The treatment strategies for RA and the QOL of RA patients, which is evaluated in daily practice using the EQ-5D, have changed significantly since the introduction of biological disease-modifying anti-rheumatic drugs (bDMARDs).

Objectives: To identify patient subsets with distinct EQ-5D trajectories among RA patients taking bDMARDs, and to examine the clinical features of patients whose QOL improved since bDMARD use in daily practice.

Methods: Since October 2000, we have established a large observational cohort of RA patients at our institute Institute Of Rheumatology, Rheumatoid Arthritis (IORRA). Essentially, all RA patients who attend our clinic are given questionnaires, including the EQ-5D, Disease Activity Score 28 (DAS28), and the Japanese version of the Health Assessment Questionnaire (J-HAQ), every 6 months. More than 5,000 RA patients are included in this cohort, of whom 785 patients who received bDMARDs for at least 3 years were enrolled in this study. The EQ-5D scores of these 785 patients were recorded biannually for 3 years, and latent class analysis of the temporal trends in the EQ-5D score based on posterior probabilities was performed after initiation of bDMARDs. The clinical characteristics of each latent class were then compared.

Results: The 785 patients (107 taking infliximab, 341 etanercept, 100 tocilizumab, 131 abatacept, 90 golimumab, and 16 certolizumab pegol) were classified into four classes based on time-related changes in their EQ-5D scores: Class 1 (n = 160), patients with a consistently low score < 0.6 despite use of bDMARDs; Class 2 (n = 314), patients with a consistently moderate score of 0.7; Class 3 (n = 229), patients whose score improved from 0.7 to 0.9 after use of bDMARDs; and Class 4 (n = 82), patients with a consistently high score of 0.9. When comparing the patients in Classes 2 and 3, whose EQ-5D scores before bDMARD use were similar, the patients in Class 3 had a younger age ($p<0.001$), shorter disease duration ($p<0.001$), higher DAS28 score ($p<0.001$), lower J-HAQ score ($p=0.038$), and more frequent use of non-steroidal agents ($p=0.002$) than those of Class 2 patients.

Conclusion: The results of this study suggest that QOL is less likely to improve in patients with RA whose disabilities and QOL deterioration have already become established despite use of bDMARDs. We also determined the clinical features of RA patients whose QOL improved after initiation of bDMARDs.

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FR10116

SUBCUTANEOUS TOCILIZUMAB IN MONOTHERAPY OR IN COMBINATION WITH CSDMARD IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS: OBSERVATIONAL STUDY TO DESCRIBE REAL-WORLD DRUG RETENTION RATE AT 12 MONTHS

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Background: Rate of discontinuation and drug survival of biologic therapies in rheumatoid arthritis (RA) is about 60-70% in real life at one year¹. In France, all biologics 1st prescription and yearly renewal are reimbursed, restricted to hospital rheumatologists, with renewal and monitoring done by both office-based or hospital rheumatologists.

Objectives: To evaluate the 12-month drug retention rate, efficacy and tolerance of tocilizumab (TCZ) subcutaneous (sc) in RA patients (pts).

Study design: prospective, multicentre, observational 18-month study. Pts: moderate to severe active RA requiring TCZ sc as prescribed in real life.

Primary endpoint: drug retention rate of TCZ sc at 12 months in pts followed by hospital- and office-based rheumatologists, estimated using Kaplan-Meier method. **Secondary endpoints:** pts' characteristics, concomitant treatments, adherence to TCZ sc using the Compliance Questionnaire for Rheumatology (CQR5), efficacy, safety of TCZ sc and QoL using EQ-5D. **Statistical analysis:** pts with ≥ 1 TCZ injection were analyzed for safety. Pts fulfilling inclusion and non-inclusion criteria were analyzed for efficacy.

Results: 291 pts were recruited, 286 were analyzed for safety and 285 for efficacy.

Baseline: mean age 56.2 $\pm$ 12.5 years, females: 74.7%, at least 1 co-morbidity: 71.9%, mean RA duration 9.4 $\pm$ 9.0 years, RF and/or ACPA: 83.4%, erosive RA: 60.8%, mean DAS28-ESR 4.77 $\pm$ 1.21. Past RA treatments were csDMARDs in 94.4%, biologics in 62.8%. EQ-5D Health state was 0.53 $\pm$ 0.19. TCZ Mono (i.e. without csDMARD) was initiated in 124 (43.5%), TCZ Combo in 158 (55.4%) pts, 84.8% of whom received MTX (17.3 $\pm$ 4.4mg/w). Glucocorticoids (GCs) were used in 48.9% of the pts (9.99 $\pm$ 9.36mg/day).

Follow up: 161 and 148 pts completed M12 and M18 visits. 138 pts withdrew including AE 61, lack of efficacy 37, pts/doctor wish 24. At M12, drug retention rate was 63.6%: 62.6% in Mono, 64.3% in Combo (Fig.1); with similar results for pts $\leq$ 65 years old and for pts $\leq$ 30Kg/m². 5 Mono pts had ongoing csDMARD and 9 Combo pts had no csDMARD. 15.3% and 19.0% used GCs, 16.19 $\pm$ 11.95mg/d in the Mono and 17.36 $\pm$ 16.65mg/d in the Combo groups. Total number of TCZ injections was 36.74 $\pm$ 25.84 done by pt in 54.0%. Mean time between 2 TCZ injections was 8.48 $\pm$ 10.70 days. Adherence to TCZ was high in 86.5% of the 89 pts who completed CQR5 at month 12. It was 52.9% for the 121 pts who completed pts diary over the month 12-month 18 period. Mean DAS28 in all, Mono and Combo were 1.91 $\pm$ 1.11, 1.66 $\pm$ 1.02, 2.12 $\pm$ 1.14 respectively. EULAR good and moderate responses were respectively 61.3 and 7.7% in all; 67.2 and 4.9% in Mono; 56.8 and 9.9% in Combo pts. EQ-5D improved in all domains with a change from baseline of 0.11 $\pm$ 0.29. 234 (81.8%) pts had at least 1 adverse event (AE), 46 (16.1%) had at least 1 serious AE including 11 infections, 2 GI perforations and 2 deaths (pneumopathy and bronchial carcinoma).

Figure 1. Kaplan-Meier curve of the drug retention rate by SC TCZ in mono vs combo - Efficacy population

Conclusion: At 12 months, drug retention rate was 63.6% in patients receiving TCZ sc in real life, with no difference between Mono and Combo groups. EULAR good/moderate response was 69.0%. QoL improved in all EQ-5D domains. No new safety signal occurred.

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THE COMPARATIVE RISK OF OSTEOPOROTIC FRACTURES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TNF INHIBITORS VERSUS OTHER BIOLOGICS: A NATION-WIDE COHORT STUDY IN KOREA

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Background: Rheumatoid arthritis (RA) is associated with an increased risk of osteoporosis and osteoporotic fracture, but little is known about comparative risk of osteoporotic fractures between biologic agents.

Objectives: To investigate the comparative risk of osteoporotic fractures among RA patients who initiated TNF inhibitors, abatacept, and tocilizumab.

Methods: We identified patients aged ≥ 40 years with at least two ICD-10 diagnosis codes for RA who initiated TNF inhibitor, abatacept, or tocilizumab from the 2005-2015 Korean National Health Insurance Service datasets. The primary outcome was a composite osteoporotic fracture endpoint of spine, hip, forearm or humerus fractures requiring hospitalization. Secondary outcomes were spinal and non-spinal fractures. Follow-up period started from the day after the first dispensing date of the study drug to the earliest date among the following events: discontinuation of the study drugs, outcome occurrence, disenrollment, end of study dataset, or death. Propensity score (PS) matching with a variable ratio of 10:1 was conducted for TNF inhibitor versus abatacept initiators and for TNF inhibitor versus tocilizumab initiators to adjust for baseline confounding. We estimated hazard ratio (HR) and 95% confidence interval (CI) of osteoporotic fracture risks comparing TNF inhibitors to abatacept or tocilizumab by Cox proportional hazard models stratified by a matching ratio.

Results: We included 2,339 TNF inhibitor initiators and 594 abatacept initiators, and 2,486 TNF inhibitor initiators and 647 tocilizumab initiators in each PS-matched cohort. The incidence rates per 100 person-years for the primary outcome were 1.57 and 1.65 for TNF inhibitor and abatacept initiators, and 1.69 and 2.05 for TNF inhibitor and tocilizumab initiators, respectively. The HR (95% CI) for the primary outcome was 1.10 (1.54-2.23) comparing TNF inhibitors versus abatacept and it was 1.00 (0.53-1.92) comparing TNF inhibitor versus tocilizumab initiators. We also did not find any significant difference for secondary outcomes (Table1).

Table 1. Risk of osteoporotic fractures in TNF inhibitor initiators vs. abatacept initiators and tocilizumab initiators

	TNF inhibitor (n=2,339)			Abatacept (n=594)			HR (95% CI)
	Events	Py	IR per 100 PY	Events	Py	IR per 100 PY	
Primary outcome							
Osteoporotic fracture	47	2,998	1.57	12	727	1.65	1.10 (1.54-2.23)
Secondary outcomes							
Spinal fracture	25	3,018	0.83	8	731	1.10	0.95 (0.41-2.20)
Non-spinal fracture	22	3,022	0.73	4	737	0.54	1.52 (0.41-5.65)
	TNF inhibitor (n=2,468)			Tocilizumab (n=647)			HR (95% CI)
	Events	Py	IR per 100 PY	Events	Py	IR per 100 PY	
Primary outcome							

Osteoporotic fracture	54	3,196	1.69	16	781	2.05	1.00 (0.53-1.92)
Secondary outcomes							
Spinal fracture	29	3,221	0.90	10	788	1.27	0.98 (0.43-2.24)
Non-spinal fracture	25	3,225	0.78	6	793	0.76	1.03 (0.36-2.90)

Conclusion: We did not find a significant difference in the risk of osteoporotic fractures between TNF inhibitor and abatacept initiators, or between TNF inhibitor and tocilizumab initiators in this Korean population-based cohort study.

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FRI0118

INFECTION OUTCOMES IN PATIENTS WITH RA TREATED WITH ABATACEPT AND OTHER DMARDS: RESULTS FROM A 10-YEAR INTERNATIONAL POST-APPROVAL STUDY

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Background: The abatacept global post-marketing epidemiology programme consists of observational studies based on biologic disease registries and healthcare claims databases to assess infection and malignancy risks associated with abatacept treatment, as used in routine clinical practice.

Objectives: To evaluate the risk of infection in patients with RA treated with abatacept versus conventional synthetic (cs)DMARDs and other biologic (b) or targeted synthetic (ts)DMARDs.

Methods: Data were analysed from five cohorts: two biologic registries (the Anti-Rheumatic Therapy in Sweden register and the Rheumatoid Arthritis Observation of Biologic Therapy German registry), a disease registry (FORWARD, The National Databank for Rheumatic Diseases in the USA) and two healthcare claims databases (the population-based British Columbia Canadian RA Cohort and the US Optum Research Database). Crude incidence rates (per 1000 patient-years of exposure) with 95% CIs were calculated for hospitalised infections and opportunistic infections. Adjusted risk ratios (RRs) with 95% CIs were estimated using multivariate models adjusting for demographics, co-morbidities and other potential confounders within each database and were subsequently pooled using a random effects model for meta-analyses.

Results: From all cohorts, patients treated with abatacept (6400), csDMARDs (137K) and other b/tsDMARDs (54K) were followed up for a mean of 2.3–3.7, 2.2–6.2 and 2.3–4.7 years, respectively. Patients were mainly female (71–86%), with a mean age ranging from 49–63 years, and 3–18% had a history of prior severe infections across treatment groups/cohort. A greater number of abatacept-treated patients had a history of ≥ 2 prior biologics (44–85% vs csDMARDs, 11% [FORWARD] and other b/tsDMARDs, 0–19%). In abatacept-treated patients, incidence rates for hospitalised infections ranged from 16–56 and opportunistic infections from 0.4–7.8 (Table). Adjusted RRs (95% CIs) for abatacept vs csDMARDs (range: 0.3 [0.2, 0.7] to 2.2 [1.3, 3.7]; pooled estimate: 1.2 [0.6, 2.2]) and abatacept vs other b/tsDMARDs (range: 0.5 [0.3, 0.8] to 1.3 [0.8, 2.1]; pooled estimate: 0.9 [0.6, 1.3]) showed no increased risk in hospitalised infections.

Conclusion: In this large, international post-marketing epidemiology programme, pre-specified infection risks were more frequent with abatacept than csDMARDs and b/tsDMARDs in some, but not all, cohorts. Increased risks for individual outcomes/cohort may be attributed to prior biologic exposure, study design and practice pattern differences. These data are consistent with the current safety profile of abatacept.

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