

## Cost-Effective Tapering Algorithm in Rheumatoid Arthritis Patients: Combination of Multibiomarker Disease Activity Score and Autoantibody Status

Hagen M, et al. The Journal of Rheumatology, 2018: November 26.

**Objective:** Analyze the effect of a risk-stratified DMARD tapering algorithm based on MBDA and ACPA on treatment costs for patients with rheumatoid arthritis in sustained remission. To show that tapering or stopping DMARDs in RA patients in sustained clinical remission is feasible and cost-effective, especially in patients with low risk of relapse based on ACPA negativity and low MBDA status.

### Baseline & Methods:

Post-hoc retrospective analysis of direct treatment costs for 146 patients from the RETRO prospective randomized study.

- MBDA & ACPA status at baseline (BL) in three arms:
  - Arm 1: Continuation of all DMARDs (n=46)
  - Arm 2: Tapering all DMARDs by 50% (n=47)
  - Arm 3: Taper DMARDs by 50% at 6 months then STOP (n=53)
- Patients were followed for 1 year and direct treatment costs were evaluated every 3 months.
- MBDA and ACPA were used for predictors creating a risk-stratified tapering algorithm based on relapse rates.
- Patients were from the prospective randomized RETRO study: RA diagnosis for at least 12 months in stable clinical remission (defined by DAS28-ESR <2.6) and taking stable doses of conventional or biologic DMARDs for at least 6 months.
- Relapse was defined as DAS28-ESR > 2.6.
- At every visit, (BL, months 3, 6, 9 & 12) direct costs assessed for each patient including cDMARD, bDMARD and corticosteroids. Costs for MBDA and ACPA were included in BL costs.
- Indirect costs (consultation, hospitalization, physiotherapy) were not considered.

### Commercial and Clinical Applications:

- MBDA is an independent predictor for relapse (P=0.01)
- The distribution of MBDA positively differed significantly (P=0.018) between the three treatment arms.
- Tapering or stopping cDMARDs/bDMARD using an algorithm with MBDA and ACPA was shown to provide substantial cost savings.

### Conclusions:

Overtreatment can be prevented and costs can be saved if tapering is performed in RA patients with low relapse risk based on ACPA and MBDA status. Such an approach can combine the interests of patients (safety, overtreatment), rheumatologists (personalized medicine) and health insurance (costs).

### Results

All patients were in a sustained clinical remission with a mean DAS20-ESR of 1.71 (+0.056) at baseline.

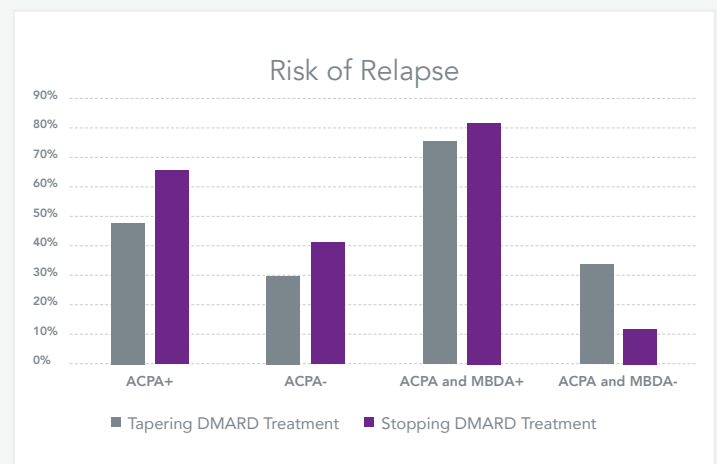
- 79.5% (n=116) were on cDMARDs with MTX
- 39% (n=57) were on bDMARDs
- 56.2% (n=82) were ACPA+
- 43.2% (n=63) MBDA >30

Treatment Costs: Defined patients who did not flare as successfully tapered and calculated their cost saved costs for cDMARDs and bDMARDs.

Direct treatment costs for double-negative or single-positive groups (n=41) would have been €372,245.16 for full dose treatment over 1 year.

Tapering or stopping for low risk groups allowed a reduction of €219,712.03 in drug costs which equates to an average cost reduction per patient of €5358.83.

When using only ACPA status for relapse prediction, overall cost reduction was lower €184,580.00 and an average patient cost reduction of €4394.76 with a higher relapse risk.



**TABLE 1** Cost reduction adapted to risk factors for relapse: model based on ACPA status only

Arms	ACPA-	ACPA+	Total
Arm 1 (Control)	BL = €128,302.32 M12 = €128,302.51 -€0* (n = 17)	BL = €209,984.76 M12 = €209,984.76 -€0* (n = 23)	BL = €338,287.08 M12 = €338,287.27 -€0* (n = 40)*
Arm 2 (Tapering)	BL = €92,962.44 M12 = €44,436.58 <b>-€48,525.86</b> (n = 14)	BL = €222,054.56 M12 = €114,116.31 <b>-€107,938.25</b> (n = 14)	BL = €315,017.00 M12 = €158,552.89 <b>-€156,464.11</b> (n = 28)
Arm 3 (Stopping)	BL = €39,585.12 M12 = €11,469.26 <b>-€28,115.86</b> (n = 14)	BL = €49,231.20 M12 = €13,883.65 -€35,347.55** (n = 10)	BL = €39,585.12 M12 = €11,469.26 <b>-€28,115.86</b> (n = 14)
All			BL = €354,602.12 M12 = €170,022.12 <b>-€184,580.00</b> (n = 42)

**TABLE 2** Cost reduction adapted to risk factors for relapse: model based on ACPA status combined with MBDA score

Arms	ACPA-/MBDA-	ACPA-/MBDA+	ACPA+/MBDA-	ACPA+/MBDA+	Total
Arm 1 (Control)	BL = €80,286.80 M12 = €80,286.80 -€0* (n = 10)	BL = €64,853.52 M12 = €64,853.52 -€0* (n = 7)	BL = €159,185.88 M12 = €159,185.88 -€0* (n = 16)	BL = €73,568.88 M12 = €73,568.88 -€0* (n = 7)	BL = €377,895.08 M12 = €377,895.08 -€0* (n = 40)
Arm 2 (Tapering)	BL = €70,839.24 M12 = €27,619.32 <b>-€43,219.92</b> (n = 8)	BL = €35,983.20 M12 = €16,817.20 <b>-€19,166.00</b> (n = 6)	BL = €189,480.00 M12 = €91,013.56 <b>-€98,466.44</b> (n = 12)	BL = €46,434.56 M12 = €23,102.75 -€23,331.81 (n = 2)	BL = €296,302.44 M12 = €135,450.08 <b>-€160,852.36</b> (n = 26)
Arm 3 (Stopping)	BL = €42,208.32 M12 = €9446.40 <b>-€32,761.92</b> (n = 8)	BL = €11,236.80 M12 = €1499.06 -€9737.74** (n = 6)	BL = €33,734.40 M12 = €7636.65 <b>-€26,097.76</b> (n = 7)	BL = €24,406.80 M12 = €6247.00 -€18,159.80** (n = 3)	BL = €75,942.72 M12 = €17,083.05 <b>-€58,859.67</b> (n = 15)
All					BL = €372,245.16 M12 = €152,533.13 <b>-€219,712.03</b> (n = 41)

Values in bold are absolute saved costs. \*No cost reduction, owing to study design. \*\*No cost reduction, owing to high relapse risk.

BL: baseline assessment at start of tapering; M12: Month 12 followup; ACPA: anticitrullinated protein antibodies; MBDA: multibiomarker disease activity.