FOUR-WEEK CHANGES IN COLLAGEN DEGRADATION BIOMARKERS ARE ASSOCIATED WITH 24-WEEK CLINICAL RESPONSE IN PSORIATIC ARTHRITIS: *A BIOMARKER-GUIDED STRATIFICATION APPROACH*

R. Malmkvist[1,2], A.-C. Bay-Jensen[2], D. Sinkeviciute[2], S. Francis Thomsen[1,3], M. Asser Karsdal[2], K. Lozenski[4], L. Seridi[5], S. Gao[5], W. Chen[5], D. Murphy[6]

[1] University of Copenhagen, Denmark, [2] Nordic Bioscience A/S, Denmark, [3] Bispebjerg Hospital, Denmark,
[4] Johnson & Johnson, Horsham, PA, USA, [5] Johnson & Johnson, Spring House, PA, USA, [6] Johnson & Johnson, San Diego, CA, USA

This material is distributed for scientific purposes by Johnson & Johnson Innovative Medicine and is not for promotional use.

Key Take-home message

Early dynamic changes in ECM remodelling biomarkers identify biologically distinct subgroups of patients with PsA that are associated with subsequent symptom alleviation

Biologic-naïve patients with active PsA
DISCOVER-2 study (NCT03158285)
***n* = 254**

→ **Baseline**
Serum sample
ECM biomarker measurement

→ **Week 4**
Serum sample
ECM biomarker measurement

→ **Calculate Δ4-week**
(change from baseline)
Standardise & Winsorise
Iterative biomarker selection

→ ***K*-means clustering**
(*k* = 2)



→ **Week 24**
Clinical response
(ACR20/50, PASI 75/90/100, enthesitis & dactylitis resolution)

Background & Objective

To determine whether early changes in extracellular matrix (ECM) remodelling biomarkers identify biologically distinct subgroups of patients with psoriatic arthritis (PsA) and whether such profiles are associated with subsequent symptom alleviation

Methods

Patients:
254 biologic-naïve patients with active PsA

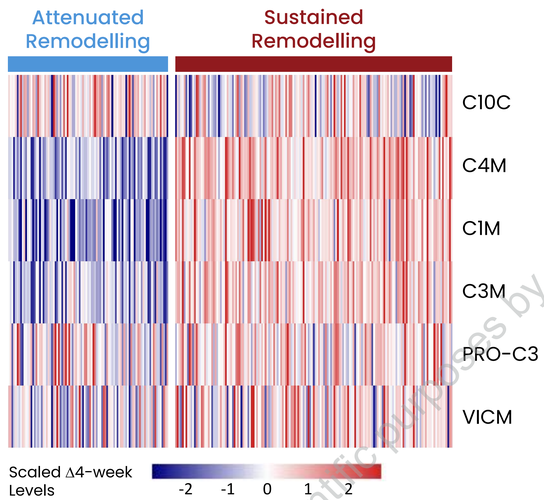
Biomarkers:
Reduced panel included:
Hypertrophic chondrocytes (C10C), collagen degradation (C4M, C1M, C3M), fibrosis marker (PRO-C3), and inflammatory marker (VICM)

Statistics:

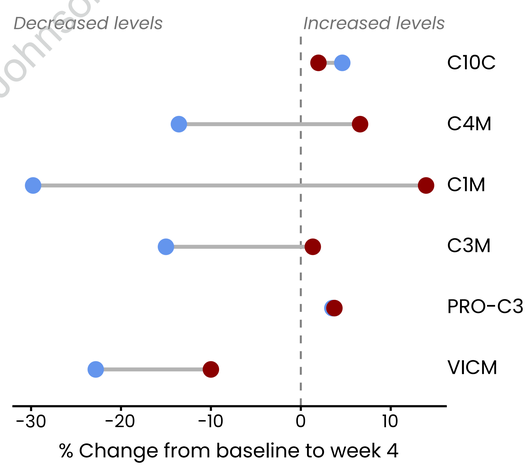
- Changes from baseline to week 4 (Δ4-week) calculated, Winsorised (1.5×IQR) and standardised
- *K*-means clustering (Euclidean distance); *k* = 2 selected by silhouette and elbow methods
- Biomarker reduction: iterative, stability-based approach (adjusted Rand Index ≥ 0.9)
- Associations with week 24 responses assessed using adjusted logistic regression (age, sex, baseline CRP, treatment arm)

Results

Heatmap of standardised changes (Δ4-week) in ECM biomarker levels across patients



Δ4-week biomarker changes in the two identified clusters



Baseline characteristics by cluster

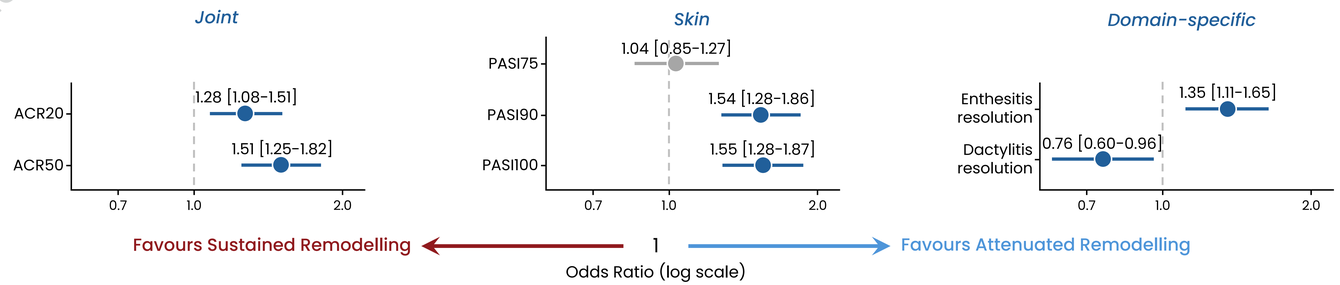
	Attenuated Remodelling (*n* = 93)	Sustained Remodelling (*n* = 161)	*P* value
Age, years	46 (34, 55)	45 (38, 53)	1.000
Sex, female	35 (37.6%)	80 (49.7%)	1.000
CRP, mg/L	2.0 (1.2, 3.6)	1.1 (0.6, 2.4)	**< 0.001**
PsA duration, years	3.8 (1.4, 8.4)	4.5 (2.5, 8.0)	1.000
PASI	6.9 (3.2, 16.6)	5.4 (2.4, 11.4)	1.000
vdH-S	22.0 (8.5, 45.5)	14.5 (6.5, 33.0)	1.000
Treatment arm			1.000
Placebo	23 (24.7%)	62 (38.5%)	
Q4W	35 (37.6%)	43 (26.7%)	
Q8W	35 (37.6%)	56 (34.8%)	
Biomarkers at baseline			
C10C, ng/mL	3123 (2707, 3581)	3255 (2859, 3830)	0.096
C4M, ng/mL	47.2 (38.9, 59.6)	36.4 (30.5, 47.6)	**< 0.001**
C1M, ng/mL	106.8 (80.3, 160.3)	68.9 (46.1, 108.7)	**< 0.001**
C3M, ng/mL	18.0 (14.1, 22.7)	15.0 (12.4, 18.3)	**< 0.001**
PRO-C3, ng/mL	11.4 (9.2, 15.2)	10.7 (8.9, 14.1)	0.121
VICM, ng/mL	11.4 (6.7, 17.6)	7.0 (3.9, 13.1)	**0.001**

Associations between Attenuated Remodelling cluster vs Sustained Remodelling cluster and week 24 response

Model adjusted for age, sex, baseline CRP, and treatment arm

Odds ratios (ORs) with 95% CIs (log scale)

Blue = *P* < 0.05
Grey = Not significant



Two distinct ECM remodelling trajectories at week 4 are associated with differential clinical responses at week 24

ACR70 and MDA responses were omitted due to low responder count

Scan the QR code
The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Rikke Malmkvist
rija@nordicbio.com
/rikke-malmkvist