Multi-Biomarker Disease Activity (MBDA) Score and Prediction of Radiographic Progression in a Randomized Study of Patients with Early Rheumatoid Arthritis (RA) Treated with Methotrexate Alone or with Adalimumab


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OBJECTIVES

In early RA patients from the OPERA cohort, to investigate:
- MBDA score at baseline and change (±) in MBDA score at 3 months as predictors of clinical remission at 6 months and radiographic progression at 1 year and
- The added value of baseline MBDA score in predicting Disease Activity Score including C-reactive protein (DAS28-CRP) remission at 6 months and radiographic progression at 1 year.

METHODS

- In the investigator-initiated, double-blind randomized controlled OPERA study, treatment-naïve early RA patients (N=180) were randomized to MTX + adalimumab (MTX + ADA) group (n=90) or MTX + placebo group (n=90).
- C-reactive protein was assayed from serum samples at 0 and 12 months.
- The MBDA score, calculated based on serum concentrations of CRP, interleukin-6 (IL-6), chitinase-like protein 1 (YKL-40), vascular endothelial growth factor A (VEGFA), matrix metalloproteinase 1 and 3 (MMP-1 and -3), and vasoactive intestinal peptide 1 (VIP1-28), serum amyloid A (SAA1), leptin and resistin, on a scale of 1-100, was determined at baseline and 3, 6, and 12 months.
- Baseline MBDA score was defined as low (<30), moderate (30-44), and high (>44).

RESULTS

- **BASELINE CHARACTERISTICS**
  - Characteristics were consistent with recent RA onset and were similar between treatment arms and patients who did/did not progress radiographically (Table 1).
  - Median (interquartile range [IQR]) DAS28-CRP was 5.6 (3.8-6.6); MBDA score was 59 (12-90); TSS was 2 (0-31).
  - MBDA score was low (<30) in 8/180 (4%) patients, moderate (30-44) in 34/180 (19%) patients, and high (>44) in 178/180 (98%) patients. DAS28-CRP was moderate (3.4-4.4) in 118/180 (65%) patients, high (>4.4) in 62/180 (34%) patients, and very high (>5.5) in 16/180 (9%) patients.

- **BASELINE MBDA SCORE AND ΔMBDA SCORE AS PREDICTORS FOR DAS28-CRP REMISSION AT 6 MONTHS**
  - Logistic regression analysis showed that baseline MBDA score was not predictive for remission at 6 months, odds ratio (OR)=1.03 (95% CI, 0.98-1.05) (Table 2).
  - ΔMBDA score was an independent predictor of DAS28-CRP remission at 6 months (OR=0.98; 95% CI: 0.96-1.00) (Table 2).

- **BASELINE MBDA SCORE AND ΔMBDA SCORE AS PREDICTORS FOR RP AT 12 MONTHS**
  - In logistic regression analysis baseline MBDA score (OR=1.03; 95% CI: 1.91-1.00) was significantly associated with RP at 12 months in univariate analyses (Table 3).
  - ΔMBDA score was not associated with RP at 12 months in univariate and multivariate analyses (Table 3).

- **CONCLUSION**
  - In this double-blind randomized controlled trial of treatment-naïve patients with early RA, MBDA score was an independent predictor of DAS28-CRP remission at 6 months, and baseline MBDA score was an independent predictor of radiographic progression at 12 months.
  - Furthermore, the MBDA score had a clinical added value to baseline anti-CCP positive patients in predicting low risk of radiographic progression.

Table 1: Baseline Demographic, Clinical, and Radiographic Characteristics. Values are median and range unless otherwise stated.

Table 2: Univariate and Multivariate Logistic Regression Analyses for Prediction of Clinical Remission (DAS28-CRP ≤ 3.2) at 6 Months

Table 3: Prediction of Radiographic Progression at 12 Months (ΔTSS ≥ 2)

Figure 1: Median MBDA score by Treatment Group

Figure 2: Risk of radiographic progression stratified by baseline MBDA score (A) or baseline DAS28-CRP (B).

Figure 3: Changes of MBDA score (A) and DAS28-CRP (B) over time.