DISCREPANCIES BETWEEN THE RHEUMATOID ARTHRITIS PATIENT POPULATION IN RANDOMIZED CONTROLLED TRIALS OF BIOLOGICS AND THAT IN REAL-WORLD SETTINGS: A STUDY USING THE IORRA COHORT

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Background: Randomized controlled trials (RCTs), which are currently considered to provide the highest level of evidence, include patients with high disease activity and exclude those with comorbidities often seen in real-world settings. With the increasing recognition of the importance of real-world evidence, attention is being paid to discrepancies between RCT-based evidence and the patient population in routine clinical practice; however, factors causing these gaps in the context of rheumatoid arthritis (RA) are available.

Objectives: To evaluate the proportion of patients meeting the inclusion criteria in RCTs of biologics for the treatment of RA conducted in Japan using the real-world IORRA cohort.

Methods: The inclusion criteria used in Phase 2 or Phase 3 RCTs of the following biological DMARDs (bDMARDs) were extracted: infliximab (IFX), etanercept (ETN), adalimumab (ADA), golimumab (GLM), certolizumab (CZP), abatacept (ABT), tocilizumab (TCZ), and infliximab (IFX-BS). Patients participating in the IORRA study during the period when each RCT was conducted (Cohort A) and those who initiated treatment with each bDMARD at our institute in 2016 (Cohort B) were included in the analysis. The proportion of RA patients in Cohorts A and B who met the RCT inclusion criteria was assessed.

Results: A total of 19 RCTs were conducted in Japan (IFX; 2, ETN; 1, ADA; 2, GLM; 2, CZP; 3, ABT; 2, TCZ; 6, IFX-BS, 1). Key trial inclusion criteria were: age, RA duration, tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), methotrexate (MTX) use, corticosteroid use, and prior bDMARD therapy. The number of patients participating in the IORRA analysis during the period when each RCT was conducted ranged from 1,777 to 6,843 (mean: 5,470) (Cohort A). The median/average [range] proportion of RA patients meeting the RCT inclusion criteria was 0.6%/2.3% [range: 0.0%-16.2%]. The proportion by criterion was 93.9%/92.4% [59.7%-99.9%] for age, 68.8%/67.1% [9.0%-99.6%] for RA duration, 11.6%/16.0% [4.5%-33.0%] for SJC, 14.6%/17.2% [3.7%-33.9%] for TJC, 27.8%/32.1% [20.1%-49.8%] for CRP, 60.2%/58.7% [43.7%-66.8%] for ESR, 14.8%/40.6% [13.1%-73.9%] for MTX use, 99.5%/99.3% [98.5%-99.8%] for prednisolone (PSL) use, and 91.9%/92.0% [85.6%-98.0%] for prior bDMARD use. In Cohort A, the proportion of RA patients meeting the RCT inclusion criteria was low, particularly with respect to SJC, TJC, and MTX use. Among 337 patients who initiated bDMARD therapy at our institute in 2016, a total of 139 biologic-naive patients (IFX; 3, ETN; 33, ADA; 11, GLM; 21, CZP; 17, ABT; 25, TCZ; 28, IFX-BS; 1) were included in the analysis (Cohort B). In Cohort B, the median/average [range] proportion of RA patients meeting all RCT inclusion criteria was 0%/8.2% [0.0%-54.2%]. The proportion by criterion was 100%/99.1% [94.1%-100%] for age, 20.8%/26.5% [0.0%-57.1%] for SJC, 11.8%/17.0% [0.0%-50.0%] for TJC, 33.3%/34.9% [0.0%-66.7%] for CRP, 58.3%/57.3% [0.0%-75.0%] for ESR, 23.5%/35.5% [0.0%-100%] for MTX use, and 100%/100% [0.0%-100%] for PSL use. As in Cohort A, the proportion of RA patients meeting the inclusion criteria was low in Cohort B, particularly with respect to SJC, TJC, and MTX use.

Conclusion: It is important to note that evidence from RCTs of bDMARDs is based on a limited RA population in real-world settings.