Conclusion: Substantial heterogeneity exists among registries regarding AE assessment within the JAK-pot collaboration. These differences must be taken into account when analysing the safety of JAKi across different countries in collaborative studies. For comparative analyses, stratified analyses by country are required to account for differential AE assessment and varying degrees of potential under-reporting.

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EFFECTS OF RANKL INHIBITION ON PROMOTING HEALING OF BONE EROSION IN RHEUMATOID ARTHRITIS USING HR-pQCT: A 2-YEAR, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Background: Partial repair of bone erosions in rheumatoid arthritis (RA) is known from high-resolution peripheral quantitative computer tomography (HR-pQCT) studies in patients with moderate to high disease activity using biologics [1]. Whether RANKL inhibition by denosumab is efficacious in healing existing erosions in RA patients with low disease activity or in remission on conventional synthetic DMARDs is uncertain.

Objectives: To evaluate the effects of denosumab on erosion healing at 2-4 metacarpophalangeal head as determined by HR-pQCT in patients with RA with stable disease.

Methods: This was a randomized, placebo-controlled, double-blind study. RA patients with disease activity score 28 joints (DAS28) ≤ 5.1 were randomized (1:1) to subcutaneous denosumab 60mg or placebo once every six months for 24 months. The primary outcome was erosion healing at MCP 2-4 on HR-pQCT at 12 months. The effects of denosumab on erosion and joint space parameters on HR-pQCT and radiographs, disease activity and health assessment questionnaire-disability index (HAQ-DI) were also examined.

Results: At 24 months, HR-pQCT images were analyzed in 98 patients. Baseline demographic, clinical characteristics and imaging parameters were comparable between the two treatment groups (table 1). Seventeen patients in each group (placebo group: 17/52, 32.6%; denosumab group: 17/50, 34.0%) achieved sustained low disease activity (DAS28 ≤ 3.2) throughout the 24 months. At 12 months, changes in erosion parameters on HR-pQCT were similar between the two groups. At 24 months, new erosions (19% vs 9%, $p=0.009$) and erosion progression (34% vs 16%, $p<0.001$) were more common in the placebo group than the denosumab group. Erosion healing was seen in a significantly higher proportion of patients in the denosumab group (20% vs 6%, $p=0.045$) at 24 months. The details of the changes in HR-pQCT erosion parameters are shown in figure 1. No significant differences in the changes in joint space parameters on HR-pQCT, van der Heijde-Sharp erosion score, DAS28 and HAQ-DI were observed between the two groups at 12 and 24 months.

Conclusion: Although no differences in erosion parameters were observed at 12 months, denosumab was more efficacious than placebo in erosion repair on HR-pQCT after 24 months.

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Table 1. Baseline clinical, demographic, disease activity parameters and medications

	Placebo (n=55)	Denosumab (n=55)	Total (n=110)
Age	56.5 $\pm$ 7.1	57.2 $\pm$ 8.5	56.8 $\pm$ 7.8
Gender (Female)	47 (86)	41 (75)	88 (80)
Disease duration (years)	8.5 $\pm$ 6.8	7.3 $\pm$ 6.9	7.9 $\pm$ 6.8
Rheumatoid factor positive	40 (72)	38 (69)	78 (71)
ACPA positive	43 (78)	44 (80)	87 (79)
DAS28-CRP	2.43 $\pm$ 0.83	2.6 $\pm$ 0.92	2.51 $\pm$ 0.88
DAS28-CRP $\geq$ 3.2	8 (15)	13 (24)	21 (19)
HAQ-DI (0-3)	0.31 $\pm$ 0.38	0.46 $\pm$ 0.47	0.39 $\pm$ 0.43
csDMARDs	49 (89)	52 (95)	101 (92)
Combination csDMARDs	26 (47)	33 (60)	59 (54)
Glucocorticoids	5 (10)	5 (9)	10 (9)
vdH- Sharp erosion score	10.4 $\pm$ 18.4	8.9 $\pm$ 13.8	9.6 $\pm$ 16.2
vdH- Sharp JSN score	12.4 $\pm$ 17.7	11.5 $\pm$ 17.2	11.9 $\pm$ 17.4
Lumbar spine aBMD, g/cm ²	0.914 $\pm$ 0.147	0.930 $\pm$ 0.143	0.922 $\pm$ 0.145
Total hip aBMD, g/cm ²	0.837 $\pm$ 0.102	0.847 $\pm$ 0.146	0.841 $\pm$ 0.125
Femoral neck aBMD, g/cm ²	0.681 $\pm$ 0.099	0.695 $\pm$ 0.128	0.687 $\pm$ 0.114

Data are reported as mean $\pm$ SD or number (%). ACPA: Anti-cyclic citrullinated peptide antibody; DAS28: disease activity score 28; csDMARDs: conventional synthetic disease modifying anti-rheumatic drug. HAQ-DI: health assessment questionnaire disability index; vdH- Sharp score: Van der Heijde- Sharp score; aBMD: areal bone mineral density

Figure 1. Changes in erosion parameters by HR-pQCT. (A) Percentage of patients with overall erosion healing; (B) Outcome of individual erosion with healing, progression and new erosion detected across study period; change in (C) mean erosion volume; (D) total erosion volume; (E) erosion width; (F) erosion depth and (G) marginal osteosclerosis per patient.

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