OP0061 TIGHT CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TARGETED THERAPIES ACROSS THE COVID-19 PANDEMIC ERA

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Background: The ongoing coronavirus disease 2019 (COVID-19) pandemic and subsequent waves still represent a healthcare issue. Their impact on the treat-to-target (T2T) strategy in rheumatoid arthritis (RA) patients has been seldom investigated. Difficult access to rheumatology outpatient clinic, laboratory and imaging investigations as well as nationwide containment measures could potentially affect disease activity and tight-control strategy. Recently, we reported how a telephone-based tight control strategy ensured satisfactory management of RA treated with targeted therapies during the first wave of the pandemic [1]. However, the performance of our different patterns of healthcare delivery across different pandemic waves has not been studied yet.

Objectives: To analyze the impact of different patterns of healthcare delivery on remission of RA patients treated with targeted therapies during the first wave (2020) and second/third waves (2021) of pandemic compared to the pre-pandemic period (2019).

Methods: In this observational real-life study, data of our cohort of RA patients treated with biologic or targeted synthetic drugs were extracted from a longitudinal registry. Clinical Disease Activity Index (CDAI) was analyzed in the same period from 22nd of February to 18th of May for three consecutive years: before the pandemic (2019), during the first wave (2020), and during the second/third waves (2021). During the first wave, patients could choose whether to receive home drug delivery or to maintain their face-to-face visits, in the other periods only in-person visits were delivered. A generalized linear model with the binomial error was fitted to evaluate the difference in the proportion of patients in CDAI remission. Quantile regression was used to compare the median of CDAI in difficult-to-treat (D2T) patients [2]. In both models, the correlation of different measurements on the same patient was considered.

Results: In the pre-pandemic period (2019), 407 RA patients were included in this study. During the first wave (2020) we analyzed 450 patients, of whom 359 patients chose in-person visits, while 91 patients home drug delivery and virtual visit. Finally, 540 patients were included in 2021 (second/third wave). The percentages of patients in CDAI remission were similar in the three periods (prevalence ratio 1.07, p-value 0.423 between 2020 and 2019, and 1.01, p-value 0.934 between 2021 and 2019). The CDAI remission rate was 40.55% (N=163), 43.18% (N=155) and 40.82% (N=220) in 2019, 2020 and 2021, respectively. The disease activity profile during the three periods is reported in detail in the Table 1 below. Among our cohort of D2T patients, the median value of CDAI before (2019), during the first wave (2020), and during the second/third wave (2021) changed significantly (p= 0.053 between 2020 and 2019 and p=0.006 between 2021 and 2019).

Table 1.

RA patients	CDAI	2019		2020		2021	
		No. missing	N (%)	No. missing	N (%)	No. missing	N (%)
	Remission	0	163 (40.55%)	89	155 (43.18%)	6	220 (40.82%)
	Low	0	151 (37.56%)	89	140 (39.00%)	6	227 (42.12%)
	Moderate/ high	0	88 (21.89%)	89	64 (17.83%)	6	92 (17.07%)

Conclusion: Although the pandemic has imposed changes in our healthcare delivery, these different strategies seem to be effective in ensuring satisfactory management of RA treated with targeted therapies. The approaches modulated in the context of the different periods have been a feasible compensation for ensuring disease control even in D2T patients.

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[1] Ann Rheum Dis 2021;80:1243-1245

[2] Ann Rheum Dis 2021;80:31–5.

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OP0062 EFFICACY AND SAFETY OF ADALIMUMAB WITH LOW AND HIGH DOSE-METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE: THE RANDOMISED CONTROLLED MIRACLE STUDY

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that causes not only joint pain but also bone destruction resulting in impairment of quality of life. Tumor necrosis factor inhibitors have improved prognosis of patients with rheumatoid arthritis dramatically, especially in combination with methotrexate, however, the optimal dose of the concomitant methotrexate is unclear.

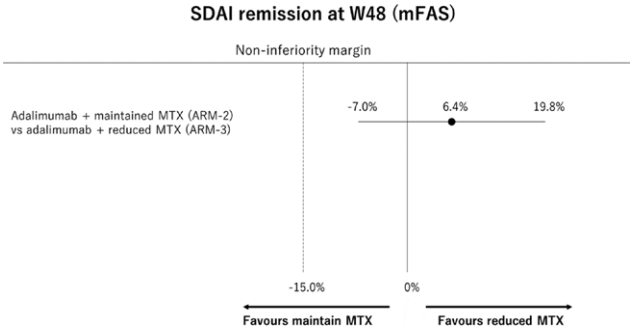
Objectives: To evaluate the efficacy and safety of adalimumab in combination with reduced dose of methotrexate in patients with early RA with inadequate response to methotrexate.

Methods: The MIRACLE study was a multinational, randomized, open-label study in patients with RA with inadequate response to methotrexate conducted in Asia. It compared low dose and high dose methotrexate upon starting adalimumab. Methotrexate-naive patients with RA with a disease duration of less than two years started methotrexate at 6 to 8 mg/week and increased it to the maximum tolerable dose by week 12. Patients who have not achieved remission according to simplified disease activity index (SDAI) despite methotrexate ≥ 10 mg/week at week 24 were randomised to the maximum tolerable dose of

methotrexate group (10 to 25 mg/week) or the reduced dose group (6 to 8 mg/week) and started to receive subcutaneous adalimumab 40 mg every other week. The primary endpoint was non-inferiority in the achievement of SDAI remission at week 48 in the reduced dose group compared with the maximum tolerable dose group with a non-inferiority margin of -15% based on two-sided 90% confidence interval. (NCT03505008)

Results: A total of 300 patients were enrolled in the study. Among them, 291 started methotrexate and were included in the analysis. The mean age was 57.7±15.2 years, female was 74.6%, and the mean disease duration from the diagnosis of RA was 21.1±56.2 days. Anti-CCP antibody was positive in 211 (73.0%) and the mean SDAI at study enrollment was 26.5±12.4. At week 24, with the mean dose of methotrexate of 12.6±2.9 mg/week, 108 patients (37.1%) achieved remission according to SDAI and continued MTX monotherapy. 134 patients (46.0%) were randomised and started adalimumab with 68 patients in the maximum tolerable dose group and 66 patients in the reduced dose group. At week 48, the remission achievement rates were 38.4 % and 44.8 %, respectively, with the adjusted risk difference of the reduced dose group to the maximum tolerable dose group of 6.4% (-7.0% to 19.8%, 90% CI), which met the criterion for noninferiority. No significant difference was found in health assessment questionnaire disability index ≤0.5 (59.1% vs 62.0%, respectively, p=0.72) and in radiological remission rates (Δmodified total Sharp score ≤0.5, 66.3% vs 62.0 %, respectively, p=0.59). Adverse drug reactions tended to be more frequent in the maximum tolerable dose group than in the reduced dose group (22.1% vs 9.1%, respectively, p=0.06).

Conclusion: The MIRACLE randomised study demonstrated that, in patients with inadequate response to methotrexate, the efficacy of adalimumab with reduced dose of concomitant methotrexate was not inferior to that with maximum tolerable dose of methotrexate with better safety profile.



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OP0063

OLOKIZUMAB IMPROVES PATIENT REPORTED OUTCOMES IN MODERATE TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS PATIENTS INADEQUATELY CONTROLLED BY METHOTREXATE (MTX-IR): RESULTS FROM THE PHASE 3 RANDOMIZED CONTROLLED TRIAL, CREDO 2

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Background: Olokizumab (OKZ) is an interleukin-6-inhibitor for treatment of Rheumatoid Arthritis (RA). In these analyses, we present patient reported outcomes (PROs) reported by MTX-IR patients with moderate to severely active RA treated with OKZ vs adalimumab (ADA) or placebo in a phase 3 randomized controlled trial (RCT) (ClinicalTrials.gov number, NCT02760407).

Objectives: To assess the effect of OKZ treatment compared with placebo and ADA in patient global assessment of disease activity (PtGA), pain, physical function (HAQ-DI), fatigue (FACIT-F) and health related quality of life (SF-36 physical (PCS) and mental (MCS) component summary and domain scores) and work participation (WPS-RA) at week 12.

Methods: 1648 patients receiving MTX were randomized to receive SQ injections: 1) OKZ 64 mg every 2 weeks (q2w, n=464), 2) OKZ 64 mg q4w (n=479), 3) ADA 40 mg q2w (n=462) and 4) placebo q2w (n=243). At week 14, non-responders: subjects without ≥ 20% improvements in both swollen and tender joint counts, added rescue medication (sulfasalazine and/or hydroxychloroquine) to study treatment. Between groups differences in least-squares mean (LSM) changes from baseline were analyzed.

Results: At week 12, treatment with both OKZ doses and ADA resulted in statistically greater LSM changes from baseline than placebo across all PROs, including 7 of 8 domains of SF-36 with exception of role emotional (Table 1 and Figure 1). Reported work and household work impairments, days productivities were reduced by half and missed household work days because of arthritis were all improved (p<0.01) with OKZ and ADA treatment. PROs further improved to week 24 in the active treatment arms. Post hoc analyses demonstrated that a higher proportion of patients receiving both doses of OKZ as well as ADA reported improvements ≥ minimum clinically important differences vs placebo (p<0.01) across all PROs, indicating clinically meaningful benefits on an individual patient basis. Estimates of numbers needed to treat indicated that between 5 and 10 patients would need to be treated to achieve these benefits. More patients in both OKZ groups reported scores ≥ normative values in PtGA, HAQ-DI and SF-36 PCS scores; with ADA in PtGA and HAQ-DI.