Table 1. Results of secondary efficacy endpoints at week 12, 24, 36 and 48 in ITT set.

	Secondary efficacy endpoints							
	ACR20 (%)		ACR50 (%)		ACR70 (%)		DAS28-CRP (mean)	HAQ-DI (mean)
Duration	HLX01	Placebo	HLX01	Placebo	HLX01	Placebo	HLX01	Placebo
Baseline							5.49	5.43
Week 12	48.1	32.6	21.9	10.9	4.4	5.4	3.89	4.47
Week 24	60.7	35.9	36.6	18.5	15.3	12.0	3.39	4.37
Week 36	60.1	48.9	46.4	31.5	32.2	17.4	2.88	3.51
Week 48	73.8	62.0	55.2	40.2	39.9	27.2	2.82	3.51

Conclusion: Comparing with placebo plus MTX, HLX01 plus MTX showed significantly improved clinical outcomes and comparable safety profiles in Chinese patients with moderately to severely active RA who had inadequate responses to MTX, demonstrating HLX01 in combination with MTX as a well-tolerated, safe and efficient treatment option.

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AB0198

EFFICACY AND SAFETY AFTER TRANSITION FROM REFERENCE ADALIMUMAB TO CT-P17 (ADALIMUMAB BIOSIMILAR: 100 MG/ML) IN COMPARISON WITH THE MAINTAINED TREATMENT (CT-P17 OR REFERENCE ADALIMUMAB) IN PATIENTS WITH MODERATE-TO-SEVERE ACTIVE RHEUMATOID ARTHRITIS: 1-YEAR RESULT

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Background: Therapeutic equivalence of CT-P17 to reference adalimumab (ref-adalimumab) has been shown in patients with moderate-to-severe active rheumatoid arthritis (RA) through primary 24-week results [1]. Here, efficacy, pharmacokinetics (PK), safety and immunogenicity results up to 52-week, including transition data from ref-adalimumab to CT-P17 are presented.

Objectives: To evaluate efficacy, PK, safety and immunogenicity when switched from ref-adalimumab to CT-P17 compared to maintaining CT-P17 or ref-adalimumab.

Methods: In this study, 648 moderate-to-severe active RA patients despite methotrexate treatment were randomized (1:1) to either CT-P17 or ref-adalimumab and treated with doses of 40 mg every 2 weeks up to Week 24. Prior to dosing at Week 26, 608 patients were randomized again to either maintaining their treatments or being switched from ref-adalimumab to CT-P17. Efficacy, PK, safety, and immunogenicity were assessed up to Week 52.

Results: After the second randomization, 303 patients continued with CT-P17, 153 patients continued with ref-adalimumab and 151 patients switched from ref-adalimumab to CT-P17 treatments, up to Week 48. Demographics and baseline characteristics were similar among the 3 groups. Sustained and comparable efficacy in terms of ACR20/50/70 response rates was achieved not only in the maintenance groups (CT-P17 or ref-adalimumab) but also in the switched from ref-adalimumab to CT-P17 group up to Week 52 (Figure 1).

Figure 1. ACR 20/50/70 Response Rates up to 1 Year. Abbreviation: ref-adalimumab, reference adalimumab. Note: There were patients who could not visit the study site due to COVID-19 pandemic and were counted as nonresponder for ACR response at Week 52.

In terms of PK, mean trough serum concentration (C_{trough}) were maintained after Week 24 in all 3 groups. The observed mean C_{trough} were within the reported therapeutic ranges of ref-adalimumab trough levels in RA patients (5-8 µg/mL).

The safety profile after transition was comparable among the 3 groups (Table 1). The most common treatment-emergent adverse events (TEAEs) was neutropenia. Similar proportions of patients in all 3 groups experienced at least 1 TEAE: injection site reactions, hypersensitivity/allergic reactions and infections. One malignancy (basal cell carcinoma; unrelated) was reported in the ref-adalimumab maintenance group. Safety data accumulated over 1 year also showed comparable results among the 3 groups. Anti-drug antibody (ADA) and neutralizing antibody (NAb) results were similar among the 3 groups. At Week 52, the proportions of patients who had ADA/NAbs were 28.4%/24.8% patients in CT-P17 maintenance, 27.0%/24.3% patients in ref-adalimumab maintenance and 28.3%/26.3% patients in switched to CT-P17 groups.

Conclusion: Single transition from ref-adalimumab to CT-P17 was efficacious and safe without increase in immunogenicity. Also, efficacy, PK, safety and immunogenicity profiles were comparable between CT-P17 and ref-adalimumab up to Week 52.

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Table 1. Overview of TEAEs from Weeks 26 to 52 (Safety Population – second random subset)

Patients, n (%)	Second Randomization		
	CT-P17 Maintenance (N=303)	Ref-ada Maintenance (N=152)	Switched to CT-P17 (N=152)
≥1 TEAE	121 (39.9)	69 (45.4)	73 (48.0)
≥1 TESA	6 (2.0)	3 (2.0)	5 (3.3)
≥1 TEAE leading to study drug discontinuation	3 (1.0)	2 (1.3)	5 (3.3)
≥1 TEAE classified as hypersensitivity/allergic reactions	2 (0.7)	1 (0.7)	0 (0)
≥1 TEAE classified as injection site reactions	1 (0.3)	4 (2.6)	1 (0.7)
≥1 TEAE classified as infection	54 (17.8)	41 (27.0)	28 (18.4)
≥1 TEAE classified as malignancy	0 (0)	1 (0.7)	0 (0)

Abbreviations: Ref-ada, reference adalimumab; TEAE, treatment-emergent adverse event; TESA, treatment-emergent serious adverse event.

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AB0199

PLACEBO AND NOCEBO RESPONSES IN RANDOMIZED CONTROLLED TRIALS OF NON-TUMOR NECROSIS FACTOR BIOLOGICS AND JANUS KINASE INHIBITORS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS SHOWING INSUFFICIENT RESPONSE TO TUMOR NECROSIS FACTOR INHIBITORS: A META-ANALYSIS

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Background: Placebo and nocebo responses have important consequences for the development of pharmaceutical drugs and the design of randomized controlled trials (RCTs). They can lead to the incorrect measurement of treatment-related efficacy and adverse effects (AEs).

Objectives: The goal of this study was to evaluate the frequency and magnitude of placebo and nocebo responses in placebo-controlled RCTs of non-tumor necrosis factor (TNF) biologics and Janus kinase (JAK) inhibitors in patients with rheumatoid arthritis (RA) showing an insufficient response to TNF inhibitors.

Methods: We performed a meta-analysis on the rates of placebo response, AEs, severe AEs (SAEs), and withdrawal owing to AEs in placebo-controlled randomized clinical trials (RCTs) of non-TNF biologics and JAK inhibitors in patients with RA showing an insufficient response to TNF inhibitors.

Results: Nine RCTs contained a total of 3,442 patients (1,840 experimental subjects and 1,602 controls). The pooled incidence of an ACR20 response rate in placebo-treated patients was 22.1% (95% CI 16.4–29.1%) and 27.9% (95% CI 24.5–31.6%) in RCTs of non-TNF inhibitors and JAK inhibitors, respectively. A strong negative correlation was observed between drug efficacies (ACR20 response) and AE rates in the placebo arm, indicating that the greater the placebo response, the weaker the nocebo response ($r = -0.762$, $P = 0.017$). A strong positive correlation was observed between drug efficacies (ACR20 response) in the placebo and active comparator, indicating that the greater the placebo response, the greater the treatment response ($r = 0.737$, $P = 0.003$). The pooled estimate in placebo-treated patients with at least one AE was 71.8% (95% CI 57.4–82.7%) and 58.7% (95% CI 52.8–64.3%) in RCTs of non-TNF inhibitors and JAK inhibitors, respectively. The pooled estimate in placebo-treated patients who withdrew from treatment owing to an AE was 3.8% (95% CI 2.7–5.3%) and 4.0% (95% CI 2.7–6.0%) in RCTs of non-TNF inhibitors and JAK inhibitors, respectively. A strong positive correlation was observed between AE rates in the placebo and active arms, indicating that the greater the nocebo response, the stronger the AE rate in the active arm ($r = 0.855$, $P = 0.003$).

Conclusion: The frequency of the placebo and nocebo responses was 22.1% vs. 27.9% and 71.8% vs. 58.7% in placebo-controlled RCTs of non-TNF inhibitors and JAK inhibitors for RA, respectively, and the greater the placebo response, the weaker the nocebo response and the greater the efficacy.

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AB0200

TRENDS IN THE CHOICE OF FIRST BIOLOGIC AND TARGETED SYNTHETIC DMARD IN RHEUMATOID ARTHRITIS PATIENTS: 20-YEARS JOURNEY OF HUR-BIO REAL-LIFE REGISTRY

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Background: In the last 20 years, there have been extraordinary improvements and practice-changing developments in the management of rheumatoid arthritis (RA). Exploring the pathogenetic mechanisms first enabled clinicians to use anti-tumor necrosis factor (TNF) alpha agents, then drugs targeting different molecules. Parallel to these developments, treatment guidelines have been changed accordingly. Meanwhile, how these developments have been reflected into the real-world practice is a question of interest.

Objectives: In this study, we aimed to explore the first biologic agent trends of our 20-years of single-center experience.

Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a single center biological disease modifying anti-rheumatic drug (DMARD) registry since 2005. Patients who were started biologics before 2005 were registered retrospectively. In brief; demographic data, treatment-related data (including adverse events) and disease-related data of RA patients have been recorded in HUR-BIO. Until the end of the 2020, 21 different rheumatologists contributed to the development of HUR-BIO. In this study, distribution of the first-line biologic agents was calculated according to 5-year periods starting from the 2001. Also, demographic and serologic data of RA patients were reported.

Results: A total of 2080 RA patients was registered in HUR-BIO by the end of 2020. Of these patients, 79.5% was female. Mean age at the starting of bDMARD was 53.3 ± 17.8 years. Rate of rheumatoid factor and anti-cyclic citrullinated peptide positivity was 67.6% and 61.0%, respectively. 65 (3.2%), 335 (16.1%), 858 (41.2%) and 822 (39.5%) patients were prescribed with their first bDMARD in 2001-2005, 2006-2010, 2011-2015 and 2016-2020, respectively. There was a trend towards the increasing prescription of non-Anti-TNF bDMARDs over time.

Table 1. Distribution of first biologic DMARDs in RA patients according to 5-years periods

	2001-2005	2006-2010	2011-2015	2016-2020	Total
Adalimumab	15 (23.1)	111 (33.0)	187 (21.8)	153 (18.6)	466 (22.4)
Etanercept	30 (46.2)	154 (45.8)	229 (26.7)	54 (6.6)	467 (22.4)
Infliximab	20 (30.8)	58 (17.3)	64 (7.5)	7 (0.9)	149 (7.1)
Golimumab	0	0	37 (4.3)	43 (5.2)	80 (3.8)
Certolizumab	0	0	37 (4.3)	68 (8.3)	105 (5.0)
Anti-TNF	65 (100)	323 (96.4)	554 (64.5)	325 (39.5)	1267 (60.9)
Tofacitinib	0	0	6 (0.7)	212 (25.8)	218 (10.5)
Tocilizumab	0	0	9 (1.0)	102 (12.4)	111 (5.3)
Rituximab	0	12 (3.6)	136 (15.8)	84 (10.2)	232 (11.1)
Abatacept	0	0	153 (17.8)	99 (12.0)	252 (12.1)
Non-Anti-TNF	0	12 (3.6)	304 (35.5)	497 (60.5)	813 (39.1)
Total	65 (100)	335 (100)	858 (100)	822 (100)	2080 (100)

Approval years of drugs in Turkey; Infliximab: 2003, etanercept:2004, adalimumab: 2005, golimumab: 2013, certolizumab: 2014, abatacept: 2010, tocilizumab: 2013, rituximab:2009, tofacitinib: 2015,

Conclusion: Real-life practice in RA seems consistent with treatment guidelines. Use of non-Anti-TNF bDMARDs becoming more frequent year-by-year. Jak kinase inhibitor has risen through the last 5 years. Next decade may be the years of Jak kinases inhibitors.

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AB0201

CHANGES IN THE PRESCRIPTION PATTERNS OF THE SECOND-LINE BIOLOGIC AND TARGETED SYNTHETIC DMARD IN RHEUMATOID ARTHRITIS PATIENTS: 20-YEARS JOURNEY OF HUR-BIO REAL-LIFE REGISTRY

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