

Collagen Turnover Biomarkers Associate with Active Psoriatic Arthritis and Decrease with Guselkumab Treatment in a Phase 3 Clinical Trial (DISCOVER-2)

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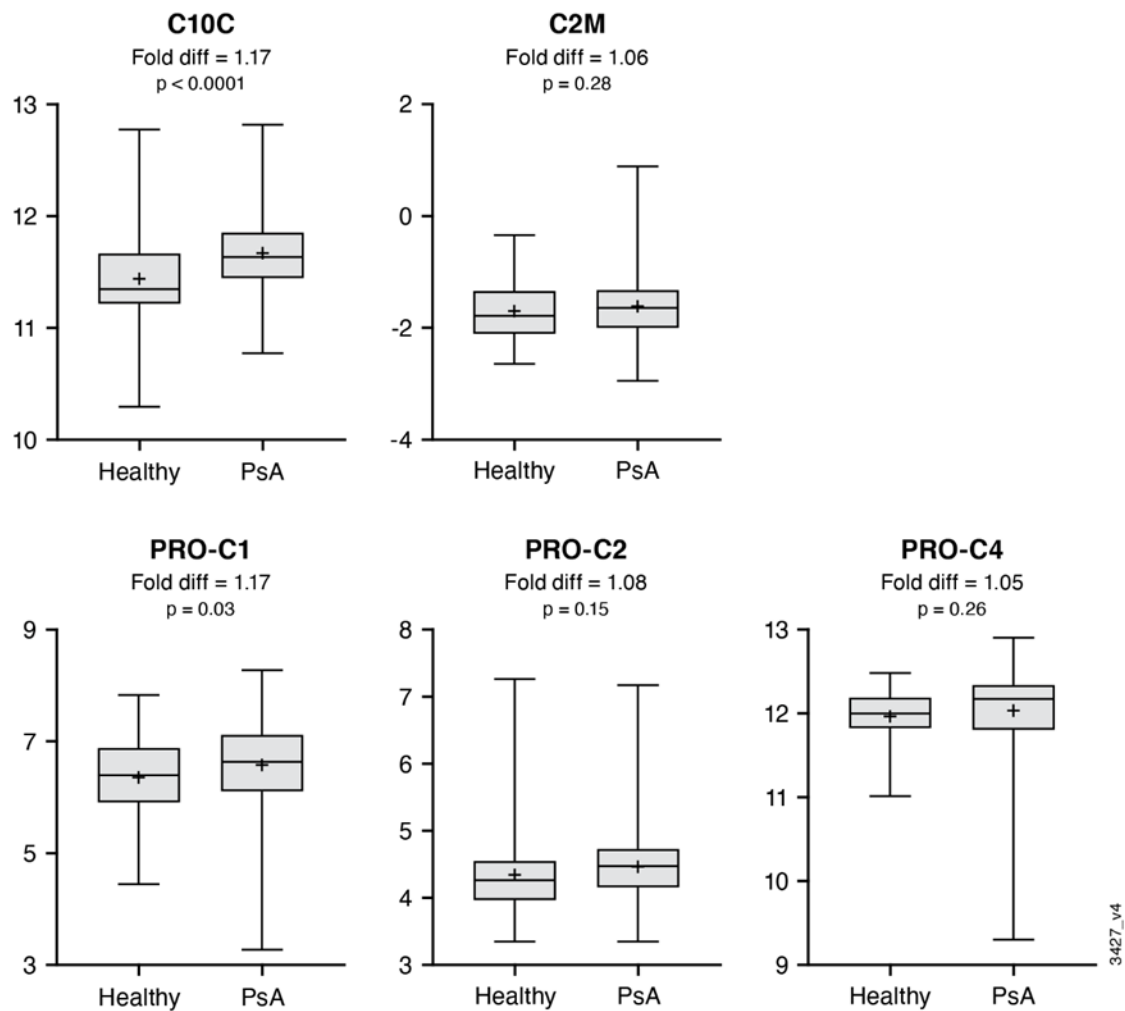
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Supplementary Figure 1. Collagen Degradation and Formation Biomarkers in the Serum of PsA Patients Compared to Healthy Controls

Healthy controls (N=76) were demographically matched (age and sex) to PsA biomarker subset (N=260). Values are median (plus [+] marks represent mean). Boxes represent interquartile range, while whiskers represent the minimum and maximum values. adj, adjusted; PsA, psoriatic arthritis; adj p<0.05



Supplementary Table 1. Mean Biomarker Concentrations at Baseline in the Guselkumab and Placebo Groups and Healthy Subjects

	Guselkumab		Guselkumab		Placebo		Healthy	
	100 mg Q4W		100 mg Q8W					
Patients, N	82		92		86		76	
Biomarker	Log₂ (ng/mL)	SD	Log₂ (ng/mL)	SD	Log₂ (ng/mL)	SD	Log₂ (ng/mL)	SD
C1M	6.50	0.83	6.27	0.87	6.48	1.05	4.73	0.29
C2M	-1.66	0.67	-1.54	0.64	-1.64	0.56	-1.70	0.52
C3M	4.04	0.40	3.96	0.39	4.06	0.43	3.30	0.44
C4M	5.43	0.44	5.36	0.47	5.40	0.56	4.83	0.37
C6M	4.92	0.54	4.89	0.55	5.02	0.55	3.46	0.67
C10C	11.66	0.28	11.70	0.33	11.65	0.37	11.44	0.39
PRO-C1	6.52	0.89	6.66	0.70	6.54	0.73	6.36	0.73
PRO-C2	4.47	0.53	4.47	0.46	4.45	0.55	4.35	0.77
PRO-C3	3.58	0.50	3.60	0.49	3.45	0.54	3.03	0.44
PRO-C4	12.02	0.59	12.04	0.42	12.05	0.37	11.97	0.31
PRO-C6	3.24	0.53	3.29	0.50	3.18	0.48	2.77	0.47

Q4W, every 4 weeks; Q8W, every 8 weeks; SD, standard deviation

Supplementary Table 2. Efficacy results at Week 24 for patients in the DISCOVER-2 Biomarker Subset and the overall DISCOVER-2 study population.

Response at Week 24	DISCOVER-2 Biomarker Subset			DISCOVER-2 Study Cohort		
	Guselkumab 100 mg		Placebo	Guselkumab 100 mg		Placebo
	Q4W	Q8W		Q4W	Q8W	
Patients, N	82	92	86	245	248	246
ACR20	55 (67.1%)	54 (58.7%)	22 (25.6%)	156 (63.7%)	159 (64.1%)	81 (32.9%)
ACR50	22 (26.8%)	33 (35.9%)	6 (7.0%)	81 (33.1%)	78 (31.5%)	35 (14.2%)
PASI75*	64 (78.0%)	72 (78.3%)	21 (24.4%)	144/184 (78.3%)	139/176 (79.0%)	42/183 (23.0%)
PASI90*	49 (59.8%)	55 (59.8%)	8 (9.3%)	112/184 (60.9%)	121/176 (68.8%)	18/183 (9.8%)

Data reported as n (%) or n/N (%).

*PASI responses were assessed in patients with $\geq 3\%$ body surface area psoriatic involvement and an Investigator's Global Assessment score of ≥ 2 at baseline. All patients included in the Biomarker Subset met these criteria.

ACR20/50, $\geq 20\%/ \geq 50\%$ improvement in American College of Rheumatology response criteria; PASI75/90, $\geq 75\%/ \geq 90\%$ improvement in Psoriasis Area and Severity Index score; Q4W, every 4 weeks; Q8W, every 8 weeks

Supplementary Table 3. Guselkumab Reduces Serum levels of C1M, C3M, C4M, and C6M Relative to Baseline Levels and Relative to Placebo

Biomarkers		Guselkumab 100 mg		Placebo →	Guselkumab 100 mg		
		Q4W	Q8W	Guselkumab Q4W	Q4W	Q8W	
C1M	W4 vs BL	0.01	0.15	0.78	W4: Guselkumab vs placebo	0.34	0.52
	W24 vs BL	<0.0001	<0.0001	0.02	W24: Guselkumab vs placebo	0.002	0.05
	W52 vs BL	<0.0001	<0.0001	<0.0001			
C3M	W4 vs BL	0.10	0.24	0.87	W4: Guselkumab vs placebo	0.49	0.59
	W24 vs BL	<0.0001	<0.0001	0.17	W24: Guselkumab vs placebo	0.01	0.04
	W52 vs BL	0.0001	<0.0001	<0.0001			
C4M	W4 vs BL	0.10	0.15	0.88	W4: Guselkumab vs placebo	0.34	0.33
	W24 vs BL	<0.0001	<0.0001	0.23	W24: Guselkumab vs placebo	0.01	0.01
	W52 vs BL	<0.0001	<0.0001	<0.0001			

Supplementary Table 3. Guselkumab Reduces Serum levels of C1M, C3M, C4M, and C6M Relative to Baseline Levels and Relative to Placebo

Biomarkers		Guselkumab 100 mg		Placebo →	Guselkumab 100 mg		
		Q4W	Q8W	Guselkumab Q4W	Q4W	Q8W	
C6M	W4 vs BL	0.02	0.15	0.78	W4: Guselkumab vs placebo	0.34	0.40
	W24 vs BL	<0.0001	<0.0001	0.02	W24: Guselkumab vs placebo	0.07	0.04
	W52 vs BL	<0.0001	<0.0001	<0.0001			

GUS Q4W, N=82; GUS Q8W, N=92; placebo, N=86. Adj, adjusted; BL, baseline; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week

All values were adjusted p values.

Bolded values indicate significant difference (p<0.05).