

Supplementary Material

Supplementary Table 1. Demographic and clinical characteristics of ERA patients at diagnosis, according to BMD at DEXA.

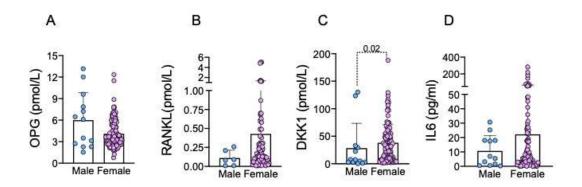
Bone Mineral Density (BMD)

| Variable | Normal BMD (N = 22) (31.0 %) | Osteopenic or osteoporotic (N = 49) (69.0 %) | P |
|--|---------------------------------------|---|-------|
| Age (years) | 53.91 ± 2.36 | 61.20 ± 1.39 | 0.007 |
| Gender, female (%) | 19 (86.4) | 47 (95.9) | 0.169 |
| Symptom duration (months) | 5.36 ± 0.71 | 5.78 ± 0.48 | 0.630 |
| VERA (%) | 9 (40.9) | 16 (32.7) | 0.341 |
| BMI (Kg/m ²) | 28.08 ± 0.79 | 24.34 ± 0.51 | 0.001 |
| Obese (BMI \geq 30 kg/m2) (%) | 7 (31.8) | 4 (8.2) | 0.011 |
| Erosive, n(%) | 3 (13.6) | 19 (38.8) | 0.029 |
| Seropositive (%) | 13 (59.1) | 36 (73.5) | 0.175 |
| ACPA positive (%) | 10 (28.6) | 35 (71.4) | 0.034 |
| IgM-RF positive (%) | 11 (50.0) | 26 (53.1) | 0.507 |
| IgA-RF positive (%) | 5 (22.7) | 16 (32.7) | 0.290 |
| ESR (mm/1st h) | 45.14 ± 5.43 | 37.96 ± 3.27 | 0.211 |
| CRP (mg/L) | 0.77 ± 0.91 | 0.67 ± 0.10 | 0.644 |
| IL-6 (pg/mL) | 21.99 ± 9.38 | 34.00 ± 8.04 | 0.195 |
| SJC44 | 9.45 ± 1.41 | 9.61 ± 0.98 | 0.975 |
| TJC44 | 12.91 ± 1.96 | 13.86 ± 1.07 | 0.459 |
| DAS | 3.72 ± 0.22 | 3.65 ± 0.12 | 0.645 |
| HAQ | 1.28 ± 1.63 | 1.13 ± 0.10 | 0.537 |
| Sharp score | 0.64 ± 0.50 | 1.57 ± 0.46 | 0.041 |
| Larsen Score | 0.55 ± 0.42 | 1.51 ± 0.44 | 0.039 |
| DAS44 remission at 3 months FU, n(%) | 6 (31.6) | 9 (19.6) | 0.232 |
| DAS44 remission at 6 months FU, n(%) | 8 (38.1) | 20 (40.8) | 0.524 |
| DAS44 remission at 12 months FU, n(%) | 8 (36.4) | 17 (35.4) | 0.572 |
| Joint damage progression at 12 months FU, n(%) | 2 (9.1) | 21 (42.9) | 0.005 |

Data are shown as mean \pm s.e.m. or n (%). **VERA**, very early Rheumatoid Arthritis; **BMI**, body mass index; **ACPA**, Anti-Citrullinated Protein Antibodies; **IgA/IgM-RF**: Immunoglobulin-A or Immunoglobulin M isotypes Rheumatoid Factor; **ESR**, Erythrocyte Sedimentation Rate; **CRP**, C-Reactive Protein; **IL-6**, interleukin-6; **SJC44**, swollen joint count over 44 joints; **TJC44**, tender joint

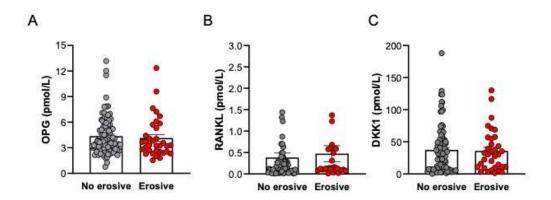
count over 44 joints; **DAS44**, Disease Activity Score measured on 44 joints; **HAQ**, Health Assessment Questionnaire.

Supplementary Figure 1



Supplementary Figure 1(A-D). Plasma levels of bone-derived biomarkers and IL-6 in ERA patients based on gender. (A) OPG (B) RANKL (C) DKK1 and (D) IL-6 plasma levels in ERA patients stratified based on gender. A p < 0.05 was considered statistically significant. ERA: Early Rheumatoid Arthritis; OPG: Osteoprotegerin; RANKL: receptor activator of nuclear factor kappa beta; DKK1: Dickkopf1.

Supplementary Figure 2



Supplementary Figure 2(A-C). Plasma levels of bone-derived biomarkers in ERA patients based on baseline presence of bone erosions. (A) OPG (B) RANKL and (C) DKK1 plasma levels in ERA patients stratified based on the presence of baseline bone erosions at plain radiographs of hands and feet. ERA: Early Rheumatoid Arthritis; OPG: Osteoprotegerin; RANKL: receptor activator of nuclear factor kappa beta; DKK1: Dickkopf1.