TB cases occurred with tofacitinib treatment. One malignancy (thyroid cancer) was reported. Severe (>3 ULN) elevation of liver enzymes or increases of CPK above normal were infrequent (<1%); no severe cytopenias were reported. Lipid increases occurred in 10% of pts. Tofacitinib was withdrawn in 40 pts (13.9%) due to lack of efficacy (n=20; 7%), AEs (n=11; 3.8%) or other reasons (n=9; 3.1%), such as loss of follow-up, pregnancy, access issues or travel. Limitations include limited pt numbers and follow-up of exposure.

Conclusions: In the RW LA setting, tofacitinib was used mostly as 2nd-line therapy; no new safety signals emerged vs clinical trials. SIEs and HZ were uncommon; no cases of TB/other OIs occurred, but were seen in the clinical program.

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AB0420 THE SAME TREATMENT RESPONSE OF MONO- AND COMBINED-MTX TREATMENT IN DMARDS-NAÏVE TURKISH PATIENTS WITH SEROPOSITIVE RHEUMATOID ARTHRITIS AND THE IMPORTANCE OF PULMONARY TOXICITY

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Background: Methotrexate (MTX) is the anchor drug for the treatment of rheumatoid arthritis (RA). There are important guidelines suggesting mono-MTX treatment at first for pharmacologic treatment of RA (1,2). We thought that these recommendations should be evaluated in different geographic regions and ethnic groups because of genetic factors.

Objectives: Therefore, we aimed to compare the efficacy and adverse effect profile of mono-MTX and combined-MTX treatments in patients with DMARDs-naïve Turkish patients with seropositive RA.

Methods: Hundred patients with seropositive RA (mean age: 47.4±12.0 years, 63 females and 37 males) were included. Patients were excluded the past history of using for synthetic or biologic DMARDs or moderate-high dose steroid (>10mg/day), viral hepatitis, transaminase elevations, and other contra-indications for MTX. Then they were divided as mono-MTX (n=57) and combined-MTX (n=43) groups.

Results: There was no difference between groups in age (p=0.34), sex (p=0.104), age of onset (p=0.10), MTX-weekly dose (p=0.228), the score of DAS28 (p=0.783), RF level (p=0.473), and CCP level (p=0.592) at the beginning. Patients of combined-DMARDs group used higher dose of prednisolone than patients of mono-MTX group (p=0.011). The change of DAS28 scores was not different between groups. CRP levels of combined-MTX group were higher than mono-MTX group both beginning and at 6th month. The frequencies of adverse events were not different between groups. GI adverse events are the first line in both groups (28% vs.16.3%). The frequencies of dose decrease (7% vs. 14%) or stop (7% vs. 4.7%) for MTX were also not different between groups (p=0.288, p=0.257). The frequencies of other adverse effects were less than 5%. MTX dose decrease or stop have been moderately correlated with pulmonary involvement (r=0.4, p=0.02).

Conclusions: Both mono-MTX and combined-MTX treatment had similar efficacy and safety profile in Turkish patients with seropositive RA as reported in studies of other countries suggesting no any advantage of combined MTX compared to mono-MTX (3). The frequency of MTX-stopping in our study was similar to this systematic review (9%). As a conclusion, MTX should also be the first choice of the treatment of RA in our country. Pulmonary adverse events should not be ignored.

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AB0421 RAPAMYCIN REDUCES DISEASE ACTIVITY THROUGH RESTORING REGULATORY T CELL NUMBERS IN PATIENTS WITH ACTIVE REFRACTORY RHEUMATOID ARTHRITIS

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Background: $CD4^+CD25^+Foxp3^+$ T regulatory (Treg) cells play a key role in peripheral tolerance. Rapamycin was approved by the FDA to preserve renal allografts and to be efficacious in patients with several autoimmune diseases [1].

Objectives: To investigate the status of Treg cells in active refractory rheumatoid arthritis (RA) and the effects of rapamycin on patients with RA.

Methods: Forty-five active refractory RA patients were enrolled. Rapamycin was used at a dose of 0.5 mg every 2 days [the preliminary, open-label clinical trial of rapamycin (Clinical Trials.gov number: ChiCTR-IPR-17010307)]. Clinical improvement and immunological assessments were performed before 1st rapamycin dose and 12 weeks post treatment. Blood samples were obtained from RA patients and 75 healthy volunteers for estimation of $CD4^+$ T cell subsets.

Results: Two patients dropped out due to non-compliance. As compared to healthy controls (median of Treg cells: 33.32 cell/ul), the absolute counts of circulating Treg cells were significantly decreased in patients with active refractory RA (median: 27.17 cell/ul; P=0.046). While the median ratios of Th17/Treg cells in patients with active refractory RA (median: 0.26) were significantly higher than those of healthy volunteers (median: 0.19; P=0.029). No difference in the absolute counts of circulating Th17 cells and Th1 cells was observed between patients with active refractory RA and healthy subjects. Rapamycin treatment led to clinical improvement with the median post-treatment DAS28-ESR decreasing when compared to baseline (from 4.19 to 3.78) in active refractory RA patients. Sixteen patients (16/43 patients, 37.21%) achieved an EULAR moderate response and 6 patients (6/43 patients, 13.95%) reached good response at week 12. Rapamycin administration resulted in an increase in the absolute counts of Treg cells in active refractory RA patients, from a median of 27.17 cell/ul (at week 0) to 37.57 cell/ul (at week 12) (P=0.041). The ratios of Th17/Treg cells shows a reduction from a median of 0.26 at baseline to 0.20 at week 12, but the difference is not significant (P =0.376). No significant difference was observed in the absolute counts of circulating Th17 and Th1 cells after rapamycin treatment. Interestingly, we observed that Treg cells increased before the complete remission of the disease (DAS28 score <2.6) in patients with active refractory RA. At week 12, the mean dose of prednisone which refractory RA patients were receiving decreased from 11.98 mg/d to 8.31 mg/d, with a dose reduced by ≥30% than that at baseline. The categories of DMARDs use were also reduced (P<0.05). No serious adverse events was observed during the 12-week period of rapamycin treatment.

Conclusions: Reduced absolute number of Treg cells was found in the patients with active refractory RA, indicating an imbalance between Th17 and Treg cells. Rapamycin elicits rapid improvement of disease activity via restoring circulating Treg cells numbers in patients with active refractory RA.

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AB0422 1,25-DIHYDROXYVITAMIN D3 MODULATES T CELLS DIFFERENTIATION AND IMPACTS ON THE PRODUCTION OF ASSOCIATED-CYTOKINES FROM CHINESE HAN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Recent studies have suggested that vitamin D may play a role in select inflammatory diseases including rheumatoid arthritis (RA). Epidemiological studies suggest that there is an association between vitamin D deficiency and susceptibility to RA.

The present study sought to investigate effects of 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) on T cells differentiation and associated cytokines in Chinese Han patients with early rheumatoid arthritis (RA). The results reported that 1,25(OH)2D3 inhibits the synthesis of Th1 cytokines IFN-γ, Th17 cytokines IL-17, IL-22, IL-6, TNF-α, and up-regulates Th2 cytokine IL-4, which indicated that the possible immunoregulatory role and bone-sparing effects of 1,25(OH)2D3 in RA through modulation of the Th1/Th17 and Th2 cytokine balance.

Objectives: To study effects of 1,25-dihydroxyvitamin D3 ($1,25(OH)_2D_3$) on T cells differentiation and associated cytokines in patients with early rheumatoid arthritis (RA).

Methods: The level of Th1, Th2, Th17 and Treg cell were detected with BDFACS Calibur flow cytometer. IFN-γ, TNF-α, IL-2, IL-4, IL-6, IL-10, IL-17 and IL-22 were examined in 54 patients with incipient RA using a cytometric bead array (CBA).

Results: After 72 hours of incubation of peripheral blood mononuclear cells (PBMCs) with $1,25(OH)_2D_3$ in RA patients, the levels of IFN-γ, TNF-α, IL-2, IL-6 and IL-17 significantly decreased compared to those of the control. $1,25(OH)_2D_3$ had no significantly impact on the levels of IL-4, IL-10 and IL-22. The levels of Th17 and the ratio of Th17/Treg significantly decreased in $1,25(OH)_2D_3$ treated