SUPPLEMENTARY APPENDIX

Effects of Interleukin-1β Inhibition on Incident Hip and Knee Replacement:

Exploratory analyses from a randomized, double-blind, placebo-controlled trial

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Supplementary Table 1: Terms used by the investigators to describe the nature of the AEs and incidence rates in patients with and without medical history of OA

AE preferred term	AE lower level term	OA in medical history (N = 1569)(%)	No OA in medical history (N = 8492)(%)
Nodal OA	**Total**	**0**	**2 (0)**
	Heberden's nodes	0	2 (0)
OA	**Total**	**236 (15)**	**267 (3.1)**
	Ankle OA	4 (0.3)	6 (0.1)
	Arthrosis	4 (0.3)	12 (0.1)
	Coxarthrosis	19 (1.2)	33 (0.4)
	Degenerative joint disease	4 (0.3)	7 (0.1)
	Elbow OA	3 (0.2)	3 (0)
	Erosive OA	1 (0.1)	0
	Finger OA	0	7 (0.1)
	Foot OA	4 (0.3)	3 (0)
	Generalised OA	0	1 (0)
	Generalized OA	1 (0.1)	4 (0)
	Gonarthrosis	12 (0.8)	39 (0.5)
	Hand OA	6 (0.4)	8 (0.1)
	Hip arthrosis	3 (0.2)	14 (0.2)
	Hips OA	11 (0.7)	12 (0.1)
	Knee OA	12 (0.8)	21 (0.2)
	Localised OA	1 (0.1)	0
	Localized OA	0	1 (0)
	OA hip	2 (0.1)	6 (0.1)
	Omarthrosis	5 (0.3)	9 (0.1)

	O.A. shoulders	1 (0.1)	3 (0)
	OA	8 (0.5)	25 (0.3)
	OA aggravated	139 (8.9)	14 (0.2)
	OA deformans	0	1 (0)
	OA flare up	1 (0.1)	1 (0)
	OA knee	14 (0.9)	30 (0.4)
	OA knees	3 (0.2)	8 (0.1)
	OA shoulders	2 (0.1)	2 (0)
	Osteoarthrosis	0	6 (0.1)
	Osteoarthrosis generalized	0	1 (0)
	OA, generalized, involving hand	0	1 (0)
	OA, localized, primary, involving forearm	0	1 (0)
	Rhizarthrosis	0	1 (0)
	Shoulder OA	9 (0.6)	15 (0.2)
	Thumb OA	3 (0.2)	7 (0.1)
	Toe OA	1 (0.1)	0
	Wrist OA	4 (0.3)	2 (0)

AE, adverse event; OA, osteoarthritis

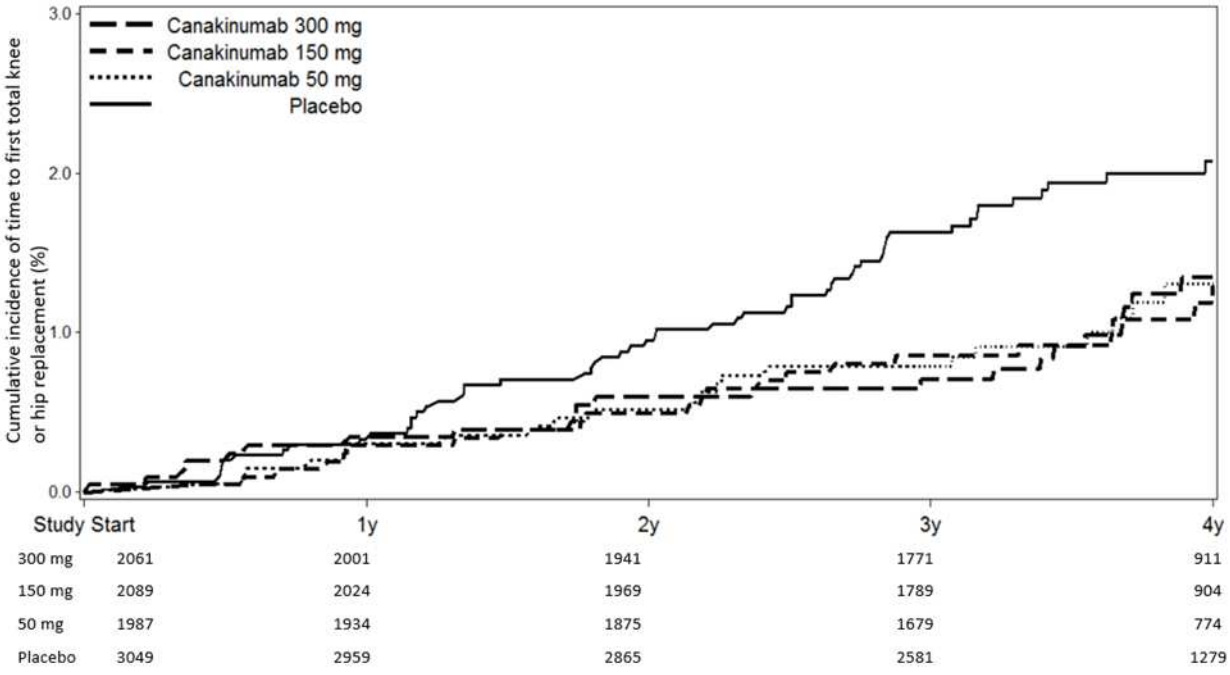
Supplemental Table 2: Baseline clinical characteristics by medical history of OA and treatment group

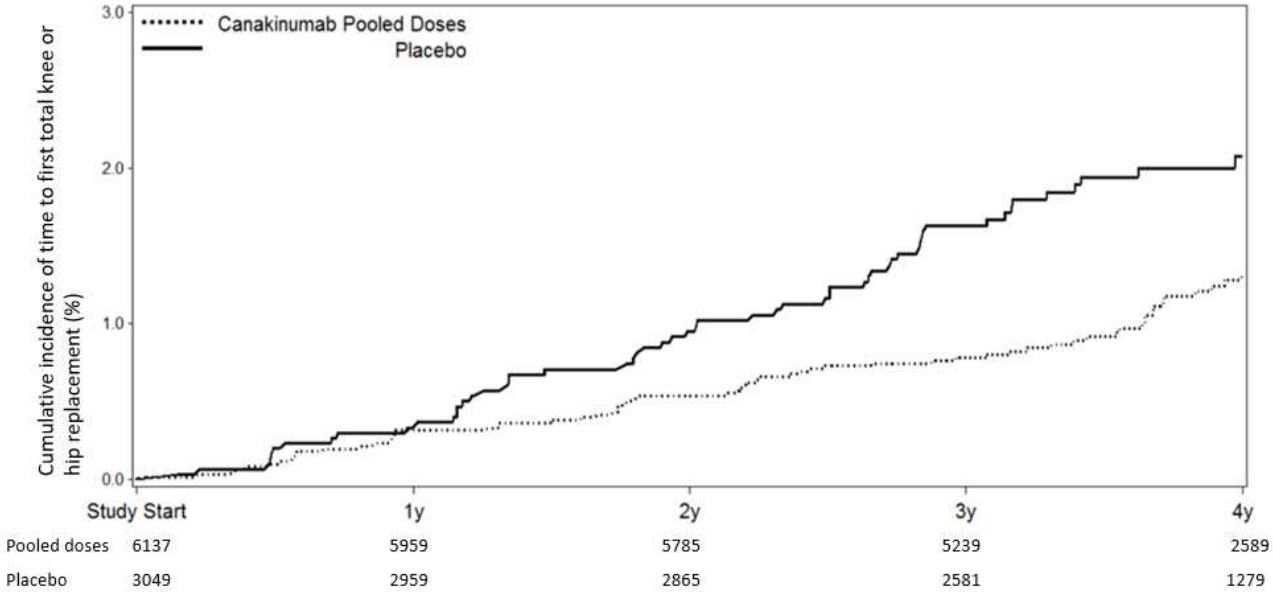
	Medical history of OA		**No OA in the medical history**	
Demographic variable[1]	**Canakinumab Pooled (N=1073)**	**Placebo (N=496)**	**Canakinumab Pooled (N=5644)**	**Placebo (N=2848)**
Age – y	64.9 (9.1)	64.3 (8.9)	60.4 (10.7)	60.5 (10.7)
Sex, F – no. (%)	390 (36.3)	165 (33.3)	1332 (23.6)	700 (24.6)
Weight (kg)	93.6 (21.5)	95.9 (21.6)	87.54 (19.6)	87.30 (19.7)
BMI (kg/m^2)	32.7 (6.5)	33.0 (6.7)	30.2 (5.7)	30.2 (5.8)
Waist circumference (cm)	109.2 (16.0)	110.1 (16.4)	104.3 (14.5)	104.1 (14.7)
Smoking, current smoker (%)	244 (22.7)	105 (21.2)	1357 (24.0)	660 (23.2)
Smoking, former smoker (%)	531 (49.5)	256 (51.6)	2603 (46.1)	1363 (47.9)
hsCRP (mg/L) (median, q1-q3)	4.15 (2.80-7.00)	4.10 (2.75-6.75)	4.35 (2.85-7.25)	4.05 (2.75-7.15)

1) Values are mean (SD), unless otherwise noted

BMI, Body Mass Index; hsCRP, high sensitivity C-reactive protein; OA, Osteoarthritis

Supplemental Figure 1. Cumulative incidence of THR or TKR in participants treated with placebo compared to canakinumab at 50 mg, 150 mg, or 300 mg administered once every three months (A, top); and placebo compared to all participants treated with canakinumab regardless of dose (B, bottom). Data are shown on an intention-to-treat basis for trial participants without a prior history of gout, gouty arthritis, or rheumatoid arthritis.





Supplemental Figure 2: Cumulative incidence of the secondary supportive sensitivity endpoint of worsening OA symptoms or new OA adverse events in participants treated with placebo compared to canakinumab at 50 mg, 150 mg, or 300 mg administered once every three months. Data are shown on an intention-to-treat basis for those with peripheral OA at study entry.