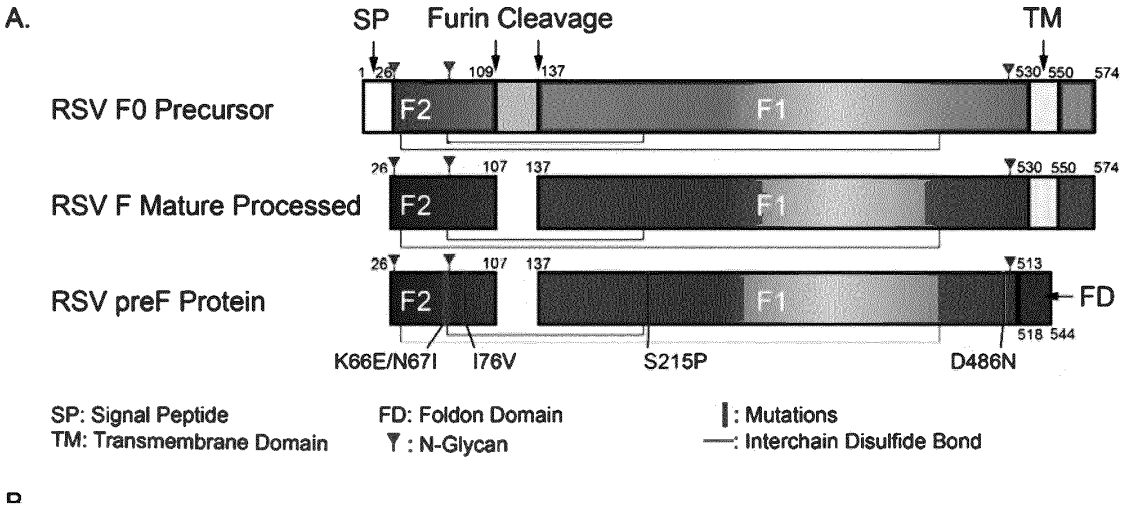

A.
SP
Furin Cleavage
TM
RSV F0 Precursor
RSV F Mature Processed
RSV preF Protein
F2
F1
FD
K66E/N67I
I76V
S215P
D486N
SP: Signal Peptide
TM: Transmembrane Domain
FD: Foldon Domain
: N-Glycan
: Mutations
: Interchain Disulfide Bond

B

FIG. 1

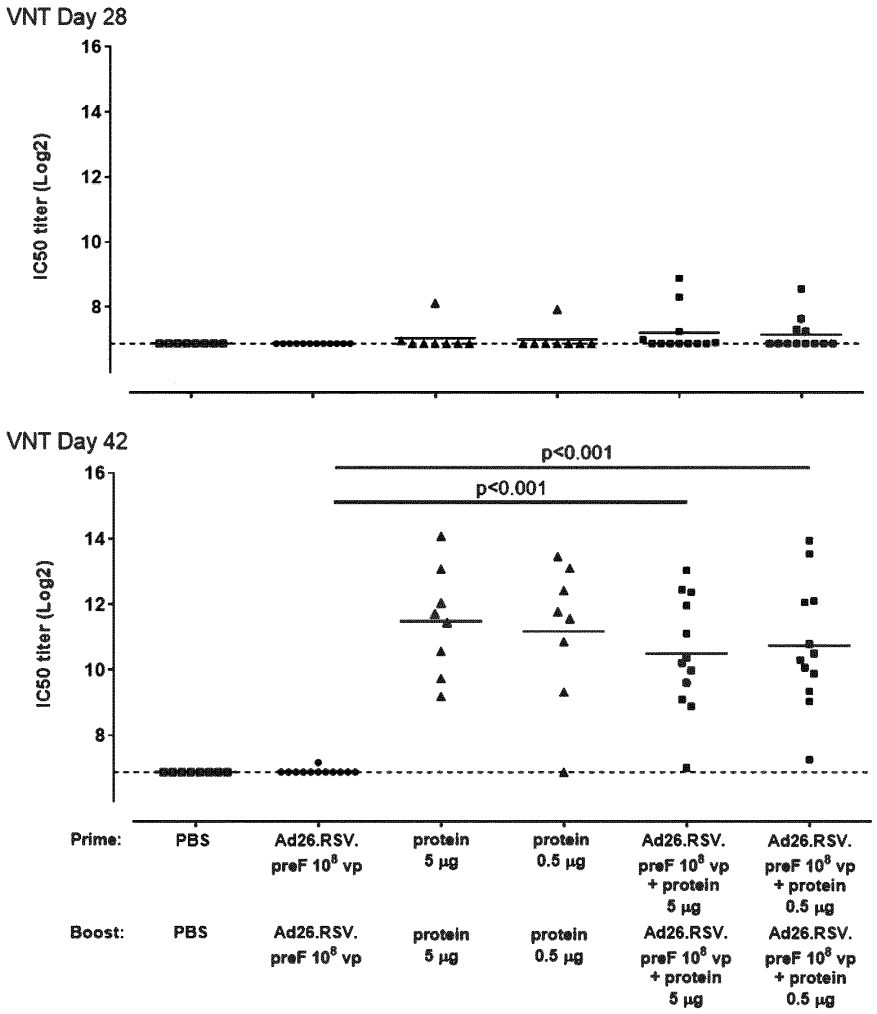

VNT Day 28
IC50 titer (Log2)
16
14
12
10
8
VNT Day 42
IC50 titer (Log2)
p<0.001
p<0.001
16
14
12
10
8
Prime: PBS
Ad26.RSV. preF 10^8 vp
protein 5 µg
protein 0.5 µg
Ad26.RSV. preF 10^8 vp + protein 5 µg
Ad26.RSV. preF 10^8 vp + protein 0.5 µg
Boost: PBS
Ad26.RSV. preF 10^8 vp
protein 5 µg
protein 0.5 µg
Ad26.RSV. preF 10^8 vp + protein 5 µg
Ad26.RSV. preF 10^8 vp + protein 0.5 µg

FIG. 2

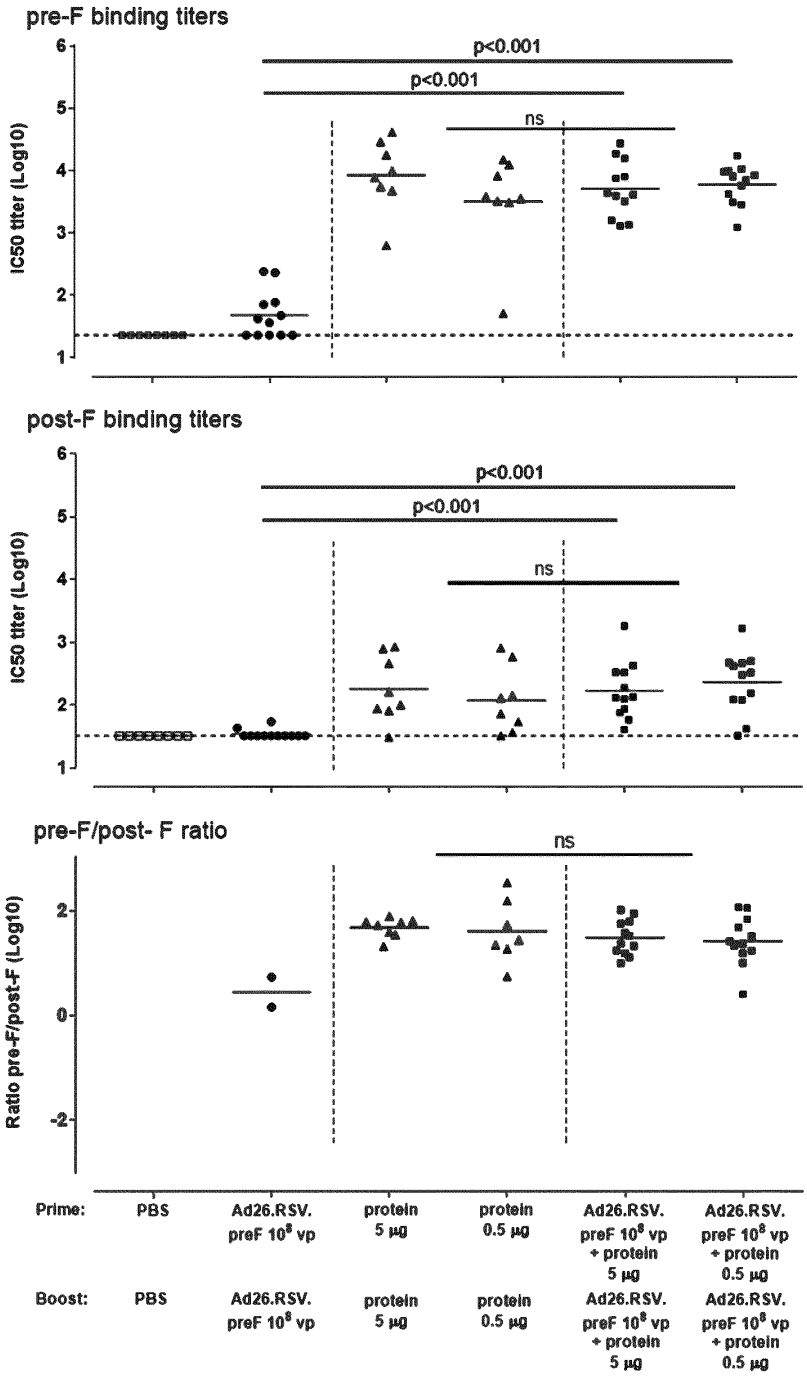

pre-F binding titers
IC50 titer (Log10)
p<0.001
p<0.001
ns
post-F binding titers
IC50 titer (Log10)
p<0.001
p<0.001
ns
pre-F/post- F ratio
Ratio pre-F/post-F (Log10)
ns
Prime: PBS
Ad26.RSV. preF 10^8 vp
protein 5 µg
protein 0.5 µg
Ad26.RSV. preF 10^8 vp + protein 5 µg
Ad26.RSV. preF 10^8 vp + protein 0.5 µg
Boost: PBS
Ad26.RSV. preF 10^8 vp
protein 5 µg
protein 0.5 µg
Ad26.RSV. preF 10^8 vp + protein 5 µg
Ad26.RSV. preF 10^8 vp + protein 0.5 µg

FIG 3

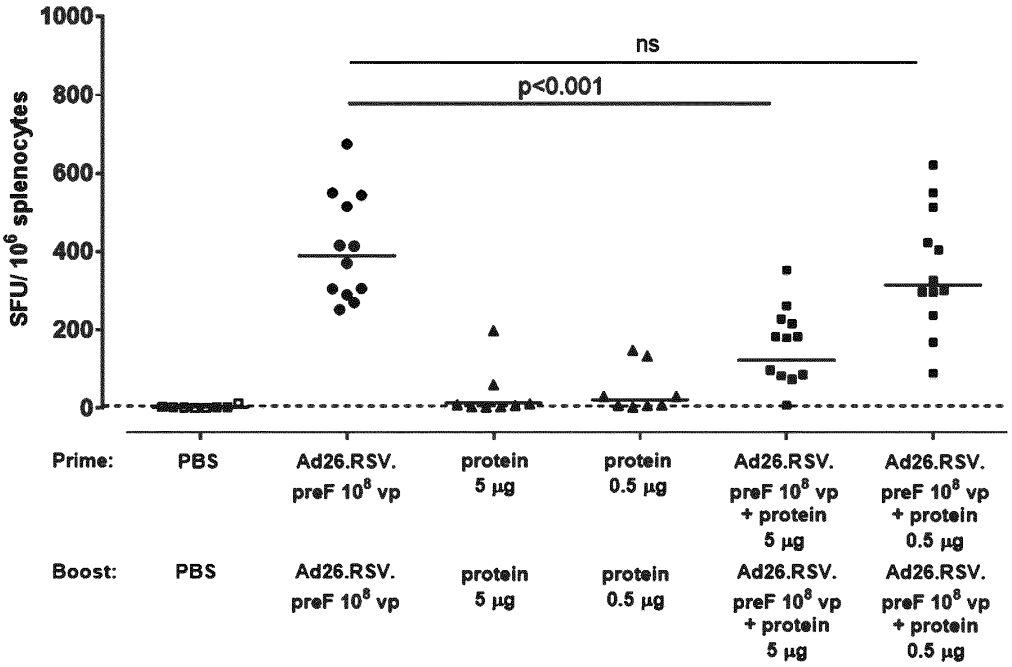

1000
800
600
400
200
0
SFU/ 10^6 splenocytes
ns
p<0.001
Prime:
PBS
Ad26.RSV. preF 10^8 vp
protein 5 µg
protein 0.5 µg
Ad26.RSV. preF 10^8 vp + protein 5 µg
Ad26.RSV. preF 10^8 vp + protein 0.5 µg
Boost:
PBS
Ad26.RSV. preF 10^8 vp
protein 5 µg
protein 0.5 µg
Ad26.RSV. preF 10^8 vp + protein 5 µg
Ad26.RSV. preF 10^8 vp + protein 0.5 µg

FIG. 4

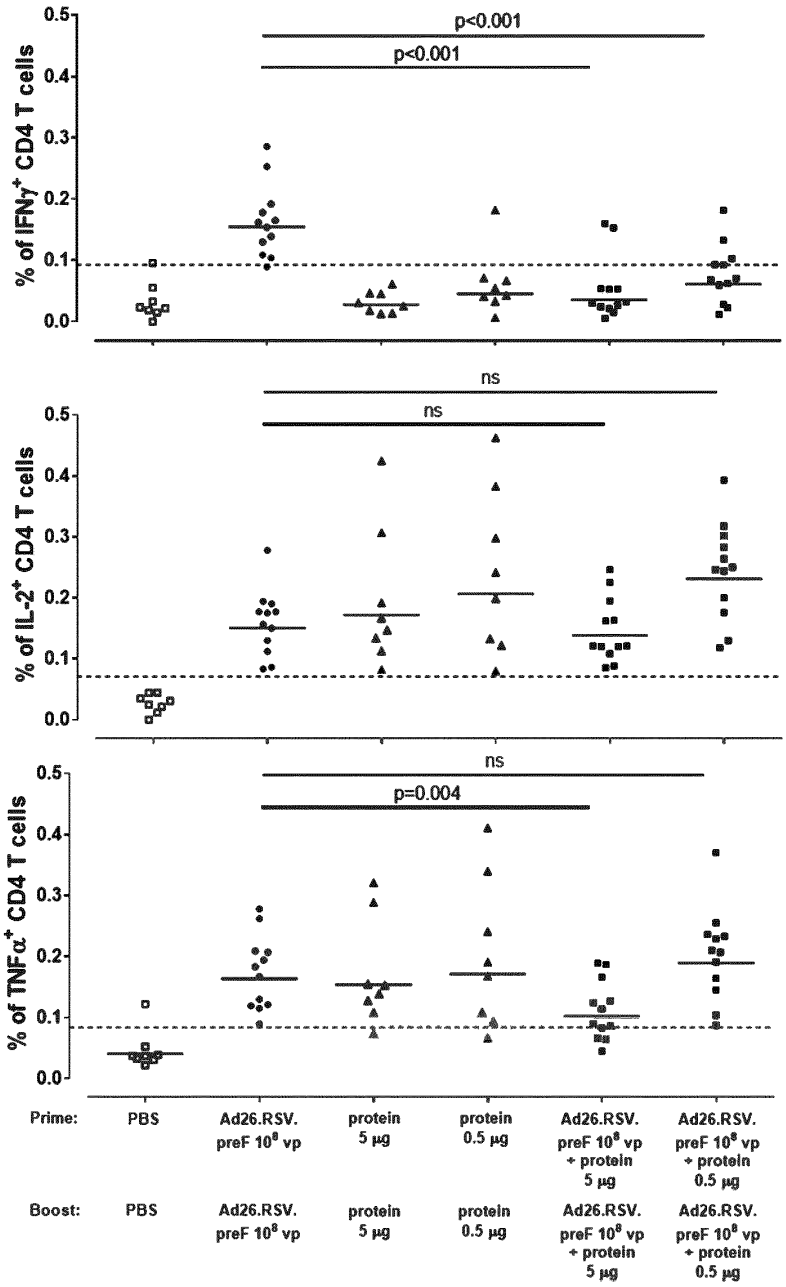

p<0.001
p<0.001
% of IFNγ+ CD4 T cells
0.5
0.4
0.3
0.2
0.1
0.0
ns
ns
% of IL-2+ CD4 T cells
ns
p=0.004
% of TNFα+ CD4 T cells
Prime: PBS
Ad26.RSV. preF 10^8 vp
protein 5 µg
protein 0.5 µg
Ad26.RSV. preF 10^8 vp + protein 5 µg
Ad26.RSV. preF 10^8 vp + protein 0.5 µg
Boost: PBS
Ad26.RSV. preF 10^8 vp
protein 5 µg
protein 0.5 µg
Ad26.RSV. preF 10^8 vp + protein 5 µg
Ad26.RSV. preF 10^8 vp + protein 0.5 µg

FIG. 5

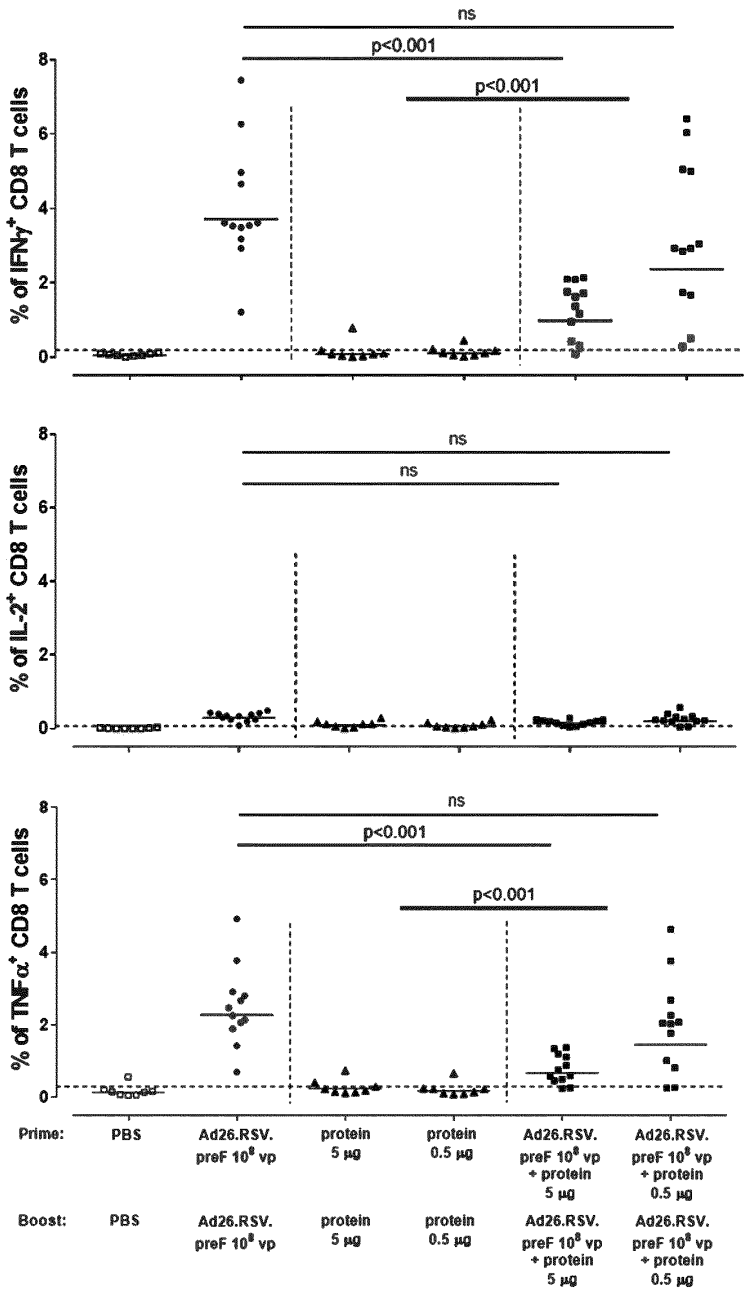

ns
p<0.001
p<0.001
% of IFNγ+ CD8 T cells
ns
ns
% of IL-2+ CD8 T cells
ns
p<0.001
p<0.001
% of TNFα+ CD8 T cells
Prime: PBS Ad26.RSV. preF 10^8 vp protein 5 µg protein 0.5 µg Ad26.RSV. preF 10^8 vp + protein 5 µg Ad26.RSV. preF 10^8 vp + protein 0.5 µg
Boost: PBS Ad26.RSV. preF 10^8 vp protein 5 µg protein 0.5 µg Ad26.RSV. preF 10^8 vp + protein 5 µg Ad26.RSV. preF 10^8 vp + protein 0.5 µg

FIG. 6

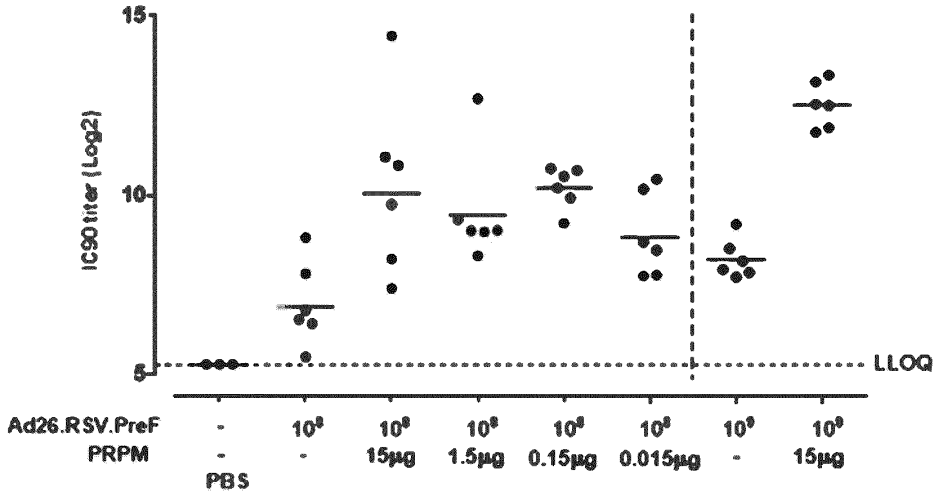

15
10
5
IC90 titer (Log2)
LLOQ
Ad26.RSV.PreF
PRPM
-
-
PBS
10^8
-
10^8
15µg
10^8
1.5µg
10^8
0.15µg
10^8
0.015µg
10^9
-
10^9
15µg

FIG. 7

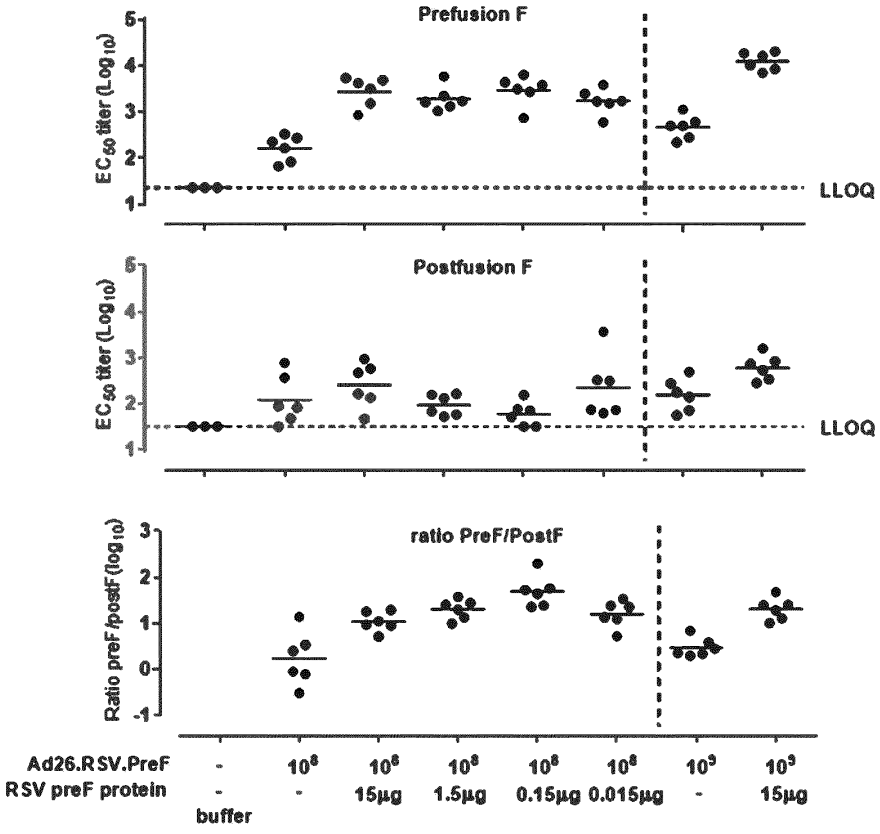

Prefusion F
EC50 titer (Log10)
LLOQ
Postfusion F
EC50 titer (Log10)
LLOQ
ratio PreF/PostF
Ratio preF /postF (log10)
Ad26.RSV.PreF - 10^8 10^8 10^8 10^8 10^8 10^9 10^9
RSV preF protein - - 15µg 1.5µg 0.15µg 0.015µg - 15µg
buffer

FIG. 8

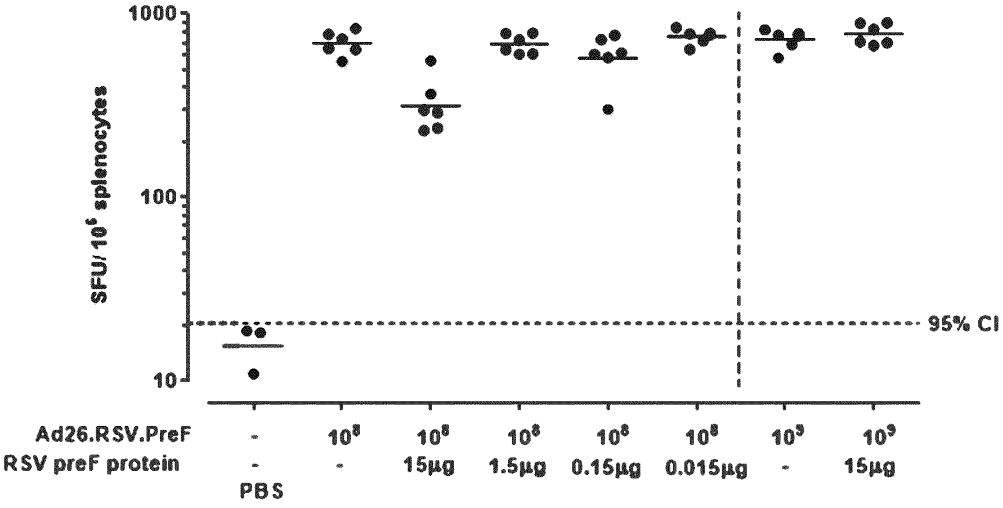

1000
100
10
SFU/ 10^6 splenocytes
95% CI
Ad26.RSV.PreF
RSV preF protein
-
-
PBS
10^8
-
10^8
15µg
10^8
1.5µg
10^8
0.15µg
10^8
0.015µg
10^9
-
10^9
15µg

Fig. 9

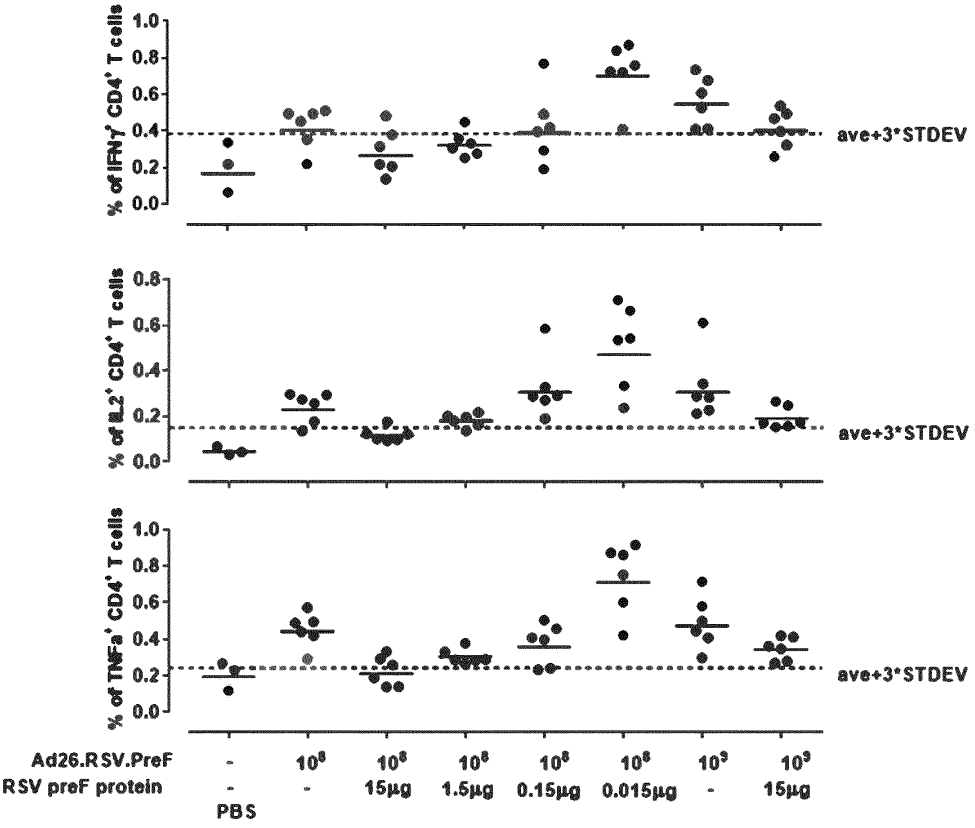

% of IFNγ+ CD4+ T cells
% of IL2+ CD4+ T cells
% of TNFa+ CD4+ T cells
ave+3*STDEV
Ad26.RSV.PreF
RSV preF protein
PBS

FIG. 10

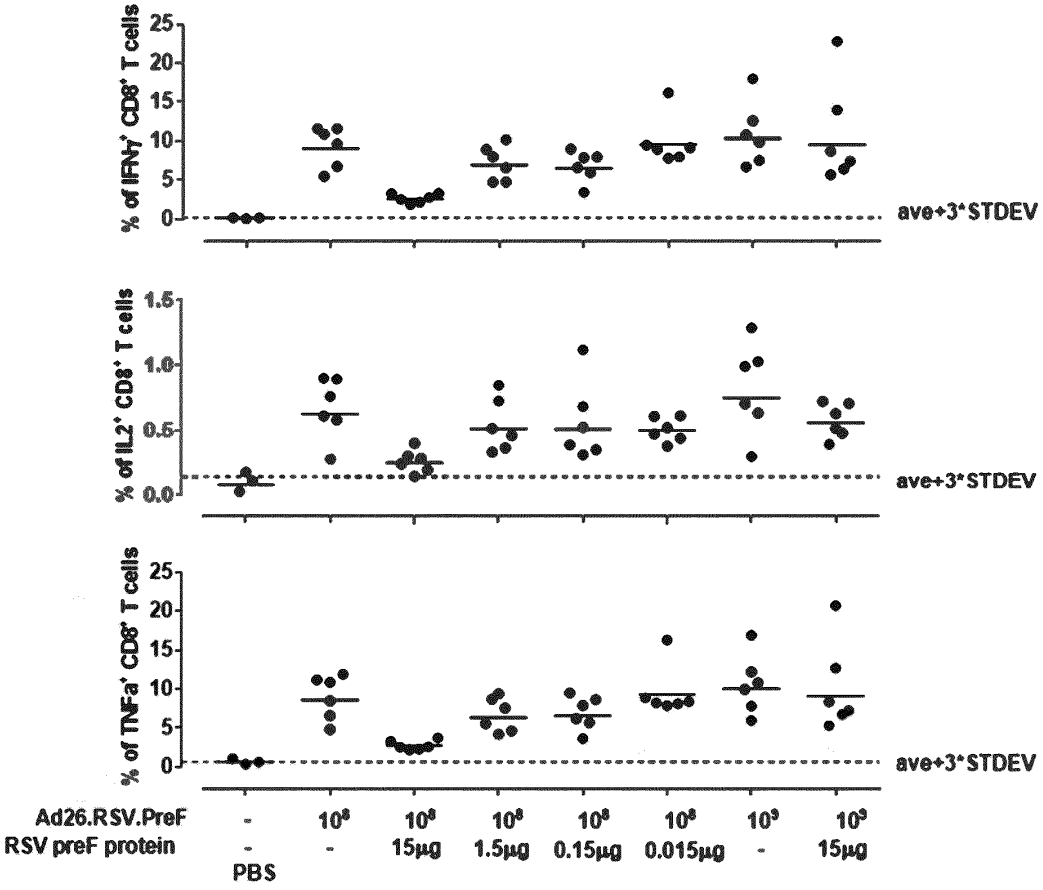

% of IFNγ+ CD8+ T cells
25
20
15
10
5
0
ave+3*STDEV
% of IL2+ CD8+ T cells
1.5
1.0
0.5
0.0
ave+3*STDEV
% of TNFa+ CD8+ T cells
25
20
15
10
5
0
ave+3*STDEV
Ad26.RSV.preF - 10^8 10^8 10^8 10^8 10^8 10^9 10^9
RSV preF protein - - 15µg 1.5µg 0.15µg 0.015µg - 15µg
PBS

FIG. 11

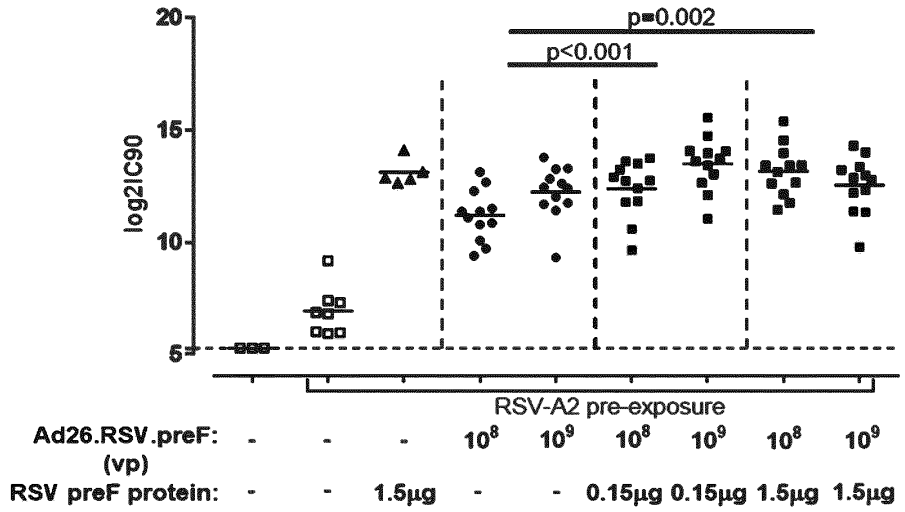

p=0.002
p<0.001
log2IC90
20
15
10
5
RSV-A2 pre-exposure
Ad26.RSV.preF: (vp) - - - 10^8 10^9 10^8 10^9 10^8 10^9
RSV preF protein: - - 1.5µg - - 0.15µg 0.15µg 1.5µg 1.5µg

FIG. 12

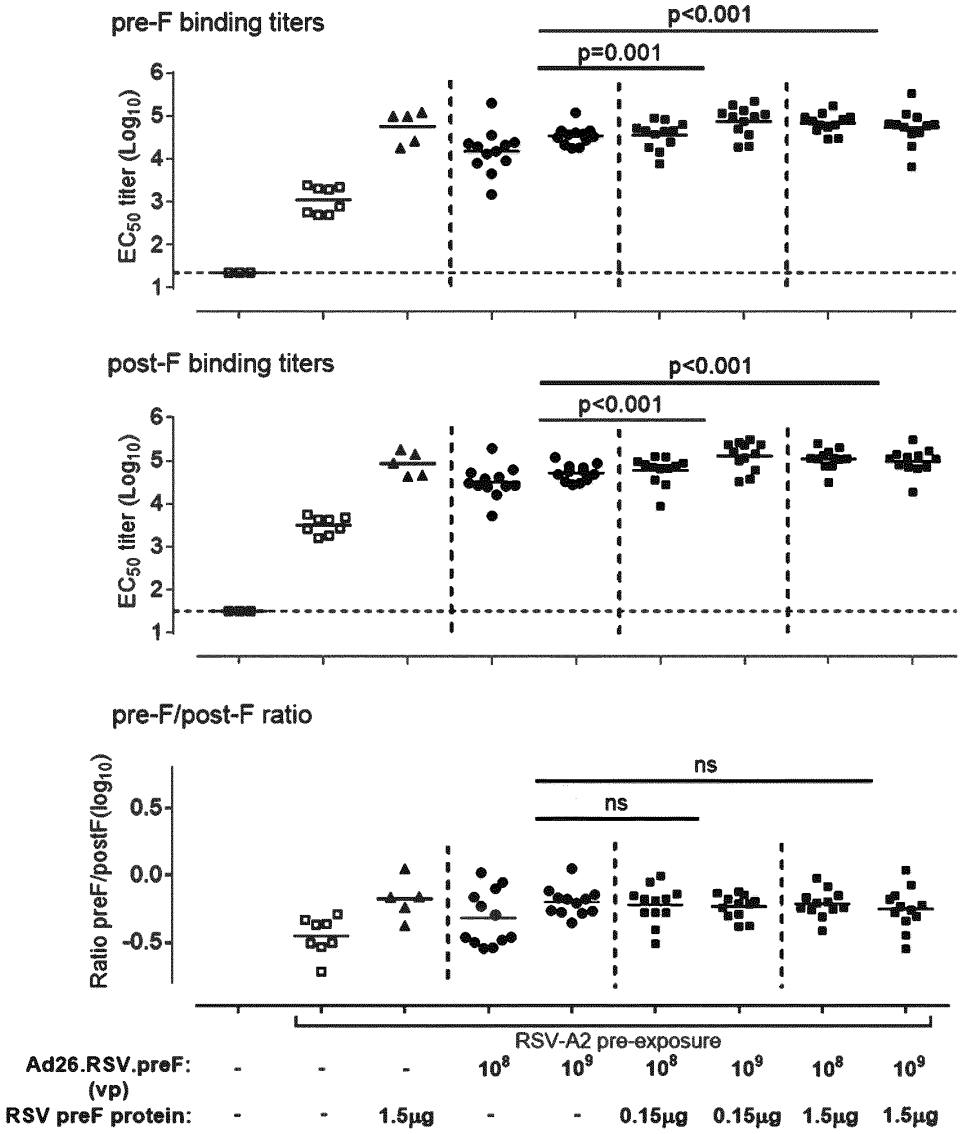

pre-F binding titers
p<0.001
p=0.001
EC50 titer (Log10)
post-F binding titers
p<0.001
p<0.001
EC50 titer (Log10)
pre-F/post-F ratio
ns
ns
Ratio preF/postF(log10)
RSV-A2 pre-exposure
Ad26.RSV.preF: (vp) - - - 10^8 10^9 10^8 10^9 10^8 10^9
RSV preF protein: - - 1.5µg - - 0.15µg 0.15µg 1.5µg 1.5µg

FIG. 13

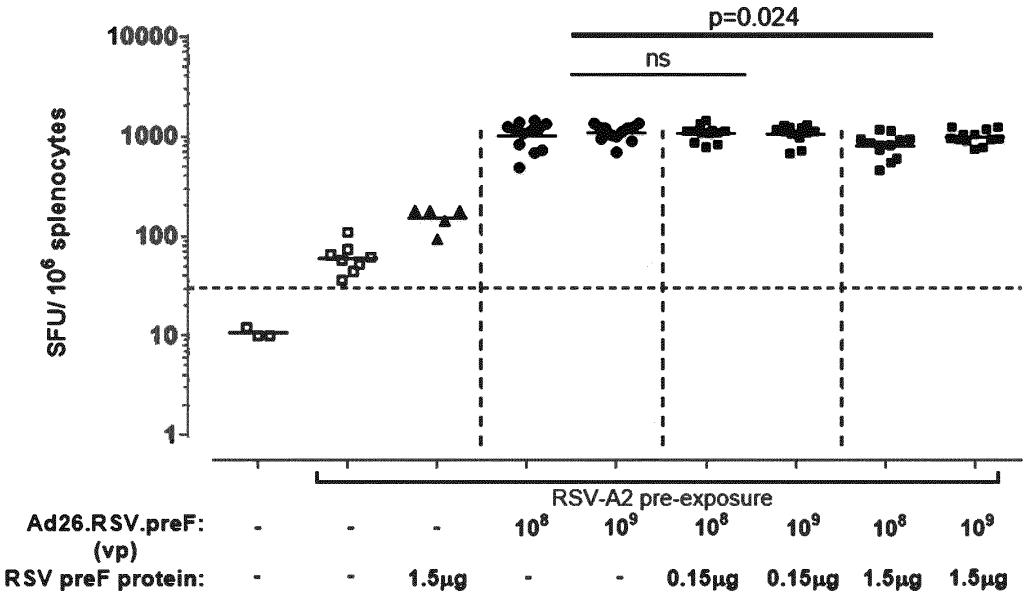

p=0.024
ns
10000
1000
100
10
1
SFU/ 10^6 splenocytes
RSV-A2 pre-exposure
Ad26.RSV.preF: (vp)
RSV preF protein:
- - - 10^8 10^9 10^8 10^9 10^8 10^9
- - 1.5µg - - 0.15µg 0.15µg 1.5µg 1.5µg

FIG. 14

CD4+

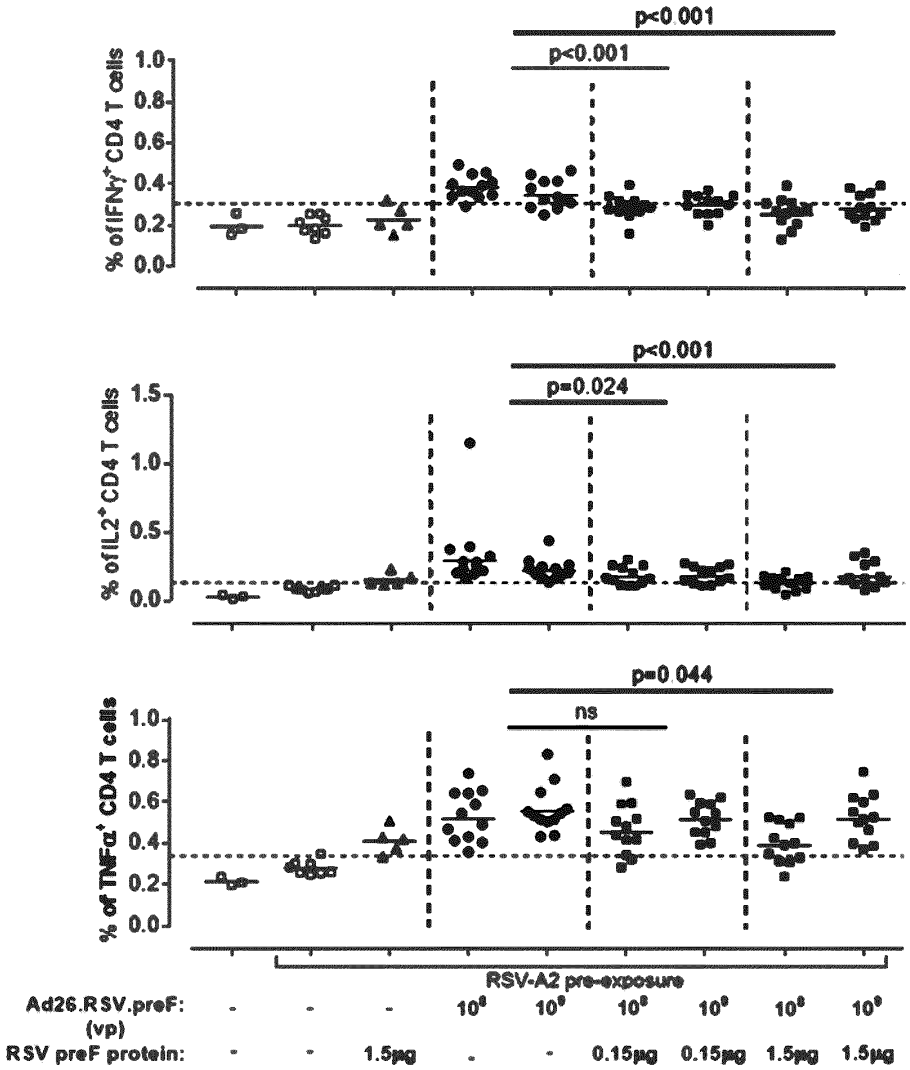

p<0.001
p<0.001
% of IFNγ+ CD4 T cells
1.0
0.8
0.6
0.4
0.2
0.0
p<0.001
p=0.024
% of IL2+ CD4 T cells
1.5
1.0
0.5
0.0
p=0.044
ns
% of TNFα+ CD4 T cells
1.0
0.8
0.6
0.4
0.2
0.0
RSV-A2 pre-exposure
Ad26.RSV.preF (vp): - - - 10^8 10^9 10^8 10^9 10^8 10^9
RSV preF protein: - - 1.5µg - - 0.15µg 0.15µg 1.5µg 1.5µg

FIG. 15A

CD8+

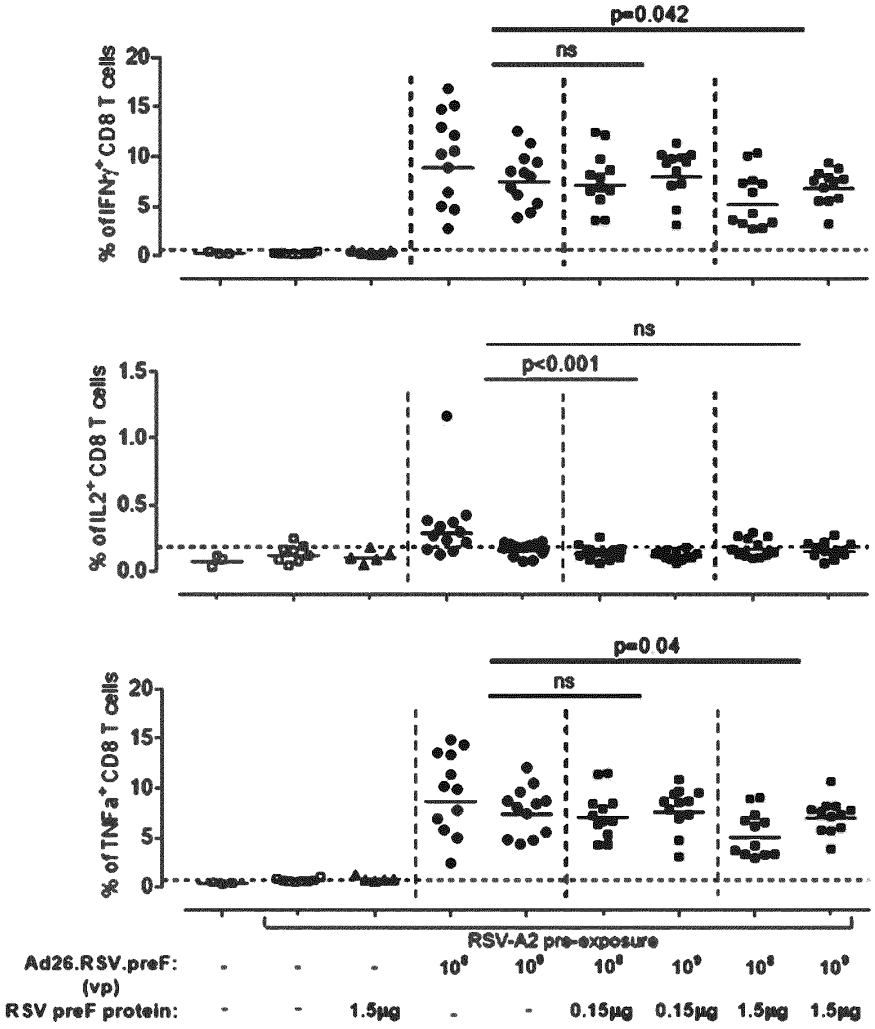

p=0.042
ns
% of IFNγ+ CD8 T cells
20
15
10
5
0
ns
p<0.001
% of IL2+ CD8 T cells
1.5
1.0
0.5
0.0
p=0.04
ns
% of TNFa+ CD8 T cells
20
15
10
5
0
RSV-A2 pre-exposure
Ad26.RSV.preF: (vp) - - - 10^8 10^9 10^8 10^9 10^8 10^9
RSV preF protein: - - 1.5µg - - 0.15µg 0.15µg 1.5µg 1.5µg

FIG. 15B

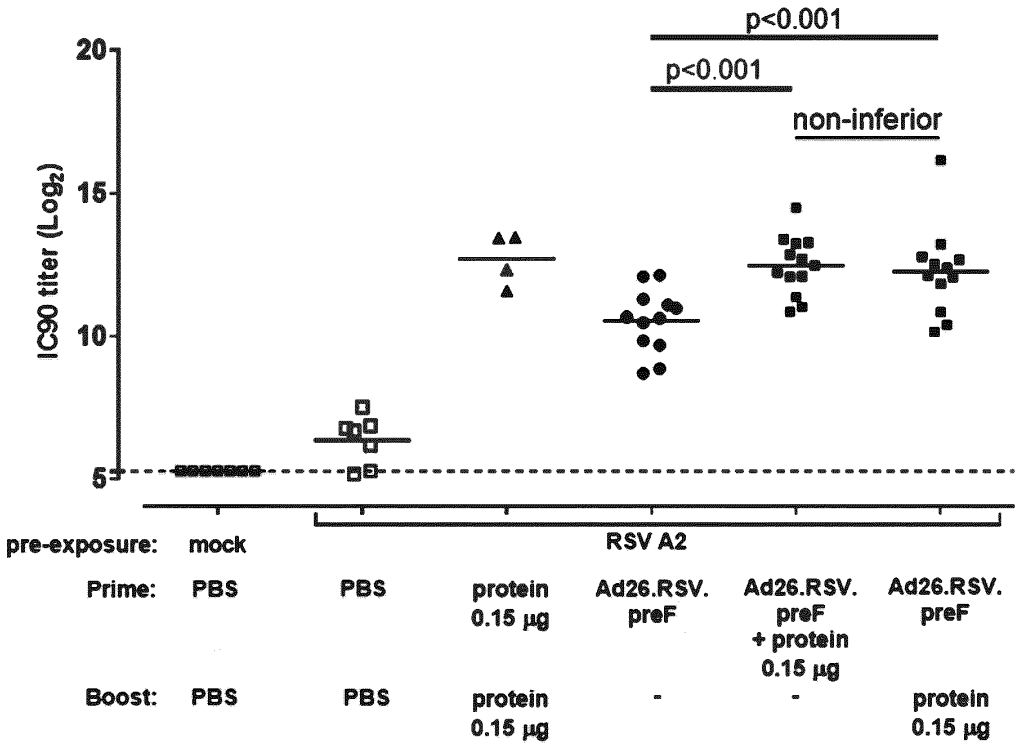

p<0.001
p<0.001
non-inferior
20
15
10
5
IC90 titer (Log2)
pre-exposure: mock
RSV A2
Prime: PBS PBS protein 0.15 µg Ad26.RSV. preF Ad26.RSV. preF + protein 0.15 µg Ad26.RSV. preF
Boost: PBS PBS protein 0.15 µg - - protein 0.15 µg

FIG. 16

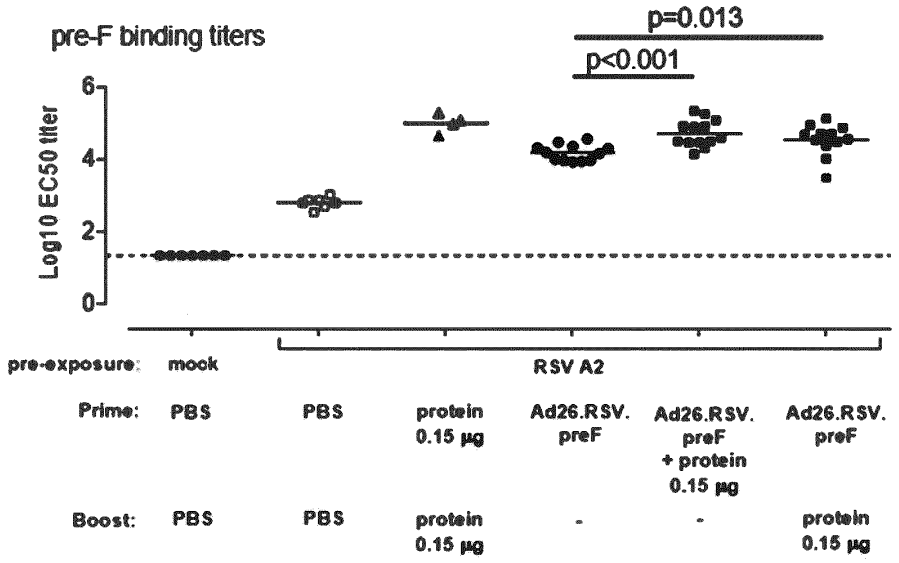


FIG.17A

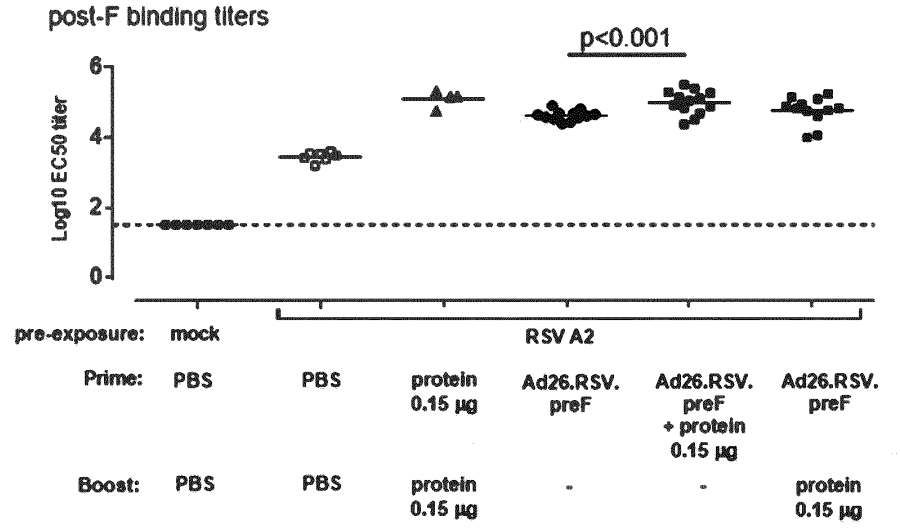


FIG.17 B

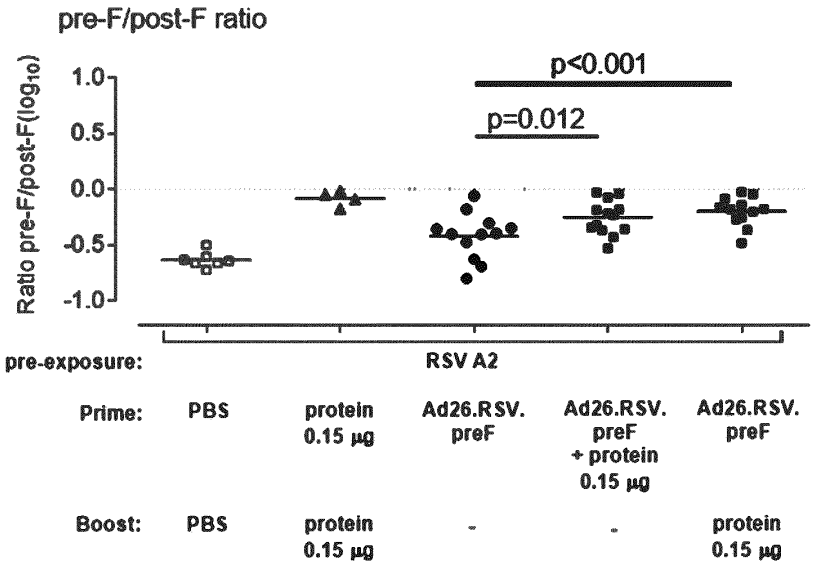

pre-F/post-F ratio
Ratio pre-F/post-F(log10)
1.0
0.5
0.0
-0.5
-1.0
p<0.001
p=0.012
pre-exposure:
RSV A2
Prime:
PBS
protein 0.15 µg
Ad26.RSV. preF
Ad26.RSV. preF + protein 0.15 µg
Ad26.RSV. preF
Boost:
PBS
protein 0.15 µg
-
-
protein 0.15 µg

FIG. 17C

CD4+

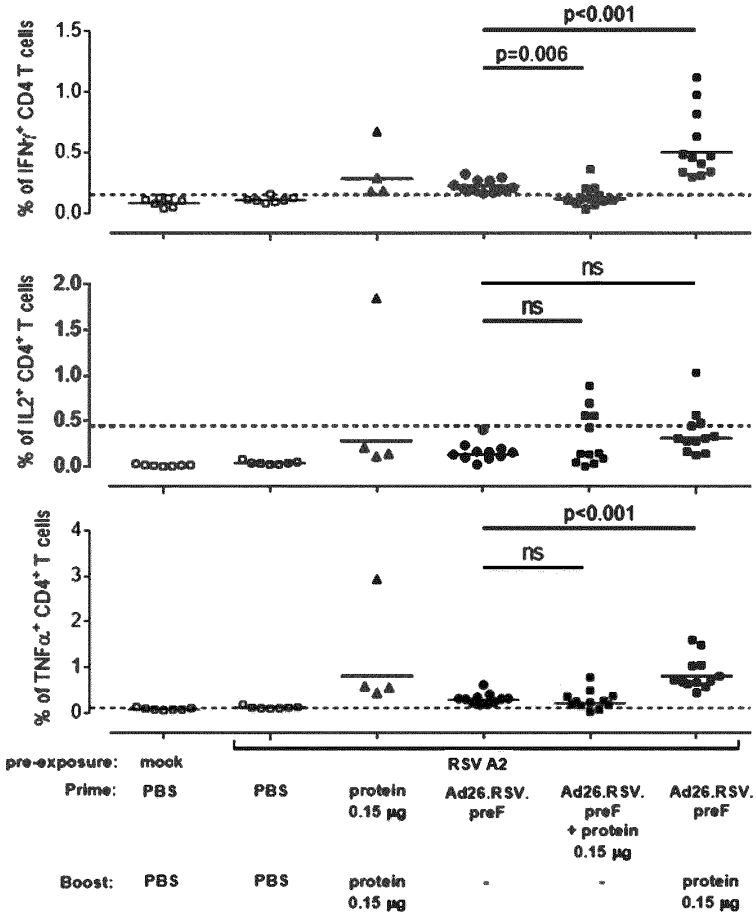

p<0.001
p=0.006
% of IFNγ+ CD4 T cells
1.5
1.0
0.5
0.0
ns
ns
% of IL2+ CD4+ T cells
2.0
1.5
1.0
0.5
0.0
p<0.001
ns
% of TNFα+ CD4+ T cells
4
3
2
1
0
pre-exposure: mock
RSV A2
Prime: PBS
PBS
protein 0.15 µg
Ad26.RSV. preF
Ad26.RSV. preF + protein 0.15 µg
Ad26.RSV. preF
Boost: PBS
PBS
protein 0.15 µg
-
-
protein 0.15 µg

FIG. 18

CD8+

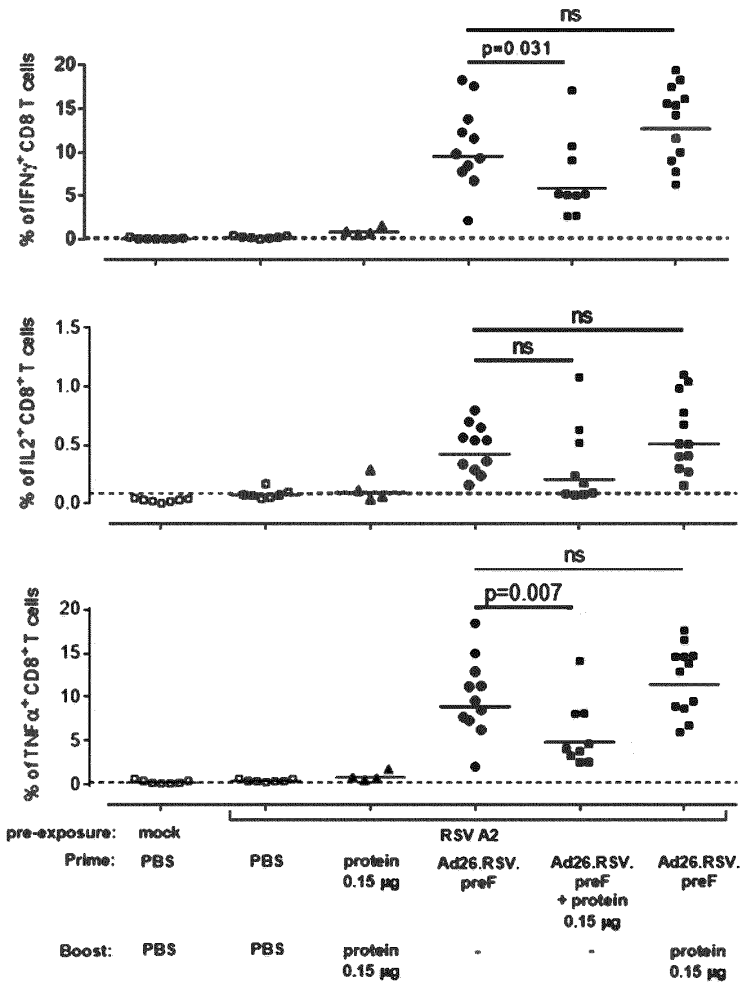


FIG. 18 (Continued)

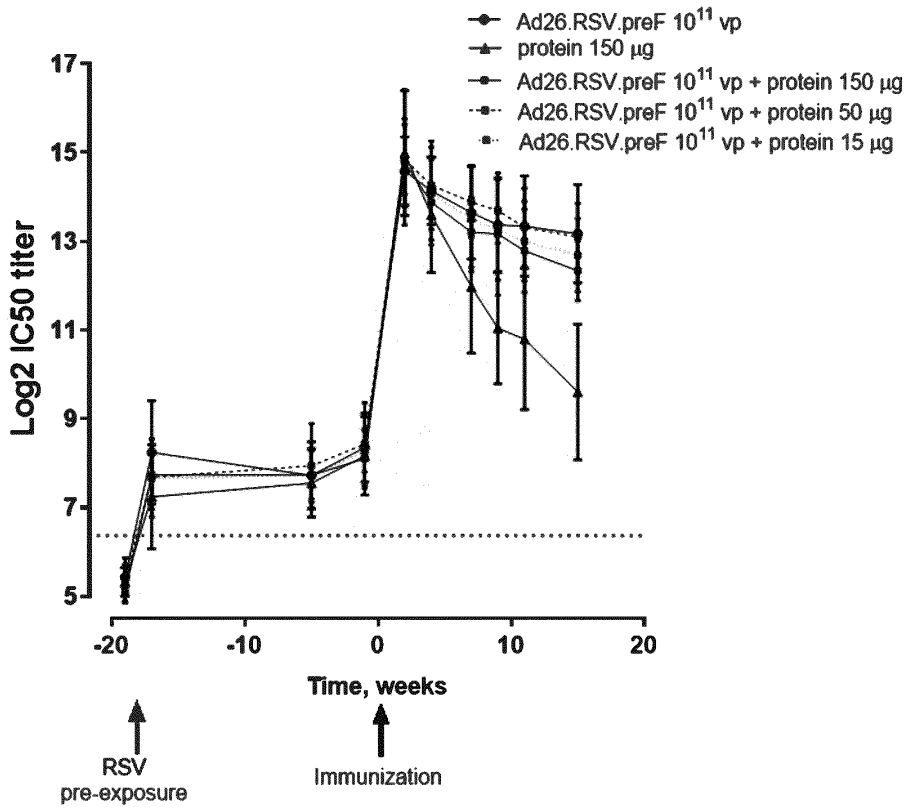

Ad26.RSV.preF 10^11 vp
protein 150 µg
Ad26.RSV.preF 10^11 vp + protein 150 µg
Ad26.RSV.preF 10^11 vp + protein 50 µg
Ad26.RSV.preF 10^11 vp + protein 15 µg
Log2 IC50 titer
17
15
13
11
9
7
5
-20
-10
0
10
20
Time, weeks
RSV
pre-exposure
Immunization

FIG. 19

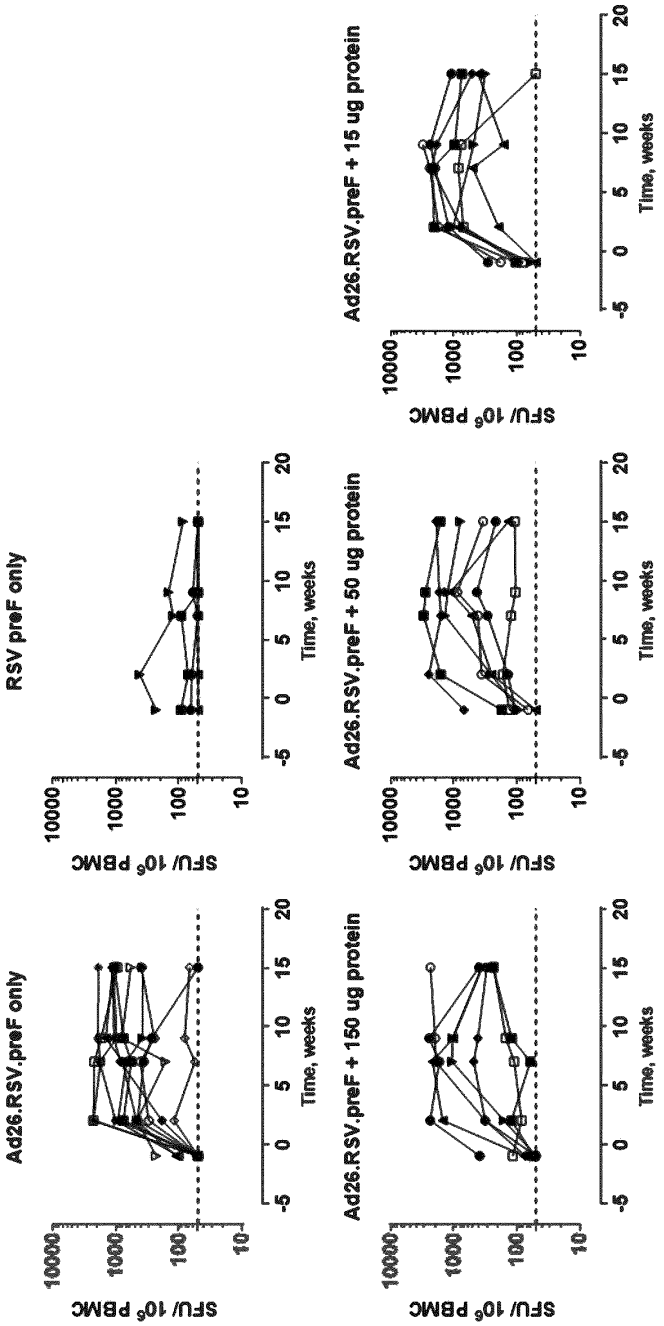

RSV preF only
Ad26.RSV.preF + 15 ug protein
Ad26.RSV.preF + 50 ug protein
Ad26.RSV.preF only
Ad26.RSV.preF + 150 ug protein
SFU/ 10^6 PBMC
Time, weeks
10000
1000
100
10
-5
0
5
10
15
20

FIG. 20

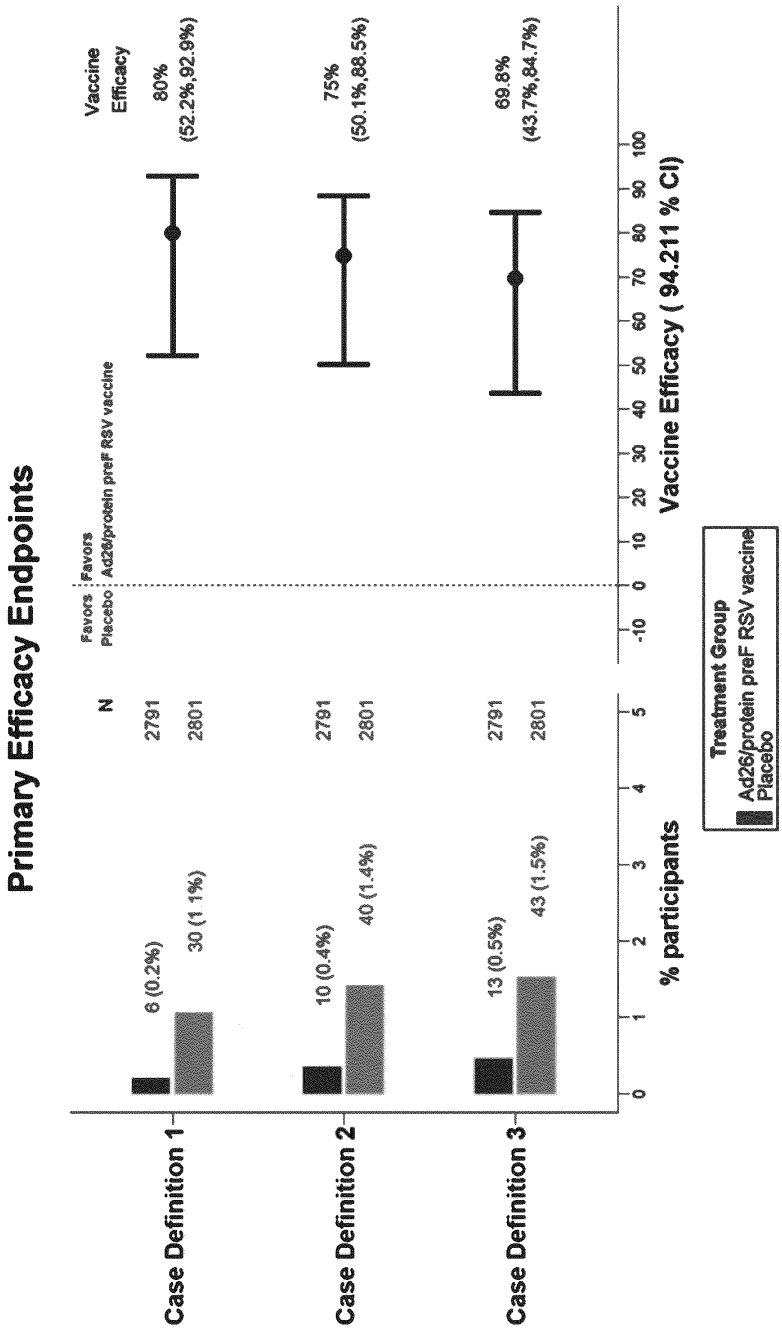

Primary Efficacy Endpoints
Favors Placebo
Favors Ad26/protein preF RSV vaccine
N
Vaccine Efficacy
Case Definition 1
2791
2801
6 (0.2%)
30 (1 1%)
80%
(52.2%,92.9%)
Case Definition 2
2791
2801
10 (0.4%)
40 (1.4%)
75%
(50.1%,88.5%)
Case Definition 3
2791
2801
13 (0.5%)
43 (1.5%)
69.8%
(43.7%,84.7%)
% participants
Vaccine Efficacy (94.211 % CI)
Treatment Group
Ad26/protein preF RSV vaccine
Placebo

FIG. 21

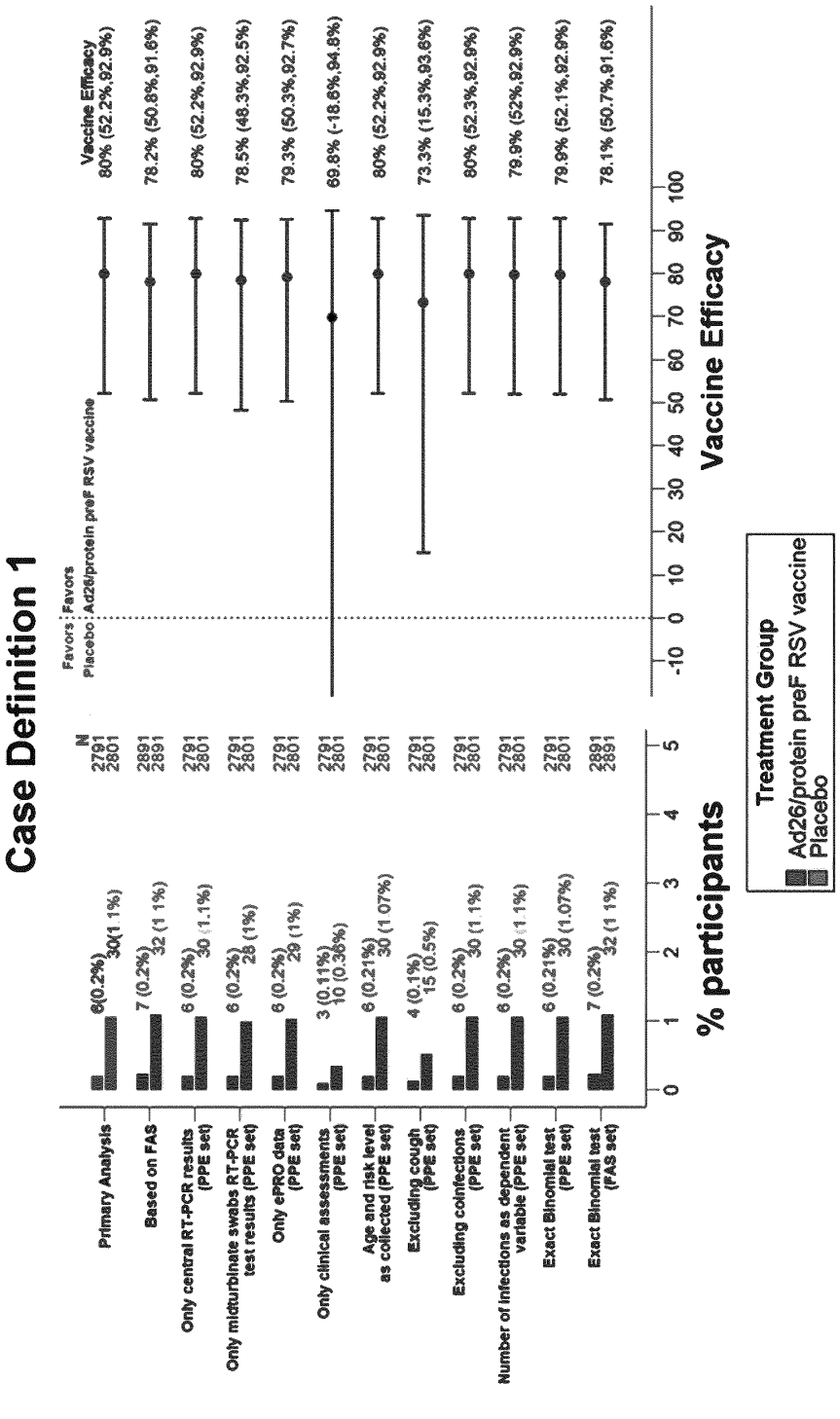

Case Definition 1
Favors : Favors
Placebo : Ad26/protein preF RSV vaccine
N
Vaccine Efficacy
Primary Analysis
6(0.2%) 30(1.1%)
2791 2801
80% (52.2%,92.9%)
Based on FAS
7 (0.2%) 32 (1.1%)
2891 2891
78.2% (50.8%,91.6%)
Only central RT-PCR results (PPE set)
6 (0.2%) 30 (1.1%)
2791 2801
80% (52.2%,92.9%)
Only midturbinate swabs RT-PCR test results (PPE set)
6 (0.2%) 28 (1%)
2791 2801
78.5% (48.3%,92.5%)
Only ePRO data (PPE set)
6 (0.2%) 29 (1%)
2791 2801
79.3% (50.3%,92.7%)
Only clinical assessments (PPE set)
3 (0.11%) 10 (0.36%)
2791 2801
69.8% (-18.8%,94.8%)
Age and risk level as collected (PPE set)
6 (0.21%) 30 (1.07%)
2791 2801
80% (52.2%,92.9%)
Excluding cough (PPE set)
4 (0.1%) 15 (0.5%)
2791 2801
73.3% (15.3%,93.6%)
Excluding coinfections (PPE set)
6 (0.2%) 30 (1.1%)
2791 2801
80% (52.3%,92.9%)
Number of infections as dependent variable (PPE set)
6 (0.2%) 30 (1.1%)
2791 2801
79.9% (52%,92.9%)
Exact Binomial test (PPE set)
6 (0.21%) 30 (1.07%)
2791 2801
79.9% (52.1%,92.9%)
Exact Binomial test (FAS set)
7 (0.2%) 32 (1.1%)
2891 2891
78.1% (50.7%,91.6%)
0 1 2 3 4 5
% participants
-10 0 10 20 30 40 50 60 70 80 90 100
Vaccine Efficacy
Treatment Group
Ad26/protein preF RSV vaccine
Placebo

FIG. 22

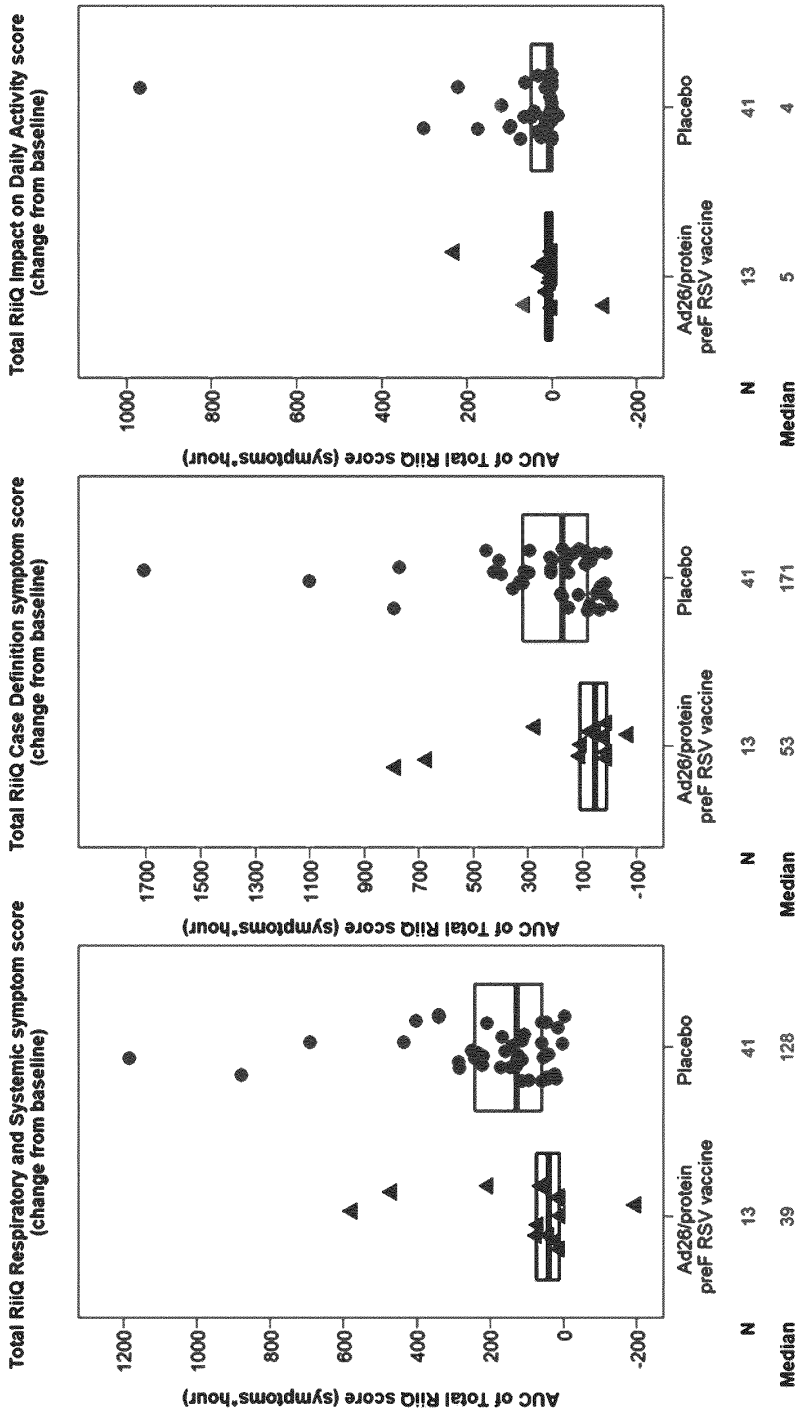

Total RiiQ Respiratory and Systemic symptom score (change from baseline)
AUC of Total RiiQ score (symptoms*hour)
1200
1000
800
600
400
200
0
-200
Ad26/protein preF RSV vaccine
Placebo
N 13 41
Median 39 128
Total RiiQ Case Definition symptom score (change from baseline)
AUC of Total RiiQ score (symptoms*hour)
1700
1500
1300
1100
900
700
500
300
100
-100
Ad26/protein preF RSV vaccine
Placebo
N 13 41
Median 53 171
Total RiiQ Impact on Daily Activity score (change from baseline)
AUC of Total RiiQ score (symptoms*hour)
1000
800
600
400
200
0
-200
Ad26/protein preF RSV vaccine
Placebo
N 13 41
Median 5 4

FIG. 23

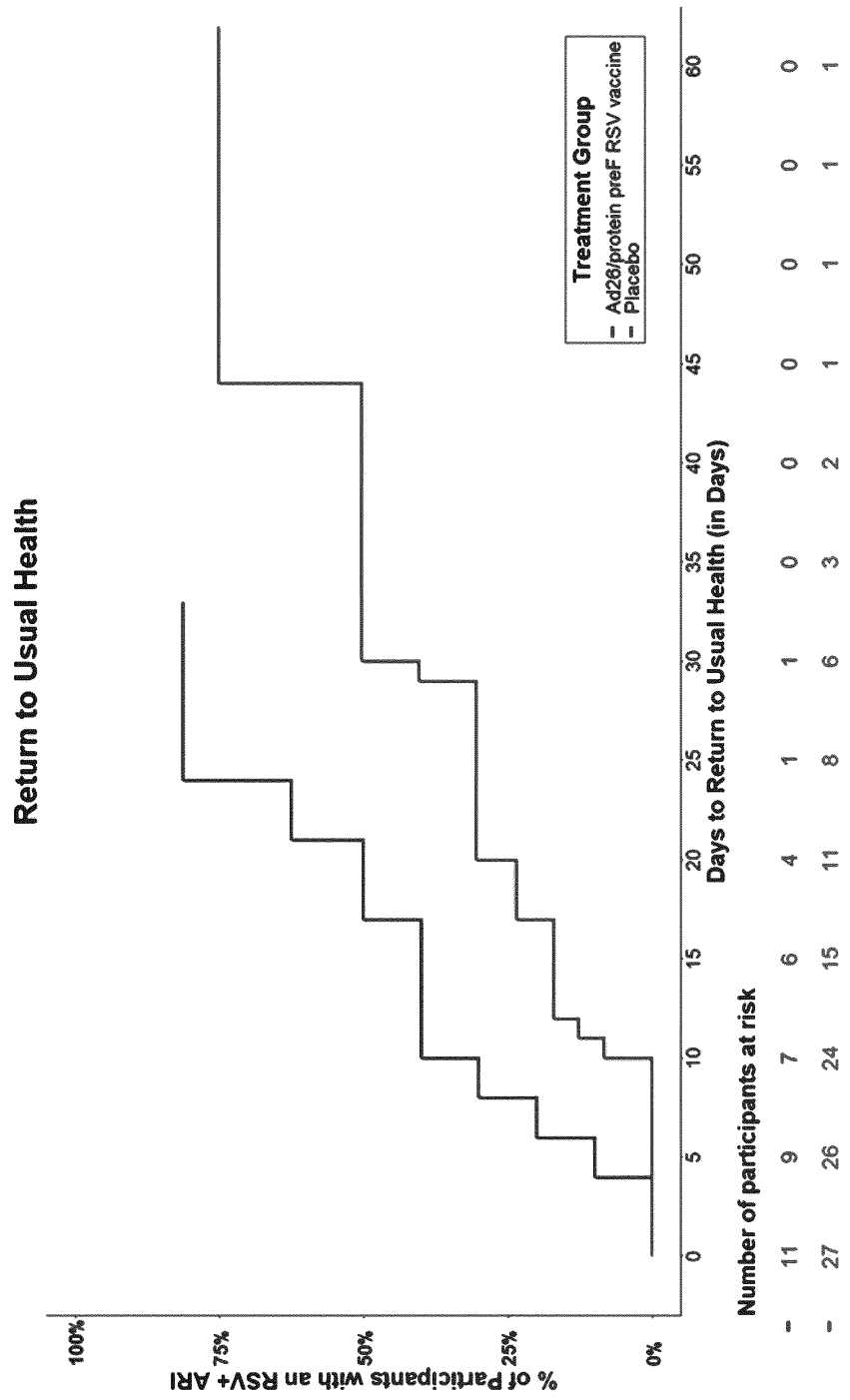

Return to Usual Health
% of Participants with an RSV+ ARI
100%
75%
50%
25%
0%
Treatment Group
Ad26/protein preF RSV vaccine
Placebo
Days to Return to Usual Health (in Days)
0 5 10 15 20 25 30 35 40 45 50 55 60
Number of participants at risk
11 9 7 6 4 1 1 0 0 0 0 0 0
27 26 24 15 11 8 6 3 2 1 1 1 1

FIG. 24

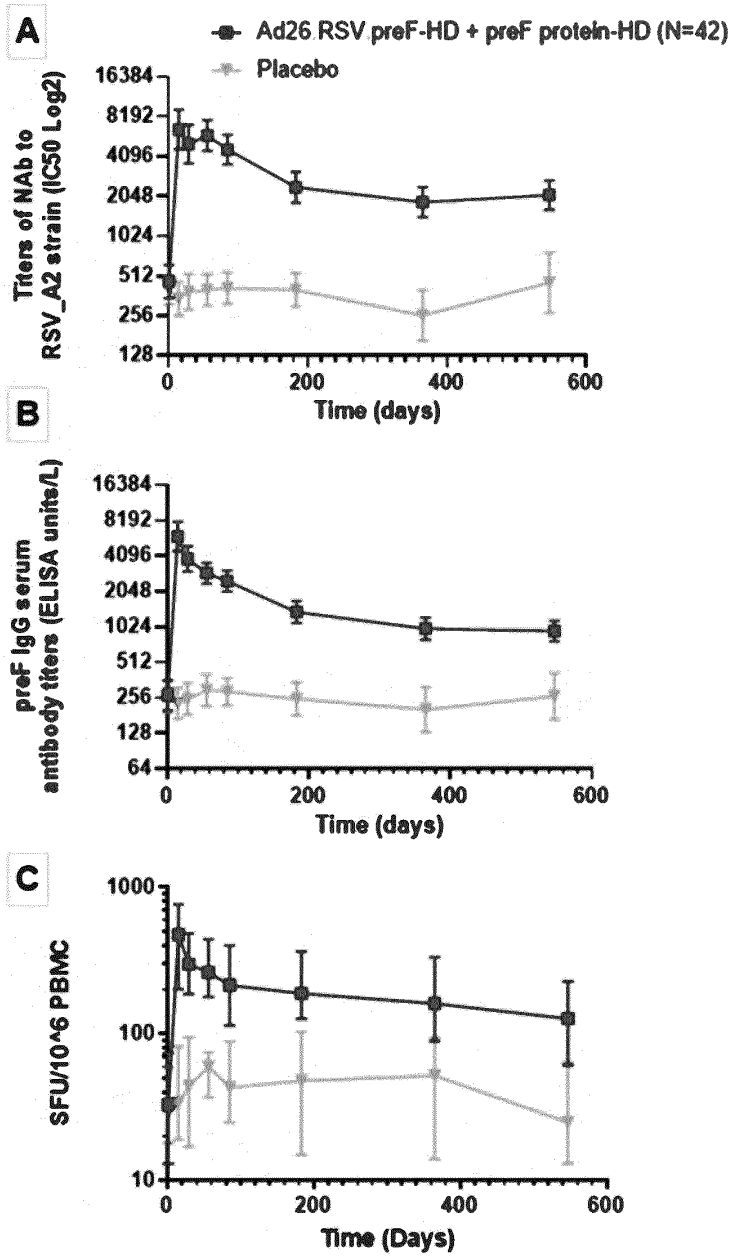
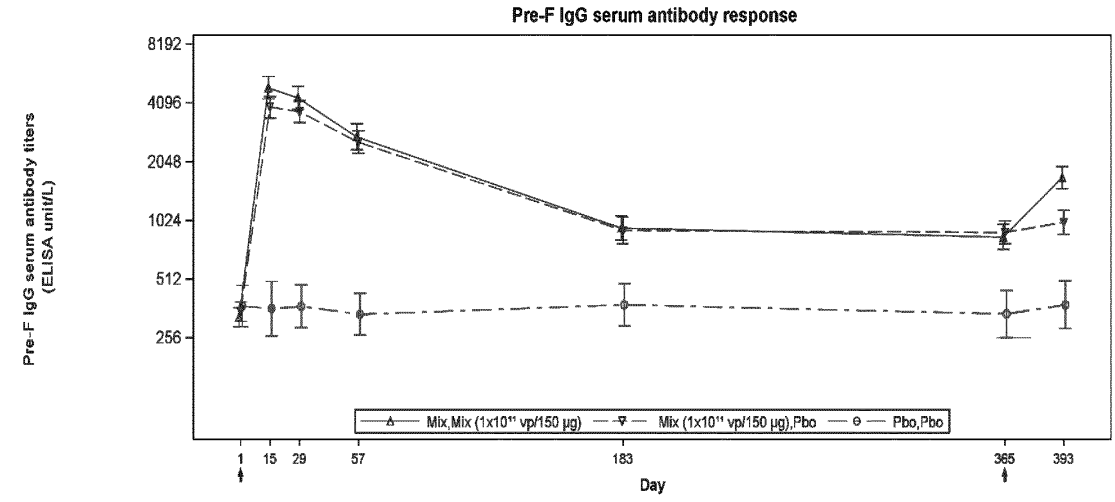
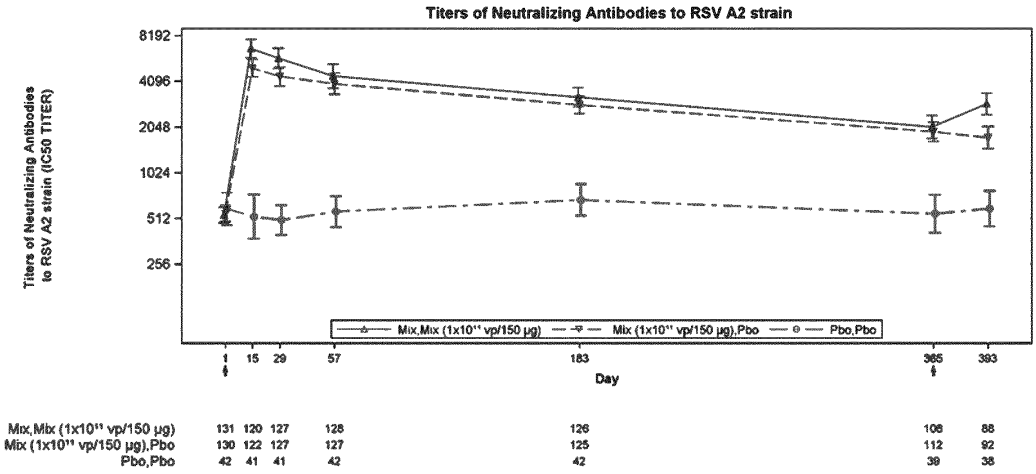

A
Ad26.RSV.preF-HD + preF protein-HD (N=42)
Placebo
Titers of NAb to RSV_A2 strain (IC50 Log2)
16384
8192
4096
2048
1024
512
256
128
0
200
400
600
Time (days)
B
preF IgG serum antibody titers (ELISA units/L)
16384
8192
4096
2048
1024
512
256
128
64
0
200
400
600
Time (days)
C
SFU/10^6 PBMC
1000
100
10
0
200
400
600
Time (Days)

FIG.25



Mix,Mix (1x10¹¹ vp/150 µg)	131	120	127	128	126	108	88
Mix (1x10¹¹ vp/150 µg),Pbo	130	122	127	127	125	112	91
Pbo,Pbo	42	41	41	42	42	39	38

FIG. 26



Mix,Mix (1x10¹¹ vp/150 µg)	131	120	127	128	126	108	88
Mix (1x10¹¹ vp/150 µg),Pbo	130	122	127	127	125	112	92
Pbo,Pbo	42	41	41	42	42	39	38

FIG. 27

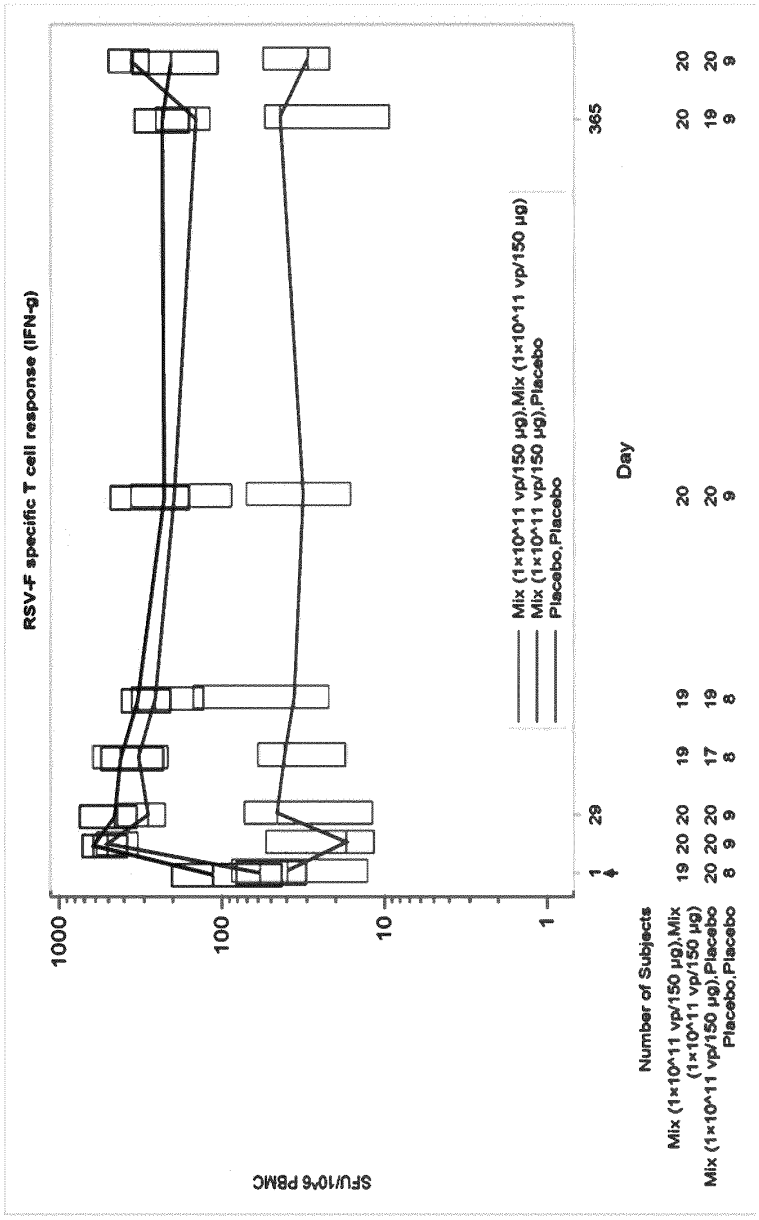

RSV-F specific T cell response (IFN-g)
SFU/10^6 PBMC
1000
100
10
1
Day
1
29
365
Mix (1×10^11 vp/150 µg),Mix (1×10^11 vp/150 µg)
Mix (1×10^11 vp/150 µg),Placebo
Placebo,Placebo
Number of Subjects
Mix (1×10^11 vp/150 µg),Mix (1×10^11 vp/150 µg) 19 20 20 19 19 20 20 20
Mix (1×10^11 vp/150 µg),Placebo 20 20 20 17 19 20 19 20
Placebo,Placebo 8 9 9 8 8 9 9 9

FIG. 28

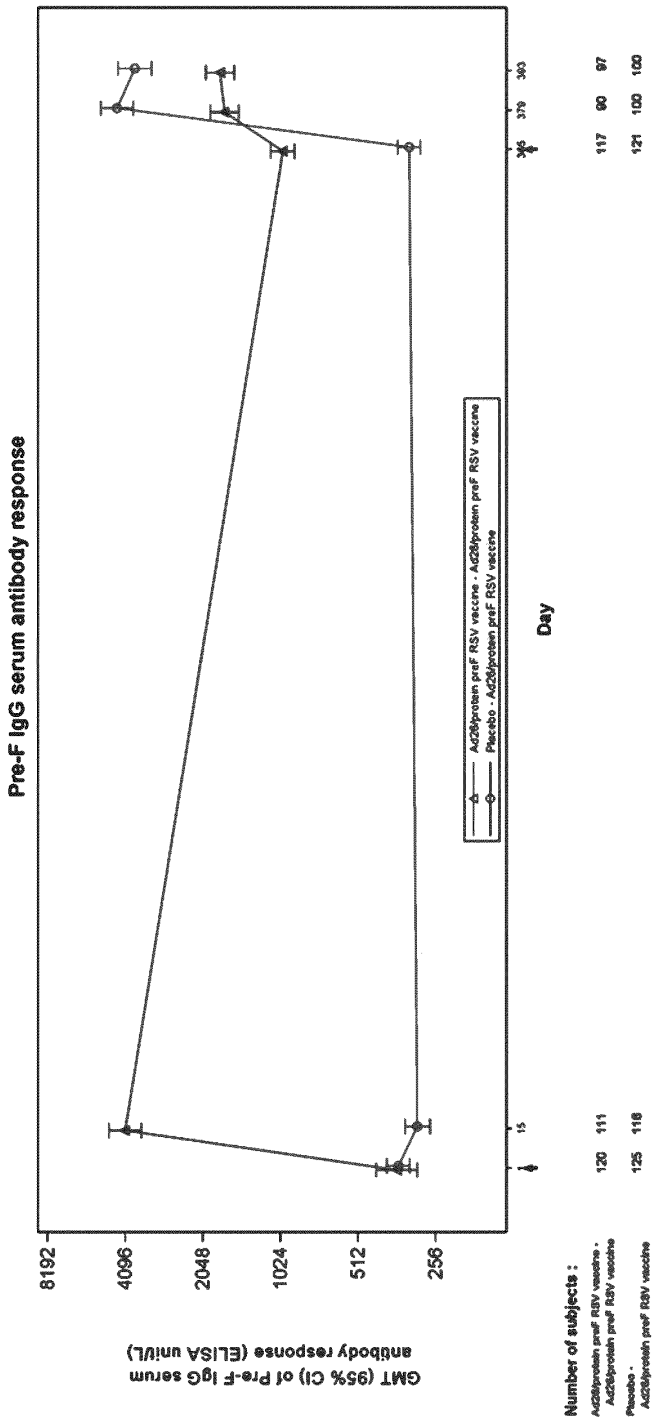

Pre-F IgG serum antibody response
GMT (95% CI) of Pre-F IgG serum antibody response (ELISA unit/L)
8192
4096
2048
1024
512
256
1
15
Day
Ad26/protein preF RSV vaccine - Ad26/protein preF RSV vaccine
Placebo - Ad26/protein preF RSV vaccine
Number of subjects :
Ad26/protein preF RSV vaccine - Ad26/protein preF RSV vaccine
120 111 117 90 97
Placebo - Ad26/protein preF RSV vaccine
125 118 121 100 100

FIG. 29

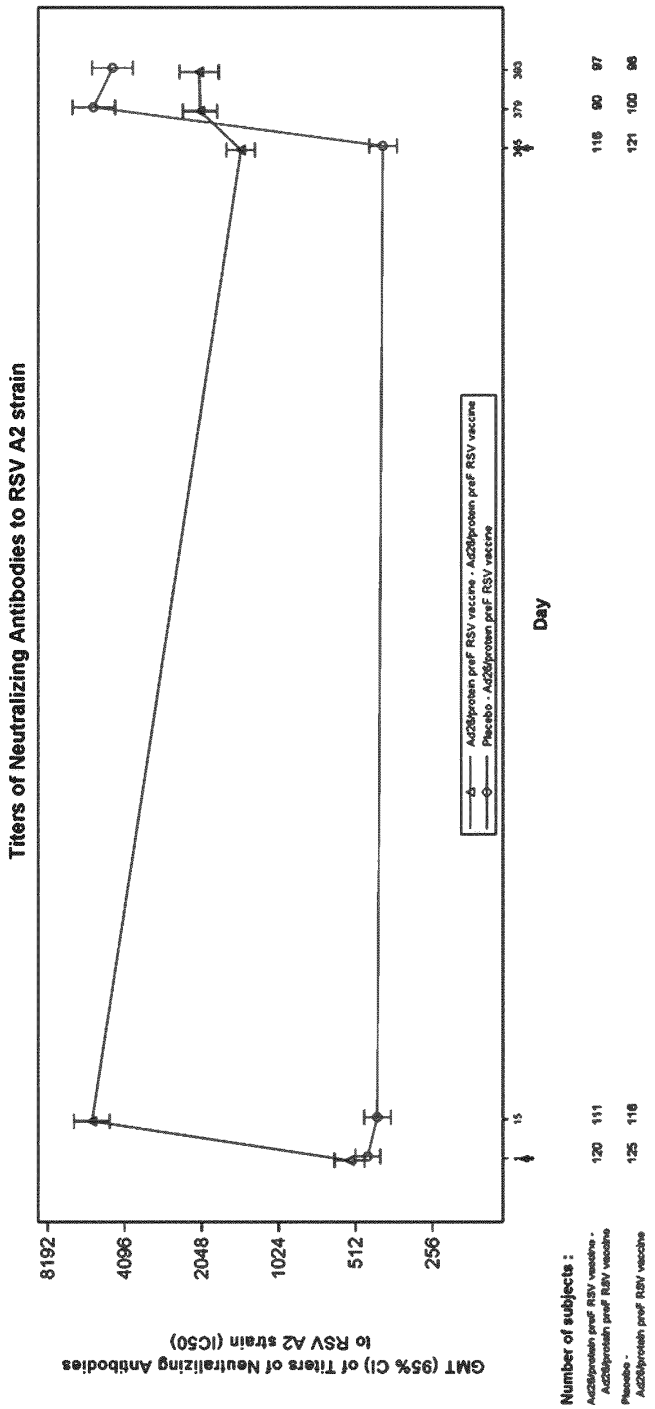

Titers of Neutralizing Antibodies to RSV A2 strain
GMT (95% CI) of Titers of Neutralizing Antibodies to RSV A2 strain (IC50)
8192
4096
2048
1024
512
256
Day
1
15
365
379
393
Ad26/protein preF RSV vaccine - Ad26/protein preF RSV vaccine
Placebo - Ad26/protein preF RSV vaccine
Number of subjects :
Ad26/protein preF RSV vaccine - Ad26/protein preF RSV vaccine 120 111 116 90 97
Placebo - Ad26/protein preF RSV vaccine 125 116 121 100 96

FIG. 30