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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

Y. H. Lee¹, G. G. Song². ¹Korea University, Rheumatology, Seoul, Korea, Rep. of (South Korea); ²Korea University Guro Hospital, Rheumatology, Seoul, Korea, Rep. of (South Korea)

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

A. İ. Ertenli¹, U. Kalyoncu¹, O. Karadag¹, L. Kılıç¹, A. Akdoğan¹, I. Dogan¹, Ş. A. Bilgen¹, E. Bilgin¹, E. Duran¹, Y. Maraş², B. Kıcak³, A. Erden², B. Armagan², A. San⁴, E. C. Bolek¹, B. Farisoğulları¹, G. K. Yardımcı¹, Z. Özsoy¹, G. Ayan¹, M. Çalgüneri¹, S. Kiraz¹. ¹Hacettepe University, Internal Medicine, Rheumatology, Ankara, Turkey; ²Ankara City Hospital, Internal Medicine, Rheumatology, Ankara, Turkey; ³Medical Park Hospital, Internal Medicine, Rheumatology, Gaziantep, Turkey; ⁴Yenimahalle Education and Research Hospital, Internal Medicine, Rheumatology, Ankara, Turkey

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

S. Kiraz¹, U. Kalyoncu¹, O. Karadag¹, L. Kılıç¹, A. Akdoğan¹, I. Dogan¹, Ş. A. Bilgen¹, E. Bilgin¹, E. C. Bolek¹, B. Kıcak², Y. Maraş³, A. Erden³, B. Armagan³, A. San⁴, E. Duran¹, B. Farisoğulları¹, G. K. Yardımcı¹, Z. Özsoy¹,