

# Multi-biomarker Disease Activity Score as a Predictor of Flare in Rheumatoid Arthritis Patients who Stop TNF-inhibitor in the POET-Study

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## Introduction

POET (Potential Optimisation Expediency of TNF-inhibitor) is a study in the Netherlands investigating TNFi (Tumor Necrosis Factor inhibitor) cessation in Rheumatoid Arthritis (RA) patients, ≥18 years old with >6 months low disease activity (LDA: DAS28 ≤3.2) or remission and on TNFi therapy >1 year. Patients were randomized 1:2 to continue or stop TNFi and followed for 12 months.

## Objectives

Prediction of flare by the multi-biomarker disease activity (MBDA) score at baseline in RA patients observed for 12 months after stopping TNFi treatment. Flare was defined three different ways.

## Methods

439 RA patients, according to ACR 1987 and/or 2010 criteria, with LDA (DAS28 ≤3.2) >6 months, were randomized to stop or continue TNFi and be sampled for serum at t=0.

MBDA scores were measured in the clinical laboratory of Crescendo Bioscience (South San Francisco, CA, USA). The MBDA score has a scale of 1–100 and disease activity categories of low (<30), moderate (30–44) and high (>44).

Separate analyses were performed for three different definitions of flare: 1) TNFi restart, 2) medication escalation or 3) clinician-reported flare, assessed over 12 months from stopping TNFi.

Univariate t-tests, median tests or Pearson  $\chi^2$  tests and multivariate logistic regressions adjusted for potential confounders were used to evaluate the association between baseline variables and each definition of flare.

Based on results of univariate and survival analyses, MBDA scores were dichotomized as high vs. moderate/low.

Patients who dropped out before 12 months without flare were counted with those who continued to have a response.

## Results

Univariate analysis showed that disease duration (p=0.012), BMI (p=0.017), DAS28-ESR (p<0.0001) and MBDA score (p<0.0001) were significantly different between patients who had a flare by any definition and patients who stayed in remission or LDA after cessation of TNFi therapy.

Adjusted for these confounders, a high MBDA score was independently associated with increased risk for TNFi restart (OR 1.85), medication escalation (OR 1.99) and clinician reported flare (OR 2.0) (Table 2). DAS28-ESR was independently associated with flare defined only as medication escalation (OR 1.48).

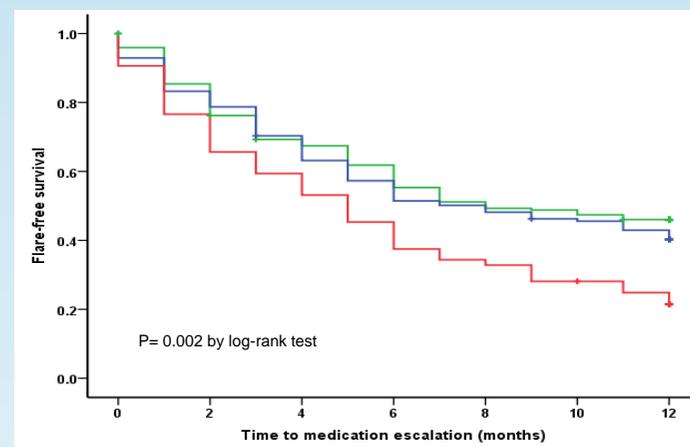
**Table 1**

Univariate associations (P-values) of baseline characteristics with occurrence of flare in the stop group at 12 months, using three definitions of flare

Characteristic	TNFi restart N=219	Medication escalation N=259	Clinician reported flare N=251
Female (%)	0.735	0.452	0.799
Age (yrs)	0.990	0.242	0.169
Disease duration (yrs)	<b>0.001</b>	<b>0.024</b>	<b>0.011</b>
BMI	<b>0.028</b>	<b>0.004</b>	0.135
RF(+)	0.530	0.340	0.865
Anti-CCP (+)	0.775	0.988	0.209
Erosiveness (%)	<b>0.020</b>	0.074	0.194
ESR mm/h	0.227	0.145	0.161
DAS28-ESR	<b>0.073</b>	<b>0.001</b>	<b>0.017</b>
MBDA score	<b>0.008</b>	<b>&lt;0.0001</b>	<b>0.002</b>
Number of TNFi	0.621	0.392	0.322
Concomitant DMARD (%)	0.670	0.379	0.852

**Figure 1**

Kaplan-Meier curve for flare-free survival for patients with low (<30, green), moderate (30–44, blue) or high (>44, red) MBDA scores at BL, based on medication escalation



**Table 2**

Regression analysis of high (>44) vs. moderate or low baseline MBDA score in the stop-TNFi group (N=439) as a predictor for flare at 12 months, defined three ways

Flare definition	OR (95% CI)	P-value
TNFi restart		
Unadjusted	2.32 (1.32–4.05)	<b>0.003</b>
Adjusted	2.17 (1.23–3.83)	<b>0.008</b>
Fully adjusted	1.85 (1.00–3.40)	<b>0.049</b>
Medication escalation		
Unadjusted	2.84 (1.52–5.31)	<b>0.001</b>
Adjusted	2.44 (1.29–4.62)	<b>0.006</b>
Fully adjusted	1.99 (1.01–3.94)	<b>0.047</b>
Clinician reported flare		
Unadjusted	2.54 (1.39–4.64)	<b>0.002</b>
Adjusted	2.31 (1.25–4.25)	<b>0.007</b>
Fully adjusted	2.00 (1.06–3.77)	<b>0.033</b>

Adjusted = adjusted for baseline DAS28-ESR (continuous); Fully adjusted = adjusted for baseline DAS28-ESR (continuous), disease duration (continuous), BMI (continuous) and erosions (yes/no).

## Conclusion

- In univariate analyses longer disease duration, higher BMI, DAS28-ESR and MBDA score assessed at cessation of TNFi were associated with RA disease flare.
- In RA patients with LDA (DAS28≤3.2), a high MBDA score was an independent predictor of flare within 12 months after discontinuing TNFi therapy.



Crescendo Bioscience® provided funds for retrieval, aliquoting, labeling and shipping of study sample and performed MBDA testing at no charge.