Methods: Forty RA and AS patients treated with etanercept (ETN) or certolizumab pegol (CZP) were included in a 12-month follow-up study. Peripheral QCT and DXA BMD were determined. Bone biomarkers, such as PTH, osteocalcin, RANKL, 25-hydroxyvitamin D (VITD), P1NP, CTX, sclerostin, DKD-1 and cathepsin K (CATHK) were assessed by ELISA.

Results: There was no further bone loss during anti-TNF treatment. Volumetric and areal BMD showed significant correlations with each other (p<0.05). Total QCT BMD after 12 months was inversely determined by disease activity at baseline in the full cohort (p=0.030). Cortical BMD was negatively determined by baseline disease activity (p=0.005) and CATHK (p=0.025). In RA, VITD-0 determined QTRABMD-12 (p=0.005). In the full cohort, the one-year change in QTRABMD was related to TNF inhibition together with VITD-0 (p=0.031). Therapy and lower CATHK determined QCORRTMD changes (p=0.006). In RA, treatment together with VITD-0 (p=0.01) or CATHK-0 (p=0.002), while in AS, treatment together with RANKL-0 (p=0.05) determined QCT BMD changes.

Conclusion: QCT confirmed that biologics may attenuate bone loss. Disease activity, CATHK, RANKL and VITD may predict the effects of anti-TNF treatment on volumetric BMD changes. There may be differences between RA and AS in this aspect.

Acknowledgements: This research was supported by Hungarian National Scientific Research Fund (OTKA) grant No. K 105073 (H.P.B. and Z.S.); by the European Union and the State of Hungary and co-financed by the European Social Fund in the framework of TAMOP-4.2.4.A/2-11/1-2012-0001 ‘National Excellence Program (Z.S.); by the European Union grant GilOP-2.3.2-15-2016-00050 (Z.S.); and by the Pfizer Investigator Initiated Research Grants no. WS1895414 and WS1696540 (Z.S.).

Disclosure of Interests: Balázs Juhász: None declared, Katalin Gulyás: None declared, Agnes Horváth: None declared, Edit Végh: None declared, Anita Pusztai: None declared, Agnes Szentpetery: None declared, Zsófia Pethö: None declared, Nóra Bodnár: None declared, Attila Hamar: None declared, Levente Bodoki: None declared, Harjjit Pal Bhattas: None declared, Eva Szekanecz: None declared, Katalin Hodosi: None declared, Andrea Domján: None declared, Szilvia Szamosi Speakers bureau: Roche, Csaba Horváth: None declared, Sándor Szántó Speakers bureau: Abbvie, MSD, Novartis, Consultant of: Abbvie, Novartis, Gabriella Szücs Speakers bureau: Roche, Boehringer, Actelion, Sager, Consultant of: Actelion, Boehringer, Hennie Raterman: None declared, Willem Lems Speakers bureau: Pfizer, Amgen, Lilly, UCS, Galapagos, Consultant of: Pfizer, Amgen, Lilly, UCS, Galapagos, Oliver FitzGerald Speakers bureau: Abbvie, Janssen, Pfizer, Consultant of: BMS, Celgene, Eli Lilly, Janssen, Pfizer, Grant/research support from: Abbvie, BMS, Eli Lilly, Novartis, Pfizer, Zoltán Szekanecz Speakers bureau: Pfizer, Roche, Abbvie, Novartis, Lilly, Sanofi, Consultant of: Pfizer, Abbvie, Novartis, Grant/research support from: Pfizer, UCS.

DOI: 10.1136/annrheumdis-2021-eular.1951

POS0044

T315 SUPPRESSES OSTEOGENIC DIFFERENTIATION IN SAOS-2 CELLS BY INHIBITING PHOSPHORYLATION OF AKT

Z. Huang1, X. Huang1, Y. Huang1, Z. Li2, Q. Huang1, T. Li2, Guangdong Second Provincial General Hospital, Department of Rheumatology and Immunology, Guangzhou, China.

Background: New bone formation is common in the late stage of various inflammatory arthritis, while osteoblasts play a vital role in this process. Activation of PI3K/Akt pathway promotes the differentiation and enhances the function of osteoblasts [1]. T315 is a novel small molecule drug, which may induce apoptosis and suppress the expression of cellular markers of chronic lymphocytic leukemia cells by disrupting PI3K/Akt pathway [2]. However, the lack of study focuses on the influence of T315 on the osteoblasts, except tumor cell lines.

Objectives: We aimed to assess the effect of T315 on human osteoblast-like Saos-2 cells, while its potential mechanism in PI3K/Akt pathway was evaluated as well.

Methods: (1) Saos-2 was stimulated with an osteogenic reagent which contained L-ascorbic acid, β-glycerophosphoric acid, and dexamethasone. The concentration of T315 was adjusted to 0μg/ml, 1μg/ml, and 2μg/ml in the culture medium. (2) Alizarin red stain and alkaline phosphatase (ALP) stain were performed at d0, d7, d14, and d21 after being treated with T315. (3) Cellular protein was extracted at d0, d3, and d6 after being treated with T315, then ALP activity was tested based on a recommendation from the manufacturer of the kit. (4) Colagen type 1ν2 Chain (Col1ν2) and osteocalcin (OCN), two osteogenic markers, were measured through western blot, with glyceraldehyde 3-phosphate dehydrogenase (GAPDH) as an endogenous control. (5) Phospho-phosphoinositol 3-kinase (pPI3K), phospho-protein kinase B (pAkt), and runt-related transcription factor 2 (Runx2) was tested through western blot as well. GAPDH or protein kinase (Akt) was chosen as an internal reference as appropriate. (6) Analysis of variance with the least significant difference was used to analyze the data. A P<0.05 was considered statistically significant.

Results: The higher concentration of T315 related to the lower mineralized area and the positive area of ALP, while longer incubation time with T315 decreased these regions as well (Figure 1A-C). (2) T315 reduced the activity of ALP accordingly (Figure 1D); (3) T315 suppressed the protein expression of Col1ν2 and OCN in a dose-dependent and time-dependent manner (Figure 1E, F). (4) T315 did not alter pPI3K, but it inhibited the phosphorylation of Akt (Figure 1G, H). (5) Runx2 was reduced because of the greater dose or longer incubation time with T315 (Figure 1).

Conclusion: T315 inhibits the differentiation of osteoblasts through inhibiting the phosphorylation of Akt. Surprisingly, pPI3K seldom changes in this process, so its detail mechanism should be investigated in further.

REFERENCES: