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**The effect of a selective CXCR2 antagonist (AZD5069) on human blood neutrophil count and innate immune functions.**

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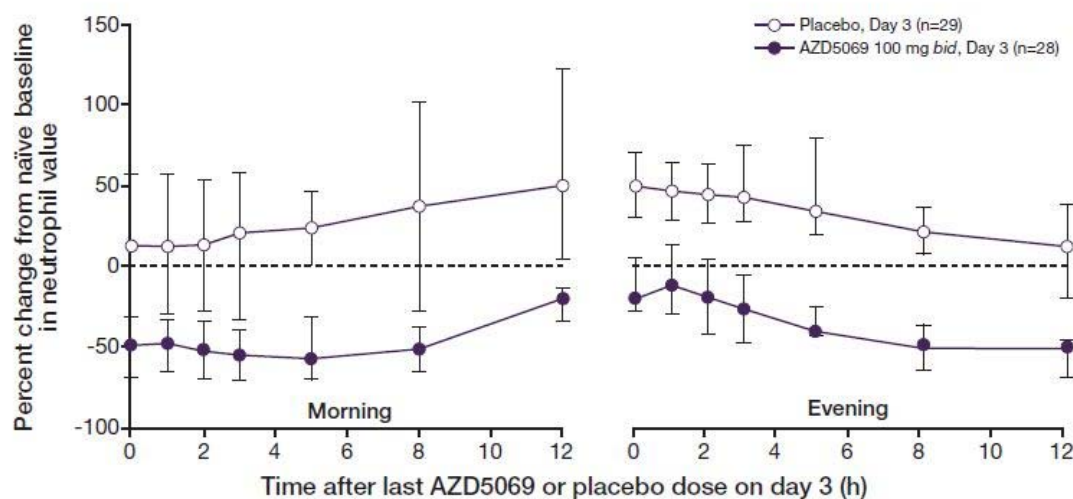
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# The effect of a selective CXCR2 antagonist (AZD5069) on human blood neutrophil count and innate immune functions

## Supplementary information

**Supplementary figure 1.** Reduction in blood neutrophil count on Day 3 of treatment period. Each point is shown as the arithmetic mean ( $\pm$  SD) neutrophil percent change from naïve (pre-treatment) baseline versus time by treatment, on linear scale.

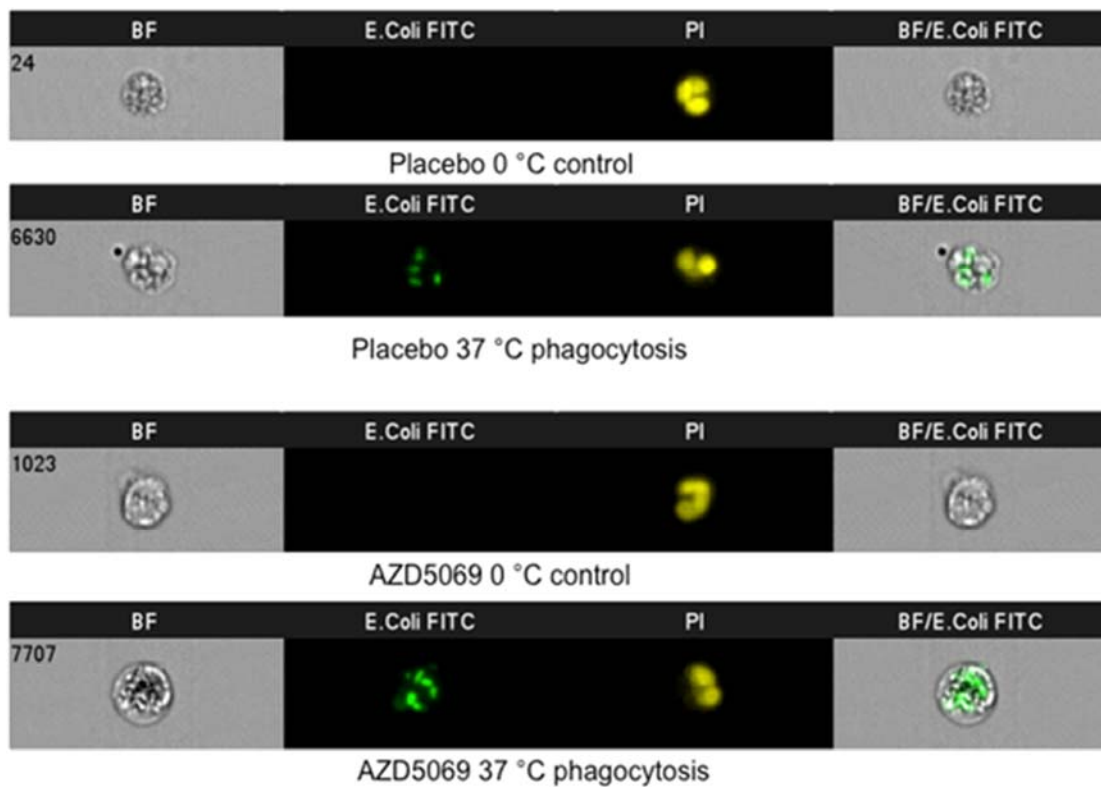


**Supplementary figure 2.** Images of neutrophils from representative subjects treated with either placebo or AZD5069.

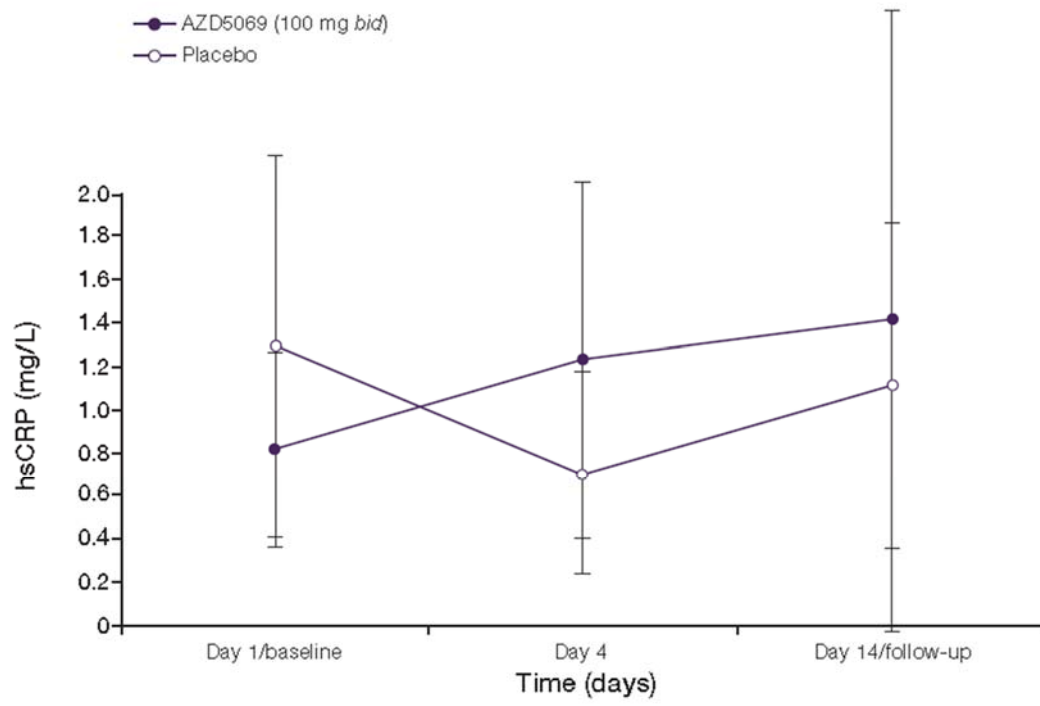
Neutrophil phagocytic function was visualised using a multispectral imaging flow cytometry instrument (Imagestream-X, Amnis). Images taken at 0°C are negative controls; phagocytosis was triggered by cell incubation at 37°C. Individual neutrophils are visualised in bright field (BF), green fluorescence (*E. coli* FITC) that shows FITC-labelled *E. coli* engulfed within the cell. After exposure

to propidium iodide (PI), which stains the cell nucleus, the figure shows typical segmented nuclei and a combination/superimposition of BF/*E. coli* FITC images.

The Phagotest assay used in this study includes the fluorescence quenching step, which neutralises FITC fluorescence in *E. coli* that are not protected by being inside the neutrophils. Thus, on the placebo 37°C phagocytosis BF/*E. coli* FITC image, bacteria attached to the surface of the neutrophil are visible but lack green fluorescence label.



**Supplementary figure 3.** Serum levels of high sensitivity C-reactive protein (hsCRP) remained low during both treatment periods. Figure shows mean values (SD).



**Supplementary table 1.** Demographics of human volunteer study population.

Variable/ Category	All subjects N=30
Age (years)	
Mean (SD)	30 (8)
Median	28
Minimum/maximum	19/45
Gender (n [%])	
Male	29(96.7%)
Female	1 (3.3%)
Race (n [%])	
White	29 (96.7%)
Other*	1 (3.3%)
Height (cm)	
Mean (SD)	178 (9)
Median	179
Minimum/maximum	158/191
Weight (kg)	
Mean (SD)	75.6 (10.7)
Median	75.0
Minimum/maximum	50.2/108.0
Body mass index (kg/m <sup>2</sup> )	
Mean (SD)	23.9 (2.5)
Median	23.9
Minimum/maximum	19.0/30.0

SD: standard deviation

\*Subject E0002033 was Middle Eastern.

**Supplementary table 2.** Circulating neutrophil counts over time in human volunteers

		Baseline	Day 2	Day 3	Day 4	Day 14
<b>Circulating neutrophil count (10<sup>9</sup>/L)</b>						
AZD5069	n	29	29	28	28	29
	mean	3.43	1.10	1.42	1.36	3.05
	SD	0.89	0.61	0.70	0.65	0.95
Change from baseline	n		29	28	28	29
	mean		-1.67	-1.34	-0.40	0.32
	SD		0.67	0.69	0.60	0.74
Placebo	n	29	29	29	29	29
	mean	3.21	3.00	2.90	2.92	3.06
	SD	0.80	0.89	0.87	0.94	0.92
Change from baseline	n		29	29	29	29
	mean		0.19	0.09	0.11	0.22
	SD		0.78	0.80	0.86	1.23

**Supplementary table 3.** Human volunteer neutrophil functional assays at the indicated timepoints.

		Day 1	Day 4	Day 14
Phagocytosis (%)	n	28	28	28
	Geometric mean	98.2	96.2	97.5
	CV%	1.4	2.4	1.5
	Arithmetic mean	98.2	96.2	97.5
	SD	1.2	2.3	1.5
	Median	98.4	96.9	97.8
95% CI		(97.7, 98.7)	(95.3, 97.1)	(96.9, 98.1)
Placebo (n=29)	n	29	29	29
	Geometric mean	97.9	97.6	98.0
	CV%	1.8	1.5	1.2
	Arithmetic mean	97.9	97.6	98.0
	SD	1.7	1.5	1.1
	Median	98.4	98.2	98.3
95% CI		(97.2, 98.6)	(97.0, 98.2)	(97.6, 98.5)
Oxidative burst (%)	n	28	28	29
	Geometric mean	99.1	99.0	98.7
	CV%	1.0	0.7	0.9
	Arithmetic mean	99.1	99.0	98.7
	SD	0.9	0.7	0.9
	Median	99.4	99.3	99.1
95% CI		(98.8, 99.5)	(98.7, 99.3)	(98.4, 99.1)
Placebo (n=29)	n	29	28	29
	Geometric mean	99.2	99.3	98.3
	CV%	0.5	0.5	2.9
	Arithmetic mean	99.2	99.3	98.3
	SD	0.5	0.5	2.7
	Median	99.4	99.3	99.1
95% CI		(99.0, 99.4)	(99.1, 99.5)	(97.3, 99.3)

CV, geometric coefficient of variation; SD, standard deviation, CI, confidence interval.