TABLE S1 Treatment-emergent adverse events (TEAEs)

MedDRA[a] preferred term, no. (%)	Placebo (n = 32)	MHAA4549A 400 mg (n = 20)	MHAA4549A 1200 mg (n = 20)	MHAA4549A 3600 mg (n = 20)	Oseltamivir (n = 8)	All (N = 100)
Total number of subjects with at least one adverse event	28 (87.5%)	18 (90%)	16 (80%)	17 (85%)	7 (87.5%)	86 (86%)
Total number of adverse events	68	33	39	52	15	207
Procedural hemorrhage	8 (25%)	6 (30%)	3 (15%)	6 (30%)	3 (37.5%)	26 (26%)
Alanine aminotransferase increased	5 (15.6%)	5 (25%)	4 (20%)	4 (20%)	2 (25%)	20 (20%)
Aspartate aminotransferase increased	3 (9.4%)	5 (25%)	3 (15%)	3 (15%)	2 (25%)	16 (16%)
Amylase increased	2 (6.3%)	1 (5%)	1 (5%)	0	0	4 (4%)
Upper respiratory tract infection	6 (18.8%)	3 (15%)	2 (10%)	3 (15%)	0	14 (14%)
Headache	5 (15.6%)	0	3 (15%)	2 (10%)	1 (12.5%)	11 (11%)
Nasal congestion	2 (6.3%)	1 (5%)	1 (5%)	3 (15%)	0	7 (7%)
Oropharyngeal pain	2 (6.3%)	0	2 (10%)	0	3 (37.5%)	7 (7%)
Nausea	2 (6.3%)	1 (5%)	0	3 (15%)	0	6 (6%)
Diarrhea	2 (6.3%)	1 (5%)	0	2 (10%)	0	5 (5%)
Nasopharyngitis	0	3 (15%)	1 (5%)	1 (5%)	0	5 (5%)
Rash erythematous	2 (6.3%)	0	0	0	0	2 (2%)

[a]MedDRA (Medical Dictionary for Regulatory Activities, v16.1) was used. Multiple occurrences of the same event in a subject were counted once in the overall incidence.

TABLE S2 Efficacy results for the ITTI population

		MHAA4549A			
Endpoint	Placebo (n = 21)	400 mg (n = 11)	1200 mg (n = 13)	3600 mg (n = 14)	Oseltamivir (n = 2)
Median qPCR AUC (log_{10} vps/mL × h)	458.1	247.2	444.4	11.3	57.4
% Reduction		46.0%	3.0%	97.5%	87.5%
(p-value)		(0.0455)	(0.9020)	(0.0051)	(0.0558)
Median cell culture AUC (log_{10} $TCID_{50}$ × h)	186.8	70.3	224.5	0.0	28.8
% Reduction		62.4%	-20.2%	100%	84.6%
(p-value)		(0.0087)	(0.8742)	(0.0023)	(0.0558)
Median qPCR peak (log_{10} vps/mL)	6.38	5.08	6.36	1.45	2.30
% Reduction		20.4%	0.3%	77.3%	63.9%
(p-value)		(0.0187)	(1.0000)	(0.0024)	(0.0947)
Median cell culture peak (log_{10} $TCID_{50}$)	4.25	1.75	4.00	0.00	1.25
% Reduction		58.8%	5.9%	100%	70.6%
(p-value)		(0.0220)	(0.9578)	(0.0023)	(0.1150)
Median composite symptom score AUC	207.7	87.5	192.1	37.7	8.1
% Reduction		57.9%	7.5%	81.8%	96.1%
(p-value)		(0.2000)	(0.8743)	(0.2887)	(0.0855)
Median total mucus weight (g)	17.28	3.24	10.63	0.66	0.00
% Reduction		81.3%	38.5%	96.2%	100.0%
(p-value)		(0.0384)	(0.2722)	(0.0443)	(0.0496)

Comparison of 400-mg, 1200-mg, and 3600-mg MHAA4549A and oseltamivir groups to placebo was performed using the nonparametric Wilcoxon rank-sum test. Percent reduction was calculated as 100%*([the median of placebo – the median of active]/the median of placebo). P-values were not adjusted for multiple testing.

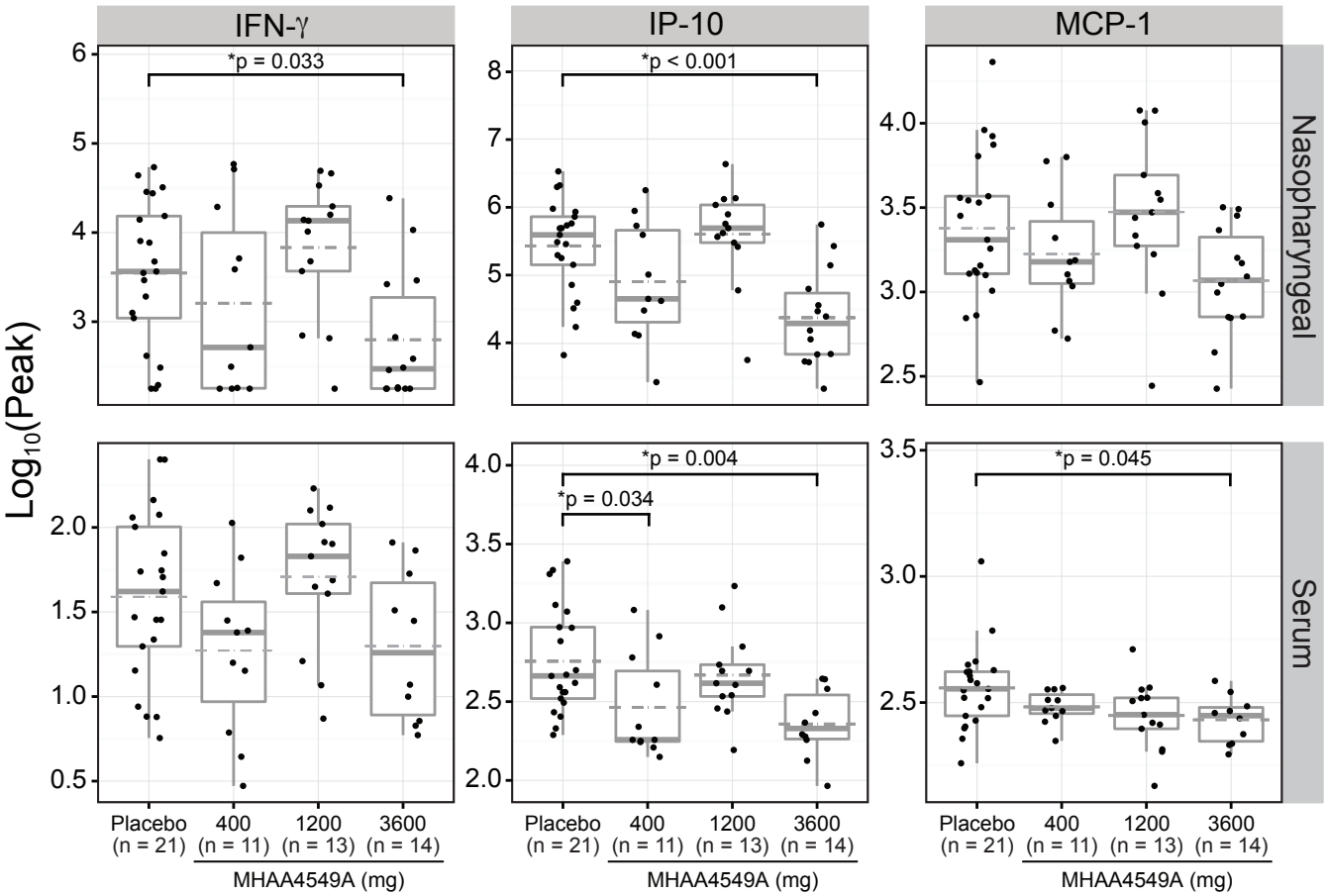

FIG S1 Effects of MHAA4549A on the peak levels of NP and serum cytokines. IFN-γ, IP-10, and MCP-1 cytokine levels were measured in the NP-derived samples (upper panels) and serum (lower panels) of all ITTI subjects. Filled circles represent the peak levels of each subject. Box plots demonstrate the variance, the median (bold line), the mean (dashed line), and interquartile range of each group. Treatment comparisons against the placebo group were performed using the Dunnett's t-test and p-values are shown only for groups that were statistically significant (*$p < 0.05$). IP-10, interferon-inducible protein-10; ITTI, intent-to-treat-infected; MCP-1, monocyte chemoattractant protein-1; NP, nasopharyngeal.