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Supplementary Materials for

A dose-dependent plasma signature of the safety and immunogenicity of the rVSV-Ebola vaccine in Europe and Africa

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Determination of the dose independence of the signature's equation

To define whether this signature was dependent or independent of the vaccine dose, it was next calculated in each dose group.

Signature assessed in low-dose vaccinees only

The ratio of cytokines/chemokines introduced in the equation was also standardized. This standardization involves the mean and standard deviation of each ratio in Geneva samples:

$$\text{IL1-Ra}^{\text{STD-LD}} = [\log10(\text{IL-1Ra}^{\text{Day 1}} / \text{IL-1Ra}^{\text{Day 0}})-0.245]/0.413$$

$$\text{IL-6}^{\text{STD-LD}} = [\log10(\text{IL-6}^{\text{Day 1}} / \text{IL-6}^{\text{Day 0}})-0.203]/0.387$$

$$\text{TNF-}\alpha^{\text{STD-LD}} = [\log10(\text{TNF}\alpha^{\text{Day 1}} / \text{TNF}\alpha^{\text{Day 0}})-0.060]/0.326$$

$$\text{IL-10}^{\text{STD-LD}} = [\log10(\text{IL-10}^{\text{Day 1}} / \text{IL-10}^{\text{Day 0}})-0.192]/0.604$$

$$\text{MCP-1}^{\text{STD-LD}} = [\log10(\text{MCP-1}^{\text{Day 1}} / \text{MCP-1}^{\text{Day 0}})-0.148]/0.231$$

The eigen values for the components were 3.29, 0.86, 0.37, 0.31 and 0.17. The single component with the eigen value greater than 1 was therefore retained. This component explained 66% of the variability of the ratios.

The equation of this principal component was:

$0.459*\text{MCP-1}^{\text{STD-LD}} + 0.464*\text{IL-1Ra}^{\text{STD-LD}} + 0.410*\text{TNF}\alpha^{\text{STD-LD}} + 0.457*\text{IL-10}^{\text{STD-LD}} + 0.464*\text{IL-6}^{\text{STD-LD}}$

The standard deviation of the signature in vaccinees was 1.81 (and the mean was 0). The coefficient in the equation was then divided by 1.81 so that the standard deviation of the signature equals 1. Thus, the final equation for the signature was:

Signature =

$0.253*\text{MCP-1}^{\text{STD-LD}} + 0.245*\text{IL-1Ra}^{\text{STD-LD}} + 0.226*\text{TNF-}\alpha^{\text{STD-LD}} + 0.252*\text{IL-10}^{\text{STD-LD}} + 0.256*\text{IL-6}^{\text{STD-LD}}$

The signature obtained in low-dose vaccinees was similar.

The Kaiser-Meyer-Olkin measure was assessed to check the adequacy of our model. The obtained values were: 0.72 for IL-1Ra, 0.81 for IL-6, 0.78 for TNF-α, 0.87 for IL-10 and 0.70 for MCP-1; the overall measure of adequacy was 0.77. We concluded that our model was adequate.

Signature assessed in high-dose vaccinees only

The ratio of cytokines/chemokines introduced in the equation was also standardized. This standardization involves the mean and standard deviation of each ratio in Geneva samples:

$$\text{IL1-Ra}^{\text{STD-HD}} = [\log10(\text{IL-1Ra}^{\text{Day 1}} / \text{IL-1Ra}^{\text{Day 0}})-1.026]/0.403$$

$$IL\text{-}6^{STD\text{-}HD} = [\log 10(IL\text{-}6^{Day\,1} / IL\text{-}6^{Day\,0})\text{-}0.626]/0.505$$

$$TNF\text{-}\alpha^{STD\text{-}HD} = [\log 10(TNF\alpha^{Day\,1} / TNF\alpha^{Day\,0})\text{-}0.337]/0.317$$

$$IL\text{-}10^{STD\text{-}HD} = [\log 10(IL\text{-}10^{Day\,1} / IL\text{-}10^{Day\,0})\text{-}0.618]/0.560$$

$$MCP\text{-}1^{STD\text{-}HD} = [\log 10(MCP\text{-}1^{Day\,1} / MCP\text{-}1^{Day\,0})\text{-}0.525]/0.243$$

The eigen values for the components were 3.15, 0.65, 0.61, 0.43 and 0.16. The single component with the eigen value greater than 1 was therefore retained. This component explained 63% of the variability of the ratios.

The equation of this principal component was:

$0.511*MCP\text{-}1^{STD\text{-}HD} + 0.468*IL\text{-}1Ra^{STD\text{-}HD} + 0.390*TNF\alpha^{STD\text{-}HD} + 0.421*IL\text{-}10^{STD\text{-}HD} + 0.437*IL\text{-}6^{STD\text{-}HD}$

The standard deviation of the signature in vaccinees was 1.77 (and the mean was 0). The coefficient in the equation was then divided by 1.77 so that the standard deviation of the signature equals 1. Thus, the final equation for the signature was:

Signature =
$0.288*MCP\text{-}1^{STD\text{-}HD} + 0.264*IL\text{-}1Ra^{STD\text{-}HD} + 0.220*TNF\text{-}\alpha^{STD\text{-}HD} + 0.237*IL\text{-}10^{STD\text{-}HD} + 0.246*IL\text{-}6^{STD\text{-}HD}$

The signature obtained in high-dose vaccinees was similar.

The Kaiser-Meyer-Olkin measure was assessed to check the adequacy of our model. The obtained values were: 0.70 for IL-1Ra, 0.84 for IL-6, 0.85 for TNF-α, 0.74 for IL-10 and 0.68 for MCP-1; the overall measure of adequacy was 0.74. We concluded that our model was adequate.
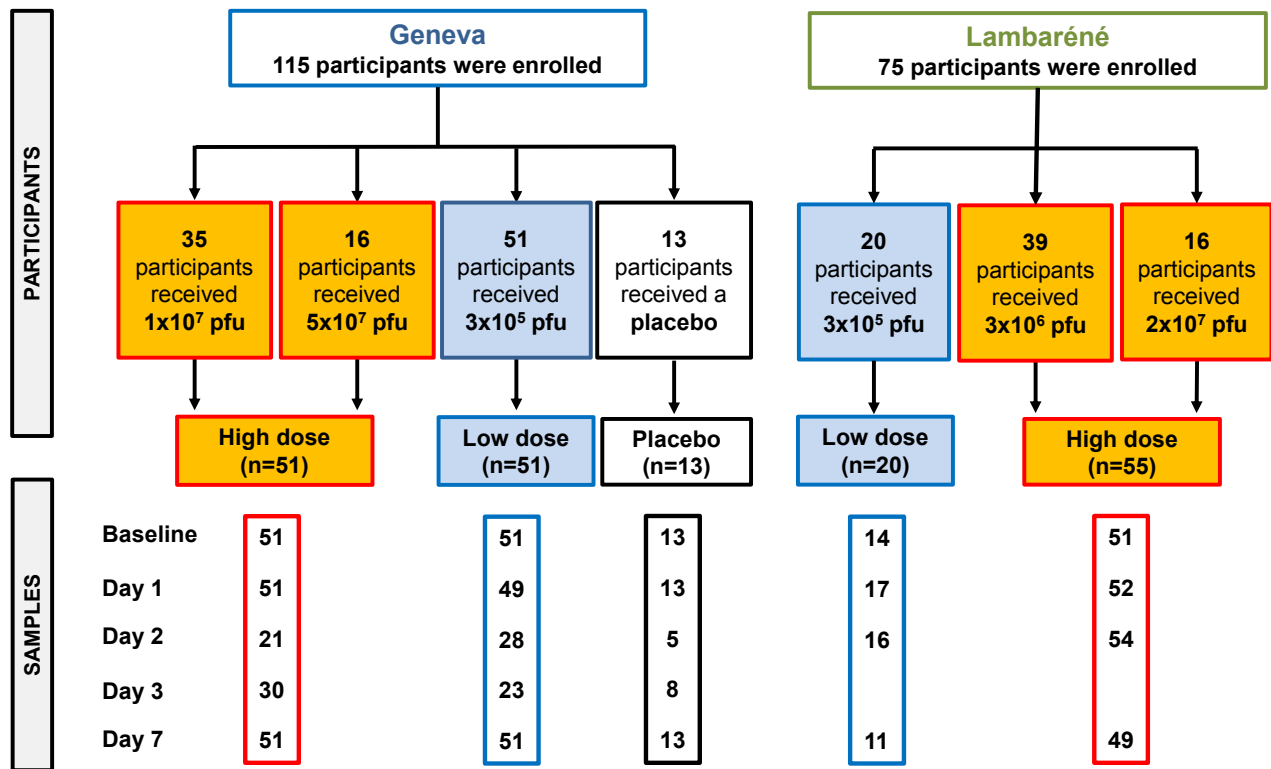
Figure S1. Study flow chart.

Flow diagram of the distribution of participants enrolled in the Geneva RCT and in the Lambaréné dose-escalation trials. The number of samples indicates samples available for/included in the analyses. In Geneva, the day 3 visit was scheduled on day 2 or 3, allowing comparison of the early kinetics of chemokines/cytokines. In Lambaréné, cytokine responses to $3x10^6$ and $2x10^7$ pfu were similar, such that these two groups of vaccinees were pooled into a "high-dose" group.
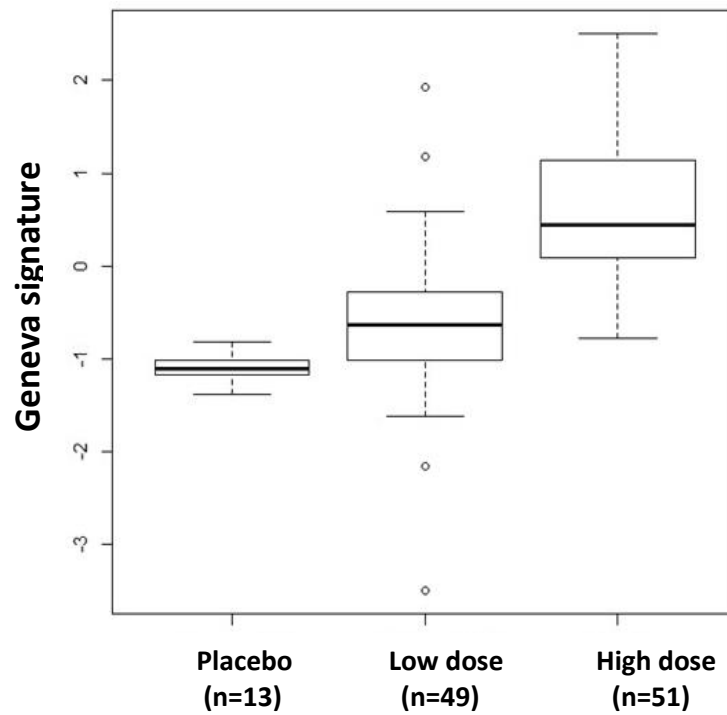
Figure S2. The plasma signature of responses to rVSV-ZEBOV in Geneva vaccinees.

This represents the signature (in arbitrary units) calculated in placebo, low-dose and high-dose vaccine recipients.
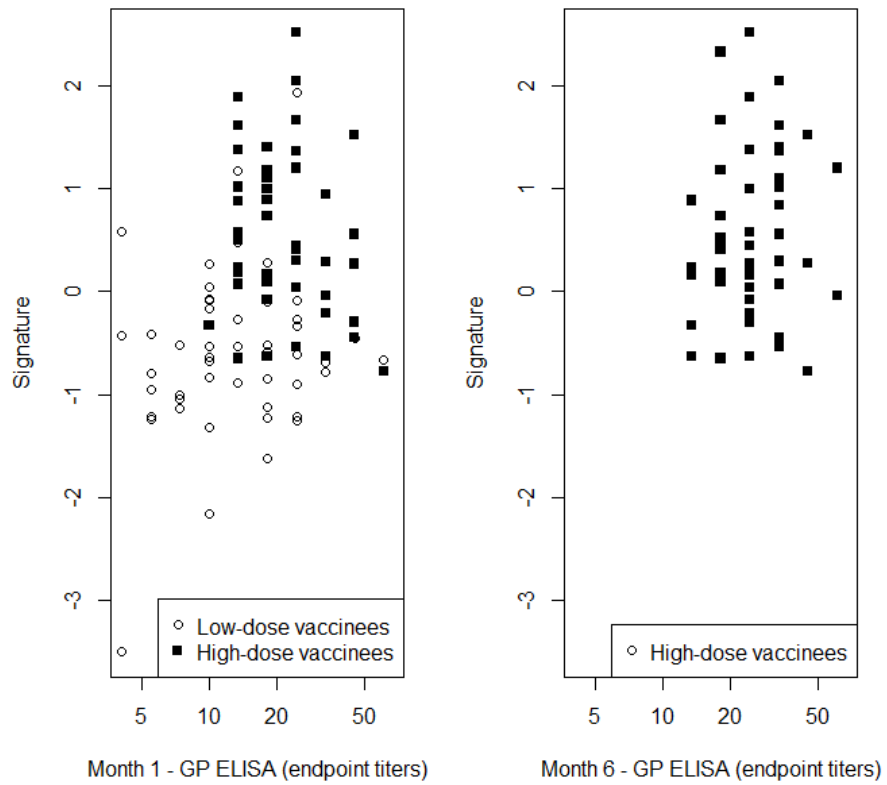
Figure S3. Associations between the plasma signature and IgG titers to EBOV-GP.

IgG antibodies to EBOV-GP had been assessed by GP-specific ELISA one month (left) and 6 months (right) following rVSV-ZEBOV immunization, as previously described (*5*). At month 6, only samples from high-dose Geneva vaccinees (n=51) were included.

A

IL1RN (IL-1RA)

CCL4 (MIP1-β)

IL6

CCL2 (MCP-1)

TNF

IL10

Placebo
Low dose
High dose

B

IL1RN (IL-1RA)

CCL4 (MIP1-β)

IL6

CCL2 (MCP-1)

TNF

IL10

Placebo
Low dose
High dose
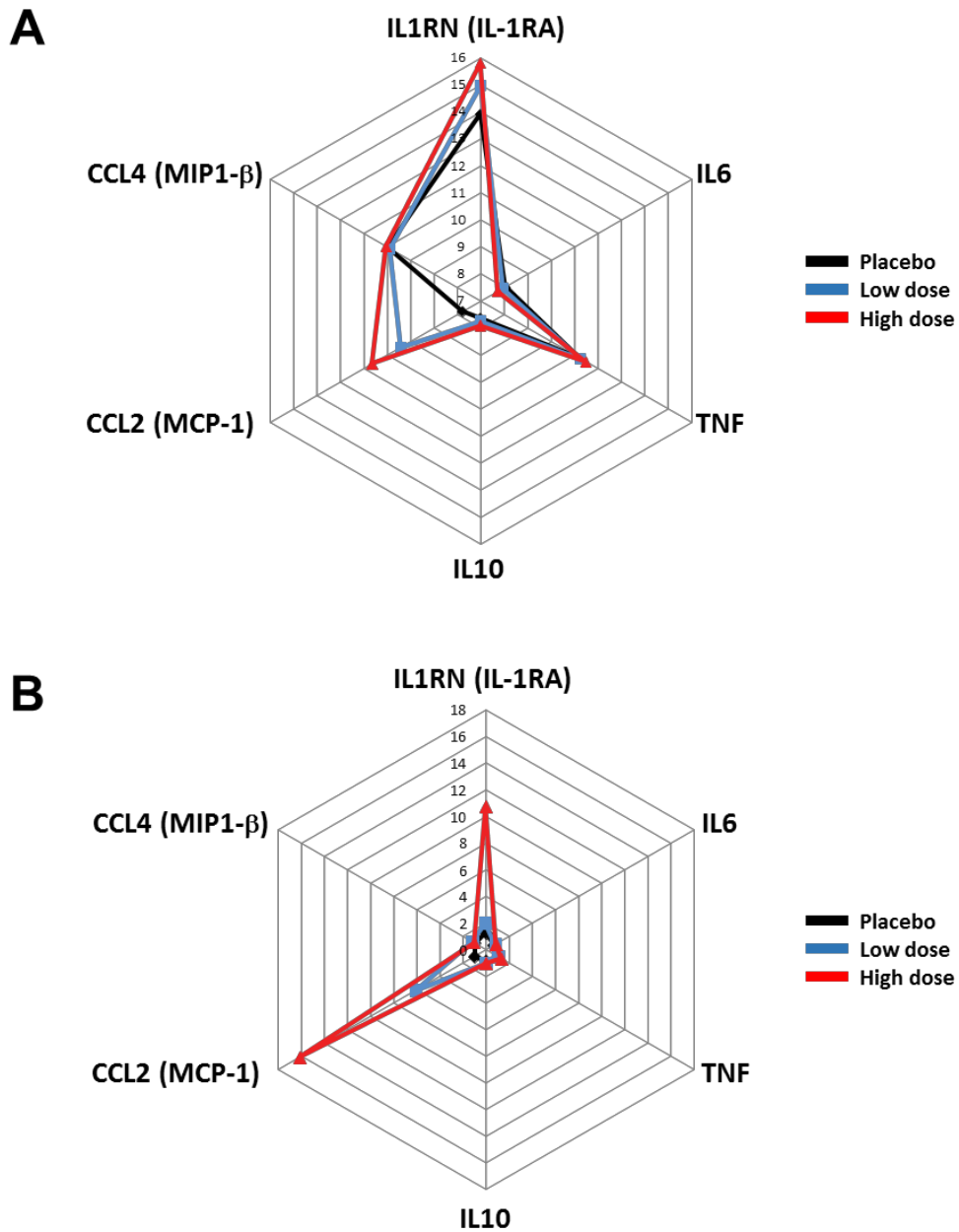
Figure S4. Relative gene expression levels and fold change in gene expression levels (compared to day 0) for cytokines and chemokines comprising the plasma signature in Geneva participants.

A. Relative gene expression levels ($\log_2$) of the markers comprising the plasma signature in Geneva participants.

B. Vaccine responses, expressed by the day 1/day 0 fold changes, are illustrated for the markers comprising the plasma signature in Geneva participants.
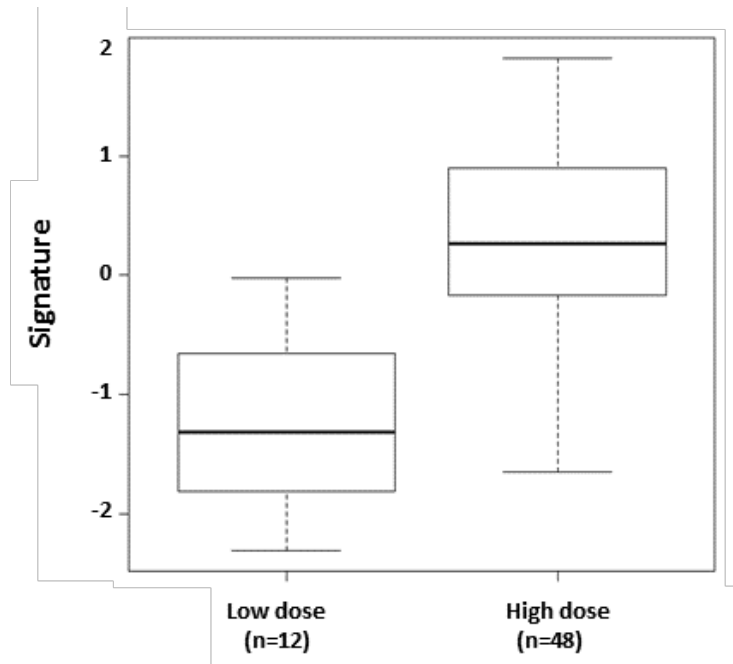
Figure S5. The plasma signature of responses to rVSV-ZEBOV defined by the Lambaréné data.

This represents the signature (in arbitrary units) calculated in low-dose and high-dose vaccine recipients.
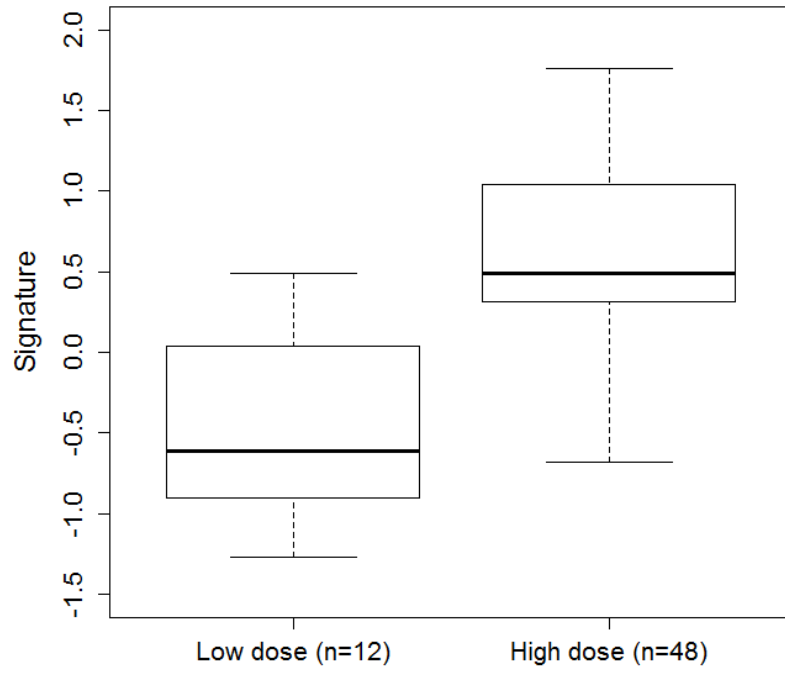
Figure S6. The Geneva plasma signature of responses to rVSV-ZEBOV applied to Lambaréné vaccinees.
This represents the signature (in arbitrary units) calculated in low-dose and high-dose vaccine recipients.
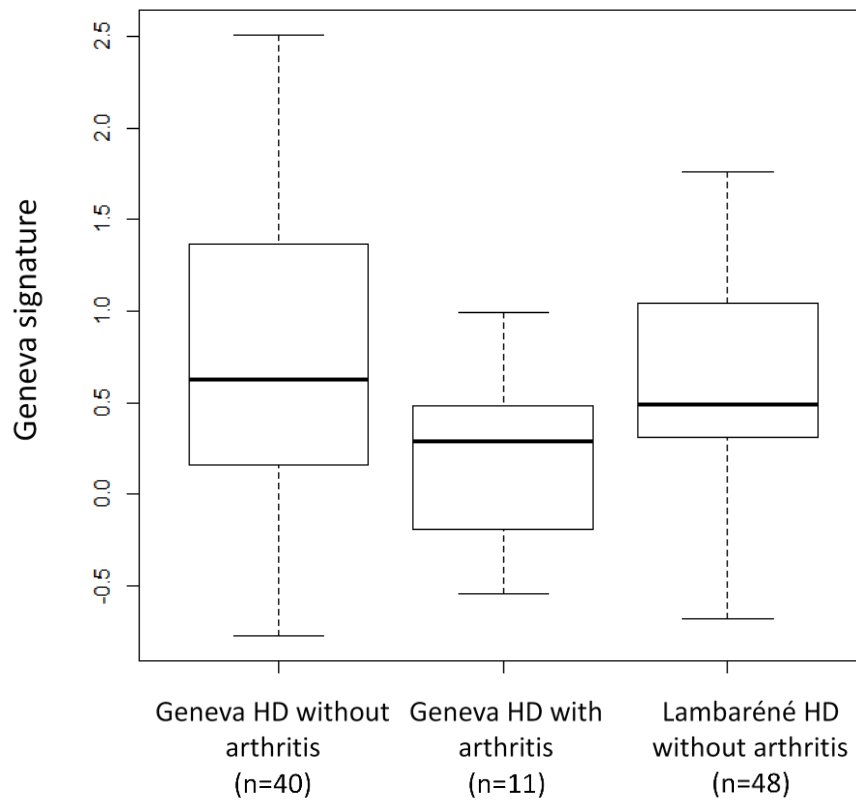
**Figure S7. The Geneva signature applied to HD vaccinees with or without arthritis in Geneva and Lambaréné.**

This represents the signature (in arbitrary units) calculated in the indicated groups of vaccinees.

Table S1. Plasma cytokines and chemokines with no significant change after rVSV-ZEBOV immunization in Geneva.

| Markers*	Days	N	Placebo GMC (95%CI)	N	Low dose (3x10⁵) GMC (95%CI)	N	High dose (10⁷ or 5x10⁷) GMC (95%CI)	Global	P vs LD	P vs HD	LD vs HD
MIP-1α	0	13	0.02 (0.01 to 0.07)	51	0.02 (0.01 to 0.03)	51	0.01 (0.01 to 0.02)	.66	>.99	.83	.70
	1	13	0.02 (0.01 to 0.07)	51	0.02 (0.01 to 0.04)	51	0.02 (0.01 to 0.03)	.91	>.99	.96	.92
	2	5	0.01 (0.01 to 0.01)	26	0.02 (0.01 to 0.05)	21	0.02 (0.01 to 0.03)	.78	.81	.92	.92
	3	8	0.03 (0.00 to 0.27)	25	0.01 (0.01 to 0.03)	30	0.01 (0.01 to 0.02)	.51	.59	.52	.99
	7	13	0.02 (0.01 to 0.08)	51	0.01 (0.01 to 0.02)	51	0.01 (0.01 to 0.02)	.40	.45	.43	>.99
	P **		.43		.28		.55				
CXCL5	0	13	743.42 (578.15 to 955.95)	51	965.27 (800.93 to 1163.33)	51	909.46 (767.78 to 1077.28)	.42	.42	.59	.89
	1	13	619.18 (453.17 to 845.99)	49	750.47 (609.63 to 923.84)	51	824.53 (697.05 to 975.34)	.37	.66	.39	.78
	2	5	696.76 (367.44 to 1321.26)	28	897.62 (700.62 to 1150.01)	21	760.31 (552.34 to 1046.58)	.62	.76	.97	.72
	3	8	578.09 (423.75 to 788.63)	23	682.17 (562.18 to 827.77)	30	719.8 (577.44 to 897.26)	.60	.76	.60	.94
	7	13	691.24 (512.9 to 931.58)	51	750.63 (618.46 to 911.06)	51	678.28 (558.15 to 824.27)	.75	.93	>.99	.76
	P **		.49		.018		.002				
IL1-β	0	13	0.02 (0.01 to 0.03)	51	0.02 (0.01 to 0.03)	51	0.01 (0.01 to 0.02)	.51	>.99	.77	.56
	1	13	0.02 (0.01 to 0.04)	51	0.03 (0.02 to 0.04)	51	0.02 (0.01 to 0.02)	.32	.86	.92	.32
	2	5	0.01 (0.01 to 0.03)	27	0.02 (0.01 to 0.05)	21	0.02 (0.01 to 0.04)	.68	.72	.89	.87
	3	8	0.01 (0.01 to 0.03)	24	0.02 (0.01 to 0.03)	30	0.02 (0.01 to 0.03)	.87	.98	.89	.93
	7	13	0.02 (0.01 to 0.05)	51	0.02 (0.01 to 0.02)	50	0.02 (0.01 to 0.02)	.56	.79	.57	.84
	P **		.30		.21		.38				
IL-8	0	13	4.53 (3.62 to 5.67)	51	3.54 (2.71 to 4.61)	51	3.90 (3.32 to 4.58)	.55	.58	.82	.81
	1	13	4.62 (3.40 to 6.27)	49	2.81 (2.08 to 3.79)	51	4.05 (3.37 to 4.86)	.054	.18	.89	.11
	2	5	4.89 (2.17 to 11.04)	28	3.46 (2.61 to 4.60)	21	5.67 (4.47 to 7.19)	.059	.61	.92	.063

Markers*			Placebo		Low dose (3x10⁵)		High dose (10⁷ or 5x10⁷)	_P_ values for comparison between dose groups ANOVA with Post-hoc Scheffe			
	3	8	3.31 (2.11 to 5.18)	23	4.90 (3.72 to 6.44)	30	4.90 (4.05 to 5.94)	.24	.29	.27	1
	7	13	4.36 (3.17 to 5.99)	51	3.49 (2.58 to 4.71)	51	3.94 (3.28 to 4.74)	.64	.72	.94	.78
	_P_ **		.30		.034		<.001				
G-CSF	0	13	0.73 (0.14 to 3.82)	51	0.29 (0.12 to 0.71)	51	0.21 (0.1 to 0.47)	.44	.63	.44	.89
	1	13	1.31 (0.28 to 6.12)	49	0.53 (0.22 to 1.28)	51	0.35 (0.15 to 0.84)	.39	.65	.40	.80
	2	5	0.91 (0.09 to 8.79)	28	0.63 (0.20 to 1.96)	21	0.69 (0.22 to 2.15)	.96	.97	.98	.99
	3	8	0.02 (0.02 to 1.86)	23	5.02 (2.65 to 9.48)	30	2.17 (0.76 to 6.18)	.012	.011	.067	.50
	7	13	0.33 (0.06 to 1.75)	51	1.00 (0.44 to 2.26)	51	0.91 (0.41 to 1.99)	.47	.49	.55	.99
	_P_ **		.098		<.001		<.001				
GM-CSF	0	13	0.02 (0.01 to 0.03)	51	0.03 (0.02 to 0.05)	51	0.01 (0.01 to 0.02)	<.001	.23	.74	.001
	1	13	0.02 (0.01 to 0.03)	49	0.02 (0.01 to 0.03)	51	0.02 (0.01 to 0.02)	.60	.79	>.99	.65
	2	5	0.02 (0.00 to 0.10)	28	0.02 (0.01 to 0.03)	21	0.01 (0.01 to 0.02)	.62	.93	.72	.74
	3	8	0.02 (0.01 to 0.06)	23	0.03 (0.02 to 0.06)	30	0.01 (0.01 to 0.02)	.15	.87	.71	.15
	7	13	0.02 (0.01 to 0.06)	51	0.02 (0.01 to 0.03)	51	0.02 (0.01 to 0.02)	.42	.99	.78	.44
	_P_ **		.72		.036		.31				

* Expressed in pg/m. IFN-γ, IL-2, IL-4 and IL-17 remained below detection levels in all samples at all time points and are not depicted.

**: Linear regression models with mixed effects were used to test the equality of geometric mean across days.

Table S2. Daily ratio of GMCs (compared to day 0) for up-regulated plasma cytokines and chemokines in Geneva participants.

	Days	Placebo Ratio of GMC (compared to day 0)	P *	Low dose Ratio of GMC (compared to day 0)	P *	High dose Ratio of GMC compared to day 0	P *
IL-1Rα	0	1		1			
	1	0.97 (0.78 to 1.21)	.81	1.77 (1.39 to 2.26)	**<.001**	10.61 (8.41 to 13.37)	**<.001**
	2	0.70 (0.51 to 0.95)	**.030**	2.36 (1.76 to 3.16)	**<.001**	2.66 (1.94 to 3.64)	**<.001**
	3	0.85 (0.65 to 1.10)	.21	1.27 (0.93 to 1.74)	.13	1.40 (1.06 to 1.84)	**.019**
	7	0.90 (0.73 to 1.12)	.37	1.19 (0.93 to 1.51)	.17	1.20 (0.95 to 1.51)	.13
IL-6	0	1		1		1	
	1	0.70 (0.35 to 1.38)	.31	1.82 (1.18 to 2.79)	**.007**	13.48 (8.29 to 21.91)	**<.001**
	2	0.72 (0.27 to 1.93)	.52	1.26 (0.74 to 2.12)	.40	1.31 (0.67 to 2.57)	.43
	3	0.56 (0.25 to 1.28)	.18	0.76 (0.43 to 1.35)	.35	1.13 (0.62 to 2.04)	.69
	7	0.44 (0.22 to 0.88)	**.026**	0.74 (0.49 to 1.14)	.17	0.82 (0.51 to 1.34)	.44
TNFα	0	1		1		1	
	1	1.30 (0.59 to 2.87)	.51	1.33 (0.78 to 2.27)	.30	3.98 (2.43 to 6.51)	**<.001**
	2	0.40 (0.13 to 1.22)	.12	2.30 (1.19 to 4.43)	**.014**	4.31 (2.18 to 8.53)	**<.001**
	3	0.66 (0.26 to 1.68)	.39	1.10 (0.54 to 2.23)	.80	2.92 (1.62 to 5.29)	**<.001**
	7	1.46 (0.66 to 3.20)	.36	1.01 (0.60 to 1.72)	.97	2.06 (1.26 to 3.38)	**.005**
IL-10	0	1		1		1	
	1	0.74 (0.39 to 1.38)	.35	2.11 (1.19 to 3.75)	**.011**	7.08 (4.68 to 10.70)	**<.001**
	2	0.28 (0.12 to 0.70)	**.010**	2.17 (1.08 to 4.34)	**.030**	2.52 (1.42 to 4.46)	**.002**
	3	0.66 (0.31 to 1.39)	.28	1.29 (0.61 to 2.72)	.51	1.15 (0.70 to 1.89)	.59
	7	0.65 (0.34 to 1.21)	.18	0.78 (0.44 to 1.38)	.40	1.10 (0.73 to 1.66)	.66
MCP-1	0	1		1		1	
	1	0.89 (0.78 to 1.02)	.11	1.40 (1.22 to 1.62)	**<.001**	3.35 (2.97 to 3.78)	**<.001**
	2	0.86 (0.71 to 1.05)	.14	1.29 (1.09 to 1.54)	**.004**	1.35 (1.14 to 1.59)	**<.001**
	3	0.95 (0.81 to 1.12)	.56	1.00 (0.84 to 1.20)	>.99	1.13 (0.98 to 1.31)	.092
	7	0.94 (0.82 to 1.08)	.38	1.05 (0.92 to 1.21)	.48	1.06 (0.94 to 1.20)	.34

MIP1-β	0	1		1		1	
	1	0.96 (0.81 to 1.149	.64	1.33 (1.14 to 1.55)	**<.001**	2.31 (2.09 to 2.56)	**<.001**
	2	0.94 (0.73 to 1.20)	.61	1.26 (1.04 to 1.52)	**.020**	1.22 (1.06 to 1.41)	**.007**
	3	1.14 (0.93 to 1.39)	.22	0.95 (0.78 to 1.16)	.63	0.90 (0.80 to 1.02)	.11
	7	1.15 (0.97 to 1.36)	.12	0.90 (0.77 to 1.04)	.17	0.84 (0.76 to 0.93)	**<.001**

* *P* values for testing the null hypothesis the equality of GMC at days 0 and 1, i.e. the ratio equals 1.

Table S3a-c. Spearman's correlation coefficients between cytokines/chemokines (Geneva).

Spearman correlation coefficients between the various cytokines/chemokines.

Table S3a, Day 1

		Day 1		
		Placebo	**Low dose**	**High dose**
IL-1Rα	IL-6	0.06 (*P*=.83)	0.47 (***P*<.001**)	0.58 (***P*<.001**)
	TNFα	0.40 (*P*=.17)	0.38 (***P*=.006**)	0.29 (***P*=.04**)
	IL-10	0.21 (*P*=.49)	0.28 (***P*=.048**)	0.45 (***P*<.001**)
	MCP-1	0.18 (*P*=.57)	0.71 (***P*<.001**)	0.72 (***P*<.001**)
	MIP1β	-0.29 (*P*=.34)	0.53 (***P*<.001**)	0.46 (***P*<.001**)
IL-6	TNFα	0.83 (***P*<.001**)	0.49 (***P*<.001**)	0.60 (***P*<.001**)
	IL-10	0.57 (*P*=0.040)	0.61 (***P*<.001**)	0.58 (***P*<.001**)
	MCP-1	0.55 (*P*=.050)	0.22 (*P*=.12)	0.56 (***P*<.001**)
	MIP1-β	-0.19 (*P*=0.54)	0.37 (***P*=.009**)	0.43 (***P*=.002**)
TNFα	IL-10	0.55 (*P*=.053)	0.65 (***P*<.001**)	0.53 (***P*<.001**)
	MCP-1	0.58 (*P*=.040)	0.42 (***P*=.003**)	0.32 (***P*=.02**)
	MIP1-β	-0.14 (*P*=0.64)	0.30 (***P*=.03**)	0.30 (***P*=.04**)
IL-10	MCP-1	0.10 (*P*=0.74)	0.29 (***P*=.045**)	0.41 (***P*=.003**)
	MIP1-β	-0.02 (*P*=0.94)	0.45 (***P*=.001**)	0.50 (***P*<.001**)
MCP-1	MIP1-β	-0.07 (*P*=0.82)	0.44 (***P*=.002**)	0.71 (***P*<.001**)

Table S3b, Day 2

		Day 2		
		Placebo	**Low dose**	**High dose**
IL-1Rα	IL-6	0.34 (*P*=.58)	0.42 (***P*=.020**)	0.45 (***P* =.040**)
	TNFα	0.67 (*P*=.22)	0.62 (***P* <.001**)	0.23 (*P*=.32)
	IL-10	-0.05 (*P*=.93)	0.42 (***P*=.030**)	-0.07 (*P*=.75)
	MCP-1	0.80 (*P*=.10)	0.23 (*P*=.26)	0.59 (***P*=.005**)
	MIP1β	-0.10 (*P*=.87)	0.18 (*P*=.37)	-0.14 (*P*=.55)
IL-6	TNFα	0.86 (*P*=.060)	0.63 (***P*<.001**)	0.33 (*P*=.15)
	IL-10	0.80 (*P*=.10)	0.35 (*P*=.070)	-0.20 (*P*=.38)
	MCP-1	0.45 (*P*=.45)	0.02 (*P*=.92)	0.33 (*P*=.14)
	MIP1-β	0.78 (*P*=.12)	0.11 (*P*=.60)	-0.03 (*P*=.91)

TNFα	IL-10	0.63 (*P*=.25)	0.35 (*P*=.070)	0.23 (*P*=.31)
	MCP-1	0.56 (*P*=.32)	0.20 (*P*=.32)	0.32 (*P*=.16)
	MIP1-β	0.67 (*P*=.22)	0.06 (*P*=.77)	0.13 (*P*=.56)
IL-10	MCP1	-0.15 (*P*=.80)	0.21 (*P*=.29)	-0.19 (*P*=.42)
	MIP1-β	0.82 (*P*=.090)	0.24 (*P*=.24)	-0.17 (*P*=.46)
MCP-1	MIP1-β	0.00 (*P*=1)	0.08 (*P*=.71)	0.27 (*P*=.24)

Table S3c, Day 3

		Day 3		
		Placebo	**Low dose**	**High dose**
IL-1Rα	IL-6	0.44 (*P*=.28)	0.19 (*P*=.38)	-0.03 (*P*=.87)
	TNFα	0.35 (*P*=.39)	0.27 (*P*=.21)	0.31 (*P*=.090)
	IL-10	0.05 (*P*=.91)	0.05 (*P*=.82)	0.26 (*P*=.17)
	MCP1	0.74 (***P*=.040**)	0.42 (*P*=.048)	0.65 (***P*<.001**)
	MIP1β	0.19 (*P*=.65)	0.30 (*P*=.16)	0.38 (***P*=.040**)
IL-6	TNFα	0.97 (***P*<.001**)	0.33 (*P*=.12)	0.57 (***P*=.001**)
	IL-10	0.00 (*P*=1)	0.43 (***P*=.040**)	0.61 (***P*<.001**)
	MCP-1	0.74 (***P*=.040**)	0.18 (*P*=.42)	-0.08 (*P*=.68)
	MIP1-β	-0.30 (*P*=.47)	-0.01 (*P*=.96)	-0.04 (*P*=.85)
TNFα	IL-10	0.00 (*P*=1)	0.44 (***P*=.040**)	0.46 (***P*=0.010**)
	MCP-1	0.79 (***P*=.020**)	0.51 (***P*=.010**)	0.11 (p=0.58)
	MIP1β	-0.46 (*P*=.25)	0.53 (***P*=.009**)	0.19 (p=0.32)
IL-10	MCP-1	0.15 (*P*=.72)	0.03 (*P*=.91)	0.15 (*P*=.42)
	MIP1β	-0.40 (*P*=.33)	-0.09 (*P*=.69)	0.23 (*P*=.23)
MCP-1	MIP1-β	-0.38 (*P*=.35)	0.31 (*P*=.14)	0.52 (***P*=.003**)

Table S4. Spearman's correlation coefficients between the day 1/day 0 ratios in Geneva participants.

Spearman correlation coefficients between the log10 of day 1/day 0 ratios.

		Day 1/day 0 ratio		
		Placebo	**Low dose**	**High dose**
IL-1Rα	IL-6	-0.12 (*P*=.69)	0.32 (***P*=.030**)	0.62 (***P*<.001**)
	TNFα	-0.09 (*P*=.78)	0.30 (***P*=.040**)	0.50 (***P*<.001**)
	IL-10	-0.37 (*P*=.21)	0.42 (***P*=.003**)	0.44 (***P*=.001**)
	MCP-1	-0.15 (*P*=.63)	0.79 (***P*<.001**)	0.74 (***P*<.001**)
	MIP1-β	-0.29 (*P*=.34)	0.79 (***P*<.001**)	0.62 (***P*<.001**)
IL-6	TNFα	-0.29 (*P*=.33)	0.53 (***P*<.001**)	0.59 (***P*<.001**)
	IL-10	0.15 (*P*=.63)	0.43 (***P*=.002**)	0.21 (p=0.13)
	MCP-1	-0.09 (*P*=.77)	0.43 (***P*=.002**)	0.53 (***P*<.001**)
	MIP1-β	-0.39 (*P*=.19)	0.36 (***P*=.010**)	0.45 (***P*=.001**)
TNFα	IL-10	0.30 (*P*=.32)	0.35 (***P*=.010**)	0.33 (***P*=.020**)
	MCP-1	-0.10 (*P*=.76)	0.40 (***P*=.005**)	0.56 (***P*<.001**)
	MIP1-β	0.15 (*P*=.61)	0.41 (***P*=.003**)	0.48 (***P*<.001**)
IL10	MCP-1	-0.03 (*P*=.93)	0.53 (***P*<.001**)	0.61 (***P*<.001**)
	MIP1-β	-0.28 (*P*=.36)	0.41 (***P*=.003**)	0.46 (***P*<.001**)
MCP-1	MIP1-β	0.66 (***P*=.010**)	0.87 (***P*<.001**)	0.84 (***P*<.001**)

Table S5. Associations between the rVSV-ZEBOV plasma signature and other AEs in Geneva participants.

Markers††	SWELLING (n=4)	NO SWELLING (n=111)	Difference/Ratio*	p-value**, ***
Signature	-0.08 (-0.97 to 0.82)	-0.13 (-0.32 to 0.06)	0.05 (-1.37 to 1.47)	0.92
IL1-RA	5.36 (1.75 to 16.39)	3.65 (2.84 to 4.68)	1.47 (0.25 to 8.59)	0.55
IL-6	6.29 (0.42 to 93.55)	3.94 (2.63 to 5.90)	1.60 (0.02 to 120.69)	0.76
TNF-a	0.58 (0.10 to 3.37)	2.26 (1.61 to 3.19)	0.26 (0.02 to 4.20)	0.23
IL-10	6.16 (0.85 to 44.78)	3.01 (2.08 to 4.34)	2.05 (0.09 to 48.18)	0.53
MCP-1	1.92 (1.20 to 3.07)	1.98 (1.72 to 2.27)	0.97 (0.47 to 2.02)	0.92
MIP1-b	1.64 (1.47 to 1.83)	1.41 (1.05 to 1.89)	0.86 (0.55 to 1.35)	0.40
	REDNESS (n=2)	**NO REDNESS (n=113)**		
Signature	0.08 (-2.45 to 2.60)	-0.13 (-0.32 to 0.05)	0.21 (-15.77 to 16.19)	0.90
IL1-RA	2.85 (0.21 to 38.83)	3.71 (2.91 to 4.75)	0.77 (0.00 to >1000)	0.88
IL-6	12.81 (0.09 to 1896.57)	3.92 (2.63 to 5.85)	3.26 (0.00 to >1000)	0.72
TNF-a	13.15 (0.08 to 2052.62)	2.09 (1.49 to 2.92)	6.30 (0.00 to >1000)	0.61
IL-10	1.65 (0.62 to 4.41)	3.12 (2.16 to 4.50)	0.53 (0.01 to 29.99)	0.41
MCP-1	1.97 (0.27 to 14.58)	1.97 (1.73 to 2.26)	1.00 (0.00 to >1000)	0.99
MIP1-b	1.84 (0.52 to 6.45)	1.63 (1.46 to 1.81)	1.13 (0.00 to >1000)	0.88
	SWEATS (n=2)	**NO SWEATS (n=113)**		
Signature	0.36 (-0.89 to 1.60)	-0.14 (-0.32 to 0.05)	0.49 (-6.86 to 7.85)	0.58
IL1-RA	6.86 (0.97 to 48.39)	3.66 (2.86 to 4.67)	1.88 (0.00 to >1000)	0.64
IL-6	11.66 (0.17 to 818.01)	3.93 (2.63 to 5.87)	2.97 (0.00 to >1000)	0.70
TNF-a	4.64 (0.23 to 94.22)	2.13 (1.51 to 2.99)	2.18 (0.00 to >1000)	0.70
IL-10	6.98 (0.81 to 60.44)	3.04 (2.11 to 4.38)	2.30 (0.00 to >1000)	0.59
MCP-1	2.32 (1.09 to 4.96)	1.97 (1.72 to 2.25)	1.18 (0.02 to 90.49)	0.74
MIP1-b	1.62 (0.95 to 2.76)	1.63 (1.46 to 1.82)	0.99 (0.05 to 19.04)	0.98
	NAUSEA (n=21)	**NO NAUSEA (n=94)**		
Signature	0.09 (-0.42 to 0.60)	-0.18 (-0.37 to 0.02)	0.27 (-0.32 to 0.85)	0.36
IL1-RA	5.77 (3.05 to 10.90)	3.36 (2.59 to 4.35)	1.72 (0.84 to 3.53)	0.14
IL-6	4.70 (1.47 to 15.00)	3.87 (2.55 to 5.87)	1.21 (0.33 to 4.45)	0.76
TNF-a	1.73 (0.85 to 3.53)	2.26 (1.54 to 3.32)	0.76 (0.33 to 1.77)	0.52
IL-10	3.92 (1.28 to 12.02)	2.93 (2.03 to 4.23)	1.34 (0.39 to 4.64)	0.63
MCP-1	2.61 (1.80 to 3.80)	1.86 (1.62 to 2.13)	1.40 (0.92 to 2.14)	0.11
MIP1-b	1.87 (1.33 to 2.64)	1.58 (1.42 to 1.76)	1.18 (0.81 to 1.73)	0.37
	DIARRHEA (n=3)	**NO DIARRHEA (n=112)**		
Signature	-1.34 (-3.54 to 0.86)	-0.10 (-0.27 to 0.08)	-1.24 (-6.03 to 3.54)	0.38
IL1-RA	1.13 (0.08 to 15.88)	3.82 (3.01 to 4.85)	0.29 (0.00 to 91.21)	0.46
IL-6	0.39 (0.01 to 12.84)	4.27 (2.88 to 6.33)	0.09 (0.00 to 171.34)	0.31
TNF-a	0.20 (0.00 to 9.57)	2.30 (1.66 to 3.20)	0.09 (0.00 to 396.19)	0.34
IL-10	0.38 (0.00 to 52.22)	3.27 (2.31 to 4.62)	0.12 (0.00 to >1000)	0.48
MCP-1	1.16 (0.46 to 2.93)	2.00 (1.75 to 2.29)	0.58 (0.08 to 4.18)	0.37
MIP1-b	0.82 (0.20 to 3.31)	1.66 (1.50 to 1.84)	0.50 (0.02 to 10.26)	0.43

	OTHER AE (n=62)	NO OTHER AE (n=53)		
Signature	-0.08 (-0.36 to 0.20)	-0.18 (-0.42 to 0.05)	0.10 (-0.27 to 0.48)	0.58
IL1-RA	3.94 (2.78 to 5.59)	3.44 (2.46 to 4.82)	1.15 (0.70 to 1.87)	0.58
IL-6	4.56 (2.59 to 8.04)	3.46 (1.98 to 6.04)	1.32 (0.59 to 2.94)	0.50
TNF-a	2.12 (1.24 to 3.63)	2.20 (1.49 to 3.25)	0.96 (0.49 to 1.89)	0.92
IL-10	3.56 (1.99 to 6.39)	2.62 (1.77 to 3.87)	1.36 (0.67 to 2.77)	0.39
MCP-1	2.01 (1.66 to 2.44)	1.93 (1.61 to 2.32)	1.04 (0.79 to 1.36)	0.78
MIP1-b	1.61 (1.39 to 1.88)	1.65 (1.42 to 1.91)	0.98 (0.79 to 1.21)	0.85

†Adverse events were included if reported within 14 days of VSV-ZEBOV immunisation.

††Mean values (95%CI).

*We report the mean difference (signature) and mean ratios (chemokines/cytokines) between participants with and without specific adverse events.

**Signature: T-tests were conducted to compare the mean signature in participants with/without specific adverse events.

***Chemokines/cytokines: *P* value for the comparison of the day 1 /day 0 ratio of plasma markers between participants with and without each adverse event. T-tests were conducted on log_{10}-transformed data.

Table S6. Association between the rVSV-ZEBOV plasma signature and the severity of AEs in Geneva participants.

		n	Signature, mean (95%CI)	p-values*
Subjective fever	*Maximal Grade 0*	66	-0.45 (-0.63 to -0.27)	
	Maximal Grade 1	32	0.18 (-0.18 to 0.55)	**<0.001**
	Maximal Grade 2	13	0.52 (-0.22 to 1.26)	
	Maximal Grade 3	4	0.56 (-0.75 to 1.87)	
Myalgia	*Maximal Grade 0*	58	-0.43 (-0.63 to -0.24)	
	Maximal Grade 1	35	0.07 (-0.31 to 0.45)	**<0.001**
	Maximal Grade 2	16	0.29 (-0.29 to 0.87)	
	Maximal Grade 3	6	0.53 (-0.16 to 1.22)	
Chills	*Maximal Grade 0*	71	-0.32 (-0.54 to -0.11)	
	Maximal Grade 1	20	-0.25 (-0.71 to 0.22)	**<0.001**
	Maximal Grade 2	18	0.41 (-0.04 to 0.86)	
	Maximal Grade 3	6	0.88 (0.07 to 1.69)	
Any AE	*Maximal Grade 0*	9	-0.70 (-1.07 to -0.34)	
	Maximal Grade 1	40	-0.34 (-0.59 to -0.08)	**0.002**
	Maximal Grade 2	48	-0.04 (-0.32 to 0.25)	
	Maximal Grade 3	18	0.37 (-0.26 to 0.99)	

* ANOVA

Table S7. Ratio of GMCs for individual chemokines/cytokines in HD Geneva vaccinees.

Marker	NO FEVER	FEVER	*P* value*
Objective fever			
IL-1Ra	9.84 (7.26 to 13.32)	13.22 (8.34 to 20.95)	.31
IL-6	12.92 (6.40 to 26.08)	15.25 (4.12 to 56.45)	.83
TNFα	4.25 (2.44 to 7.38)	3.29 (1.35 to 8.05)	.64
IL-10	5.66 (3.39 to 9.43)	13.66 (4.40 to 42.35)	.18
MCP-1	3.19 (2.69 to 3.79)	3.85 (2.75 to 5.39)	.34
MIP1-β	2.34 (2.06 to 2.67)	2.23 (1.73 to 2.87)	.73
Subjective fever			
IL-1Ra	7.64 (5.14 to 11.35)	12.69 (9.24 to 17.42)	.057
IL-6	8.29 (3.44 to 19.94)	17.57 (7.78 to 39.68)	.23
TNFα	2.53 (1.38 to 4.62)	5.10 (2.71 to 9.60)	.12
IL-10	4.39 (2.20 to 8.78)	9.19 (4.87 to 17.33)	.13
MCP-1	2.97 (2.38 to 3.70)	3.58 (2.92 to 4.39)	.23
MIP1-β	2.26 (1.91 to 2.66)	2.34 (2.01 to 2.74)	.75

	NO PAIN	PAIN	*P* value*
IL-1Ra	11.32 (7.10 to 18.06)	10.40 (7.67 to 14.09)	.76
IL-6	23.89 (7.52 to 75.86)	11.30 (5.51 to 23.19)	.29
TNFα	3.83 (1.43 to 10.31)	4.03 (2.35 to 6.89)	.93
IL-10	4.92 (1.99 to 12.17)	7.92 (4.48 to 13.99)	.39
MCP-1	2.91 (2.26 to 3.73)	3.50 (2.91 to 4.21)	.26
MIP1-β	2.05 (1.69 to 2.50)	2.40 (2.09 to 2.75)	.22

	NO MYALGIA	MYALGIA	*P* value*
IL-1Ra	9.35 (5.92 to 14.77)	11.30 (8.29 to 15.39)	.51
IL-6	9.53 (4.03 to 22.49)	16.02 (7.08 to 36.30)	.40
TNFα	**1.89 (1.41 to 2.53)**	**5.78 (3.00 to 11.10)**	**.004**
IL-10	6.59 (2.87 to 15.09)	7.34 (4.01 to 13.43)	.84
MCP-1	3.17 (2.48 to 4.07)	3.44 (2.83 to 4.19)	.62
MIP1-β	2.37 (1.97 to 2.86)	2.28 (1.97 to 2.65)	.75

	NO CHILLS	CHILLS	*P* value*
IL-1Ra	9.53 (7.06 to 12.87)	11.66 (7.80 to 17.45)	.44
IL-6	16.92 (7.28 to 39.28)	11.01 (4.50 to 26.93)	.50
TNFα	2.90 (1.64 to 5.13)	5.28 (2.58 to 10.78)	.21
IL-10	4.76 (2.51 to 9.01)	10.09 (5.01 to 20.30)	.13

MCP-1	3.12 (2.59 to 3.78)	3.56 (2.81 to 4.51)	.41
MIP1-β	2.34 (1.99 to 2.76)	2.29 (1.94 to 2.70)	.83
	NO ARTHRALGIA	**ARTHRALGIA**	*P* value*
IL-1Ra	10.60 (7.87 to 14.27)	10.63 (6.90 to 16.36)	.99
IL-6	15.21 (7.47 to 30.97)	7.65 (2.70 to 21.73)	.30
TNFα	4.09 (2.36 to 7.09)	3.49 (1.71 to 7.12)	.73
IL-10	**8.56 (4.89 to 14.97)**	**2.92 (1.62 to 5.28)**	**.016**
MCP-1	3.38 (2.81 to 4.06)	3.23 (2.87 to 3.65)	.71
MIP1-β	2.37 (1.97 to 2.86)	2.28 (1.97 to 2.65)	.75
	NO FATIGUE	**FATIGUE**	*P* value*
IL-1Ra	9.01 (5.96 to 13.62)	11.78 (8.52 to 16.29)	.32
IL-6	7.69 (3.53 to 16.77)	19.35 (8.17 to 45.84)	.13
TNFα	2.30 (1.62 to 3.28)	5.66 (2.78 to 11.54)	**.032**
IL-10	7.11 (3.48 to 14.52)	7.06 (3.66 to 13.63)	.99
MCP-1	2.95 (2.44 to 3.56)	3.64 (2.92 to 4.53)	.16
MIP1-β	2.01 (1.71 to 2.37)	2.53 (2.17 to 2.94)	.052
	NO HEADACHE	**HEADACHE**	*P* value*
IL-1Ra	8.18 (5.44 to 12.31)	12.72 (9.28 to 17.43)	.10
IL-6	7.31 (3.24 to 16.47)	20.67 (8.8 to 48.55)	.090
TNFα	2.20 (1.78 to 2.72)	6.03 (2.85 to 12.77)	**.016**
IL-10	8.84 (4.23 to 18.45)	6.06 (3.18 to 11.56)	.45
MCP-1	3.20 (2.57 to 3.99)	3.46 (2.79 to 4.28)	.63
MIP1-β	2.30 (1.94 to 2.71)	2.33 (1.98 to 2.73)	.91

*T-test on $\log_{10}$-transformed ratios

Table S8. Fold change in gene expression levels (compared to day 0) for cytokines and chemokines comprising the plasma signature in Geneva participants.

		Placebo		Low dose		High dose	
	Days	Fold change	*P* value	Fold change	*P* value	Fold change	*P* value
IL-1RN (IL-1Rα)	0	1		1		1	
	1	1.27	.11	2.00	**<.001**	10.75	**<.001**
IL-6	0	1		1		1	
	1	0.68	.27	0.78	.20	0.86	**.004***
TNFα	0	1		1		1	
	1	1.02	.49	1.07	.077	1.35	**<.001***
IL-10	0	1		1		1	
	1	0.89	.14	0.99	.99	1.04	.59
MCP-1	0	1		1		1	
	1	0.98	.51	6.08	**<.001**	16.14	**<.001**
MIP1-β	0	1		1		1	
	1	0.98	.88	1.17	**.044***	1.04	.23

* Indicates markers that are differentially expressed between day 0 and day 1 but for which the fold change does not reach the cutoff of ≥2.0.

Table S9. GMCs of up-regulated plasma markers in Lambaréné.

Markers*	Days	N	Low dose (3x10⁵ pfu) GMC (95%CI)	N	High dose (3x10⁶ or 2x10⁷ pfu) GMC (95%CI)	P values** LD vs HD
IL-1Rα	0	14	395.2 (284.8 to 548.4)	51	632.7 (513.9 to 779.0)	**.026**
	1	17	777.2 (579.3 to 1042.8)	52	8013.2 (6530.9 to 9832.0)	**<.001**
	2	16	1036.3 (792.2 to 1355.5)	54	2151.9 (1876.5 to 2467.8)	**<.001**
	7	11	453.2 (303.3 to 677.0)	50	598.8 (463.8 to 773.2)	.27
	P *		**<.001**		**<.001**	
IL-6	0	14	0.18 (0.04 to 0.80)	51	0.34 (0.18 to 0.61)	.46
	1	17	0.32 (0.12 to 0.87)	52	3.10 (2.60 to 3.69)	**<.001**
	2	16	0.24 (0.07 to 0.89)	54	0.62 (0.39 to 0.99)	.20
	7	11	0.13 (0.03 to 0.60)	49	0.34 (0.18 to 0.62)	.28
	P *		.75		**<.001**	
TNFα	0	14	4.04 (3.19 to 5.11)	51	3.91 (3.21 to 4.77)	.84
	1	17	3.86 (3.13 to 4.76)	52	5.47 (4.56 to 6.56)	**.018**
	2	16	7.38 (4.56 to 11.96)	54	6.03 (4.95 to 7.36)	.46
	7	11	4.95 (3.94 to 6.21)	49	4.25 (3.36 to 5.39)	.37
	P *		**<.001**		**<.001**	
IL-10	0	14	1.12 (0.52 to 2.38)	51	1.05 (0.69 to 1.59)	.89
	1	17	1.54 (0.87 to 2.74)	52	4.86 (3.43 to 6.90)	**.002**
	2	16	2.30 (1.19 to 4.46)	54	3.00 (2.35 to 3.82)	.47
	7	11	1.46 (0.75 to 2.86)	49	1.30 (0.90 to 1.87)	.76
	P *		**<.001**		**<.001**	
MCP-1	0	14	78.1 (67.8 to 90.0)	51	73.4 (64.21 to 83.9)	.54
	1	17	102.0 (80.9 to 128.5)	52	291.8 (245.74 to 346.6)	**<.001**
	2	16	107.2 (84.1 to 136.7)	54	120.9 (103.62 to 141.1)	.42
	7	11	73.6 (55.9 to 96.8)	49	89.9 (78.63 to 102.7)	.22
	P *		**.010**		**<.001**	
MIP1-β	0	14	54.7 (40.2 to 74.5)	51	57.8 (49.1 to 67.9)	.76
	1	17	54.9 (39.5 to 76.3)	52	85.7 (75.0 to 97.8)	**.023**
	2	16	74.2 (46.9 to 117.4)	54	55.7 (48.9 to 63.5)	.26
	P *		.31		**<.001**	

Analyses were performed including all vaccinees with available plasma samples (n=75).

*Concentrations are expressed in pg/ml.

**T-test on plasma markers after transformation of data (logarithm base 10).

Table S10. Comparison of baseline GMCs in Lambaréné and Geneva participants.

All subjects	Lambaréné			Geneva		
Markers*	N	GMC at day 0 (95%CI)	N	GMC at day 0 (95%CI)		*P* values
IL-1Rα	65	571.7 (476.1 to 686.5)	115	525.8 (471.0 to 586.8)		.44
IL-6	65	0.29 (0.17 to 0.52)	115	0.18 (0.12 to 0.28)		.20
TNFα	65	3.94 (3.35 to 4.63)	115	0.26 (0.17 to 0.41)		**<.001**
IL-10	65	1.06 (0.74 to 1.53)	115	0.09 (0.06 to 0.12)		**<.001**
MCP-1	65	74.4 (66.7 to 83.0)	115	171.6 (160.1 to 183.8)		**<.001**
MIP1-β	65	57.1 (49.5 to 65.8)	115	33.7 (29.7 to 38.2)		**<.001**

* Concentrations are expressed in pg/ml

Table S11. Daily ratio of GMCs (compared to day 0) for up-regulated plasma cytokines and chemokines in Lambaréné vaccinees.

Markers	Day	N	Low dose (3×10^5 pfu) GMC (95%CI)	*P* value	N	High dose (3×10^6 or 2×10^7 pfu) GMC (95%CI)	*P* value	*P* LD vs HD
IL-1Rα	1	12	2.62 (1.64 to 4.19)	**.002**	48	12.91 (10.07 to 16.55)	**<.001**	**<.001**
	2	11	2.84 (1.74 to 4.63)	**.002**	50	3.28 (2.60 to 4.13)	**<.001**	.61
	7	11	1.11 (0.74 to 1.67)	.61	46	0.96 (0.71 to 1.30)	.80	.57
IL-6	1	12	2.02 (0.36 to 11.23)	.44	48	8.02 (4.59 to 14.01)	**<.001**	.16
	2	11	0.50 (0.09 to 2.76)	.44	50	1.98 (1.23 to 3.20)	**.007**	.16
	7	11	0.49 (0.09 to 2.77)	.44	45	0.90 (0.53 to 1.52)	.69	.52
TNFα	1	12	1.06 (0.96 to 1.17)	.27	48	1.44 (1.27 to 1.63)	**<.001**	**<.001**
	2	11	1.55 (1.36 to 1.76)	**<.001**	50	1.66 (1.49 to 1.84)	**<.001**	.41
	7	11	1.07 (0.94 to 1.22)	.35	45	1.17 (1.02 to 1.34)	**.027**	.35
IL-10	1	12	1.80 (1.16 to 2.80)	**.024**	48	4.47 (2.64 to 7.55)	**<.0001**	**.013**
	2	11	1.55 (1.17 to 2.06)	**.013**	50	2.88 (2.04 to 4.06)	**<.0001**	**.009**
	7	11	0.87 (0.62 to 1.24)	.47	45	1.25 (0.85 to 1.84)	.2606	.18
MCP-1	1	12	1.28 (1.01 to 1.62)	.070	48	3.94 (3.38 to 4.59)	**<.001**	**<.001**
	2	11	1.21 (0.96 to 1.53)	.15	50	1.66 (1.49 to 1.86)	**<.001**	**.031**
	7	11	0.93 (0.72 to 1.19)	.57	45	1.23 (1.08 to 1.39)	**.003**	.070
MIP1-β	1	12	1.02 (0.72 to 1.45)	.91	48	1.53 (1.34 to 1.74)	**<.001**	.055
	2	11	0.99 (0.68 to 1.43)	.94	50	0.97 (0.84 to 1.13)	.72	.95

Table S12. Plasma cytokines and chemokines with no significant biological change after rVSV-ZEBOV immunization in Lambaréné.

	Day	N	Low dose (3x10^5 pfu) GMC (95%CI)	N	High dose (3x10^6 or 2x10^7 pfu) GMC (95%CI)	P
MIP1-α	0	14	0.02 (0.00 to 0.12)	51	0.08 (0.03 to 0.23)	.25
	1	17	0.06 (0.01 to 0.48)	52	0.09 (0.03 to 0.26)	.78
	2	16	0.04 (0.01 to 0.20)	54	0.08 (0.03 to 0.23)	.44
	7	11	0.07 (0.01 to 0.83)	49	0.06 (0.02 to 0.16)	.92
	P value		.42		**.025**	
CXCL5	0	14	3183.32 (1883.49 to 5380.17)	51	3418.01 (2785.68 to 4193.87)	.81
	1	17	2779.90 (1834.31 to 4212.96)	52	2755.81 (2247.63 to 3378.87)	.97
	2	16	2700.49 (1717.90 to 4245.10)	54	2492.06 (1959.88 to 3168.75)	.76
	7	11	1803.76 (1216.09 to 2675.40)	49	2329.54 (1934.38 to 2805.43)	.27
	P value		.11		**.002**	
IL-8	0	14	1.74 (0.51 to 5.96)	51	5.66 (4.57 to 7.00)	.086
	1	17	0.84 (0.28 to 2.49)	52	3.91 (2.86 to 5.35)	.015
	2	16	1.37 (0.37 to 5.10)	54	6.29 (4.95 to 8.00)	.040
	7	11	0.78 (0.19 to 3.22)	49	6.53 (5.23 to 8.16)	.015
	P value		.55		**<.001**	
G-CSF	0	14	15.28 (11.04 to 21.13)	51	12.53 (9.08 to 17.29)	0.4004
	1	17	13.28 (10.84 to 16.28)	52	15.56 (13.56 to 17.85)	0.2151
	2	16	16.86 (14.21 to 20.01)	54	15.51 (12.55 to 19.18)	0.5518
	7	11	25.07 (18.29 to 34.37)	49	18.74 (15.80 to 22.22)	0.1304
	P value		**.004**		**.038**	

* IFN-γ, IL1-β, IL-2, IL-4, IL-17 and GM-CSF remained below detection levels in all samples at all time points and are not depicted.

** Missing samples might contribute to statistically significant changes over time, but no marker exhibited significant changes compared to day 0.

Table S13. Comparison of vaccine responses (day 1/day 0 ratios) between Geneva and Lambaréné vaccinees.

	Markers	N	Lambaréné GMC at day 0 (95%CI)	N	Geneva GMC at day 0 (95%CI)	*P* values
High dose	IL-1Rα	48	12.91 (10.07 to 16.55)	51	10.61 (8.41 to 13.37)	.28
	IL-6	48	8.02 (4.59 to 14.01)	51	13.48 (8.29 to 21.91)	.22
	TNFα	48	1.44 (1.27 to 1.63)	51	3.98 (2.43 to 6.51)	**.001**
	IL-10	48	4.47 (2.64 to 7.55)	51	7.08 (4.68 to 10.70)	.21
	MCP-1	48	3.94 (3.38 to 4.59)	51	3.35 (2.97 to 3.78)	.15
	MIP1-β	48	1.53 (1.34 to 1.74)	51	2.31 (2.09 to 2.56)	**<.001**
Low dose	IL-1Rα	12	2.62 (1.64 to 4.19)	51	1.77 (1.39 to 2.26)	.17
	IL-6	12	2.02 (0.36 to 11.23)	51	1.82 (1.18 to 2.79)	.90
	TNFα	12	1.06 (0.96 to 1.17)	51	1.33 (0.78 to 2.27)	.47
	IL-10	12	1.80 (1.16 to 2.80)	51	2.11 (1.19 to 3.75)	.88
	MCP-1	12	1.28 (1.01 to 1.62)	51	1.40 (1.22 to 1.62)	.52
	MIP1-β	12	1.02 (0.72 to 1.45)	49	1.53 (1.34 to 1.74)	.24

Table S14. Correlations between signatures and biological outcomes in Lambaréné vaccinees.

Spearman's correlation coefficients between the Geneva/Lambaréné signature and biological outcomes:

- Peak VSV: $\rho=0.36$ (***P=.006***)
- VSV Day 1: $\rho=0.42$ (***P=.002***)
- VSV Day 2: $\rho=0.34$ (***P=.011***)
- Lymphopenia Day 1: $\rho=-0.50$ (***P<.001***)
- Lymphopenia Day 2: $\rho=-0.12$ (*P=.37*)
- Thrombocytopenia Day 1: $\rho=-0.13$ (*P=.32*)
- Thrombocytopenia Day 2: $\rho=-0.12$ (*P=.38*)
- Neutropenia Day 1: $\rho=0.35$ (***P=.014***)
- Neutropenia Day 2: $\rho=0.04$ (*P=.80*)
- Monocytosis Day 1: $\rho=0.18$ (*P=.17*)
- Monocytosis Day 2: $\rho=0.12$ (*P=.35*)

Table S15. Comparative frequencies of AEs in Geneva and Lambaréné vaccinees.

	Geneva		Lambaréné		P values*	
	Low-dose (n= 51)	High-dose (n=51)	Low-dose (n=20)	High-dose (n=55)	Geneva LD vs. Lambaréné LD	Geneva HD vs. Lambaréné HD
Pain (%)	11 (22)	38 (75)	3 (15)	31 (56)	.74	.067
Objective fever (%)	1 (2)	13 (25)	1 (5)	10 (18)	.49	.48
Subjective fever (%)	12 (24)	32 (63)	1 (5)	18 (33)	.093	**.003**
Chills (%)	15 (30)	27 (54)	0 (0)	4 (7)	**.007**	**<.001**
Myalgia (%)	20 (39)	34 (67)	2 (10)	12 (22)	**.022**	**<.001**
Arthralgia (%)	7 (14)	8 (16)	2 (10)	17 (31)	1	.072
Headaches (%)	17 (34)	30 (58)	9 (45)	30 (55)	.42	.70
Fatigue (%)	34 (66)	31 (61)	10 (50)	23 (42)	.28	.055

*Fisher's exact test

LD: low dose; HD: high dose

Table S16. Associations between the Geneva plasma signature and the severity of AEs in Lambaréné vaccinees.

		n	Signature, mean (95%CI)	P values*
Subjective fever	*Maximal grade 0*	43	0.31 (0.09 to 0.52)	.47
	Maximal grade 1	15	0.57 (0.22 to 0.91)	
	Maximal grade 2	2	0.37 (0.25 to 0.49)	
	Maximal grade 3	0	/	
Myalgia	*Maximal grade 0*	48	0.33 (0.12 to 0.54)	.29
	Maximal grade 1	9	0.69 (0.44 to 0.94)	
	Maximal grade 2	3	0.11 (-0.66 to 0.88)	
	Maximal grade 3	0	/	
Chills	*Maximal grade 0*	56	0.34 (0.16 to 0.52)	.15
	Maximal grade 1	4	0.86 (0.27 to 1.46)	
	Maximal grade 2	0	/	
	Maximal grade 3	0	/	
Any AE	*Maximal grade 0*	20	-0.06 (-0.35 to 0.24)	**.001**
	Maximal grade 1	32	0.64 (0.43 to 0.85)	
	Maximal grade 2	8	0.40 (-0.04 to 0.84)	
	Maximal grade 3	0		