



Comparison of the efficacy and safety of biologic agents between elderly-onset and young-onset RA patients: the ANSWER cohort study

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Title. Comparison of the efficacy and safety of biologic agents between elderly-onset and young-onset RA patients: The ANSWER Cohort Study

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Ethics approval

This observational study was conducted as per the Declaration of Helsinki and was approved by the ethics committees of all seven institutes.

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Conflict of interest

Sadao Jinno has received speaking fees from AbbVie G.K., Asahi Kasei Pharma., Bristol-Myers Squibb., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K.,

Janssen Pharmaceutical K.K., and Mitsubishi Tanabe Pharma, and Ono Pharmaceutical Co.. Akira Onishi reports grants from Advantest, personal fees from Asahi Kasei Pharma, personal fees from Chugai Pharmaceutical Co., Ltd., personal fees from Eli Lilly Japan K.K., personal fees from Ono Pharmaceutical Co., personal fees from Mitsubishi Tanabe Pharma, personal fees from Takeda Pharmaceutical Company Limited, personal fees from Daiichi Sankyo Co. Ltd. Motomu Hashimoto and Koichi Murata belong to the department that is financially supported by five pharmaceutical companies (Tanabe-Mitsubishi, Chugai, Ayumi, UCB-Japan and Asahi-Kasei), Nagahama city and Toyooka city. Motomu Hashimoto has received speaking fees from Mitsubishi Tanabe Pharma and Bristol-Myers Squibb; and has received research grants from Eli Lilly and Eisai. Koichi Murata has received a speaking fee and/or consulting fee from Eisai Co., Ltd.. Tohru Takeuchi has received grants from Chugai Pharmaceutical Co. Ltd, personal fees from Astellas Pharma Inc, Chugai Pharmaceutical Co. Ltd, Mitsubishi Tanabe Pharma Corporation, AbbVie GK, Bristol Myers Squibb, AYUMI Pharmaceutical Co., Daiichi Sankyo Co. Ltd, Eisai Co. Ltd, Takeda Pharmaceutical Co. Ltd, and Asahi Kasei Corporation. Yuichi Maeda received a research grant and/or speaker fee from Eli Lilly Japan K.K., Chugai Pharmaceutical Co. Ltd., Pfizer Inc., Bristol Myers Squibb, and Mitsubishi Tanabe Pharma Corporation. Kosuke Ebina has received speaking fees from AbbVie G.K., Asahi Kasei Pharma., Astellas Pharma Inc., AYUMI Pharmaceutical Co., Bristol Myers Squibb, Chugai Pharmaceutical Co. Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Corporation, and Ono Pharmaceutical Co., Sanofi K.K., Taisho, and UCB Japan; and has received research grants from AbbVie G.K., Asahi Kasei Pharma., Astellas Pharma Inc., Chugai Pharmaceutical Co. Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceutical Co., Taisho, and UCB Japan. Yonsu Son has received speaking fees from Actelion, Bristol-Myers Squibb., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., and Mitsubishi Tanabe Pharma,

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Author contributions

Conceived and designed the study: Sadao Jinno, Maureen Dubreuil. Analyzed the data: Sadao Jinno, Akira Onishi. Collection of data: Sadao Jinno, Akira Onishi, Kengo Akashi, Motomu Hashimoto, Wataru Yamamoto, Koichi Murata, Tohru Takeuchi, Takuya Kotani, Yuichi Maeda, Kosuke Ebina, Yonsu Son, Hideki Amuro, Ryota Hara, Masaki Katayama, Jun Saegusa, and Akio Morinobu. Sadao Jinno prepared the initial draft of the manuscript. All the authors were involved in revising the manuscript critically for content. All authors read and approved the final manuscript.

Data availability

The datasets generated and/or analyzed during the current study are not publicly available. Patients did not provide consent to raw data sharing during the data collection for this

purpose. All aggregated data relevant to the study are included in the article or uploaded as supplementary information.

Related congress abstract publications

We presented the data as a poster at the 2019 Annual American College of Rheumatology/Association of Rheumatology Professionals Annual Meeting and an abstract has therefore been published: Jinno S, Onishi A, Akashi K, Hashimoto M, Yamamoto W, Murata K, Takeuchi T, Kotani T, Maeda Y, Ebina K, Son Y, Amuro H, Hara R, Katayama M, Saegusa J, Morinobu A. Are There Differences in Efficacy and Safety of Biological Disease-modifying Antirheumatic Drugs Between Elderly-onset and Young-onset Rheumatoid Arthritis? [abstract]. *Arthritis Rheumatol.* 2019; 71 (suppl 10).

Abstract

Background: The objective of the study was to compare efficacy and safety of biological disease-modifying antirheumatic drugs (bDMARDs) between elderly-onset rheumatoid arthritis (EORA) and young-onset rheumatoid arthritis (YORA) patients.

Methods: Patients with rheumatoid arthritis (RA) aged ≥ 18 years enrolled in a Japanese multicenter observational registry between 2009 and 2018 who had moderate or high disease activity when initiating bDMARDs were included. EORA was defined as RA with onset at 60 or over. After propensity score weighting for differences in confounding factors, generalized estimating equations were used to assess the relationship between age of RA onset and bDMARD clinical effectiveness at 48 weeks after starting a bDMARD.

Results: Among a total of 7183 patients in the registry, 2815 (39.2%) were identified as EORA. The proportion of patients on bDMARDs was lower in the EORA as compared to the YORA (18.3 % vs 28.0 %, $p < 0.001$). Of the 989 bDMARD initiators, 364 (36.8%) were identified as EORA. The median follow-up duration was 48 weeks both in the EORA and in the YORA. After adjusting for differences in baseline characteristics between the two age groups, there was no significant difference in Clinical Disease Activity Index scores at 48 weeks (mean difference 1.01, 95%CI=-0.62-2.64, $p=0.22$). There was a non-significant trend toward lower remission in EORA (OR=0.52, 95%CI=0.24-1.14, $p=0.10$), and low disease activity/remission was similar (OR=0.86, 95%CI=0.29-2.52, $p=0.77$). Drug retention (HR=0.95, 95%CI=0.55-1.35, $p=0.78$) and

discontinuations due to adverse events (HR=0.78, 95%CI=0.38-1.18, p=0.22) were similar between the two age groups after adjustment for confounders.

Conclusion: In RA patients initiating bDMARDs, improvements in clinical disease at 48 weeks were similar between EORA and YORA. Drug retention and adverse events discontinuation was similar between the two age groups.

Keywords: Adult; Age of Onset; Aged; Arthritis, Rheumatoid /epidemiology; Antirheumatic Agents / therapeutic use; Arthritis, Rheumatoid / drug therapy; Biological Products/ therapeutic use*; Outcome and Process Assessment, Health Care; Disease Progression; Registries

INTRODUCTION

Rheumatoid arthritis (RA) among elderly people is an increasingly important health concern. A recent large RA registry in the United States showed that approximately one-fourth of the enrolled patients were diagnosed after the age of 60 years [22]. In a Swiss prospective observational cohort for early RA and undifferentiated arthritis (disease duration after the first symptom <1 year), the peak age at disease onset was between 50 and 60 years and was ≥ 60 years in 38.2 % of the 592 patients [25]. In Japan, where the population has aged rapidly in recent decades, one of the large registry studies showed the peak age at onset of RA has shifted from 50–59 to 60–69 years of age over the past decade [20]. In fact, it is not uncommon to see patients who develop RA over the age of 70 or even 80 in a typical Japanese practice.

Elderly onset-rheumatoid arthritis (EORA) is usually defined as disease onset after 60 years of age [5]. Literature is limited as to whether incidence of EORA is rising, but several environmental factors might be contributing to the increase of EORA. Cigarette smoking and periodontitis have been identified as risk factors for RA. One study reported that higher prevalence of periodontitis among the first baby boomers might have been associated with increased number of EORA in Japan [20]. The baby-boomer generation also has a greater prevalence of smoking than subsequent birth cohorts [18]. In addition to increased longevity, birth cohort effects associated with increased exposure to certain extrinsic risk factors might lead to increased number of EORA in some countries.

Patients with elderly-onset rheumatoid arthritis (EORA) can present with higher disease activity at diagnosis, greater disability, and a greater burden of comorbidities than those with young-onset rheumatoid arthritis (YORA) [6,16,26,33]. It is not entirely clear why these discrepancies arise between the two age groups, but one study reported EORA patients had higher IL-6 levels and lower TNF- α levels as compared to YORA patients[3], suggesting different cytokines may be involved in pathogenesis between the two age groups. Despite potentially greater disease severity and disability, previous studies showed patients with EORA receive biological disease-modifying antirheumatic drugs (bDMARDs) less frequently than those with YORA [27,32]. This disparity is likely driven by both providers and patients. Provider factors, such as concern for toxicity or less experience with intensive treatment in elderly RA patients, may lead to a less use of bDMARDs in EORA. Patient-related factors, such as fear of receiving treatments with potentially marked side effects, may also be associated with less use of bDMARDs in EORA. Alternatively, intensive therapy with bDMARDs may be avoided under the misconception that it is not necessary to control disease in patients with EORA.

Data regarding the efficacy and safety of bDMARDs among EORA patients have been either inconsistent or scarce. Most studies involving elderly RA patients were conducted based on age at time of treatment, but not age at RA onset, which makes it difficult to accurately assess response to bDMARDs. For example, one registry reported TNF inhibitors (TNFi) were slightly less effective in patients aged >65 years, but disease duration was longer in the elderly group (mean 14.3 years) as compared to those < 65 years (mean 11.5 years)[12]. The evidence for efficacy and safety of non-TNFi bDMARDs in EORA is even more scarce.

With a potentially growing number of EORA patients and wide adoption of a treat-to-target strategy for RA, it is important to know if bDMARDs can be used effectively and safely in patients with EORA. The objective of this study was to investigate if there are differences in efficacy and safety of bDMARDs between EORA and YORA by utilizing the data from multicenter observational cohort in Japan.

METHODS

Study design and data source. The Kansai Consortium for Well-being of Rheumatic Disease Patients (ANSWER) cohort is an observational multi-center registry of patients with RA in the Kansai district of Japan. Data from patients at seven institutes (Kyoto University, Osaka University, Osaka Medical College, Kansai Medical University, Kobe University, Nara Medial University, and Osaka Red Cross Hospital) were included. ANSWER is an ongoing prospective cohort study of adult patients with RA [8,14]. Serial disease assessments including laboratory blood work and treatment history were recorded. The data from 2009 to 2017 were retrospectively analyzed. In this study, we included all RA patients aged ≥ 18 years with disease activity score in 28 joints-erythrocyte sedimentation rate (DAS28-ESR) ≥ 3.2 at the time of bDMARD initiation. Patients were treated according to the Japan College of Rheumatology guideline [21], similar to the EULAR and ACR guidelines, with a csDMARDs, primarily MTX with or without glucocorticoids, followed by the addition of bDMARDs or other csDMARDs, using the treat-to-target approach [29,30]. Those with serial disease activity and treatment record that were fully available after bDMARD initiation were included. Those who had 2 or more disease activity assessments (at the time of bDMARD initiation and at least 3 months after bDMARD initiation) were included for analysis. The

following bDMARDs were used: abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, and tocilizumab. Januse kinase inhibitors (JAKi) such as tofacitinib was also included in the study since the treatments are being positioned after conventional synthetic DMARDs (csDMARDs) failure like bDMARDs. Other bDMARDs such as rituximab were not permitted for use in patients with RA in Japan during the study period. Patients with RA fulfilled the 1987 American College of Rheumatology (ACR) or 2010 ACR/European League Against Rheumatism (EULAR) criteria. EORA was defined as RA onset at age 60 or older. YORA was defined as RA with onset between 18 and 59. Baseline demographic data including age, sex, tender joint count, swollen joint count, patient global assessment (PtGA), physician global assessment (PGA), baseline disease activity (CDAI), disease duration of RA, type of bDMARDs, number of previously administered bDMARDs, reasons for discontinuation of bDMARDs, dates of both starting and discontinuing bDMARDs, concomitant use of methotrexate (MTX), glucocorticoids, sulfasalazine, and other csDMARDs such as leflunomide, bucillamine, iguratimod, and tacrolimus were collected. Baseline disease activity was defined as an activity measured at the time of bDMARD initiation. Other baseline demographic features such as rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) positivity, and modified Health Assessment Questionnaire disability index (mHAQ-DI) score were also collected. Drug retention was retrospectively evaluated as the time until definitive treatment interruption. Temporary discontinuations followed by reintroduction of the same medication were not recorded as discontinuations. As a part of requirement for cohort participation, physicians were mandated to report a reason for discontinuation of bDMARDs. The reasons for

discontinuation were as follows; drug inefficacy, achievement of clinical remission, toxic adverse events, patient preference (including financial reason), loss to follow up, and other. The primary outcome was CDAI score at 48 weeks. The secondary outcomes included achievement of CDAI remission, a composite outcome of low disease activity (LDA) or remission, and bDMARDs retention and adverse even at 48 weeks after initiated a bDMARD.

The study was approved by the ethics committee of Kobe University (approval number 1738) as well as the ethics committees of all participating institutions. The study was conducted in accordance with the Declaration of Helsinki. In our institute, the institutional review board waived the requirement for patients' informed consent because this study utilized only existing data collected in clinical practice. The opportunity to refuse participation in the research was ensured for the research subjects. The study was approved by the institutional review board of all 7 institutes.

Statistical Analysis. A propensity score approach was used to account for differences in potential confounding factors and predictors of outcome. Logistic regression model was used to calculate the propensity score defined as the probability of age at RA onset based on patient covariates. Prespecified potential confounding factors and predictors of the outcome were age, sex, RA duration, baseline disease activity, RF and ACPA positivity, mHAQ-DI, concomitant glucocorticoid, MTX, and csDMARDs, type of bDMARD (TNFi versus non-TNFi), and number of previously administered bDMARDs [7,9,11,17]. The analyses were based on basic stabilized inverse probability weighting to reduce the variability of weights and standard errors of estimated treatment effects. When covariate balance showed standardized differences were 10% or more, the

covariates were also included in subsequent marginal models. We used a generalized estimating equation (GEE) model incorporating inverse probability weighting for CDAI and remission, and the marginal structural Cox model for bDMARD retention and adverse events to account for clustering effects by individual and time-varying covariates [19]. Missing data on the outcomes of patients who discontinued their participation before 48 weeks were imputed using a last observation carried forward analysis. Statistical analyses were performed using SAS version 9.3 and R version 3.4.1 (R Development Core Team, Vienna, Austria). $P < 0.05$ were considered statistically significant.

RESULTS

Patient Characteristics. Among a total of 7183 patients in the registry, 2815 (39.2%) were identified as EORA. The proportion of patients on bDMARDs was lower in the EORA as compared to the YORA (18.3 % vs 28.0 %, $p < 0.001$). Of the 989 bDMARDs initiators, 364 (36.8%) were identified as EORA (Table 1). The mean age of EORA at the time of bDMARD initiation was 72.8 years while that of YORA was 54.5. The EORA group had more males, shorter disease duration, and a lower percentage of RF positivity. The percentage of ACPA positivity was similar between the two groups. The EORA had significantly higher baseline DAS28-ESR, SDAI, and mHAQ-DI score compared with the YORA while the baseline CDAI score was similar between the two groups. MTX usage was less frequent, and lower MTX dosage was used in the EORA. Glucocorticoid usage was similar between the two groups. Sulfasalazine was used more

frequently in the EORA. The EORA group received bDMARDs as the first agent more frequently as compared to the YORA.

Figure 1 shows an overall bDMARDs selection by the age group. Approximately half of patients received TNFi in both groups. Abatacept was chosen more frequently (29% vs 20%, $p=0.03$) while tocilizumab was chosen less frequently (16% vs 23%, $p=0.009$) in the EORA as compared to the YORA. The use of JAKi was less common in both groups.

Age RA onset and clinical effectiveness at 48 weeks. Of the 989 bDMARDs initiator, 79.3% (784/989) had the outcomes at 48 weeks. The median follow-up duration was 48 weeks both in the EORA and the YORA. After adjusting for differences in baseline characteristics between the two age groups, there was no significant difference in Clinical Disease Activity Index scores at 48 weeks (mean difference 1.01, 95%CI=-0.62-2.64, $p=0.22$) (Table 2). There was a non-significant trend toward lower remission in EORA (OR=0.52, 95%CI=0.24-1.14, $p=0.10$), and low disease activity/remission was similar (OR=0.86, 95%CI=0.29-2.52, $p=0.77$).

We also conducted additional analyses that included only disease duration without age to estimate propensity score because it is logically impossible to adjust both age and disease duration simultaneously based on the definition of EORA. The standardized mean difference in disease duration between EORA and YORA was -0.073 indicating an adequate balance between the two age groups. The analysis using a GEE model incorporating inverse probability weighting showed no significant difference in CDAI score at 48 weeks between the two age groups (mean difference -0.41, 95% CI= -10.90-2.76, $p=0.91$).

Drug retention and adverse events. Overall, 136 (37.4%) and 243 (38.8%) treatment courses were stopped by 48 weeks in the EORA and YORA, respectively. A total of 27 (7.4%) and 51 treatment courses (8.2%) were stopped in each group due to adverse events. Drug retention (HR=0.95, 95%CI=0.55-1.35, p=0.78) and adverse events discontinuation (HR=0.78, 95%CI=0.38-1.18, p=0.22) were similar between the two age groups after adjustment for other confounders (Figure 2).

DISCUSSION

In this analysis of a large Japanese RA registry, there was no significant difference in clinical improvement at 48 weeks between EORA and YORA patients who initiated bDMARDs. In addition, drug retention and adverse events discontinuation was similar between the two age groups, suggesting bDMARDs can be used as effectively and safely in patients with EORA as those with YORA. To the best of our knowledge, this is the first report in the real-world setting comparing the efficacy and safety of overall bDMARDs between the two groups.

Our results have important clinical implications. As previously described, EORA patients can present with more severe disease activity than the YORA [16]. However, as our study and previous studies showed, EORA patients may not be treated with bDMARDs as commonly as younger individuals [32]. Delays in effective therapy may be associated with uncontrolled inflammation and subsequent joint destruction, leading to a negative impact on physical function and development of comorbidities. Furthermore, a recent study reported the prevalence of sarcopenia was relatively high at 37.1% in patients with RA, and age was one of the risk factors while the use of bDMARDs was

protective for sarcopenia [31]. Therefore, this study suggests that it is reasonable to initiate effective treatments such as bDMARDs in EORA patients with active disease given that they are at risk of developing rapid decline of physical function, and the efficacy and safety of bDMARDs can be comparable between EORA and YORA.

We found there was no significant difference in CDAI improvement at 48 weeks between the EORA and YORA. Our finding is consistent with previous post hoc analyses of randomized control trial that showed efficacy of TNFi (etanercept, infliximab, or adalimumab) in patients with EORA [1,23]. The efficacy was similar across all age groups in contrast to the results of large cohort studies that enrolled patients with longstanding RA [2,10,13,15,28]. These results indicate that disease duration may have a greater impact on outcomes than onset age.

Although the proportion of patients achieving LDA or remission was similar between the two groups, there was a non-significant trend toward less remission in the EORA. This difference could be due to a presence of comorbidities such as knee osteoarthritis in the EORA that can negatively impact PtGA despite effective treatment of bDMARDs. In fact, our results showed mean PtGA visual analogue scale at 48 weeks was significantly higher in the EORA as compared to the YORA (36.1 vs 31.5, $p=0.02$). However, mean tender joint counts (1.3 vs 1.4, $p=0.64$), mean swollen joint counts (1.1 vs 1.1, $p=0.69$), and mean PGA visual analogue scale (12.7 vs 12.3, $p=0.73$) at 48 weeks were similar between the two groups. In such patients, LDA can be an alternative and valid treatment target.

Drug retention and adverse events discontinuation was similar between the EORA and YORA in our population. The sub-analysis showed adverse events rates due to

infections were also similar between the two groups. Our results are in support of a previous observational study that reported a similar safety profile of TNFi between the two groups [13,24]. Although there are other observational studies indicating an increased risk for adverse events or infections in elderly patients treated with TNFi compared with younger patients [4,10], such discrepancies could arise from differences in study population since most studies assessed the safety profile of young-onset RA who had relatively long disease duration. Nevertheless, providers should choose wisely which patients with EORA are safely treated with bDMARDs given that they can be susceptible to infections due to concomitant comorbidities. Conversely, it is important to keep in mind that physical dysfunction in EORA patients may worsen without timely and effective treatment.

The present study had some limitations. First, a selection bias might have occurred given the nature of a retrospective cohort study. Healthier patients in the EORA group could be selected more frequently for bDMARD treatment than those with YORA. However, we have adjusted for available confounders such as disease duration, baseline disease activity, mHAQ-DI, or concomitant use of glucocorticoid between the two groups. Second, the study population was predominantly Japanese. Our results may not be generalizable to other patient populations due to differences in patient factors or practice patterns. Third, disease activity criteria were used for outcome assessments in the present study while response criteria remain standard outcome measures for clinical trials. The strengths of this study include a large multi-center cohort of RA patients with prospectively collected detailed longitudinal clinical data including both clinical outcomes and adverse events, and also a more sophisticated statistical model adjusting for

potential confounders using GEE model incorporating inverse probability weighting and the marginal structural Cox model.

In conclusion, in RA patients initiating a bDMARD, improvements in clinical disease at 48 weeks were comparable between EORA and YORA. Drug retention and adverse events discontinuation was similar between the two age groups. Further investigation is warranted in other datasets to draw more conclusive estimates on the efficacy and safety of bDMARDs in patients with EORA.

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TABLE 1.

Clinical characteristics of elderly-onset RA and young-onset RA patients at initiation of bDMARDs

Characteristic	EORA (<i>n</i> = 364)	YORA (<i>n</i> = 625)	P-value
Age, median years (IQR)	73 (67-77)	56 (45-65)	<0.001
Female sex, <i>n</i> (%)	266 (73.2)	528 (84.5)	<0.001
Disease duration, median years (IQR)	3 (1-6)	8.5 (2-16.5)	<0.001
RF-positive, <i>n</i> (%)	268 (73.7)	513 (82.1)	0.002
ACPA-positive, <i>n</i> (%)	306 (84.2)	531 (84.9)	0.78
TJC, median (IQR)	3 (2-7)	4 (2-7)	0.59
SJC, median (IQR)	3 (2-6)	3 (1-6)	0.36
PtGA VAS (0-100mm), median (IQR)	63 (42-78)	60 (37-74)	0.09
PGA VAS (0-100mm), median (IQR)	38 (23-57)	38 (24-60)	0.73
DAS28-ESR, median (IQR)	4.9 (4.2-5.9)	4.7 (4.0-4.7)	0.001
SDAI, median (IQR)	19 (14-29)	19 (13-27)	0.11
CDAI, median (IQR)	17 (12-25)	17 (12-24)	0.48
mHAQ-DI, median (IQR)	1 (0.50-1.38)	0.63 (0.25-1.13)	<0.001
MTX use, <i>n</i> (%)	210 (57.8)	402 (64.4)	0.05
MTX dosage (mg/week), median (IQR)	8 (6-10)	10 (6-12)	0.04
Glucocorticoid use, <i>n</i> (%)	152 (41.9)	257 (41.1)	0.90
Glucocorticoid dosage (mg/day), median (IQR)	5.0 (3.5-7.5)	5.0 (3.0-7.5)	0.87
Sulfasalazine use, <i>n</i> (%)	91 (25.1)	87 (13.9)	<0.001

Other DMARDs use, n (%)	75 (20.7)	150 (24.0)	0.23
1 ST bDMARD (%)	247 (63.2)	371 (52.8)	<0.001
2 nd bDMARD (%)	74 (18.9)	161 (22.9)	0.12
>3 rd bDMARD (%)	70 (17.9)	171 (24.3)	0.01

Data are no. (%) patients or median IQR

Demographic and clinical characteristics at initiation of bDMARDs summarized as median for continuous data and as numbers (percentages) for categorical data. T-test or Wilcoxon signed-rank test and the chi-squared test were used to compare the clinical characteristics between the 2 groups for continuous variables and categorical variables, respectively. bDMARDs biological disease-modifying antirheumatic drugs, CDAI clinical disease activity index, DAS28-ESR Disease Activity Score 28-erythrocyte sedimentation rate, EORA elderly-onset rheumatoid arthritis, mHAQ modified Health Assessment Questionnaire, MTX methotrexate, ACPA anti-citrullinated protein antibodies, PtGA patient global assessment, PGA physician global assessment, RF rheumatoid factor, SDAI simplified disease activity index, SJC swollen joint count, TJC tender joint count, YORA young-onset rheumatoid arthritis, VAS visual analogue scale

TABLE 2.

Outcome comparisons at 48 weeks between EORA and YORA

	Mean difference	95% CI	P-value
Primary outcome			
CDAI	1.01	-0.62 to 2.64	0.22
Secondary outcomes			
TJC	0.20	-0.60 to 1.00	0.62
SJC	0.33	-0.36 to 1.01	0.35
PtGA VAS	2.81	-6.01 to 11.63	0.53
PGA VAS	2.91	-0.91 to 6.74	0.14
SDAI	0.99	-1.11 to 3.09	0.87

A generalized estimating equation model incorporating inverse probability weighting was used to compare the outcomes between the two groups. CDAI clinical disease activity index, elderly-onset rheumatoid arthritis, PtGA patient global assessment, PGA physician global assessment, SDAI simplified disease activity index, SJC swollen joint count, TJC tender joint count, YORA young-onset rheumatoid arthritis, VAS visual analogue scale

Figure 1. Overall bDMARD selection by the age group. EORA=elderly-onset rheumatoid arthritis, YORA=young-onset rheumatoid arthritis, ABT = abatacept, ADA = adalimumab, CZP = certolizumab pegol, ETN = etanercept, GLM =golimumab, IFX = infliximab, JAKi= Januse kinase inhibitors, TCZ = tocilizumab

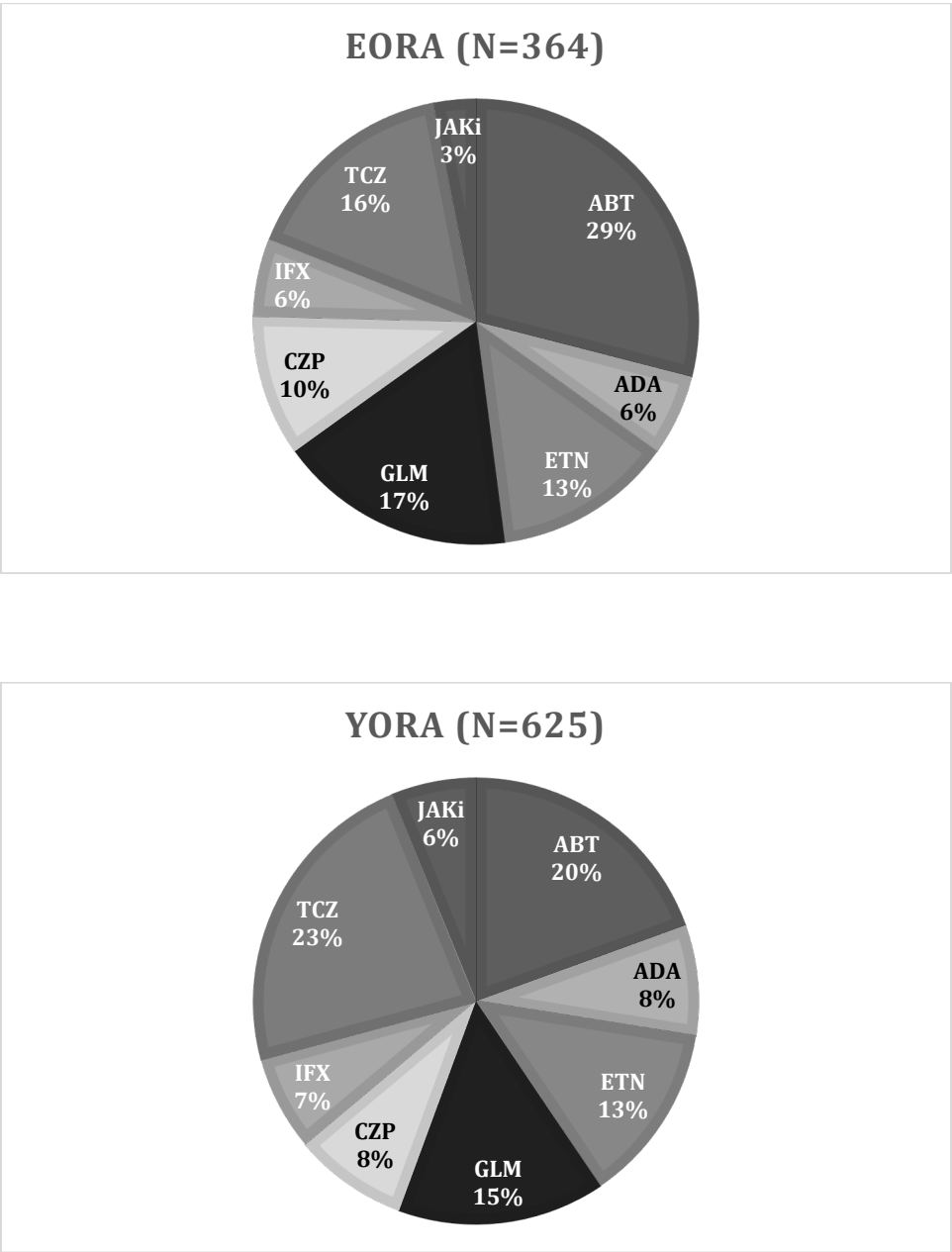
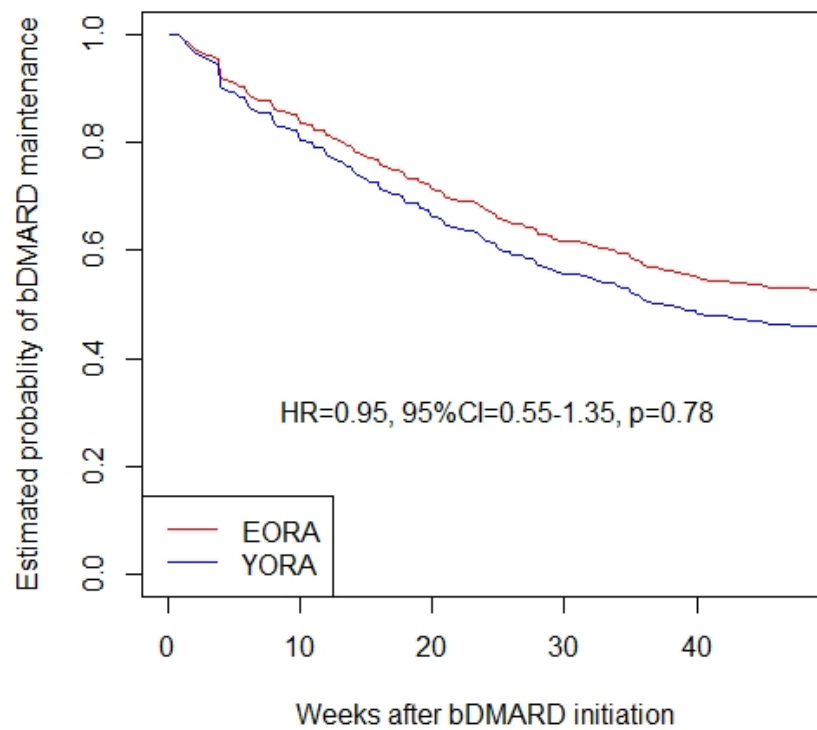


Figure 2. Adjusted drug retention and adverse event among EORA and YORA patients EORA=elderly-onset rheumatoid arthritis, YORA=young-onset rheumatoid arthritis

A. Adjusted drug retention between EORA and YORA



B. Adjusted adverse event between EORA and YORA

