

Most TE HZ infections were mild to moderate and non-serious; 6 were serious; 2 were recurrences. No visceral TE HZ occurred across the FIL RA program; there was 1 case each of genital, disseminated, and ophthalmic HZ. The disseminated HZ occurred in a pt with prior HZ history. Lymphopenia was not associated with HZ during the PBO-controlled W12 period.

Conclusion: HZ was more common in both FIL groups vs ADA or MTX up to 52 weeks but comparable vs PBO during the 12-week placebo-controlled period. In multivariate analyses, prior history of HZ, Asian region, and age ≥ 50 years were associated with increased HZ risk.

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Rheumatoid arthritis - prognosis, predictors and outcome

POS0093

HETEROGENEITY IN ADVERSE EVENT ASSESSMENT BETWEEN COUNTRIES PARTICIPATING IN AN INTERNATIONAL COLLABORATION OF REGISTRIES OF RHEUMATOID ARTHRITIS PATIENTS USING JANUS KINASE INHIBITORS (THE JAK-POT STUDY)

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Background: Industry, regulators, and the rheumatology community have recognized the need for observational studies to monitor the safety of new anti-rheumatic agents. Registries provide a unique opportunity to understand the safety of newer therapies, but pharmacovigilance studies require large number of patients to evaluate rare drug-related adverse-events (AEs). Because JAK-inhibitors (JAKi) have only recently been approved for the treatment of rheumatoid arthritis, it makes sense to combine data from several registries in order to obtain a sufficiently large sample size to promote earlier detection of adverse events.

Objectives: The purpose of this analysis was to evaluate how AEs are assessed in the various registries in preparation for a collaborative pharmacovigilance analysis, and present preliminary results.

Methods: The “JAK-pot” collaboration includes 19 RA registries. The principal investigators of the participating registries were sent a structured questionnaire on AE assessment and 18 (94%) provided complete responses on the AE assessment procedures of their registries. We present simple descriptive statistics of the AE assessment procedures employed by the participating registries.

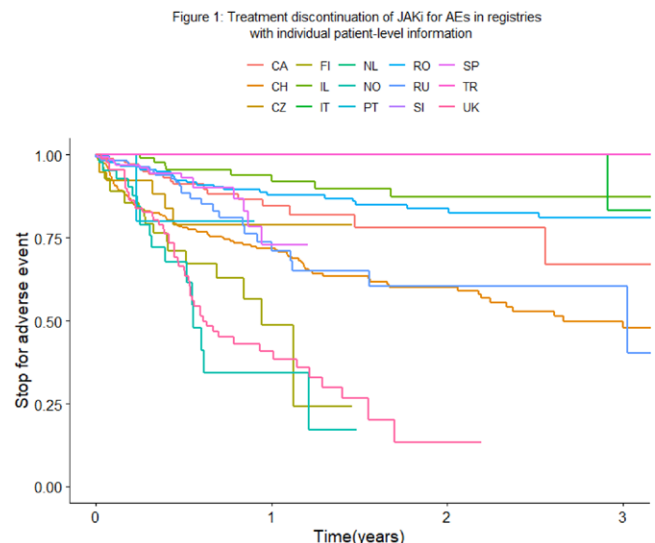
Results: The 19 registries represent 7186 patients initiating a JAKi (Table 1), who are on average 57 years old, with a mean disease duration 11 years, seropositive (83%), female (82%) and with moderate disease activity at treatment initiation.

Table 1.

Country, registry	N° of patients on JAKi included
Austria, BIOREG	87
Belgium, TARDIS	2113
Canada, RHUMADATA	363
Czech Republic, ATTRA	197
Denmark, DANBIO	506
Finland, ROB-FIN	229
Germany, RABBIT	620
Italy, GISEA	244
Israel, I-RECORD	96
Netherlands, METEOR	4
Norway, NOR-DMARD	97
Portugal, REUMA.PT	44
Romania, RRBR	252
Russia, ARBITER	428
Slovenia, biorx.si	141
Spain, BIOBADASER	139
Switzerland, SCQM	738
Turkey, TURKBIO	404
UK, BSRBR	484

After ineffectiveness, AEs was the second most common reason for JAKi discontinuation (25.5%), with large differences between registries (Figure 1).

Of the participating registries, 2 registries do not collect AEs, while 16 (89%) assess incident AEs, by means of a pre-specified extraction form (3 registries), by free text (5 registries), by a combination of both (6 registries) and/or the use of linkage to external electronic records (3registries). AEs are coded using a pre-defined coding system by 11 registries (MeDRA (8), other (3)), but nearly all are recording the severity of the AE (15, 94%), AE related-death (15, 94%), or AE-related hospitalisation (15, 94%). AEs of special interest, such as serious infections (15, 94%), thromboembolic events (15, 94%), or shingles (9, 56%), are recorded by most registries. Incident AEs are linked by the treating physician to specific therapies in 11 registries (69%), while the other 5 registries extrapolate potential causal associations based on therapy start and stop dates. A pre-specified adjudication process for AEs is made only by 5 registries (31%).



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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POS0094

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 ± 7.1	57.2 ± 8.5	56.8 ± 7.8
Gender (Female)	47 (86)	41 (75)	88 (80)
Disease duration (years)	8.5 ± 6.8	7.3 ± 6.9	7.9 ± 6.8
Rheumatoid factor positive	40 (72)	38 (69)	78 (71)
ACPA positive	43 (78)	44 (80)	87 (79)
DAS28-CRP	2.43 ± 0.83	2.6 ± 0.92	2.51 ± 0.88
DAS28-CRP>3.2	8 (15)	13 (24)	21 (19)
HAQ-DI (0-3)	0.31 ± 0.38	0.46 ± 0.47	0.39 ± 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 ± 18.4	8.9 ± 13.8	9.6 ± 16.2
vdH- Sharp JSN score	12.4 ± 17.7	11.5 ± 17.2	11.9 ± 17.4
Lumbar spine aBMD, g/cm ²	0.914 ± 0.147	0.930 ± 0.143	0.922 ± 0.145
Total hip aBMD, g/cm ²	0.837 ± 0.102	0.847 ± 0.146	0.841 ± 0.125
Femoral neck aBMD, g/cm ²	0.681 ± 0.099	0.695 ± 0.128	0.687 ± 0.114

Data are reported as mean ± 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

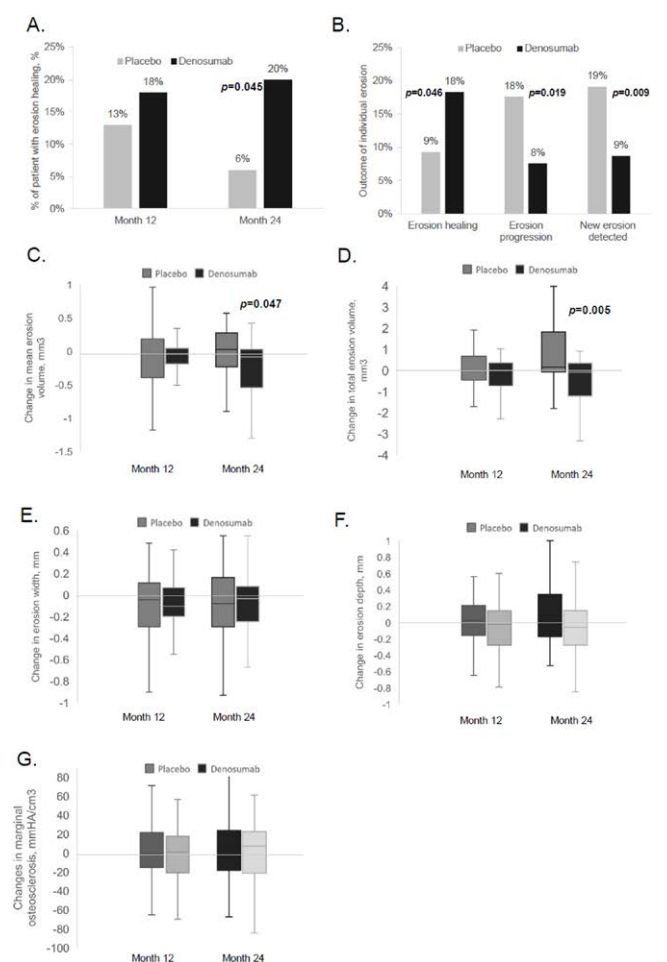


Figure 1. Changes in erosion parameters by HR-pQCT. (A) Percentage of patients with overall erosion healing; (B) Outcome of individual erosion with healing, progression and new erosion detected across study period; change in (C) mean erosion volume; (D) total erosion volume; (E) erosion width; (F) erosion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

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