

ONLINE SUPPLEMENTARY MATERIAL

Supplementary Table 1. Radiographic assessments during the study

Time point	Campaign 1	Campaign 2	Campaign 3
	Double-blind phase	Open-label extension	Open-label extension
Baseline	X	X	X
6 months	X	X	
12 months	X	X	X
18 months		X	
24 months			X
36 months			X

X indicates that the images were assessed or reassessed.

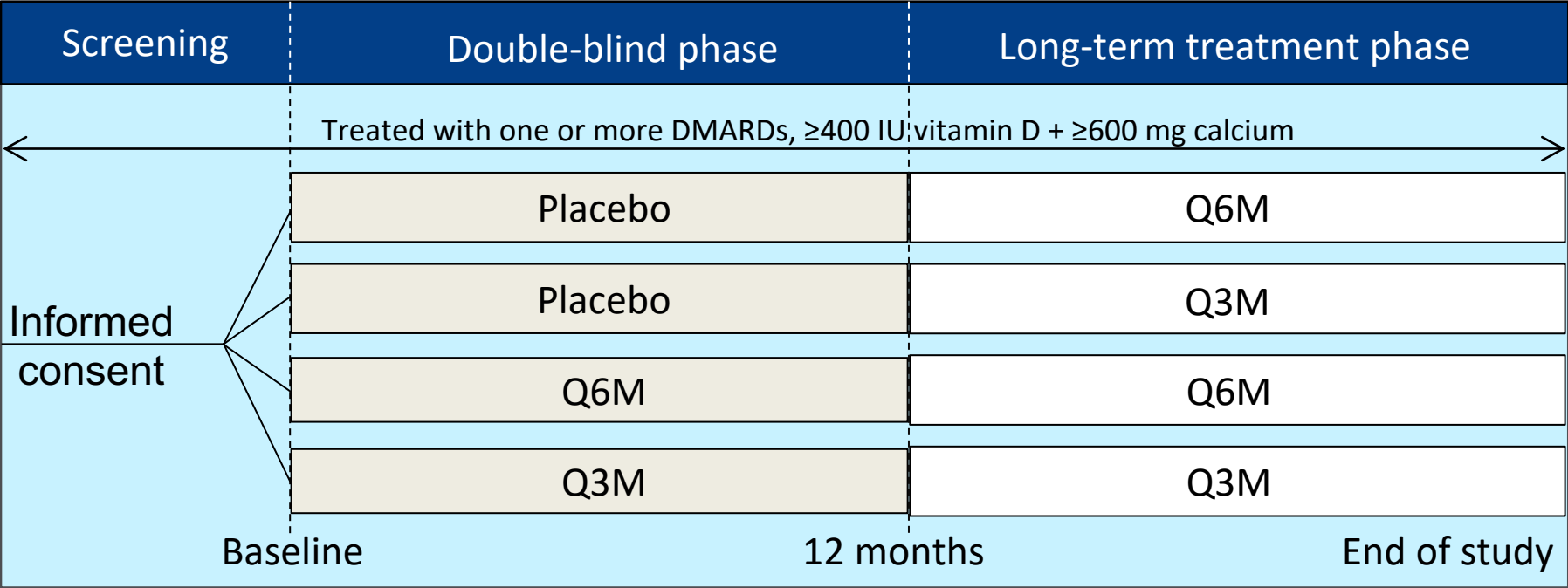
Supplementary Table 2. Changes in mTSS after 12 months during campaigns 1 (double-blind period) and 3 (current open-label extension).

Treatment group	Changes in mTSS after 12 months			
	Campaign 1 ^a		Campaign 3	
	n	Change (95% CI)	n	Change (95% CI)
Placebo	218	1.49 (0.99, 1.99)	-	-
Placebo/Q6M	-	-	105	1.29 (0.74, 1.84)
Placebo/Q3M	-	-	101	1.60 (0.88, 2.31)
Q6M	217	0.99 (0.49, 1.49)	191	1.25 (0.66, 1.84)
Q3M	219	0.72 (0.41, 1.03)	193	0.98 (0.55, 1.41)

^aTakeuchi et al., Ann Rheum Dis 2019;78:899-907

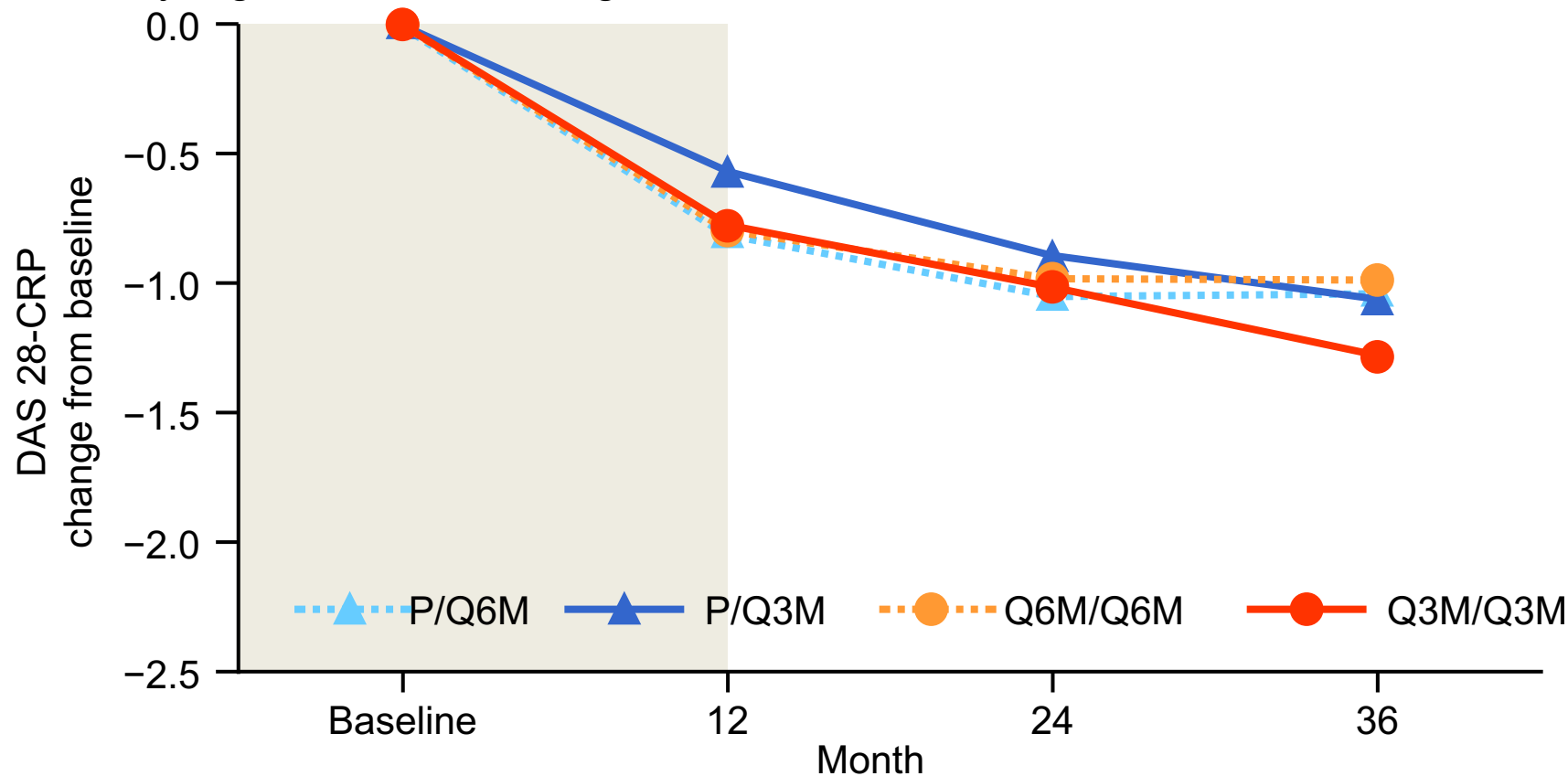
CI confidence interval; mTSS modified total Sharp score; Q3M, denosumab 60 mg every 3 months; Q6M, denosumab 60 mg every 6 months.

Supplementary Figure 1. Study design



DMARDs, disease-modifying anti-rheumatic drugs; Q3M, denosumab 60 mg every 3 months; Q6M, denosumab 60 mg every 6 months.

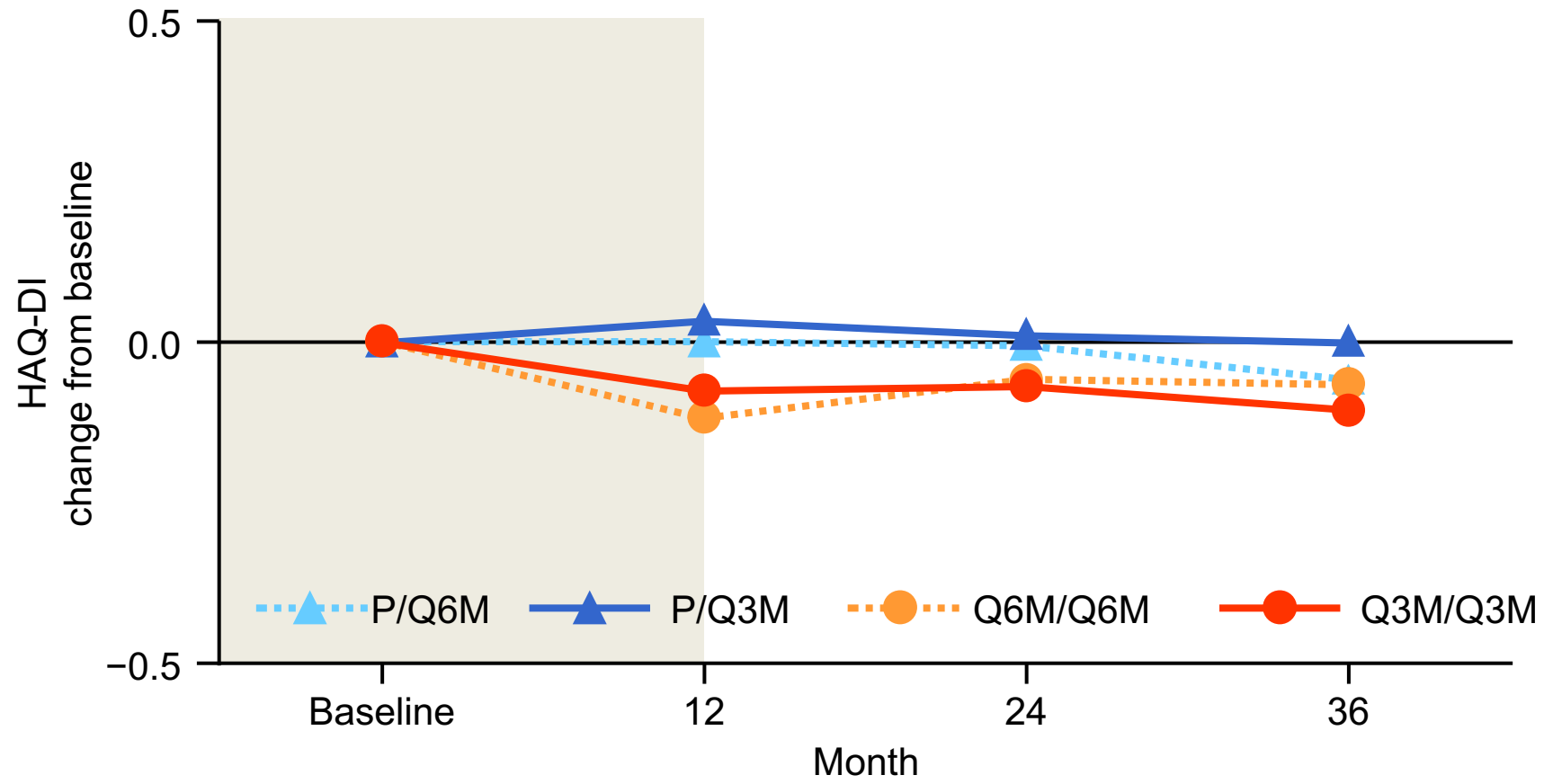
Supplementary Figure 2. Mean change in DAS28-CRP from baseline



P/Q6M (n)	105	100	52
P/Q3M (n)	101	93	52
Q6M/Q6M (n)	190	172	95
Q3M/Q3M (n)	192	173	96

DAS28-CRP, Disease Activity Score using 28 joints and C-reactive protein; P/Q3M, placebo for 12 months followed by denosumab 60 mg every 3 months; P/Q6M, placebo for 12 months followed by denosumab 60 mg every 6 months; Q3M/Q3M, denosumab 60 mg every 3 months for 12 months followed by denosumab 60 mg every 3 months; Q6M/Q6M, denosumab 60 mg every 6 months for 12 months followed by denosumab 60 mg every 6 months.

Supplementary Figure 3. Mean change in HAQ-DI from baseline

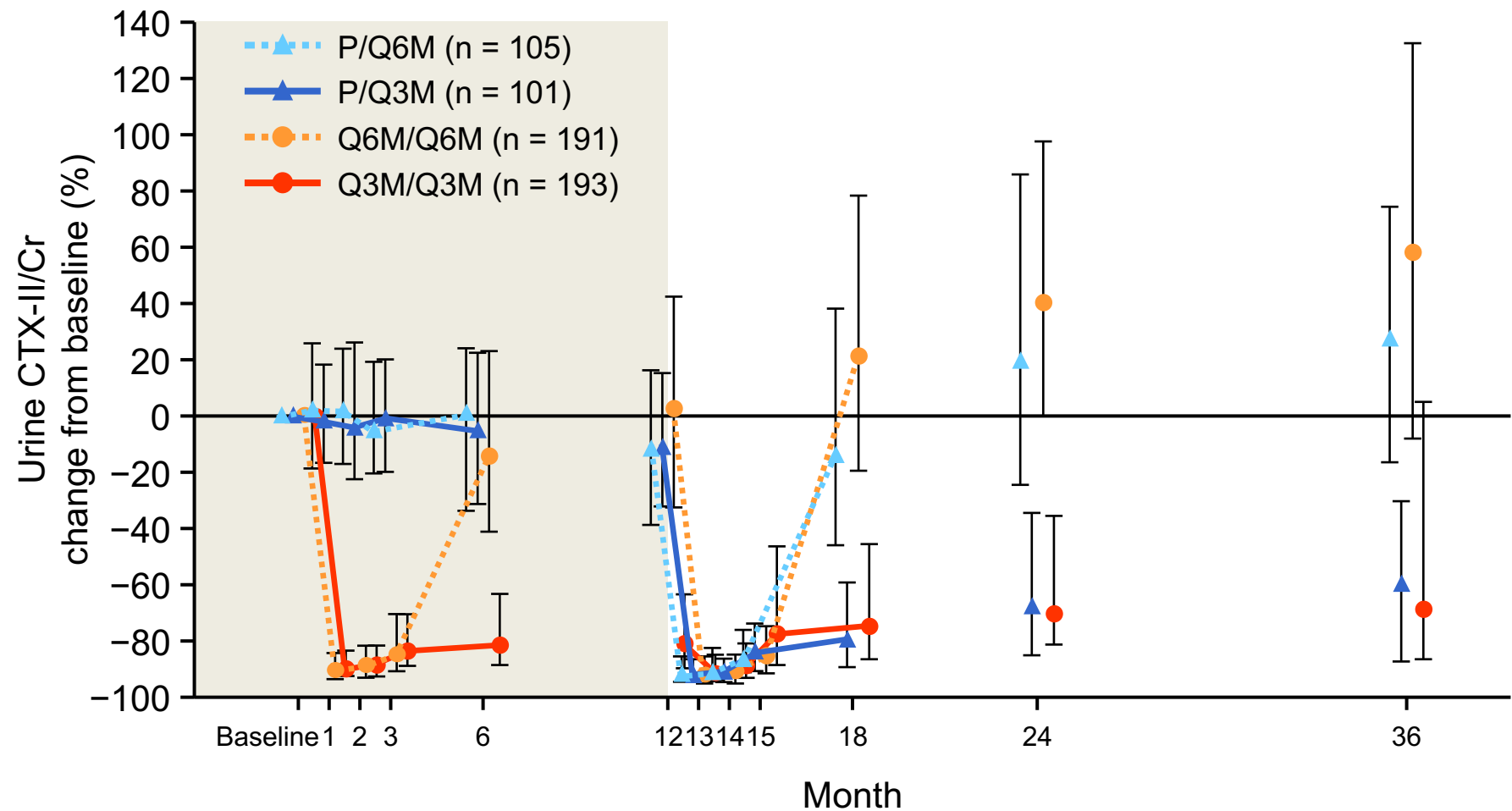


P/Q6M (n)	105	100	52
P/Q3M (n)	101	93	52
Q6M/Q6M (n)	190	172	95
Q3M/Q3M (n)	192	173	96

HAQ-DI, Health Assessment Questionnaire Disability Index; P/Q3M, placebo for 12 months followed by denosumab 60 mg every 3 months; P/Q6M, placebo for 12 months followed by denosumab 60 mg every 6 months; Q3M/Q3M, denosumab 60 mg every 3 months for 12 months followed by denosumab 60 mg every 3 months; Q6M/Q6M, denosumab 60 mg every 6 months for 12 months followed by denosumab 60 mg every 6 months.

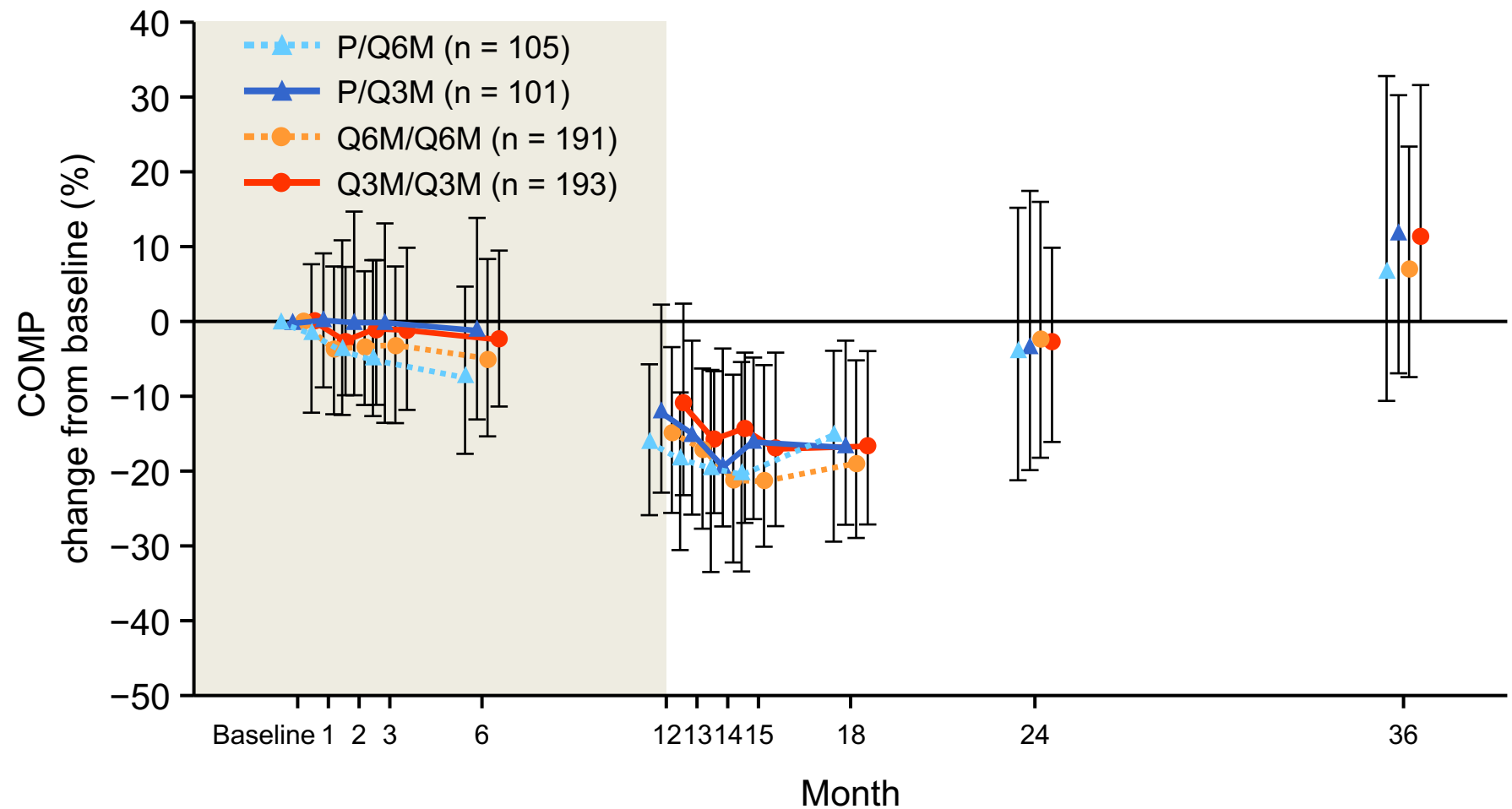
5

Supplementary Figure 4 (A). Percent change in urine C-telopeptide of type II collagen/creatinine from baseline to each visit



Median (interquartile range).
CTX-II/Cr, C-telopeptide of type II collagen adjusted for creatinine; P/Q3M, placebo for 12 months followed by denosumab 60 mg every 3 months; P/Q6M, placebo for 12 months followed by denosumab 60 mg every 6 months; Q3M/Q3M, denosumab 60 mg every 3 months for 12 months followed by denosumab 60 mg every 3 months; Q6M/Q6M, denosumab 60 mg every 6 months for 12 months followed by denosumab 60 mg every 6 months.
Long-term radiography analysis set.

Supplementary Figure 4 (B). Percent change in cartilage oligomeric matrix protein from baseline to each visit



Median (interquartile range).
COMP, cartilage oligomeric matrix protein; P/Q3M, placebo for 12 months followed by denosumab 60 mg every 3 months; P/Q6M, placebo for 12 months followed by denosumab 60 mg every 6 months; Q3M/Q3M, denosumab 60 mg every 3 months for 12 months followed by denosumab 60 mg every 3 months; Q6M/Q6M, denosumab 60 mg every 6 months for 12 months followed by denosumab 60 mg every 6 months.
Long-term radiography analysis set.

7