RAPAMYCIN INDUCES REMISSION IN PATIENTS WITH RIGHT VENTRICLE DIASTOLIC DYSFUNCTION IN RA

Background:
Th17/Treg cells have been reported to inhibit differentiation of Th17 and promote growth of FoxP3 (Treg) cells reduced in RA patients (EULAR Abstract). Moreover, rapamycin has been shown to reduce joint cartilage and bone. However, many patients do not achieve satisfactory disease control by current therapy with high risk of adverse reactions. We have reported that absolute number of peripheral regulatory T (Treg) cells reduced in RA patients (EULAR Abstract). Moreover, rapamycin has been shown to inhibit differentiation of Th17 and promote growth of FoxP3 + Treg cells by inhibiting mTOR pathway [1].

Objectives:
To observe the therapeutic efficacy of rapamycin on the reduction of disease activity, increase in Tregs and decrease in Th17 to restore balance of Th17/Treg cells in RA patients with high disease activity (DAS28 ≥2.6).

Methods:
Fifty RA patients who treated with two kinds of DMARDs for more than half a year did not achieve remission (DAS28 ≥2.6) were enrolled and were treated with rapamycin at a dose of 0.5 mg every 2 days for 24 weeks. The absolute number of CD4+ T cell subsets in peripheral blood from these patients were assessed by flow cytometry combined with internal standard beads before the treatment as baseline and at week 24 after treatment. Meanwhile, the DAS28, the dosage of corticosteroids and immunosuppressant were also recorded.

Results:
Rapamycin treatment reduced the disease activity and induced remission (DAS28<2.6) in 44.9% of active RA patients. Their DAS28 was reduced from a median 2.9 (at week 0) to 1.9 (at week 24) (P<0.001) and the absolute number of peripheral Treg cells was increased from 27.14±15.11 cells/μl (at week 0) to 36.59±17.23 cells/μl (at week 24) (P<0.002). The ratios of Th17/Treg cells also had a significant decrease from 0.36±0.29 at baseline to 0.27±0.20 at week 24 (P<0.041). In contrast, the decrease in the absolute number of Th17 cells was not statistically significant (P=0.846). After the treatment, the proportion of patients taking glucocorticoids decreased from 66.0% to 64.0% and the mean dosage of prednisone decreased from 8.89 mg/d to 7.70 mg/d. And the usages of DMARDs were also reduced (P<0.001).

Conclusions: Rapamycin combined with low level of conventional therapy effectively reduced disease activity and induced remission among RA patients who received long-term conventional treatment without remission (DAS28 ≥2.6) by increasing the absolute number of Treg cells and restoring the balance of Th17 cells and Treg cells. As the research progresses, rapamycin is likely to become a promising therapeutic candidate.

REFERENCE:

Disclosure of Interest: None declared

FR0064 RIGHT VENTRICLE DIASTOLIC DYSFUNCTION IN EARLY RHEUMATOID ARTHRITIS PATIENTS: RISK FACTORS AND THE EFFECT OF ANTI-RHEUMATOID THERAPY
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Objectives: To determine the frequency of diastolic dysfunction of the right ventricle (RVDD) in patients (pts) with early rheumatoid arthritis (RA) prior to therapy with basic anti-inflammatory drugs (DMARDs), examine its relationship with traditional risk factors of cardiovascular disease and markers of inflammation, to study the effect of anti-rheumatic therapy administered in accordance with "treat to target" (T2T) principles on RVDD in early RA pts during 18 month follow-up.

Methods: A total of 66 pts with early RA (ACR/EULAR criteria, 2010) were included: 71% of women, age 56±6.1 years, disease duration 6±9 months; DAS28 5.3 [5.0, 6.2], positive for ACCP (100%)/RF (87%), without prior administration of DMARDs and glucocorticoids. All pts underwent blood pressure monitoring (BP), echocardiography, tissue Doppler imaging. Methotrexate (MT) therapy was started in all pts with an escalation of the dose up to 30 mg/week subcutaneously. In case of no remission 3 months later, MT was added with biologic therapy (BT): Adalimumab, Certolizumab pegol, Abatacept, Rituximab. After 18 months 29 (44%) pts achieved remission. Antihypertensive therapy was administered in 51 (77%) pts: ACE inhibitors, ARBs, beta-blockers, calcium antagonists, diuretics.

Results: At baseline RVDD was detected in 16 (24%) pts. RVDD related factors that remained associated on a multivariable forward stepwise linear regression analysis were body mass index (BMI) (β-coefficient (95% CI) 0.3 [-0.003; -0.008], SDAI 0.2 [-0.009; -0.001], carotid atherosclerosis (CA) 0.2 [-0.3,0.01], disease duration 0.2 [-0.02,0.001]. Multiple coefficient of determination (R2) was 38% (p<0.03). After 18 months the incidence rate of RVDD decreased from 24% to 18%, p=0.05. The dynamics of diastolic function was multidirectional. RVDD was normalised in 10 (63%) of 16 RA pts with RVDD (p=0.02). All of them had effective control of BP and achieved remission, 67% of pts with normalised RVDD received MT+BT. 5 (31%) pts with new cases of RVDD and 6 pts with preserved RVDD did not reach the target values of BP and RA remission.

Conclusions: Presens of CA, higher BMI, SDAI and disease duration strongly associated with the incidence rate of RVDD. A significant decrease of RVDD in case of achieved targeted BP values and RA remission was observed during 18 month therapy of early RA pts in accordance with "T2T" principles.

Disclosure of Interest: None declared