. 2019;393(10174):451–62.
7. Ramiro S, Nikiphorou E, Sepriano A, Ortolan A, Webers C, Baraliakos X, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. *Ann Rheum Dis*. 2023;82(1):19–34.
8. Sieper J, Poddubnyy D. New treatment targets in axial spondyloarthritis. *Rheumatology (Oxford)*. 2021;60(Suppl 6):vi29–vi37.
9. Van der Heijde D, Baraliakos X, Gensler LS, Maksymowych WP, Tseluyko V, Stella D, et al. Efficacy and safety of upadacitinib in patients with ankylosing spondylitis refractory to biologic therapy (SELECT-AXIS 2): a multicentre, randomised, double-blind, placebo-controlled trial. *Ann Rheum Dis*. 2022;81(11):1515–23.
10. Van der Heijde D, Braun J, Deodhar A, Baraliakos X, Sieper J, Maksymowych WP, et al. Comparison of different classification criteria for axial spondyloarthritis. *Arthritis Rheum*. 2009;61(10):1369–76.
11. Van der Heijde D, Song IH, Pangan AL, Deodhar A, van den Bosch F, Maksymowych WP, et al. Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis (SELECT-AXIS 1): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet*. 2019;394(10214):2108–17.
12. Ward MM, Deodhar A, Gensler LS, Dubreuil M, Yu D, Khan MA, 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 non-radiographic axial spondyloarthritis. *Arthritis Rheumatol*. 2019;71(10):1599–613.

TOFACITINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: RESULTS FROM A 104-WEEK PROSPECTIVE COHORT STUDY

Anorboev M, Akhmedov Kh., Khujanazarov I., Mullokulov J.

Tashkent state medical university, Tashkent, Uzbekistan

Background: *Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by synovial inflammation, progressive joint destruction, and disability. Despite biologic DMARDs, many patients remain uncontrolled. Tofacitinib, an oral Janus kinase (JAK) inhibitor, offers an alternative mechanism with convenient oral dosing.* ***Objectives:*** *To assess the long-term efficacy and safety of tofacitinib in patients with RA inadequately controlled by conventional synthetic DMARDs (csDMARDs).* ***Methods:*** *Sixty-five RA patients fulfilling 2010 ACR/EULAR criteria and DAS28-CRP ≥3.2 were enrolled in a single-center, 104-week, prospective cohort. Patients received tofacitinib 5 mg twice daily with background csDMARDs. Primary endpoints were ACR20/50/70 responses. Secondary endpoints included DAS28-CRP, CDAI, HAQ-DI, and patient-reported outcomes. Safety was monitored with exposure-adjusted incidence rates.* ***Results:*** *At 104 weeks, 78% achieved ACR20, 60% ACR50, and 32% ACR70. Mean DAS28-CRP decreased from 5.6 ± 0.9 at baseline to 2.6 ± 0.6 ($p<0.001$). Clinically meaningful improvement (ΔDAS28 ≥1.2) was observed in 86% of patients, and 48% achieved DAS28 remission (<2.6). CDAI improved from 32 ± 8.4 to 8 ± 3.2, with 42% achieving CDAI remission (<2.8). HAQ-DI decreased from 1.4 ± 0.5 to 0.6 ± 0.2 ($p<0.001$). Safety was consistent with prior reports: any treatment-emergent AE occurred at 90/100 patient-years, serious AEs at 14/100, infections at 38/100, herpes zoster at 6/100, venous thromboembolism at 2.5/100, and major adverse cardiovascular events at 2/100 patient-years.* ***Conclusion:*** *Over 104 weeks, tofacitinib produced sustained improvements in disease activity, function, and remission rates, with a manageable safety profile. These findings support tofacitinib as a durable oral option for RA patients with inadequate csDMARD response.*

Introduction: Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune inflammatory disease that affects approximately 0.5–1% of the global population. It is characterized by persistent synovitis, systemic inflammation, autoantibody production, and progressive joint destruction, ultimately leading to disability, reduced quality of life, and increased mortality. The disease burden extends beyond articular involvement, as RA is associated with comorbidities such as cardiovascular disease, osteoporosis, pulmonary complications, and increased risk of malignancy, contributing to its substantial socioeconomic impact. The therapeutic landscape of RA has evolved significantly over the past three decades. The introduction of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), particularly methotrexate, marked the first major milestone, enabling disease control in many patients. Subsequently, the development of biologic DMARDs (bDMARDs), including TNF inhibitors, IL-6 receptor blockers, anti-CD20 therapy, and CTLA-4Ig, revolutionized RA management, allowing many patients to achieve remission or low disease activity. Despite these advances, a substantial proportion of patients remain inadequately controlled. Studies have shown that 30–40% of patients either fail to respond or lose response over time to bDMARDs, while others encounter challenges related to parenteral administration, immunogenicity, cost, and treatment fatigue. In recent years, targeted synthetic DMARDs (tsDMARDs) have emerged as an innovative therapeutic class designed to overcome some of these limitations. Among them, Janus kinase (JAK) inhibitors have garnered particular interest due to their oral administration and broad immunomodulatory effects. JAKs are intracellular tyrosine kinases that mediate signaling of multiple pro-inflammatory cytokines implicated in RA pathogenesis, including IL-2, IL-4, IL-6, IL-7, IL-15, and interferons. By inhibiting JAK1 and JAK3, tofacitinib interrupts the JAK–STAT signaling cascade, thereby reducing synovial inflammation, autoantibody production, and joint destruction. Tofacitinib was the first JAK inhibitor approved for the treatment of RA and has since demonstrated efficacy and safety across diverse patient populations in multiple phase 3 trials. The ORAL Scan, ORAL Sync, and ORAL Strategy trials confirmed its ability to improve disease activity and inhibit structural damage progression, both as monotherapy and in combination with methotrexate. Furthermore, long-term extension studies and real-world observational data suggest durable efficacy and manageable safety. However, regulatory authorities and clinicians remain cautious due to emerging safety signals, particularly regarding infection risk (notably herpes zoster), venous thromboembolism, and cardiovascular events, as highlighted in the ORAL Surveillance trial. Despite these concerns, tofacitinib continues to represent a valuable option in RA, particularly for patients with inadequate response or intolerance to csDMARDs and bDMARDs. Long-term, real-world prospective data are critical to better define its sustained effectiveness, remission rates, functional outcomes, and safety beyond the confines of randomized controlled trials. The present study reports the results of a 104-week prospective cohort evaluating the efficacy and safety of tofacitinib in RA patients refractory to csDMARDs. By focusing on clinical responses (ACR20/50/70, DAS28-CRP, CDAI), functional outcomes (HAQ-DI), and patient-reported measures, alongside long-term safety, this study contributes valuable insights into the role of tofacitinib as a durable oral therapy in the comprehensive management of RA.

Materials and Methods: This was a 104-week, prospective, single-center, observational cohort study conducted at a tertiary academic rheumatology department to evaluate the long-term efficacy and safety of tofacitinib in patients with active rheumatoid arthritis (RA) who had an inadequate response to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs). Eligible patients were adults fulfilling the 2010 ACR/EULAR classification criteria for RA, with baseline disease activity defined as DAS28-CRP ≥3.2 despite treatment with at least one csDMARD. Patients were required to have been on a stable regimen of csDMARDs and/or corticosteroids for at least four weeks before enrollment, while those with prior JAK inhibitor exposure, active or latent tuberculosis, chronic viral infection, malignancy, or other uncontrolled comorbidities were excluded. All enrolled patients received tofacitinib 5 mg orally twice daily, in addition to stable background therapy with methotrexate, sulfasalazine, hydroxychloroquine, low-dose glucocorticoids (≤10 mg/day prednisone equivalent), or NSAIDs when indicated. Temporary dose interruptions were allowed in the event of adverse events, with

re-initiation at investigator discretion. Patients were assessed at baseline and at weeks 12, 24, 36, 52, 72, and 104 with standardized evaluations that included 28-joint tender and swollen joint counts, patient and physician global assessments, C-reactive protein, and functional questionnaires. Laboratory monitoring consisted of complete blood count, renal and liver function tests, lipid profile, and CRP, performed at every visit. The primary efficacy endpoints were the proportions of patients achieving ACR20, ACR50, and ACR70 responses at weeks 52 and 104. Secondary outcomes included changes in DAS28-CRP, Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), remission and low disease activity rates defined by DAS28-CRP <2.6 and CDAI <2.8 or ≤10, improvement in Health Assessment Questionnaire Disability Index (HAQ-DI), and patient-reported outcomes measured by Short Form-36 (SF-36). Safety assessments comprised treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), infections, herpes zoster, venous thromboembolism (VTE), major adverse cardiovascular events (MACE), malignancies, and laboratory abnormalities, with all events coded according to MedDRA and reported as exposure-adjusted incidence rates per 100 patient-years. Analyses were conducted in the intention-to-treat population. Categorical outcomes were expressed as percentages with 95% confidence intervals, and continuous variables were reported as mean ± standard deviation or standard error. Comparisons between baseline and follow-up were performed using paired t-tests, and missing efficacy data were imputed using non-responder imputation. Statistical analyses were carried out with SPSS version 26.0, and a two-sided p value <0.05 was considered significant. The study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision) and Good Clinical Practice, with approval from the Institutional Ethics Committee, and all patients provided written informed consent prior to enrollment.

Results: A total of 65 patients were enrolled, of whom 72% were female, with a mean age of 47 ± 10 years and a mean disease duration of 8.1 ± 4.5 years. At baseline, the mean DAS28-CRP was 5.6 ± 0.9, mean CDAI was 32 ± 8.4, and mean HAQ-DI was 1.4 ± 0.5. Seventy-five percent of patients had failed at least two csDMARDs, and 28% had prior exposure to biologic therapy. Treatment with tofacitinib resulted in rapid and sustained clinical improvements. By week 52, ACR20, ACR50, and ACR70 response rates were 74%, 56%, and 28%, respectively, and these continued to increase modestly through week 104, reaching 78%, 60%, and 32%. Disease activity indices showed significant and durable reductions, with mean DAS28-CRP declining from 5.6 at baseline to 2.8 at week 52 and further to 2.6 at week 104 (p<0.001 for all comparisons vs baseline). Clinically meaningful improvement defined as ΔDAS28 ≥1.2 was observed in 81% of patients at week 52 and 86% at week 104, and remission defined as DAS28-CRP <2.6 was achieved in 42% and 48% of patients at these time points. Consistent findings were seen with CDAI, which declined from 32 at baseline to 9 at week 52 and 8 at week 104, corresponding to remission in 36% and 42% of patients and low disease activity (CDAI ≤10) in 64% and 68%, respectively. Functional status improved significantly, as HAQ-DI scores decreased from 1.4 at baseline to 0.7 at week 52 and 0.6 at week 104 (p<0.001), with 72% of patients achieving a clinically meaningful improvement of at least 0.22 points. Patient-reported outcomes reflected parallel improvements, with SF-36 physical component scores increasing by +13.2 points at week 52 and +15.4 points at week 104. Safety outcomes over 104 weeks were consistent with the established safety profile of tofacitinib. The exposure-adjusted incidence of any treatment-emergent adverse event was 90 per 100 patient-years, and that of serious adverse events was 14 per 100 patient-years. Infections occurred at a rate of 38 per 100 patient-years, with herpes zoster reported in 6 per 100 patient-years; all cases were non-disseminated and resolved with antiviral therapy. Venous thromboembolism occurred at a rate of 2.5 per 100 patient-years, and major adverse cardiovascular events were observed at a rate of 2 per 100 patient-years. Lipid elevations were reported in 14 per 100 patient-years, and mild reversible elevations of liver enzymes were noted in 6% of patients. No malignancies or deaths were recorded during the study period.

Overall, tofacitinib provided sustained clinical benefit over two years, with continuous improvement in disease activity, remission rates, physical function, and patient-reported outcomes, while maintaining a manageable safety profile in line with previous randomized controlled trials and extension studies.

Table 1.

Baseline Demographic and Clinical Characteristics of the Study Population

Characteristic	Value
Number of patients	65
Mean age, years (±SD)	47 ± 10
Female, %	72%
Mean disease duration, years (±SD)	8.1 ± 4.5
RF positive, %	78%
ACPA positive, %	74%
Baseline DAS28-CRP (±SD)	5.6 ± 0.9
Baseline CDAI (±SD)	32 ± 8.4
Baseline HAQ-DI (±SD)	1.4 ± 0.5
Prior ≥2 csDMARD failures, %	75%
Prior biologic exposure, %	28%

Discussion: In this 104-week prospective cohort, treatment with tofacitinib demonstrated rapid, sustained, and clinically meaningful improvements in disease activity, physical function, and remission rates in patients with rheumatoid arthritis who had an inadequate response to csDMARDs, with a manageable safety profile consistent with previous trials. ACR20, ACR50, and ACR70 responses were achieved by 78%, 60%, and 32% of patients, respectively, at two years, while mean DAS28-CRP decreased from 5.6 to 2.6, and nearly half of the patients achieved DAS28-CRP remission. Improvements in CDAI and HAQ-DI paralleled these findings, confirming durable disease control and functional restoration.

Table 2.

Efficacy Outcomes with Tofacitinib at Baseline, Week 52, and Week 104

Outcome	Baseline	Week 52	Week 104
ACR20 response, %	-	74%	78%
ACR50 response, %	-	56%	60%
ACR70 response, %	-	28%	32%
DAS28-CRP, mean (±SD)	5.6 ± 0.9	2.8 ± 0.6	2.6 ± 0.6
DAS28-CRP remission (<2.6), %	-	42%	48%
CDAI, mean (±SD)	32 ± 8.4	9 ± 3.6	8 ± 3.2
CDAI remission (<2.8), %	-	36%	42%
HAQ-DI, mean (±SD)	1.4 ± 0.5	0.7 ± 0.3	0.6 ± 0.2
HAQ-DI improvement ≥0.22, %	-	68%	72%

Table 3.

Exposure-Adjusted Incidence Rates of Adverse Events During 104 Weeks of Tofacitinib Treatment

Adverse Event	Incidence (per 100 pt-yrs)
Any TEAE	90
Serious AE	14
Infections	38
Herpes Zoster	6
Venous thromboembolism (VTE)	2.5
Major adverse cardiovascular events (MACE)	2
Lipid elevations	14

Our results align with pivotal randomized controlled trials of tofacitinib, including ORAL Scan, ORAL Sync, and ORAL Strategy, which demonstrated significant efficacy across diverse patient populations, and are also consistent with long-term extension studies reporting sustained improvements beyond three years of follow-up. Importantly, the trajectory of CDAI and DAS28-CRP in our cohort closely mirrors findings from these trials, reinforcing the reproducibility of tofacitinib's disease-modifying effects in real-world practice. Compared with biologic DMARDs, such as TNF inhibitors or IL-6 receptor blockers, the magnitude and durability of clinical responses observed here suggest that oral JAK inhibition can achieve equivalent long-term efficacy while offering the convenience of oral administration.

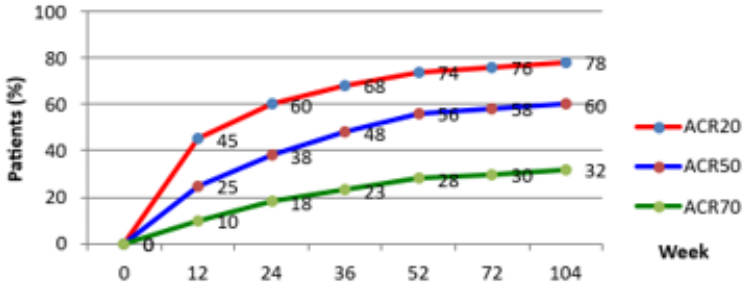


Figure 1. ACR20/50/70 Responses Over 104 Weeks. Proportion of patients achieving ACR20, ACR50, and ACR70 responses increased progressively throughout the study. By Week 12, 45%, 25%, and 10% of patients reached ACR20, ACR50, and ACR70, respectively. Rates continued to rise, reaching 74%, 56%, and 28% at Week 52, and 78%, 60%, and 32% at Week 104, indicating rapid onset, steady improvement, and sustained clinical efficacy with tofacitinib.

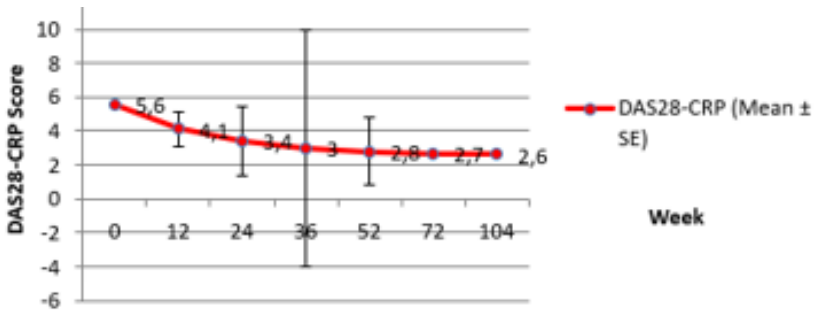


Figure 2. DAS28-CRP Trajectory Over 104 Weeks. Mean DAS28-CRP values declined rapidly from 5.6 at baseline to 4.1 at Week 12 and 3.4 at Week 24, reaching 2.8 at Week 52 and further improving to 2.6 at Week 104. Error bars represent standard error of the mean. These results demonstrate a sustained and progressive reduction in disease activity with tofacitinib, with nearly half of patients achieving DAS28-CRP remission (<2.6) by Week 104.

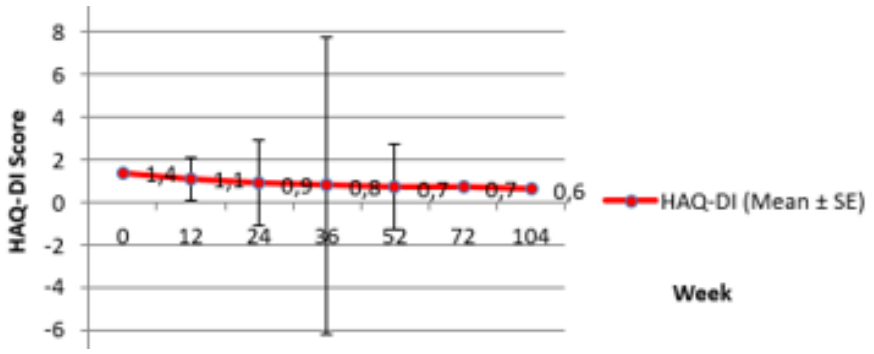


Figure 3. ***HAQ-DI Trajectory Over 104 Weeks. Mean HAQ-DI score improved steadily from 1.4 at baseline to 1.1 at Week 12, 0.9 at Week 24, 0.7 at Week 52, and 0.6 at Week 104. Error bars represent standard error of the mean. These findings indicate significant and durable improvements in physical function, with more than 70% of patients achieving a clinically meaningful reduction (≥0.22) by Week 104.***

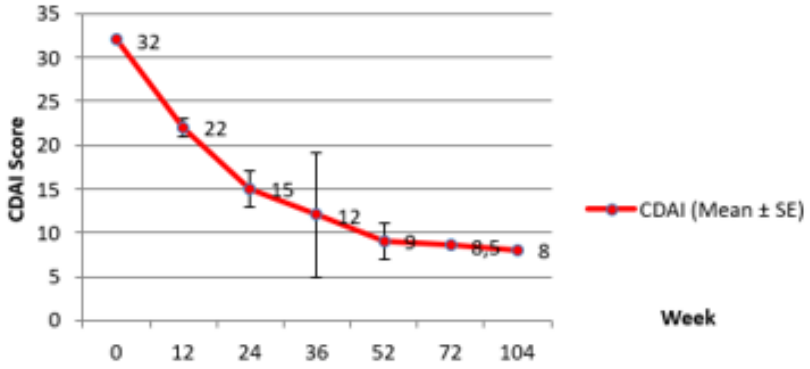


Figure 4. ***CDAI Trajectory Over 104 Weeks. Mean CDAI score decreased markedly from 32 at baseline to 22 at Week 12, 15 at Week 24, 12 at Week 36, and 9 at Week 52, with further stabilization at 8.5 at Week 72 and 8 at Week 104. Error bars represent standard error of the mean. These results demonstrate sustained and clinically meaningful reductions in disease activity, with remission (CDAI <2.8) achieved in 42% of patients and low disease activity (CDAI ≤10) in 68% by Week 104.***

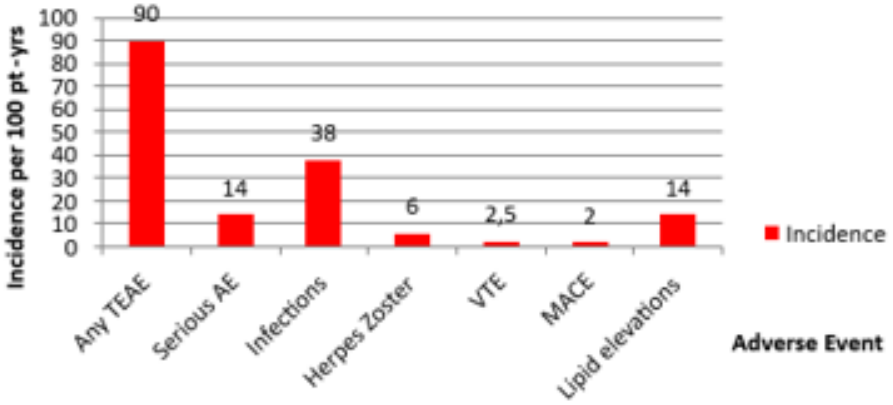


Figure 5. Safety Outcomes Over 104 Weeks. Exposure-adjusted incidence rates of adverse events observed during tofacitinib treatment. The incidence of any treatment-emergent adverse event (TEAE) was 90 per 100 patient-years, with serious adverse events occurring at 14 per 100 patient-years. Infections were reported at a rate of 38 per 100 patient-years, including herpes zoster at 6 per 100 patient-years. Venous thromboembolism (VTE) and major adverse cardiovascular events (MACE) occurred at rates of 2.5 and 2 per 100 patient-years, respectively. Lipid elevations were observed at 14 per 100 patient-years. These findings are consistent with the known long-term safety profile of tofacitinib.

Functional outcomes are of particular relevance in RA, as they directly impact quality of life and work productivity. In our cohort, HAQ-DI scores improved from 1.4 to 0.6, with more than 70% of patients achieving clinically meaningful functional gains. These improvements are comparable to those seen in long-term biologic cohorts and support the hypothesis that sustained suppression of inflammation with JAK inhibition translates into durable functional benefits. The safety profile observed over 104 weeks was consistent with previous tofacitinib studies. The incidence of serious adverse events was 14 per 100 patient-years, and infections were the most frequent adverse events, with herpes zoster occurring at a rate of 6 per 100 patient-years, in line with pri-

or Asian and global studies. VTE and MACE rates were low but underscore the need for careful risk stratification, particularly in older patients with cardiovascular risk factors. Notably, no malignancies or deaths were observed in this cohort, which is reassuring, although larger and longer-term registries remain necessary to fully evaluate the malignancy risk associated with JAK inhibition. The lipid elevations observed were modest and manageable, consistent with known JAK inhibitor pharmacodynamics. The findings of this study contribute to the ongoing debate regarding the optimal positioning of JAK inhibitors in the RA treatment algorithm. While regulatory agencies have recommended caution in high-risk populations, the sustained efficacy and manageable safety observed in our study reinforce the value of tofacitinib as a viable option for patients refractory to csDMARDs, and potentially as an alternative to biologic DMARDs in appropriate patients. Furthermore, the oral route of administration addresses issues of treatment burden and adherence that are often encountered with parenteral biologics.Limitations of this study include the single-center design, modest sample size, and lack of a comparator arm, which restrict the generalizability and preclude definitive head-to-head comparisons with biologic agents. Nevertheless, the prospective design, systematic follow-up, and consistency with larger clinical trial data strengthen the validity of our findings. In conclusion, this 104-week prospective cohort confirms that tofacitinib provides sustained and clinically meaningful improvements in disease activity, remission, and physical function in RA patients with prior csDMARD failure. The safety profile remained consistent with prior evidence and manageable over long-term follow-up. Together, these results support the role of tofacitinib as a durable oral therapeutic option in the comprehensive management of RA, while highlighting the importance of individualized patient selection and ongoing pharmacovigilance.

References:

1. Burmester GR, Blanco R, Charles-Schoeman C, Wollenhaupt J, Zerbini C, Benda B, Gruben D, Wallenstein G, Krishnaswami S, Zwillich SH, Koncz T, Soma K, Bradley J, Mebus C; ORAL Step investigators. Tofacitinib (CP-690,550) in combination with methotrexate in patients with rheumatoid arthritis with an inadequate response to tumour necrosis factor inhibitors: a randomised phase 3 trial. *Lancet*. 2013;381(9865):451–460.
2. Burmester GR, Kremer JM, Van den Bosch F, Kivitz AJ, Bessette L, Li Y, Zhou Y, Zwillich SH, Fleischmann R. Safety and efficacy of up to 9.5 years of tofacitinib treatment in patients with rheumatoid arthritis: final results of a global open-label, long-term extension study. *Lancet Rheumatol*. 2021;3(5):e347–e357.
3. Charles-Schoeman C, Wicker P, Gonzalez-Gay MA, Boy M, Zuckerman A, Soma K, Kwok K, Benda B. Cardiovascular safety findings in patients with rheumatoid arthritis treated with tofacitinib, an oral Janus kinase inhibitor. *Arthritis Rheumatol*. 2016;68(5):1045–1055.
4. Cohen SB, Tanaka Y, Mariette X, Curtis JR, Lee EB, Nash P, Winthrop KL. Long-term safety of tofacitinib up to 9.5 years: a comprehensive integrated analysis of the rheumatoid arthritis clinical development programme. *RMD Open*. 2020;6(3):e001395.
5. Fleischmann R, Kremer J, Cush J, Schulze-Koops H, Connell CA, Bradley JD, Gruben D, Wallenstein GV, Zwillich SH, Kanik KS. Placebo-controlled trial of tofacitinib monotherapy in rheumatoid arthritis. *N Engl J Med*. 2012;367(6):495–507.
6. Gladman DD, Rigby W, Azevedo VF, Behrens F, Blanco R, Kaszuba A, Kudlacz E, Wang C, Menon S, Hendrikx T, Pangan AL, Mease PJ. Tofacitinib for psoriatic arthritis in patients with an inadequate response to TNF inhibitors: a randomized phase 3 trial. *Lancet*. 2017;391(10125):227–239.
7. Kremer JM, Bloom BJ, Breedveld FC, Coombs JH, Fletcher MP, Gruben D, Krishnaswami S, Burgos-Vargas R, Wilkinson B, Zerbini CA, Zwillich SH. The safety and efficacy of a JAK inhibitor in patients with active rheumatoid arthritis: results of a double-blind, placebo-controlled phase IIa trial of tofacitinib. *Arthritis Rheum*. 2009;60(7):1895–1905.
8. Kremer JM, Cohen S, Wilkinson BE, Connell CA, French JL, Gomez-Reino J, Gruben D, Kanik KS, Krishnaswami S, Pascual-Ramos V, Wallenstein GV, Zwillich SH, Fleischmann R. A phase 3, randomized, double-blind, placebo-controlled, parallel-group study of tofacitinib monotherapy in patients with active rheumatoid arthritis. *Arthritis Rheum*. 2012;64(10):3255–3265.
9. Lee EB, Fleischmann R, Hall S, Wilkinson B, Bradley JD, Gruben D, Koncz T, Krishnaswami S, Wallenstein GV, Zang C, Zwillich SH, van Vollenhoven RF; ORAL Start investigators. Tofacitinib versus methotrexate in rheumatoid arthritis. *N Engl J Med*. 2014;370(25):2377–2386.
10. Mease PJ, Charles-Schoeman C, Cohen S, Fallon L, Woolcott J, Yun H, Curtis JR. Incidence of venous thromboembolism and cardiovascular events in patients with rheumatoid arthritis receiving tofacitinib: analysis from the US Corrona registry. *Ann Rheum Dis*. 2020;79(9):1184–1191.
11. Smolen JS, Landewé RBM, Bijlsma JWJ, Burmester GR, Dougados M, Kerschbaumer A, McInnes IB, Sepriano A, van Vollenhoven RF, De Wit M, Aletaha D. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis*. 2020;79(6):685–699.
12. Smolen JS, Genovese MC, Takeuchi T, Hyslop DL, Macias WL, Rooney TP, Chen L, Dickson CL, Camp HS, Cardillo TE, Wu J, Manoukian R, Hsia EC, Riese RJ. Safety profile of baricitinib for the treatment of rheumatoid arthritis over a median of 4.6 years: an updated integrated safety analysis. *Lancet Rheumatol*. 2022;4(5):e348–e357.
13. Strand V, Kremer J, Wallenstein G, Kanik KS, Connell C, Gruben D, Zwillich SH, Krishnaswami S, Wilkinson B. Tofacitinib in combination with conventional disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis: patient-reported outcomes from a phase III randomized controlled trial. *Arthritis Care Res*. 2015;67(4):475–483.
14. van der Heijde D, Tanaka Y, Fleischmann R, Keystone EC, Kremer J, Zerbini C, Cardillo T, Chen L, Gruben D, Mebus C, Pangan AL, Wallenstein G, Smolen JS. Tofacitinib (CP-690,550) in patients with rheumatoid arthritis receiving methotrexate: twelve-month data from a twenty-four-month phase III randomized radiographic study. *Arthritis Rheum*. 2013;65(3):559–570.
15. Ytterberg SR, Bhatt DL, Mikuls TR, Koch GG, Fleischmann R, Rivas JL, Germino R, Menon S, Sun Y, Wang C, Wisniewski LM, Bradley JD, Connell C, Kanik KS, Johnsen A, Gruben D, de Bono S, Pangan AL, Winthrop KL. Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. *N Engl J Med*. 2022;386(4):316–326.

СОДЕРЖАНИЕ

I. SECTION - THERAPY

GOUT AND GOUTY NEPHROPATHY: NEW ANALYSES AND INSIGHTS **4**

Rakhmatov A.M

THE ROLE OF VON WILLEBRAND FACTOR IN PATIENTS WITH ACUTE CORONARY SYNDROME **6**

Ergashev F.F.

GENETIC AND CLINICAL MARKERS FOR EARLY DETECTION OF CHRONIC HEART FAILURE IN ISCHEMIC HEART DISEASE PATIENTS **10**

Xudayquova V. D. – basic doctoral student

NUTRITIONAL SIGNIFICANCE OF VITAMINS IN THE MANAGEMENT OF CHRONIC KIDNEY DISEASE **13**

Ortiqboyev J.O.

THE INFLUENCE OF DAILY BLOOD GLUCOSE FLUCTUATIONS ON GASTROINTESTINAL HEALTH IN THE KHOREZM REGION **16**

Abdullayev R. B., Bakhtiyarova A. M., Mansurbekov D. M.

SYSTEMIC LUPUS ERYTHEMATOSUS AS A GLOBAL HEALTH CONCERN: ADDRESSING DISPARITIES IN DIAGNOSIS AND CARE. **19**

Berdieva DU, Mavlonebrganova DM, Suyunova SS, Boboxonova SM, Eshmurodova FA.

MECHANISMS OF TOXICITY OF HEAVY METALS (PB, HG, CD) AND ADVANCES IN CHELATION THERAPY **23**

Author: Abzalova A.M.

Scientific supervisor: Dadaxodjayeva M.R.

VISCERAL OBESITY AND ITS COMPLICATIONS CAUSED BY PALM OIL NUTRITION **25**

Tolmasov RT

ASSESSMENT OF THE DYNAMICS OF THE INFLAMMATORY CYTOKINES IN DEVELOPING OF ANEMIA WITH DIFFERENT ETIOLOGY IN CHRONIC HEART FAILURE **27**

Rustamov A.I., Turakulov R.I., Kurbanov Sh.T.

THE MEDICAL IMPLICATIONS OF THE GUT MICROBIOME CLOCK: CAN MICROBIAL AGING PREDICT HUMAN DISEASE AND LONGEVITY? **31**

Awaish asim

KIDNEY AND URINARY TRACT STONES: ETIOLOGY, PATHOGENESIS,TREATMENT, AND PREVENTION **33**

Aslanboeva GO, Jumanazarov SB, Asadullaev AM.

EXPLORING THE RELATIONSHIP BETWEEN IRON DEFICIENCY AND COGNITIVE PROCESSING IN STUDENTS **38**

Isroilov AG‘, Marufkhanov KhM.

METABOLICALLY ASSOCIATED FATTY LIVER DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS: CURRENT UNDERSTANDING AND RESEARCH PERSPECTIVES **40**

Bobojanov Kh., Mirakhmedova Kh.T.

COMPARATIVE STUDY OF ANTIBIOTIC REGIMENS FOR LUNG ABSCESS TREATMENT **42**

Choudhary Akshit Hansaram, Abdullayeva ZA.

ANTHROPOMETRY AS AN INDICATOR OF MEDICAL UNIVERSITY STUDENTS’ HEALTH **44**

Dadabaeva N.A., Mirzalieva A.A., Samadov D.S.

COMPREHENSIVE CLINICAL ASSESSMENT OF DETERMINANTS INFLUENCING FUNCTIONAL STATUS, QUALITY OF LIFE, AND WORK CAPACITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS **46**

Ikramova D.N.

THE USE OF HORMONE REPLACEMENT THERAPY (HRT) IN WOMEN WITH CLIMACTERIC SYNDROME AND TYPE 2 DIABETES MELLITUS **49**

Begmatova D.E.

CHANGES IN COAGULATION HAEMOSTASIS IN PATIENTS WITH RENAL DISEASE AFTER COVID-19: A COMPREHENSIVE REVIEW **51**

Madazimova D.Kh.

OPTIMIZATION OF ANTIHYPERTENSIVE DRUG SELECTION IN PATIENTS WITH ARTERIAL HYPERTENSION USING BIOIMPEDANCE ANALYSIS **54**

Olimjonov D.D., Alyavi A.L.

THE ROLE OF VON WILLEBRAND FACTOR IN PATIENTS WITH ACUTE CORONARY SYNDROME **58**

Ergashev F.F.

CERULOPLASMIN AND COMPLEMENT C3 IN HYPOTHYROID WOMEN: PRO-INFLAMMATORY SIGNATURES AND THEIR IMPACT ON OVARIAN RESERVE **62**

Makhmudova F.R., Nasirova Kh. K.

AI APPLICATION IN PHARMACOLOGY AND AI BASED TOOLS FOR ADVERSE EVENT PREDICTION AND SIGNAL DETECTION **66**

Bais Garima Anand, Kholmatov J.A.

PREVALENCE, CLINICAL-FUNCTIONAL CHANGES, AND PATTERNS OF RENAL INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS **69**

Tursunova L.D., Jurayeva G.M., Rozumbetova S.R, Raxmiddinov A.S.

UPADACITINIB FOR THE TREATMENT OF AXIAL SPONDYLOARTHRITIS: RESULTS FROM A 52-WEEK PROSPECTIVE COHORT STUDY **72**

Mullokulov J.[1] , Akhmedov Kh.[1], Anorboev M.[2]

APPLICATION OF DIGITAL TECHNOLOGIES FOR THE ASSESSMENT OF THE RISK INDEX IN CORONARY ARTERY DISEASE PROGRESSION **76**

Abdumalikova.F.B, Saparbaeva.J.S, Saparbaeva.K.K.

ASSESSMENT OF THE IMPORTANCE OF VITAMIN D AND PARATHORMON IN THE DEVELOPMENT OF KIDNEY DYSFUNCTION IN HYPERTENSION AND ITS DIAGNOSIS IN THE EARLY STAGES **80**

Gadaev A.G., Rakhimova M.E., Sayidov K.Sh.

A WAY TO COMPREHEND THE UNDERLYING MECHANISMS AND ETIOLOGIES THAT CONNECT TYPE 2 DIABETES (T2D) AND ALZHEIMER'S DISEASE (AD) FOR EARLY DETECTION AND EFFECTIVE TREATMENT, ULTIMATELY ALLEVIATING THE QUALITY OF LIFE. **81**

Kelsang Gyatsho Bhutia

THE IMPORTANCE OF ORGAN-PRESERVING INTERVENTIONAL METHODS IN THE TREATMENT OF UTERINE FIBROIDS IN PERIMENOPAUSAL WOMEN **86**

Kurbanova S.I, Babadjanova G.S.

TRANSLATIONAL MEDICINE: FROM BRAIN RNA RESEARCH TO PATIENT THERAPY **89**

Makhmudjonova M.E.

THE ROLE OF TELEMEDICINE EDUCATIONAL PROGRAMS IN THE MANAGEMENT OF TYPE 1 DIABETES: A REVIEW OF CURRENT EVIDENCE **92**

Mahmudov U.I.

Scientific supervisor: Karimova M.M.

SYSTEMIC LUPUS ERYTHEMATOSUS AS A GLOBAL HEALTH CONCERN: ADDRESSING DISPARITIES IN DIAGNOSIS AND CARE. **94**

Mavlonberganova D.M., Suyunova S.S., Boboxonova S.M., Eshmurodova F.A.

CHRONIC GLOMERULONEPHRITIS (CGN) **98**

Mirakhmedov Y.A

ARTERIAL HYPERTENSION IN SYSTEMIC LUPUS ERYTHEMATOSUS **100**

Mirakhmedova Kh.T., Mirzalieva A.A.

IMPACT OF ARTERIAL HYPERTENSION AND ENVIRONMENTAL FACTORS ON THE COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS IN CENTRAL ASIA **104**

Mirzaliyeva A.A, Yunusova M.R.

CLIMATE CHANGE, AIR POLLUTION, AND RESPIRATORY HEALTH: EPIDEMIOLOGICAL INSIGHTS INTO CHRONIC BRONCHITIS **106**

Nasni, Tulyaganova D.S.