Figure 2: Changes of peripheral lymphocyte subsets after immune new regulatory combination therapies (n=1415). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. Absolute number of T, B, CD4+T, CD8+T, NK, Th1, Th17 and Tregs were significantly increased (A and B). The proportion of B, Th1, CD4+T and Tregs were also increased (C and D), while the ratio of Tregs/Tregs such as Th2/Tregs and Th17/Tregs had a tendency to decrease after immune new regulatory combination therapies (E). *P<0.05, **P<0.01, ***P<0.001.

Acknowledgments: None.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.2138

AB0347 INCREASING TO OPTIMAL METHOTREXATE DOSE MIGHT BE A BETTER TRADITIONAL DMARD STRATEGY IN RA TREATMENTS: A RANDOMIZED CASE-CONTROL TRIAL OF HAKKA PEOPLE IN SOUTHERN CHINA

D. Lin¹, Y. Wen², Y. Zhang¹, Q. Chen², Y. Pan¹, L. Qing¹, J. Gu¹. ¹The 3rd Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; ²The 3rd Affiliated Hospital of Sun Yat-sen University Yuedong Hospital, Meizhou, China

Background: The optimal methotrexate (MTX) dose is defined as 0.3mg/kg/week or ≥ 20mg/week at 6 months. [1] Considering average weight of Chinese, [2] the optimal MTX should be >15mg/w. However, not more than 30% in 25191 RA cases ever had MTX treatment in CREDIT (Chinese Registry of Rheumatoid arthritis). [3] The biggest concern is side effects of MTX. Our study is to investigate whether increasing MTX would get better results accompanied with more side effects to Chinese people. **Objectives:** Hakka people have the purest genes of the majority people-Han in China. It is planned to recruit 160 RA patients in Meizhou, where is a gathering place of Hakka people.

Methods: The RA volunteers had no relief with 10mg/w oral dose of MTX with/without other 1-2 inadequate dose of DMARDs for at least 3 months. They were randomly divided into 1:1 groups. The experimental group would be treated with original DMARDs and incremental MTX (gradually increased to the optimal oral dose (0.3mg/kg/w) in the first 12 weeks and folic acid (the dose adjusted on demand with range from 5mg/w to 5mg tid). While the control group would be treated with original MTX dose(10mg/w) but incremental original DMARDs(gradually increased to the maximum dose in the first 12 weeks). The two groups would keep the treatment at 12th week last to the 36th week, and the efficacy and safety indexes would be evaluated during the whole study.

Results: 1)We planned to recruit 160 RA patients in our study. 46 Hakka RA patients were enrolled in the study so far. 2 of 46 finished the 24th week visit and 24 finished the 36th week visit. The average age is 54.2± 9.3 years old, the average weight is 59.1±11.1kg, and the female to male ratio is 41:5.

2)The average Folic acid dose is 14.4±9.5mg/w in the experimental group at the 12th week.

3)The morning stiffness time, PGA, PhGA, HAQ, DAS28 were better in experimental group after 12 weeks though slightly worse during 0-12 weeks. 100%(12) patients in experimental group, while 66.67%(8/12) in control group reach ACR20. 4) Only 1 case(5.9%,1/23)had adverse event while 6 cases (26%,6/23) occurred adverse events. All events were mild level. 1 case (4.2%, 1/23) in control group withdrew from the study because the disease was getting worse during 0-24 weeks.

Conclusion: Hakka patients in China might have better outcomes due to increasing MTX to the 0.3mg/kg/w dose than increasing the other DMARDs. Therefore, we recommended the Chinese patients choose MTX as first incremental DMARD. The appropriate dose of Folic acid plus with the optimal dose of MTX in our study is higher than previous studies (such as 13.0±4.8mg/w reported by Gaujoux-Viala, 2018[1]). We recommended Chinese patients take 15mg/w folic acid to prevent MTX side effects in view of lower folic acid level in Chinese population.[3]

References:

- Gaujoux-Viala C, Rinccheval N, Dougados M, et al. Optimal methotrexate dose is associated with better clinical outcomes than non-optimal dose in daily practice: results from the ESPOIR early arthritis cohort. *Ann Rheum Dis.* 2017 Dec;76(12):2054-2060.
- Nan Jiang, Mengtao Li, Yanhong Wang, et al. Baseline characteristics and treatments among patients with rheumatoid arthritis: the CREDIT study in China, 2016-2018. *Ann Rheum Dis.* 2019 Jun; 78 (Suppl 2) 1404-1405.

- He Y, Pan A, Hu FB, et al. Folic acid supplementation, birth defects, and adverse pregnancy outcomes in Chinese women: a population-based mega-cohort study. *Lancet.* 2016 Oct, Volume 388, Number 1, pp. S91-S91(1)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.2709

AB0348 THE EFFECTIVENESS AND SAFETY OF BARICITINIB AFTER INSUFFICIENT RESPONSE TO bDMARDs OR tsDMARDs IN PATIENTS WITH RA FROM JAPANESE MULTI-CENTER REGISTRY: 24-WEEK OUTCOMES

H. Masahiro¹, N. Takahashi², T. Kojima³ on behalf of TBCR. ¹Ichinomiya Municipal Hospital, Orthopedic Surgery / Rheumatology, Ichinomiya, Japan; ²Nagoya University Graduate School of Medicine, Orthopedic Surgery and Rheumatology, Nagoya, Japan; ³Nagoya University Graduate School of Medicine, Department of Orthopedic Surgery and Rheumatology, Nagoya, Japan

Background: EULAR has issued updated guidelines for the management of rheumatoid arthritis (RA) using conventional, biologic, and targeted synthetic DMARDs. In the 2019 update, the task force revised the preference of bDMARDs over tsDMARDs. In routine clinical practice, baricitinib is commonly used as second line or after. However, there is little information about the clinical efficacy and safety profile of baricitinib after failure of the previous agent, including another tsDMARD.

Objectives: The aim of this study was to evaluate the short-term effectiveness and safety profiles of baricitinib after insufficient response (IR) to bDMARDs or tsDMARDs in patients with RA in clinical settings.

Methods: RA patients who had been treated with baricitinib after failure of the previous agent were registered in the TBCR, a Japanese multicenter registry for RA patients treated with biologics or JAK inhibitors and followed for at least 24 weeks. Patients were divided into two groups according to the cause of failure of the previous treatment; IR ("After IR" group) and the others ("After non-IR" group). "After IR" group was further divided into four groups according to the previous agent; TNF inhibitor (TNFi group), IL-6 receptor inhibitor (IL-6Ri group), abatacept (ABT group) and tofacitinib (Tofa group). We assessed disease activities by CDAI score and drug retention rates between these groups. Furthermore, discontinuation rates due to IRs and adverse events (AEs) were evaluated.

Results: A total of 86 consecutive RA patients were registered in this study. The previous treatment was as follows; TNF inhibitor: 38 (44.2%), IL-6 receptor inhibitor: 23 (26.7%), abatacept: 11 (12.8%), tofacitinib: 13 (15.1%) and the other: 1 (1.2%). The cause of failure of the previous therapy were IRs (n=74: 86%), AEs(n=6: 7.0%) and the others (n=6: 7.0%). In "After IR" group, the most common

previous agents were TNFis (Table 1). While the percent change in CDAI was decreased at week 12 in all groups, those in Tofa group showed lower rates of improvement in CDAI compared to the others at week 24 (Figure 1). Drug retention rate at 24-week was 59.4% in TNFi group, 90.5% in IL-6Ri group, 54.5% in ABT group and 77.8% in Tofa group (Figure 2). In the present study cohort, seven patients developed herpes zoster. All seven patients were treated with antiviral agents for herpes zoster and restarted baricitinib treatment (these cases were not treated as discontinuation due to AEs in this study). The overall Cumulative discontinuation rate due to IRs and AEs at 24 weeks were 9.7% and 7.3%, respectively.

Table 1

Groups	Cases; n (%)
TNFi group	32 (43.2)
IL-6R group	21 (28.4)
ABT group	11 (14.9)
Tofa group	9 (12.2)
The other	1 (1.4)

Figure 1

Conclusion: In this study, we demonstrated the short-term effectiveness and safety profiles of baricitinib after insufficient response to bDMARDs or tsDMARDs in patients with RA in the 'real-world' setting. Baricitinib improved disease activity after failure of the previous agent, even after IR to another tsDMARD. With respect to safety, the profile is almost tolerable, although careful observation is necessary for possible complications and AEs including herpes zoster.

Disclosure of Interests: Hanabayashi Masahiro Speakers bureau: Astellas Pharma Inc., Mitsubishi Tanabe Pharma Corporation, Eisai Pharma Corporation, Chugai Pharma Corporation, abbvie, Bristol-Myers Squibb, Pfizer, Janssen Pharmaceutical K.K., Eli Lilly Japan K.K. and UCB Japan, Nobunori Takahashi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Janssen, Mitsubishi Tanabe, Ono, Pfizer, Takeda, and UCB Japan, Toshihisa Kojima Grant/research support from: Chugai, Eli Lilly, Astellas, Abbvie, and Novartis, Consultant of: AbbVie, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda

DOI: 10.1136/annrheumdis-2020-eular.6611

AB0349 EFFICACY OF TOFACITINIB THERAPY, DEPENDING ON THE USE OF DMARDs IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A REAL CLINICAL PRACTICE IN RUSSIAN FEDERATION.

A. Misiyuk¹, A. Lila¹, A. Gordeev¹, E. Galushko¹. ¹V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background:

Objectives: To evaluate how disease-modifying antirheumatic drugs (DMARDs) affects efficacy of tofacitinib (TOFA) therapy in patients with rheumatoid arthritis (RA).

Methods: We analyzed the history of 107 patients (mean age 51.4±12.1 yrs) with RA according to the 2010 ACR/EULAR criteria, from 11 regions Russian Federation, including patients who were treated at the V.A. Nasonova Research Institute of Rheumatology. These patients were non-responders to DMARDs, previously biologic therapy and were treated with TOFA in combination with DMARDs or without. 107 patients (77 woman (72%), tested positive for ACCP (76.5%)/RF (87.3%), the median disease duration was 7.5±6.6 years; the mean DAS28 score was 5.8±1.0, mean SDAI and CDAI score was 35.6±13.4 and 32.1±12.4 respectively) received TOFA for 12 months. TOFA therapy was started in all patients in dose 5 mg BID per os with escalation to 10 mg BID in 17.6% pts.

Results: The use of TOFA was accompanied by a decrease in the disease activity after 6 and 12 months of therapy. All patients were divided into 3 groups, depending on DMARDs therapy: TOFA+ methotrexate (MTX), TOFA+ another DMARDs (leflunomide, hydroxychloroquine, azathioprine), mono-therapy of TOFA. The dynamic of the disease activity in 3 groups is presenting on the table below:

Parameters	Weeks	TOFA+MTX (n=69)	TOFA+ another DMARDs (n=20)	TOFA monotherapy (n=18)
DAS28 (ESR)	baseline	5,9 ± 1,0	5,6 ± 1,1	6,0 ± 0,8
	6 months	3,5 ± 1,2*	4,1 ± 1,1*	4,2 ± 1,6*
	12 months	3,3 ± 1,0*	3,5 ± 1,3*	3,8 ± 1,2*
SDAI	baseline	36,2 ± 14,2	32,6 ± 9,5	35,3 ± 10,3
	6 months	14,4 ± 10,7*	16,7 ± 10,2*	27,3 ± 19,1*
	12 months	9,5 ± 8,0*	12,9 ± 8,6*	15,3 ± 10,2*
CDAI	baseline	32,4 ± 12,1	29,7 ± 8,9	33,2 ± 9,8
	6 months	13,3 ± 10,2*	15,6 ± 9,8*	22,4 ± 16,8*
	12 months	8,7 ± 7,6*	12,6 ± 8,2*	14,4 ± 9,6*

*p<0,05

Patients who received TOFA with MTX had lower disease activity during the therapy. Patients on mono-therapy of TOFA had higher disease activity according to DAS28, SDAI, CDAI.

Conclusion: Tofacitinib is effective ts-DMARDs for active rheumatoid arthritis on the Russian population. It shows better efficacy in combination with methotrexate, than in combination with another DMARDs (leflunomide and other) or in mono-therapy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6400

AB0350 EFFICACY OF ADDING IGURATIMOD THERAPY IN RHEUMATOID ARTHRITIS PATIENTS WHO HAD INADEQUATE RESPONSE TO BIOLOGIC DMARDs

T. Miyamoto^{1,2}, K. Yamazaki¹. ¹Seirei Hamamatsu General Hospital, Rheumatology, Hamamatsu, Japan; ²Seirei Hamamatsu General Hospital, Rheumatology, Hamamatsu, Japan

Background: Igaratimod (IGU) was newly approved in Japan in June 2012 and recommended by JCR guideline 2014 in the treatment of rheumatoid arthritis (RA). Although there have been efficacy of monotherapy and concomitant MTX in clinical trials, however, there have been no reports of concomitant biologic DMARDs (Bio).

Objectives: we investigated efficacy of concomitant IGU therapy in RA patients who had inadequate response to Bio at the author's institution.

Methods: Subjects were 107 patients adding IGU who had inadequate response to Bio from January 2014 to October 2018. Previous treatment Bio. was ADA. And baseline mean concomitant MTX was 12.3 mg/week. And baseline characteristics were Mean age 53.8 years, mean duration of illness 5.5 years, corticosteroid use 9.3% (mean 3.1 mg/day).

The course of DAS28, SDAI, CDAI and remission rates were analyzed.

Results: Mean DAS28-ESR, SDAI, CDAI were significantly decreased from the initiation of IGU treatment at 24 weeks (3.1→2.3, 7.1→2.7, 6.5→2.4), at 52 weeks (2.1, 2.4, 2.0). Remission rates of DAS28-ESR, SDAI, CDAI were 69.2%, 68.2%, 70.1% at 24 weeks, 74.8%, 78.5%, 79.4% at 52 weeks. There were no side-effect that must be stopped after adding IGU.

Conclusion: IGU might be a new RA treatment option for aiming remission in patients who had inadequate response to Bio.

References:

- [1] Hara M et al: Safety and efficacy of combination therapy of iguratimod with methotrexate for patients with active rheumatoid arthritis with an inadequate response to methotrexate: an open-label extension of a randomized, double-blind, placebo-controlled trial. *Mod Rheumatol.* 2014; 24: 410—418.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.459

AB0351 EFFICACY OF IGURATIMOD FOR RHEUMATOID ARTHRITIS IN ELDERLY PATIENTS

Y. Mochida¹, K. Harigane¹, T. Shimazaki¹, Y. Inaba², A. Nagaoka². ¹Yokohama City University Medical Center, Center for Rheumatic Diseases, Yokohama, Japan; ²Yokohama City University, Department of Orthopaedic Surgery, Yokohama, Japan

Background: Igaratimod (IGU) was started development as new non-steroidal anti-inflammatory drugs (NSAIDs), but it was changed for development as disease modifying antirheumatic drugs (DMARDs) because it showed suppression of inflammatory cytokine and inflammatory parameter which was not to be found in existing NSAIDs in the early stage of pharmacological study of drug efficacy. Although the clinical efficacy and the safety of IGU were already reported, the efficacy for elderly cases was not sufficiently analyzed.