Stable bone turnover markers corrected for age and gender during the first year of secukinumab treatment in radiographic axial spondyloarthritis

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Interleukin-17 inhibitors (IL17i) are effective treatment for radiographic axial spondylarthritis (r-axSpA), in which bone-related outcome is important. However, data on the effect of IL17i on bone metabolism are scarce (1). Therefore, our goal was to evaluate bone turnover markers (BTM) and bone regulators during one year of secukinumab treatment in r-axSpA patients in daily clinical practice.

We included r-axSpA outpatients who fulfilled the ASAS classification criteria and participated in the GLAS cohort, who started treatment with secukinumab because of active disease between April 2016 and June 2020, and had available serum samples at baseline and at ≥1 follow-up visit (3, 6, 12 months) during treatment. Demographic and clinical assessments were obtained from regular GLAS outpatient visits (2). The GLAS cohort was approved by the local ethics committees of the UMCG and MCL. All patients provided written informed consent.

Serum markers of collagen resorption (serum C-telopeptide of type I collagen: sCTX), bone regulation (osteocalcin: OC), collagen formation (procollagen type 1 N-terminal peptide: PINP) and bone mineralization (bone-specific-alkaline phosphatase: BALP) were measured and expressed in Z-scores (the number of SD from the normal mean corrected for age and gender). Laboratory evaluation of BTM has been described previously (3). Additionally, bone regulators sclerostin, a WNT bone formation signalling pathway inhibitor, and OPG, a bone resorption and osteoclastogenesis inhibitor, were measured by ELISA (R&D Systems and Biomedica Medizinprodukte GmbH). Statistical analysis was performed with SPSS Statistics 23. Generalised estimating equations were used to analyse BTM Z-scores over time within patients. *p*-values <0.05 were considered statistically significant.

24 patients were included; 46% males, mean age 46±15 years, median symptom duration 17 years (IQR 8–29), 79% HLA-B27+, median CRP 5 mg/L (IQR 2–16), 54% biological DMARD naive. Mean ASDAS was 3.8±1.0 at baseline and improved significantly to 2.6±0.8 after 1 year of secukinumab.

At baseline, median BTM Z-scores were 0.06, -0.04, 0.64 and 1.09 for sCTX, OC, PINP and BALP, respectively. BTM did not significantly change at the 3-, 6- and 12-month follow-up, with a median change of respectively +0.2 and 0.0 for sCTX, +0.1 and -0.2 for OC, -0.1 and -0.2 for PINP, and -0.2 and -0.3 for BALP (Fig. 1). Sclerostin and OPG did not significantly change over time, however, an increasing trend in levels of sclerostin (median change of 10 (IQR -6-58); *p*=0.074) was observed at 3–6 months after start of secukinumab. No significant differences in BTM and bone regulators were observed for patients who did or did not demonstrate clinical important improvement in ASDAS and for biological naive *versus* TNFi experienced patients.

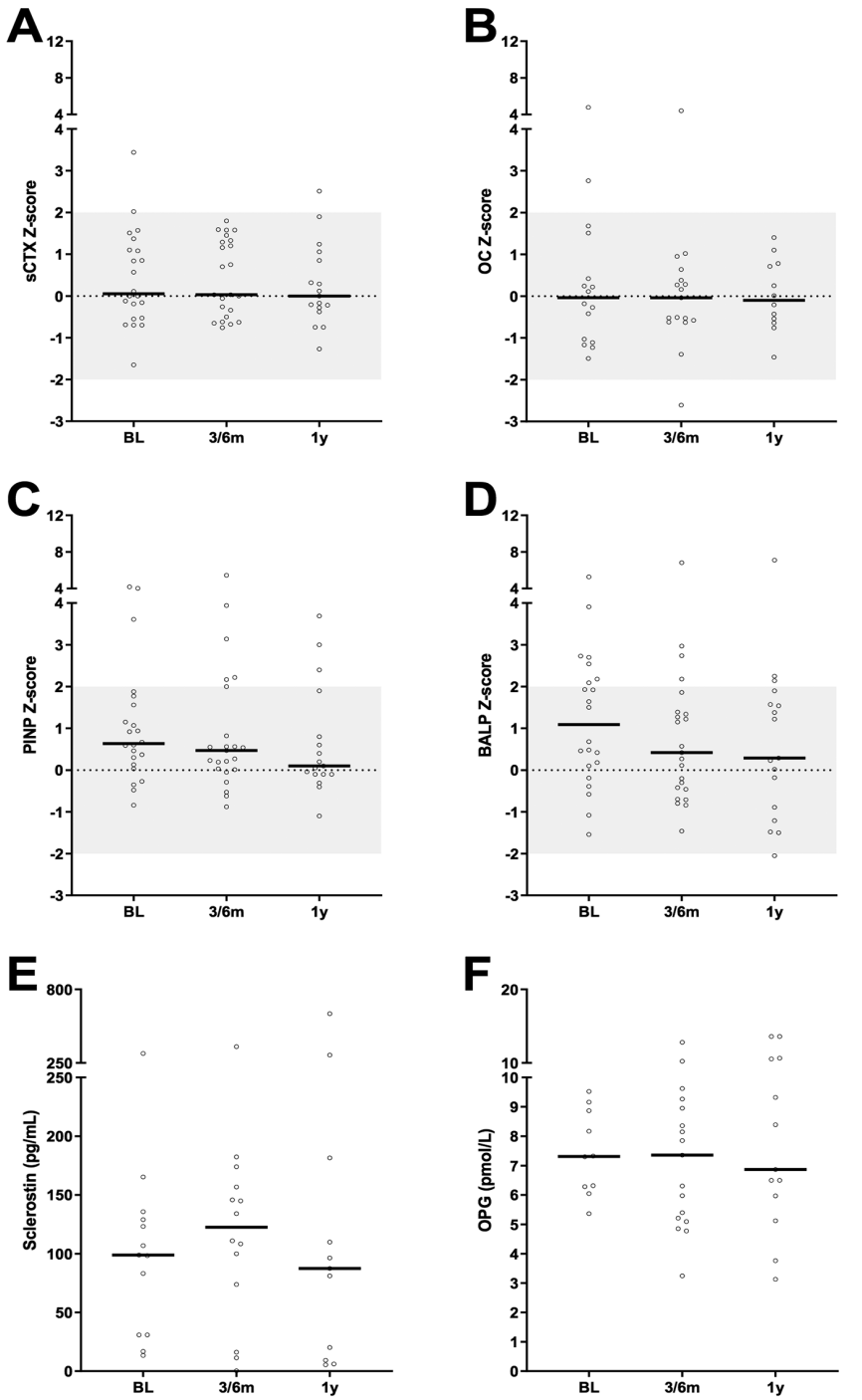

Fig. 1. Bone turnover markers sCTX (**A**), OC (**B**), PINP (**C**), BALP (**D**), and bone regulators sclerostin (**E**) and OPG (**F**) in 24 patients with r-axSpA treated with secukinumab (IL17i). Bar indicates median value and dots represent individual patient values.

These data from daily clinical practice confirm the findings of stable BTM in *post-hoc* analysis of the MEASURE 1 trial (1). An important addition is that our BTM data was corrected for the normal influence of age and gender.

In contrast to IL17i, previous studies on the effect of TNFi on BTM indicated a balance towards collagen formation and bone mineralisation during the first years of treatment (3). Possible explanation for this may be dif-

ferences in regulation of these cytokines (4). As IL17i is more pathway specific, it likely inhibits less secondary involved inflammatory pathways and cells (osteocytes, osteoclasts and osteoblasts). TNFα is a more overarching cytokine and inhibition leads to a broader downstream effect. IL17i may therefore result in less pronounced alteration in BTM and bone regulators.

To conclude, this explorative study of r-axSpA patients treated with secukinumab in daily clinical practice shows that serum levels of BTM related to bone resorption, regulation, and mineralisation as well as regulators of the bone metabolism did not significantly change during the first year of secukinumab treatment.

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Competing interests: M. Siderius is a consultant for Novartis. F. Wink has received consultany fees from Abbvie and Janssen. A. Spoorenberg has receìved grant/research support from Abbvie, Pfizer, UCB, and is a consultant for Abbvie, Pfizer, MSD, UCB, and Novartis. The other authors have declared no competing interests.

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