Disclosure of Interests: Daniel Furst Speakers bureau: CME, Consultant of: Amgen, Corbus, Galapagos, Horizon, Kadmon, Pfizer, Talaris, Grant/research support from: Corbus, CSL Behring, Galapagos, Gilead, GSK, Horizon, Kadmon, Novartis, Pfizer, Roche/Genentech, Talaris, Edward Keystone Speakers bureau: Amgen, AbbVie, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Novartis, Pfizer Pharmaceuticals, Sanofi Genzyme, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb Company, Celltrion Inc., Myriad Autoimmune, F. Hoffmann-La Roche Inc, Gilead, Janssen Inc., Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepis, Grant/research support from: Amgen, Merck, Pfizer Pharmaceuticals, PuraPharm, Jonathan Kay Consultant of: AbbVie, Inc., Boehringer Ingelheim GmbH, Celltrion Healthcare Co. Ltd., Jubilant Radiopharma, Merck & Co., Inc., Pfizer Inc., Samsung Bioepis, Sandoz Inc., Scipher Medicine, UCB, Inc., Grant/research support from: Paid to the University of Massachusetts Medical School: Gilead Sciences Inc., Novartis Pharmaceuticals Corp., Pfizer Inc., Janusz Jaworski: None declared, Rafal Wojciechowski: None declared, Piotr Wiland Speakers bureau: Eli Lilly, Sanofi Aventis, Novartis, Sandoz, Consultant of: Eli Lilly, Novartis, Sandoz, Anna Dudek: None declared, Marek Krogulec: None declared, Sławomir Jeka Speakers bureau: Novartis, Pfizer, Roche, Lilly, Teva, MSD, Abbvie, Sandoz, Egis, Medac, Consultant of: Novartis, Pfizer, Roche, Lilly, Teva, MSD, Abbvie, Sandoz, Egis, Medac, Agnieszka Zielinska: None declared, Jakub Trefler: None declared, Katarzyna Bartnicka-Masłowska: None declared, Magdalena Krajewska-Włodarczyk Speakers bureau: Abbvie, Eli Lilly, Novartis, Roche, Piotr Klimiuk: None declared, Sang Joon Lee Employee of: Celltrion, Inc., Sung Hyun Kim Employee of: Celltrion, Inc., YunJu Bae Employee of: Celltrion, Inc., GoEun Yang Employee of: Celltrion, Inc., JaeKyoung Yoo Employee of: Celltrion, Inc., TaeKyoung Kim Employee of: Celltrion, Inc.

DOI: 10.1136/annrheumdis-2021-eular.325

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.

REFERENCES:

- Mitsikostas DD, Chalarakis NG, Mantonakis LI, Delicha EM, Sfrikakis PP. Nocebo in fibromyalgia: meta-analysis of placebo-controlled clinical trials and implications for practice. *Eur J Neurol* 2012;19:672-80.
- Kravvariti E, Kitis GD, Mitsikostas DD, Sfrikakis PP. Nocebos in rheumatology: emerging concepts and their implications for clinical practice. *Nat Rev Rheumatol* 2018;14:727-40.

- Colloca L, Barsky AJ. Placebo and Nocebo Effects. *N Engl J Med* 2020;382:554-61.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.661

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.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.693

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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Background: In the last 20 years, anti-tumor necrosis factor (TNF) alpha agents re-designed the management of rheumatoid arthritis (RA). Despite this, unmet needs in the management of RA brought several drugs targeting different molecules and cytokines. It is still a research question that how did these developments changed daily-practice in RA patients who are intolerant/unresponsive to the first biological disease modifying anti-rheumatic drugs (bDMARD).

Objectives: In this study, we aimed to explore the second 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. Until the end of the 2020, 21 different rheumatologists contributed to the development of HUR-BIO. Distribution of the second-line biological agents (switch from first-line biological agent because of either adverse events or unresponsiveness) 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 776 (776/2080, 37.3%) RA patients, who was prescribed a second biological agent, was registered in HUR-BIO by the end of 2020. Of these patients, 83.7% was female. Mean age at the starting of bDMARD was 53.1 ± 13.3 years. Rate of rheumatoid factor and anti-cyclic citrullinated peptid positivity was 69.1% and 60.5%, respectively. Distribution of first-line bDMARDs was as follows: adalimumab 194 (24.9%), etanercept 209 (26.9%), infliximab 105 (13.5%), golimumab 39 (5.0%), certolizumab 35 (4.5%), abatacept 78 (10.0%), rituximab 46 (5.9%), tofacitinib 37 (4.7%), tocilizumab 33 (4.2%). 11 (1.4%), 85 (11.0%), 282 (36.3%) and 398 (51.3%) patients were prescribed with their second 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 as second-line over time.

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

	2001-2005	2006-2010	2011-2015	2016-2020	Total
Adalimumab	3 (27.3)	15 (17.6)	69 (23.9)	77 (18.9)	164 (20.8)
Etanercept	8 (72.7)	35 (41.2)	49 (17.0)	41 (10.1)	133 (16.8)
Infliximab	0	12 (14.1)	13 (4.5)	25 (6.2)	50 (5.4)
Golimumab	0	0	19 (6.6)	8 (2.0)	27 (3.4)
Certolizumab	0	0	2 (0.7)	26 (6.4)	28 (3.5)
Anti-TNF	11 (100)	62 (72.9)	152 (53.9)	177 (44.5)	402 (51.8)
Tofacitinib	0	0	4 (1.4)	73 (17.9)	77 (9.7)
Tocilizumab	0	0	12 (4.2)	81 (19.9)	93 (11.7)
Rituximab	0	22 (25.9)	53 (18.3)	32 (7.8)	107 (13.5)
Abatacept	0	1 (1.2)	61 (21.1)	35 (8.6)	97 (12.2)
Non-Anti-TNF	0	23 (27.1)	130 (46.1)	221 (55.5)	374 (48.2)
Total	11 (100)	85 (100)	282 (100)	398 (100)	776 (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: As the choice of second-line biologic and targeted synthetic DMARD, non-Anti-TNF bDMARDs, especially tofacitinib and tocilizumab becoming more frequent year-by-year. Despite that, anti-TNF agents as a group are still highly-prescribed options as second-line bDMARD.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.694

AB0202

IMPROVEMENT IN CLINICAL DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES AFTER 6 MONTHS OF TREATMENT WITH ABATACEPT, STRATIFIED BY LINE OF THERAPY, IN PATIENTS WITH RA: RESULTS FROM A LARGE, US, NATIONAL OBSERVATIONAL STUDY

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Background: RA is more responsive to treatment in the early stages of disease, and early treatment may lead to better long-term outcomes.^{1,2} Data on the effectiveness of specific drugs as first or later lines of therapy will help inform treatment sequencing.

Objectives: Data from patients enrolled in the Corrona RA Registry were used to compare the effectiveness of abatacept across lines of therapy overall (primary cohort) and in a subset of patients who were anti-citrullinated protein antibody positive (ACPA+).

Methods: Patients with RA who initiated abatacept (January 2006 to October 2020), had 6 months' follow-up (within 4–9 months of starting abatacept), had baseline (BL) and follow-up CDAI scores available, and had BL CDAI >2.8 were included. Outcomes were compared for first-, second- and third or higher-line therapy: 0, 1 or ≥2 prior biologic DMARDs or Janus kinase inhibitors, respectively. Continuous outcomes included change from BL to 6 months in mean CDAI and patient-reported pain, fatigue, and HAQ. Binary outcomes included rate of achieving minimal clinically important difference (MCID) in CDAI or modified ACR20/50/70 at 6 months. Continuous and binary outcomes were analysed using multiple linear and logistic regression, respectively. The models included line of therapy, age, sex, disease duration, work status, SC nodules, history of hypertension and depression, BL CDAI, BL patient-reported pain and BL fatigue. Additional subgroup analyses were carried out in patients with moderate/high disease activity (CDAI >10) at BL.

Results: In total, 2876 patients (2327 with BL CDAI >10; 890 ACPA+) were included; 442, 911, and 1523 patients initiated first-, second- or third/higher-line abatacept, respectively. Compared with patients on second/third/higher-line abatacept therapy, those on first-line abatacept were significantly older, had shorter disease duration, and had lower BL CDAI, pain and fatigue (all p<0.001). In adjusted analyses, patients receiving abatacept as earlier lines of therapy had significantly greater improvement from BL in mean CDAI and in patient-reported fatigue and HAQ (Table 1). There was no significant difference between lines of therapy in change in patient-reported pain. Patients receiving first-line abatacept had significantly higher odds of achieving a MCID in CDAI or modified ACR20/50/70 response (Figure 1). Similar patterns were seen when the sample was limited to patients with moderate/high disease activity or in patients who were ACPA+.

Conclusion: There were significant differences in improvement in clinical disease activity and patient-reported outcomes across lines of therapy. Better treatment responses were observed with earlier lines of abatacept therapy in the overall population, in patients who were ACPA+ and in those with moderate/high BL disease activity.

REFERENCES:

- [1] Harrold LR, et al. *Clin Rheumatol* 2017;36:1215–1220.
- [2] Monti S, et al. *RMD Open* 2015;1(Suppl 1):e000057.

Table 1. Adjusted mean change in CDAI and patient-reported outcomes from BL to 6 months after initiation of abatacept by line of therapy (primary cohort)

Adjusted outcome, mean change (SE)	First-line (n=440)	Second-line (n=898)	Third/higher-line (n=1515)	p value ^a
CDAI	-7.96 (0.33)	-7.49 (0.27)	-5.74 (0.19)	<0.001
Patient-reported pain (VAS 0–100)	-9.43 (0.69)	-7.98 (0.47)	-7.70 (0.35)	0.074
Patient-reported fatigue (VAS 0–100)	-7.49 (0.71)	-5.87 (0.51)	-4.81 (0.36)	0.002
Patient-reported HAQ	-0.16 (0.01)	-0.12 (0.01)	-0.08 (0.01)	<0.001

^aEstimated by multiple linear regression model adjusted for age, sex, disease duration, work status, SC nodules, history of hypertension and depression, BL CDAI, BL patient-reported pain and BL fatigue (factors that were identified *a priori* based on clinical experience or that differed significantly by line of therapy); p values reflect ANOVA overall test of differences across lines of therapy. VAS=visual analogue scale.