

## Supplementary Online Content

Paton NI, Goodall RL, Dunn DT, et al. Effects of hydroxychloroquine on immune activation and disease progression among HIV-infected patients not receiving antiretroviral therapy: a randomized controlled trial. *JAMA*. doi:10.1001/jama.2012.6936.

**eTable 1.** Changes in immunological and inflammatory parameters from baseline to week 48

**eFigure 1.** Change in CD8 cell activation during the trial by treatment group

**eFigure 2.** Kaplan-Meier curves of time to CD4 cell count below 350 cells/mm<sup>3</sup> by treatment group

**eFigure 3.** Comparisons of viral load values by treatment group

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Changes in immunological and inflammatory parameters from baseline to week 48<sup>a</sup>

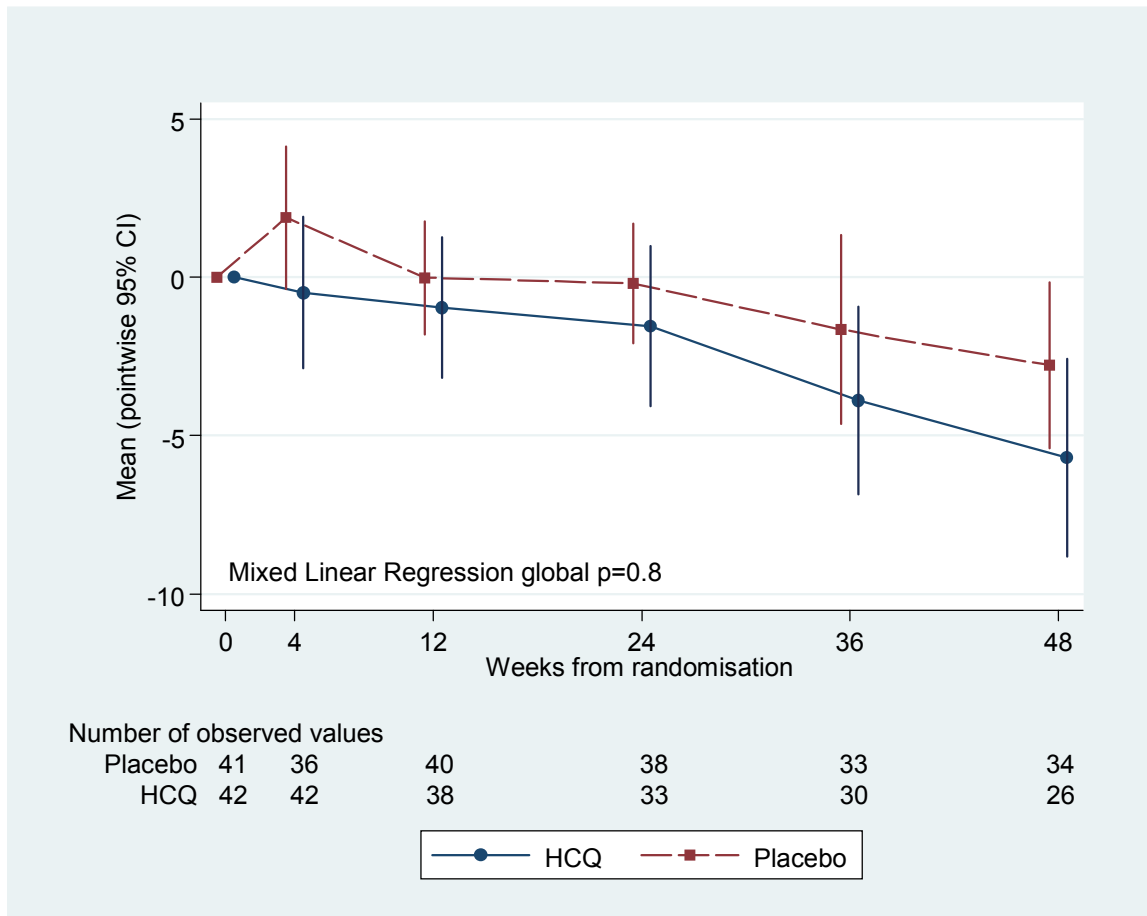
Marker <sup>c</sup>	Baseline		Change at week 24/48 <sup>a</sup>			P value <sup>b</sup>
	HCQ Mean (SD)	Placebo Mean (SD)	HCQ Mean (95% CI)	Placebo Mean (95% CI)	HCQ-Placebo (95% CI)	
IL-8 log <sub>10</sub> pg/ml	2.31 (0.91)	2.51 (0.77)	-0.31 (-0.63,0.02)	-0.23 (-0.53, 0.07)	-0.08 (-0.44, 0.29)	0.67
TNF-p55 log <sub>10</sub> pg/ml	2.88 (0.18)	2.87 (0.19)	0.09 (0.03,0.15)	0.03 (-0.02,0.08)	0.06 (-0.01,0.13)	0.11
TNF-p75 log <sub>10</sub> pg/ml	3.26 (0.18)	3.21 (0.22)	0.04 (0.00,0.09)	0.03 (-0.02,0.07)	0.01 (-0.04,0.08)	0.62
DR5 log <sub>10</sub> pg/ml	1.20 (0.08)	1.22 (0.08)	0.01(-0.02,0.04)	0.00 (-0.02,0.03)	0.00 (-0.03,0.04)	0.83
CD4-Caspase 3 %	5.1 (5.7)	7.2 (14.5)	4.8 (2.7, 6.8)	2.6 (0.1,5.0)	2.2 (-0.6,5.0)	0.12
CD4-Ki67 %	5.9 (7.1)	9.3 (13.9)	3.7 (1.4, 6.0)	3.5 (0.8, 6.2)	0.2 (-2.8, 3.2)	0.89
CD8-Caspase 3 %	5.4 (6.2)	6.0 (6.4)	5.4 (3.5, 7.4)	2.5 (0.2,4.8)	3.0 (0.4, 5.6)	0.03
CD8-Ki67 %	6.7 (7.9)	8.7 (9.6)	2.3 (0.3,4.6)	3.3 (0.7,5.8)	-0.8 (-3.7, 2.0)	0.57
CD4RA-CD27+ % Central memory	39.1 (8.8)	38.8 (11.4)	-2.2 (-3.9,-0.6)	0.1 (-1.4,1.6)	-2.3 (-4.5,-0.1)	0.04
CD4RA+CD27+ % naïve	42.9 (12.2)	44.0 (14.4)	0.3 (-1.8,2.5)	-0.8 (-1.8, 2.5)	1.2 (-1.8, 4.1)	0.78
CD4RA-CD27- % Effector	13.2 (8.5)	12.4 (8.6)	1.1 (-0.5, 2.6)	0.9 (-0.6, 2.4)	0.2 (-2.0, 2.4)	0.87
CD4RA+CD27- % Terminally differentiated	4.78 (4.80)	4.81 (4.53)	0.9 (0.1, 1.6)	-0.3 (-1.1, 0.4)	1.2 (0.2, 2.2)	0.02

<sup>a</sup> Changes at week 24 (CD4-Caspase 3, CD4-Ki67, CD8-Caspase 3, CD8-Ki67) or week 48 (all other parameters) are changes from baseline predicted using mixed linear regression models.

<sup>b</sup> p-value from parameter representing the difference in slopes between the 2 arms.

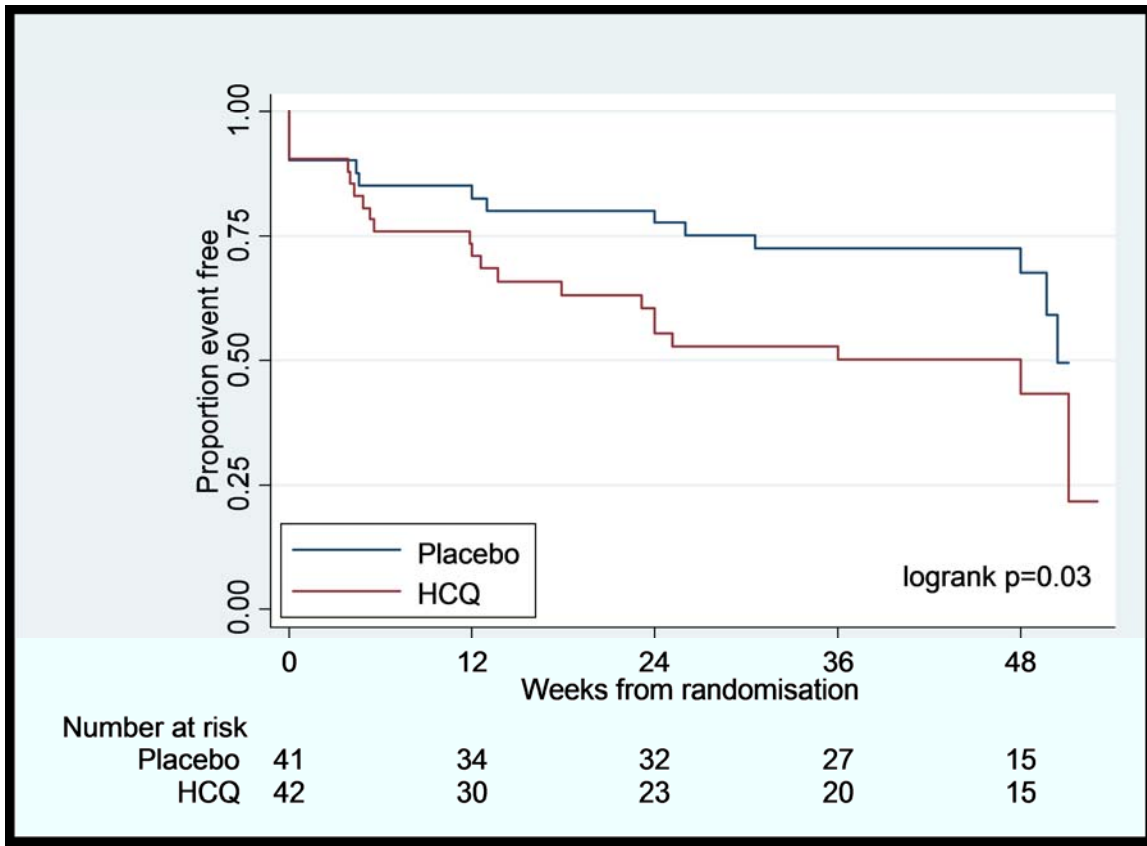
<sup>c</sup> IL-1 $\beta$ , TNF- $\alpha$  and GM-CSF were also measured but most results were below limit of detection."

**eFigure 1.** Change in CD8 cell activation during the trial by treatment group



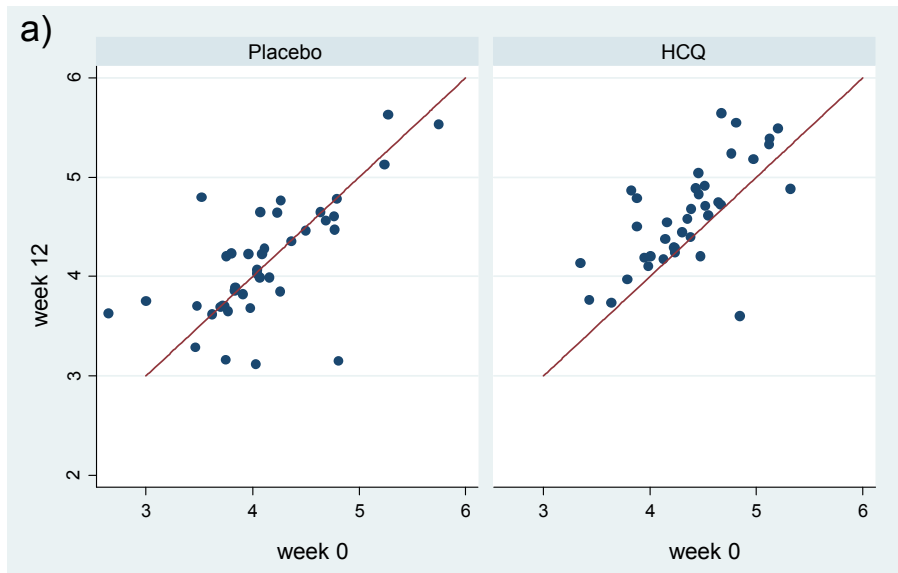
Bars indicate 95% CIs around mean values. Changes from baseline are based on empirical data, supplemented by individual predicted values for missing data obtained using a linear mixed model.

**eFigure 2.** Kaplan-Meier curves of time to CD4 cell count below 350 cells/mm<sup>3</sup> by treatment group

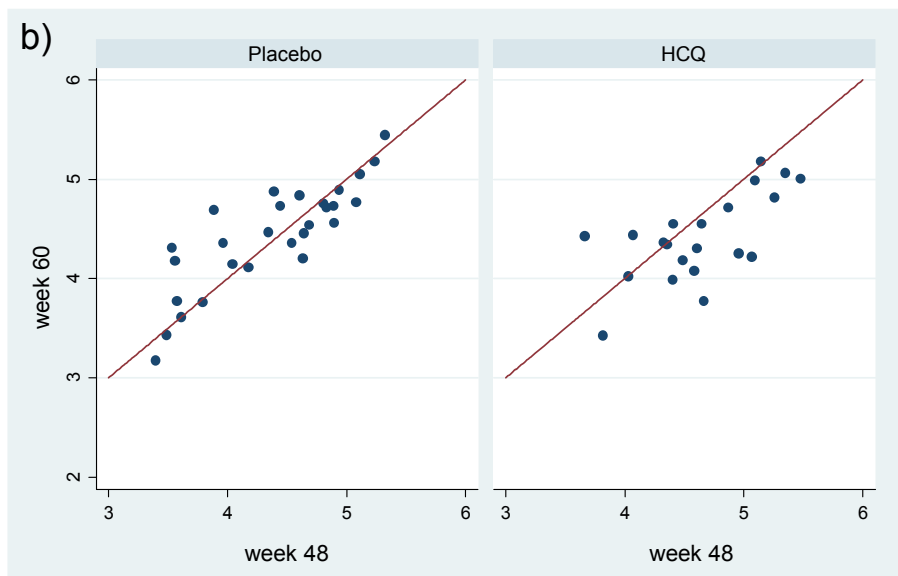


**eFigure 3a.** Comparison of viral load values at week 0 and week 12 by treatment group

**eFigure 3b.** Comparison of viral load values at week 48 and week 60 by treatment group



Individual points represent a patient's viral load result (on a logarithmic scale) at week 12 plotted against the same patient's result at week 0. The line shown is the line of equality. In the placebo group (n=40), values are evenly scattered around the line indicating that there is no systematic change in viral load between these visits. In the hydroxychloroquine group (n= 38), nearly all values lie above the line of equality, consistent with a systematic increase in viral load affecting most patients.



Individual points represent a patient's viral load result (on a logarithmic scale) at week 60 (off treatment) plotted against the same patient's result at week 48 (on treatment). In the placebo group (n=28), values are evenly scattered around the line indicating that there is no systematic change in viral load between these visits. In the hydroxychloroquine group (n=22), nearly all values lie below the line of equality, consistent with a systematic decrease in viral load affecting most patients following cessation of therapy.

• HIV RNA ( $\log_{10}$  copies/ml)  
— Line of equality