

Supporting information

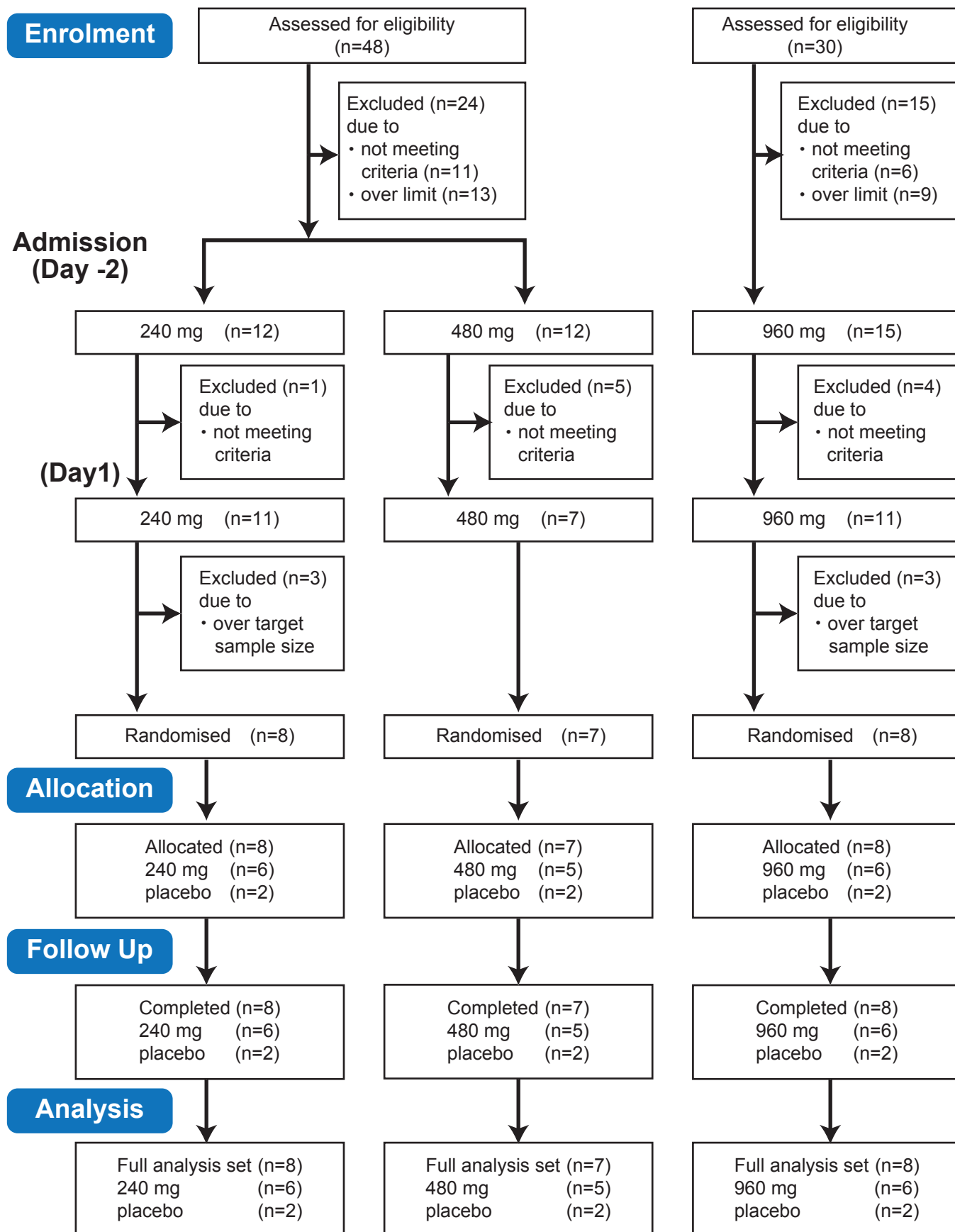


Figure S1. CONSORT flow chart

Each dose was given three times daily.

Table S1. Subject demographics shown as mean (SD)

Mean AUEC (%·h)	Placebo	AJM300 dose		
		240 mg	480 mg	960 mg
Number of patients	6	6	5	6
Age (years)	23.7 (2.4)	24.2 (4.2)	24.6 (4.3)	24.8 (4.5)
Height (cm)	171.12 (7.31)	175.43 (9.09)	172.78 (6.86)	167.00 (3.65)
Weight (kg)	65.62 (5.41)	65.35 (8.70)	66.48 (3.97)	59.98 (7.26)
BMI (kg m⁻²)	22.47(1.91)	21.18 (1.87)	22.30 (1.39)	21.48 (2.22)

BMI, body mass index; SD, standard deviation.

Table S2. PK dose proportionality assessed using a power model

PK parameters	Slope	95% CI	
		lower bound	upper bound
Day 1		AJM300	
C_{max 24h} (ng mL⁻¹)	0.930	0.343	1.517
AUC_{24h} (ng·h mL⁻¹)	1.026	0.679	1.373
Day 10			
C_{max 24h} (ng mL⁻¹)	0.611	0.275	0.946
AUC_{24h} (ng·h mL⁻¹)	0.680	0.453	0.907
Day 1		HCA2969	
C_{max 24h} (ng mL⁻¹)	1.000	0.576	1.425
AUC_{24h} (ng·h mL⁻¹)	0.986	0.667	1.305
Day 10			
C_{max 24h} (ng mL⁻¹)	0.678	0.408	0.949
AUC_{24h} (ng·h mL⁻¹)	0.678	0.413	0.942

Table S3A. Mean AUEC where the increase in lymphocyte count was $\geq 0\%$, $\geq 30\%$ and 50%

Mean AUEC (%·h)	Placebo	AJM300 dose		
		240 mg	480 mg	960 mg
Day 1				
0%	118.003	594.387	1000.177	1209.875
30%	3.379	113.170	389.327	546.608
50%	0.006	18.555	141.653	215.473
Day 10				
0%	109.139	698.558	1031.524	1197.023
30%	0.000	234.675	431.186	526.166
50%	0.000	98.512	169.276	202.027

Table S3B. Strength of the relationship (p-value) to each contrast coefficient

	Contrast coefficient				
	-3, -1, 1, 3	-3, -1, 1, 1	-5, -1, 3, 3	-1, -1, -1, 3	-3, -3, 1, 5
Day 1					
0%	98.2 (0.0000)	72.0 (0.0000)	94.7 (0.0000)	44.1 (0.0000)	79.9 (0.0000)
30%	98.0 (0.0000)	48.2 (0.0003)	85.3 (0.0000)	57.4 (0.0001)	94.8 (0.0000)
50%	94.1 (0.0003)	37.1 (0.0128)	77.7 (0.0008)	62.2 (0.0021)	98.3 (0.0003)
Day 10					
0%	94.3 (0.0000)	81.6 (0.0000)	95.2 (0.0000)	37.0 (0.0002)	70.3 (0.0000)
30%	97.8 (0.0001)	73.0 (0.0006)	95.2 (0.0001)	42.8 (0.0050)	78.9 (0.0004)
50%	96.4 (0.0086)	76.9 (0.0170)	95.7 (0.0088)	39.9 (0.0751)	75.1 (0.0182)

The strength of the relationship was obtained by eta-squared (η^2), the sum of squares (contrast)/sum of squares (total). The polynomial contrast coefficient indicates following trends: linear, -3, -1, 1, 3; upper bound, -3, 1, 1, 1; half up, -5, -1, 3, 3; lower bound, -1, -1, -1, 3; half down, -3, -3, 1, 5. (refer to Figure 4)

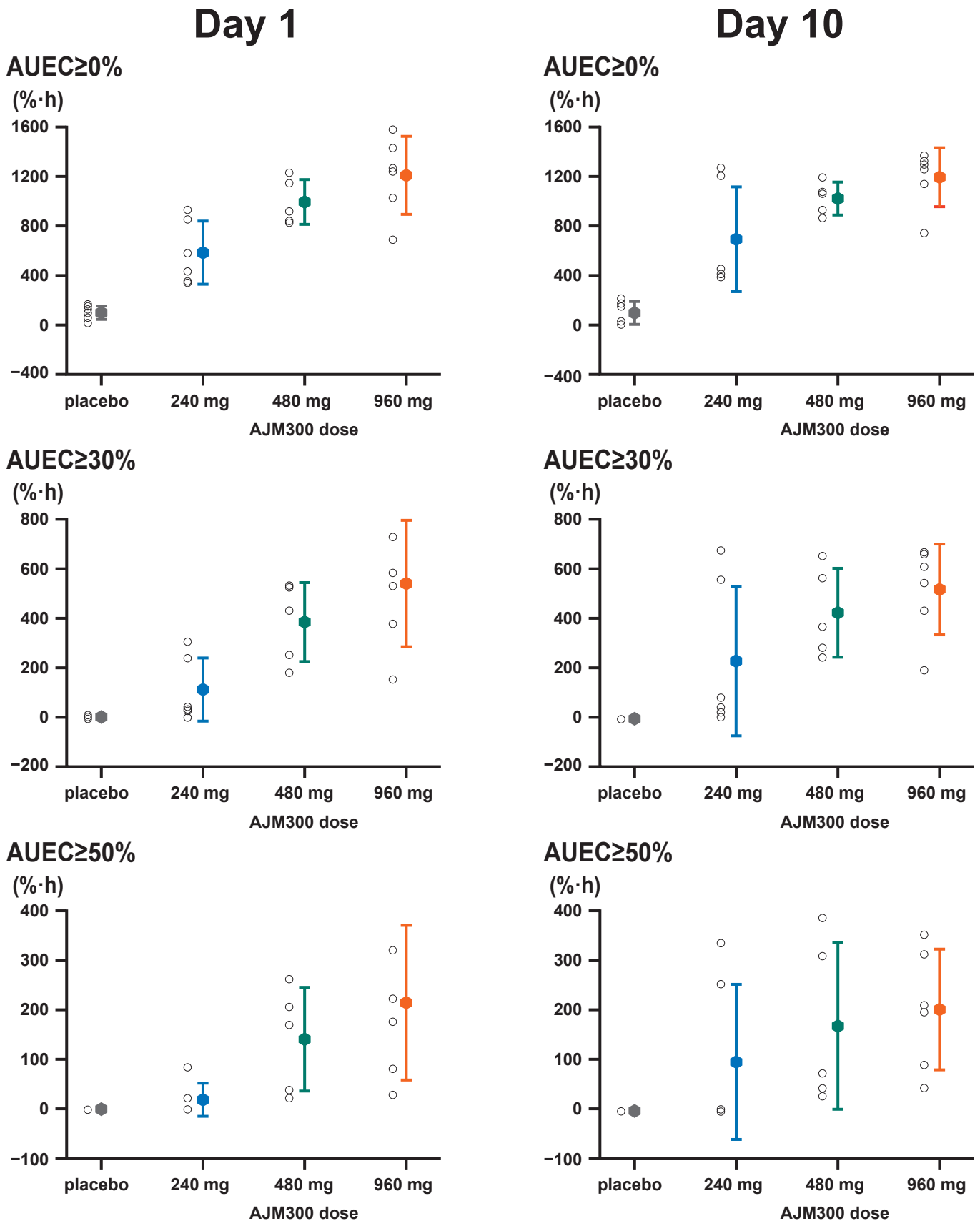


Figure S2. The mean AUECs where the increase in lymphocyte count from baseline were $\geq 0\%$ (top), $\geq 30\%$ (middle) and $\geq 50\%$ (bottom) at each dosage tested.

The comparison between the AUECs where the percentage changes were $\geq 0\%$ and $\geq 30\%$ on Day 1, and $\geq 30\%$ and $\geq 50\%$ on Day 10 versus the dose demonstrated linear trends (refer to Table S3B). Data are presented as mean \pm SD.