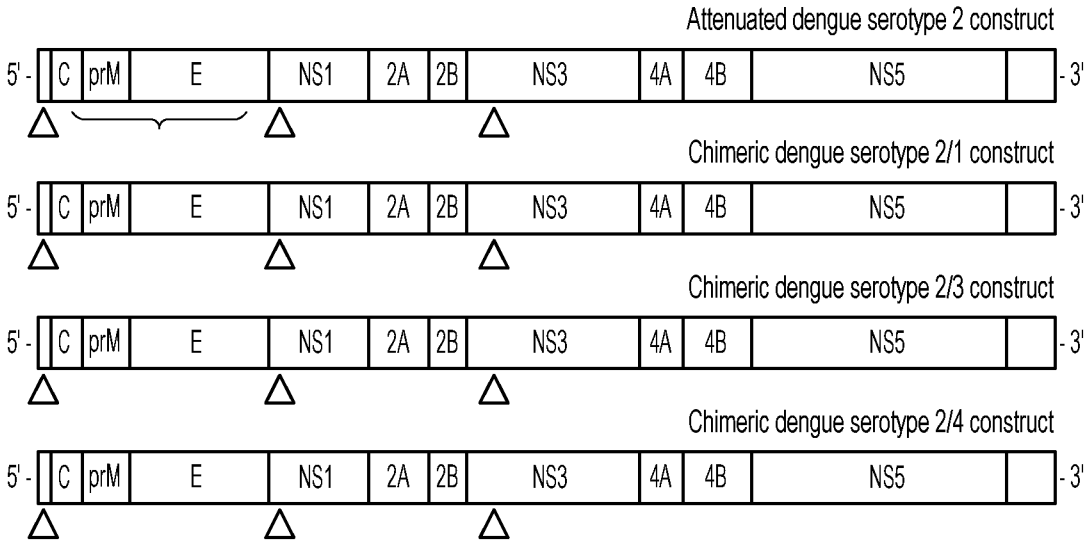

Attenuated dengue serotype 2 construct
5' -
C
prM
E
NS1
2A
2B
NS3
4A
4B
NS5
- 3'
Chimeric dengue serotype 2/1 construct
5' -
C
prM
E
NS1
2A
2B
NS3
4A
4B
NS5
- 3'
Chimeric dengue serotype 2/3 construct
5' -
C
prM
E
NS1
2A
2B
NS3
4A
4B
NS5
- 3'
Chimeric dengue serotype 2/4 construct
5' -
C
prM
E
NS1
2A
2B
NS3
4A
4B
NS5
- 3'

Figure 1

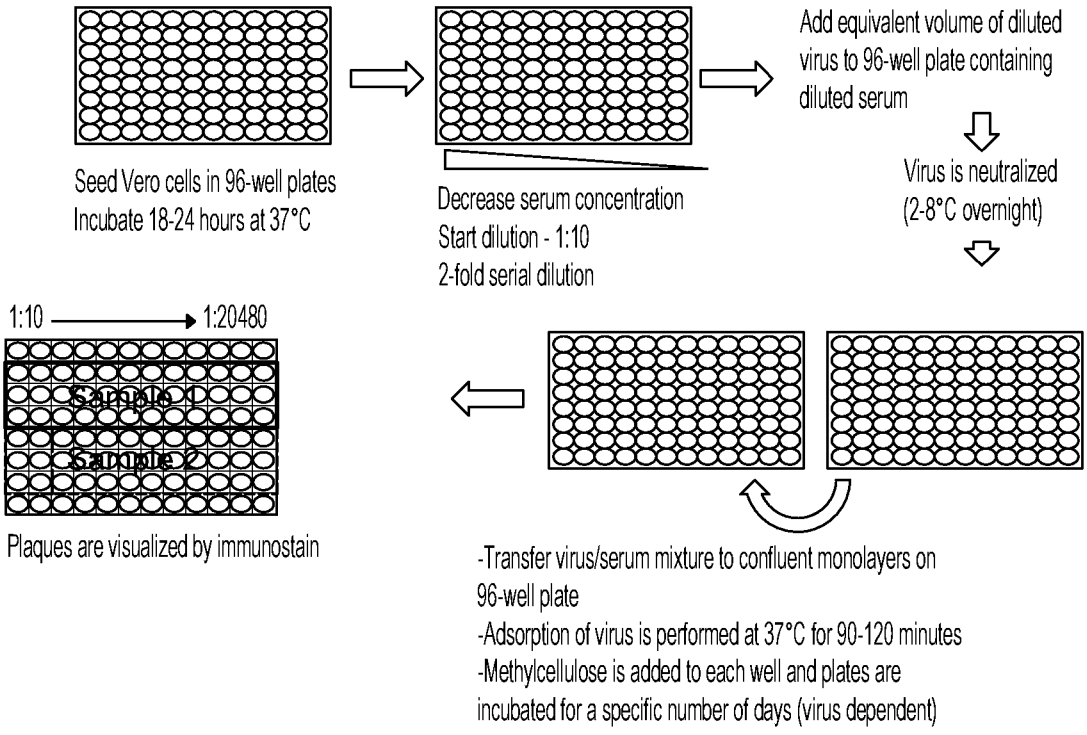

Seed Vero cells in 96-well plates
Incubate 18-24 hours at 37°C
Decrease serum concentration
Start dilution - 1:10
2-fold serial dilution
Add equivalent volume of diluted virus to 96-well plate containing diluted serum
Virus is neutralized (2-8°C overnight)
-Transfer virus/serum mixture to confluent monolayers on 96-well plate
-Adsorption of virus is performed at 37°C for 90-120 minutes
-Methylcellulose is added to each well and plates are incubated for a specific number of days (virus dependent)
1:10
1:20480
Sample 1
Sample 2
Plaques are visualized by immunostain

Figure 2

Figure 3 A

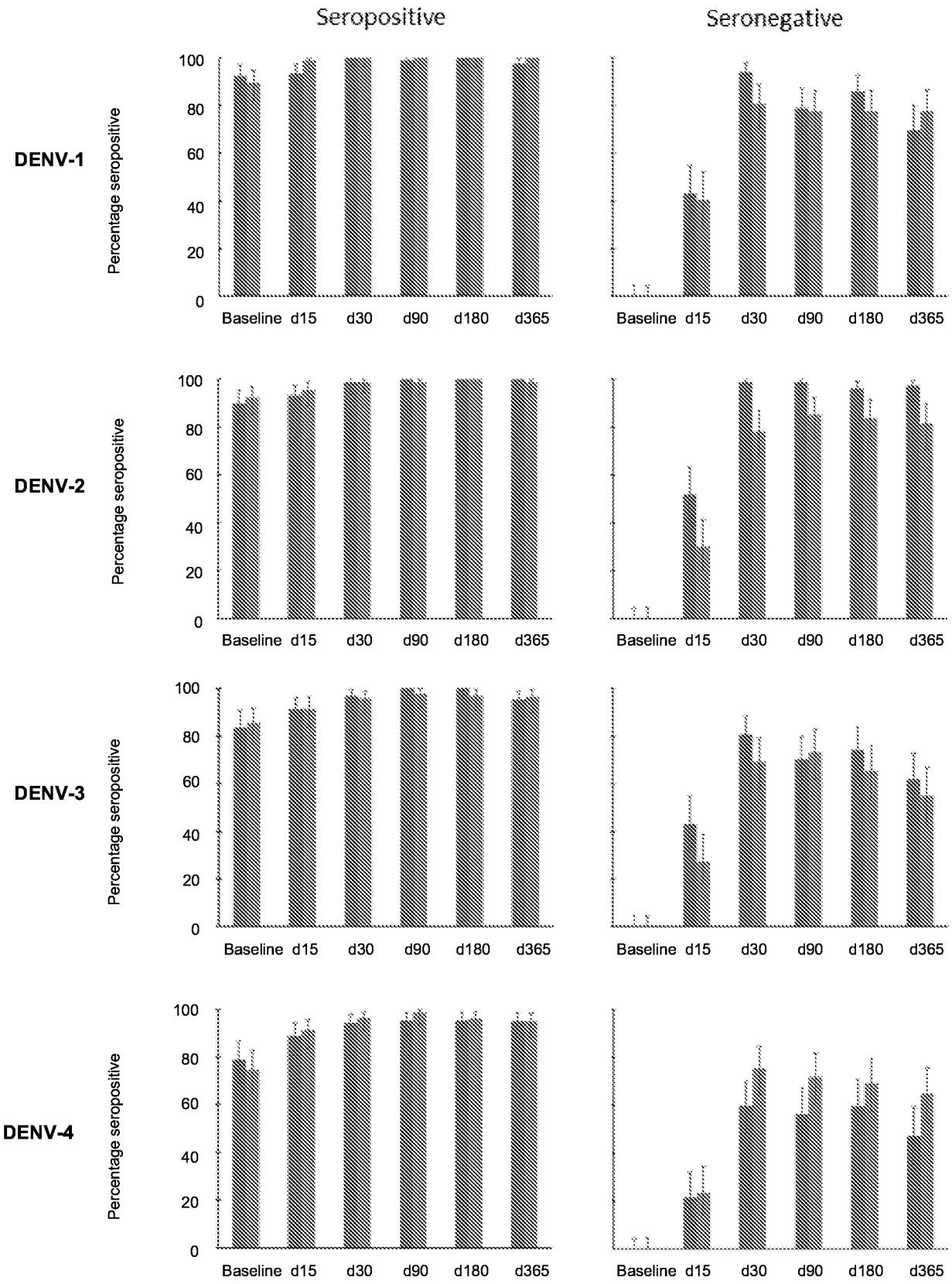

Seropositive
Seronegative
DENV-1
DENV-2
DENV-3
DENV-4
Percentage seropositive
100
80
60
40
20
0
Baseline
d15
d30
d90
d180
d365

Figure 3 B

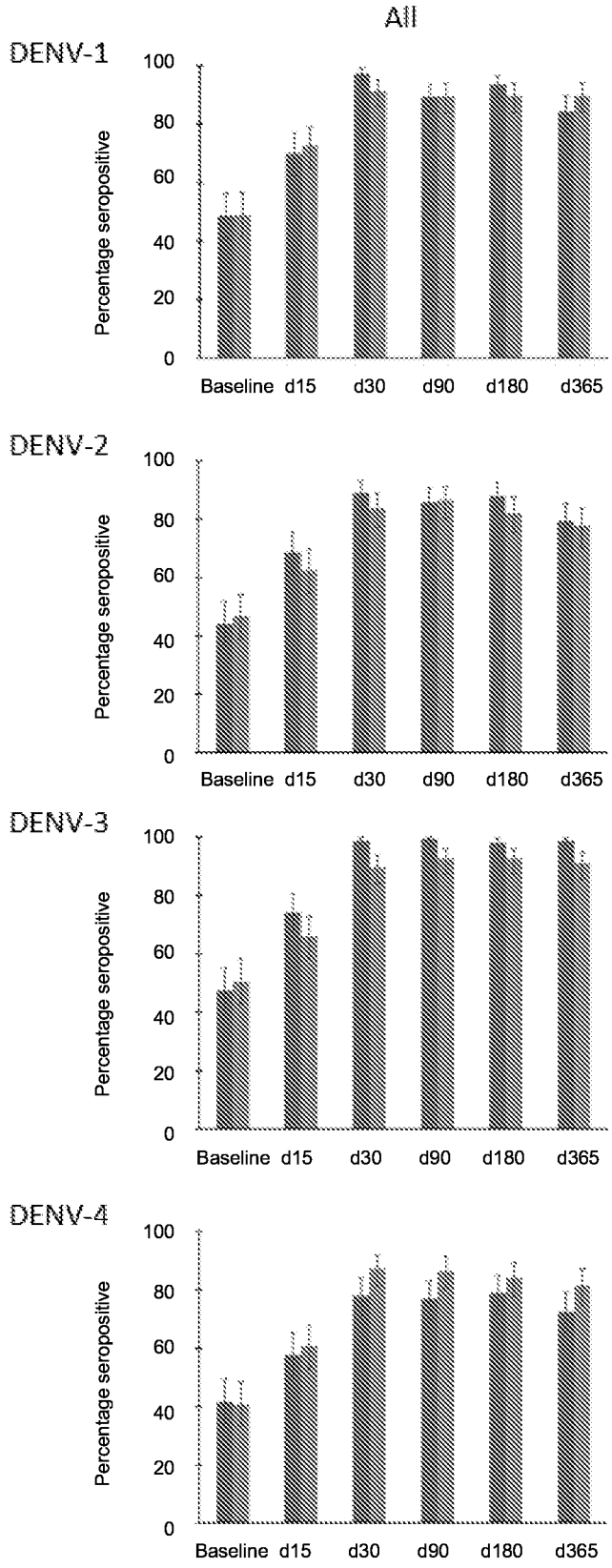

All
DENV-1
DENV-2
DENV-3
DENV-4
Percentage seropositive
100
80
60
40
20
0
Baseline
d15
d30
d90
d180
d365

Figure 4 A

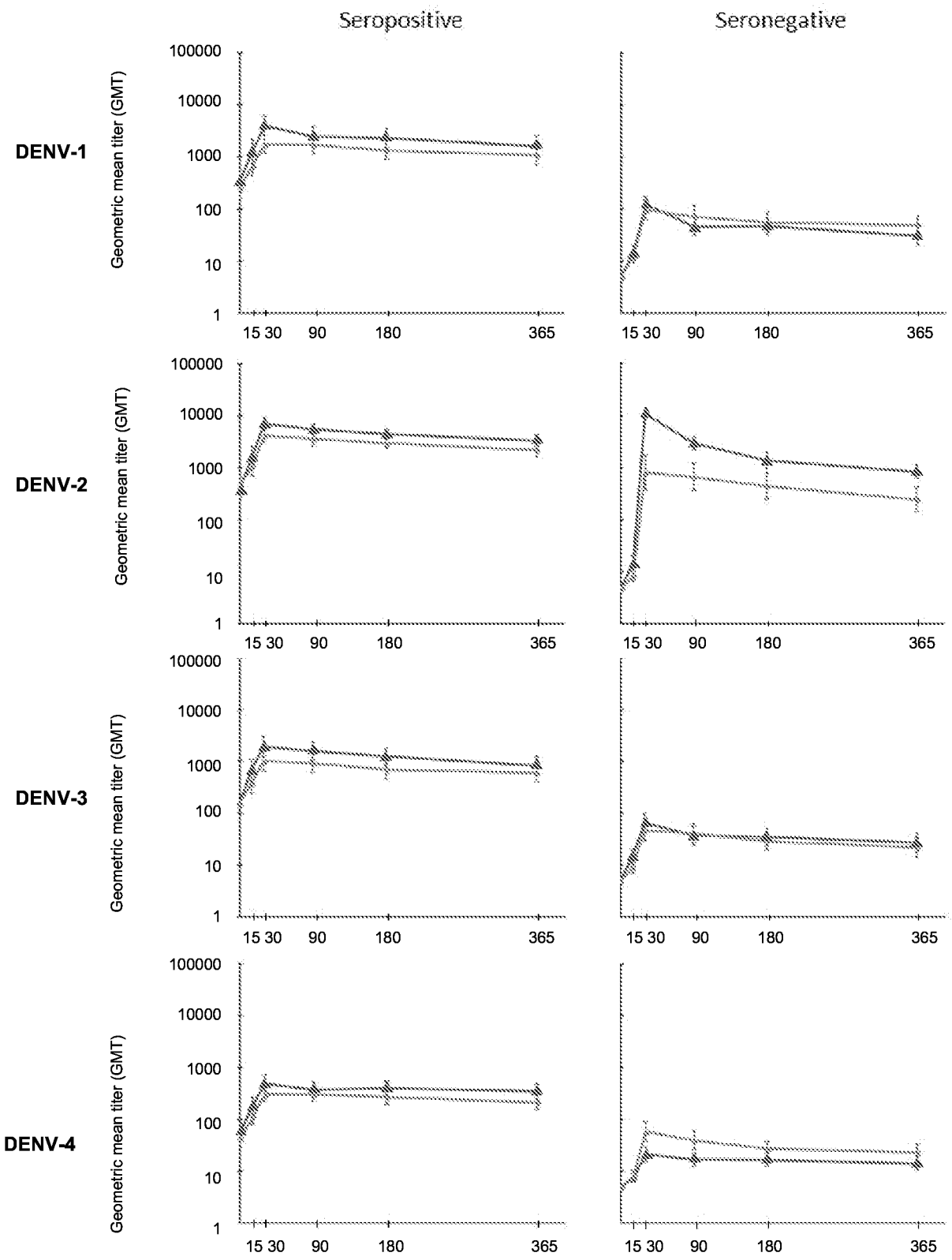

Seropositive
Seronegative
DENV-1
DENV-2
DENV-3
DENV-4
Geometric mean titer (GMT)
100000
10000
1000
100
10
1
15 30
90
180
365

Figure 4 B

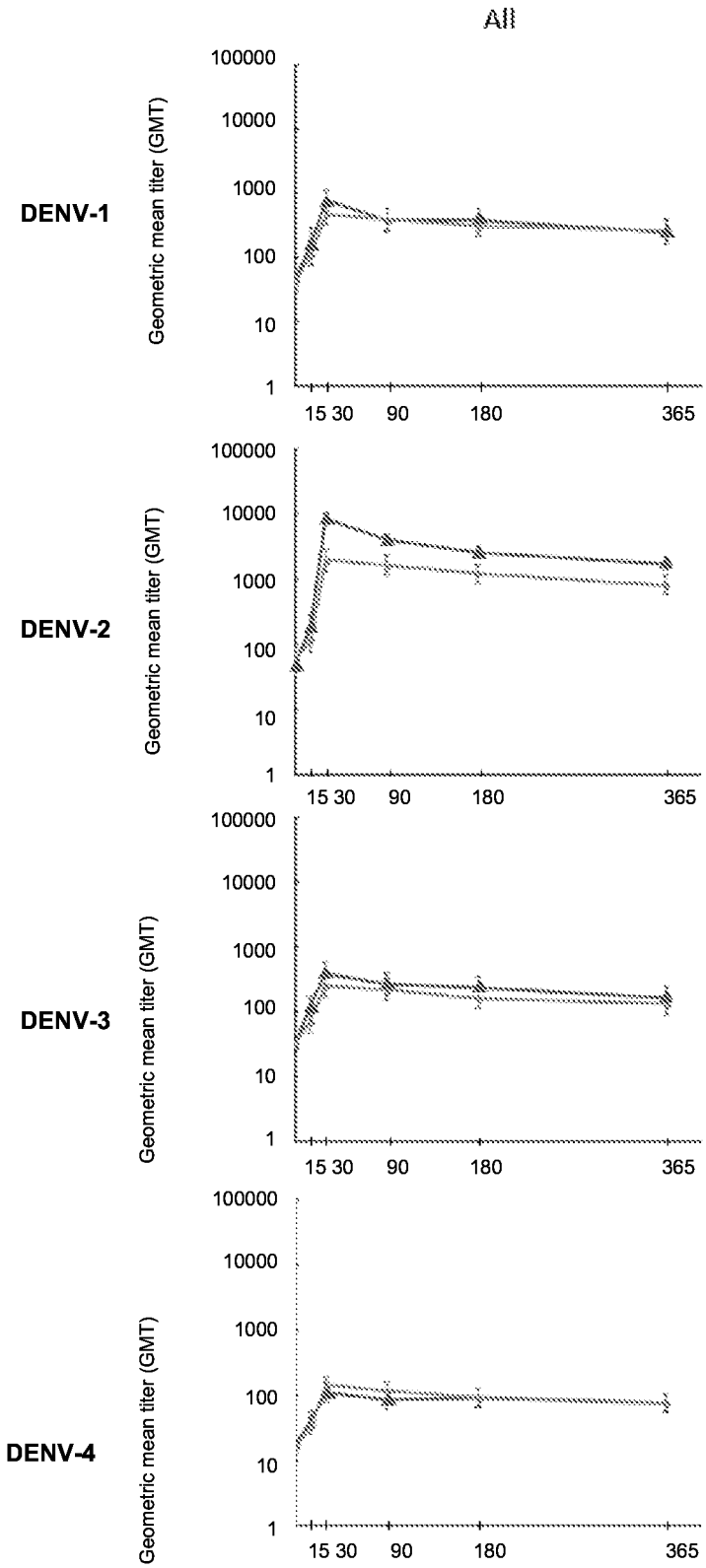

All
DENV-1
DENV-2
DENV-3
DENV-4
Geometric mean titer (GMT)
100000
10000
1000
100
10
1
15 30
90
180
365

Figure 5

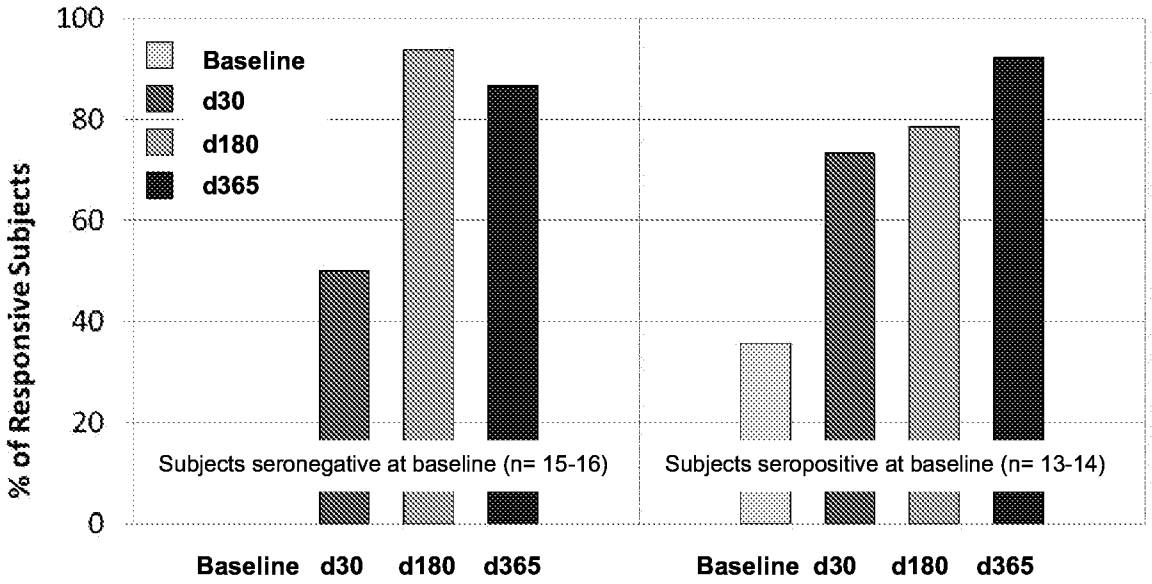

100
80
60
40
20
0
% of Responsive Subjects
Baseline
d30
d180
d365
Subjects seronegative at baseline (n= 15-16)
Subjects seropositive at baseline (n= 13-14)
Baseline d30 d180 d365
Baseline d30 d180 d365

Figure 6

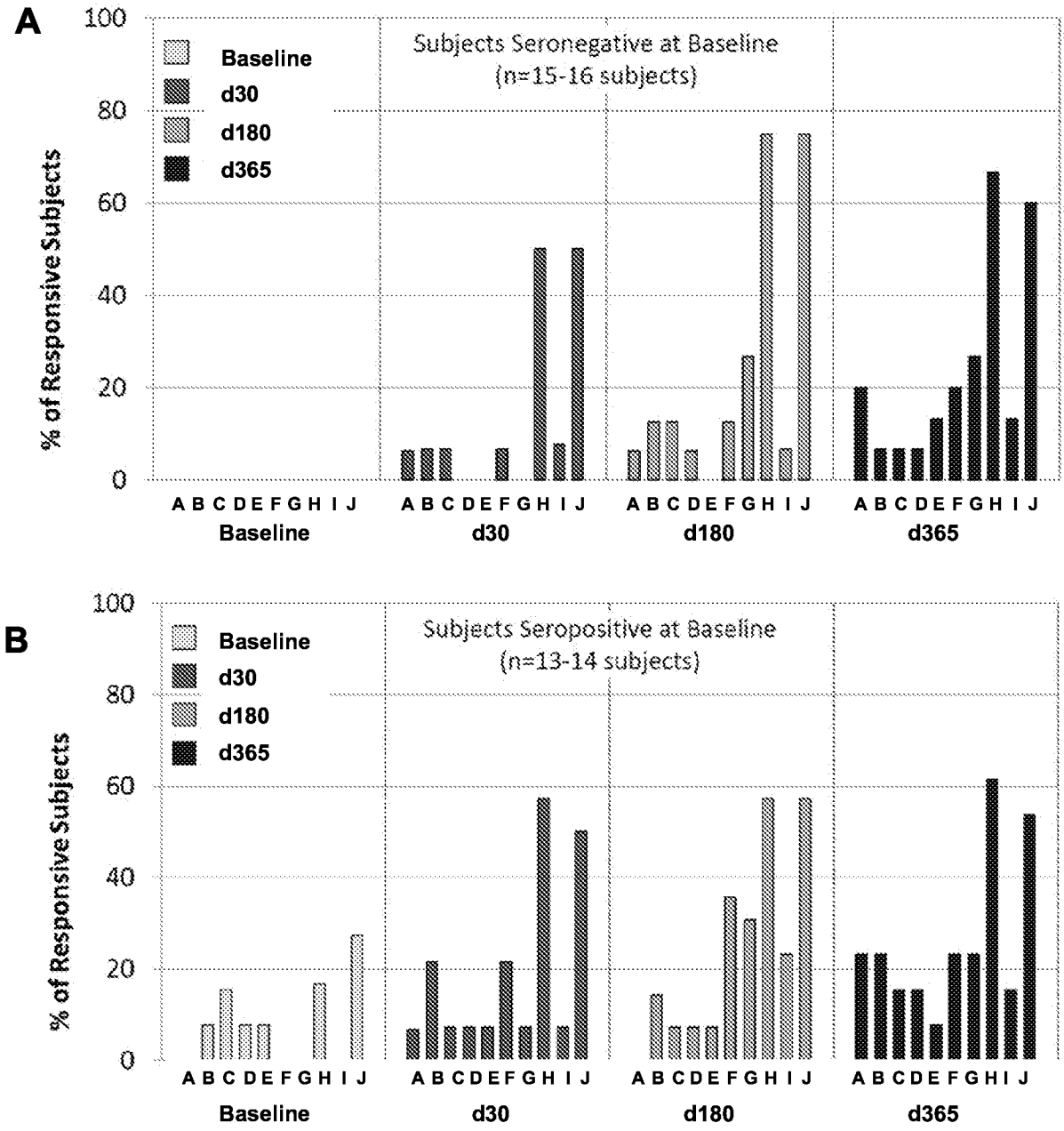

A
100
80
60
40
20
0
% of Responsive Subjects
Baseline
d30
d180
d365
Subjects Seronegative at Baseline
(n=15-16 subjects)
A B C D E F G H I J
Baseline
d30
d180
d365
B
Subjects Seropositive at Baseline
(n=13-14 subjects)

Figure 7

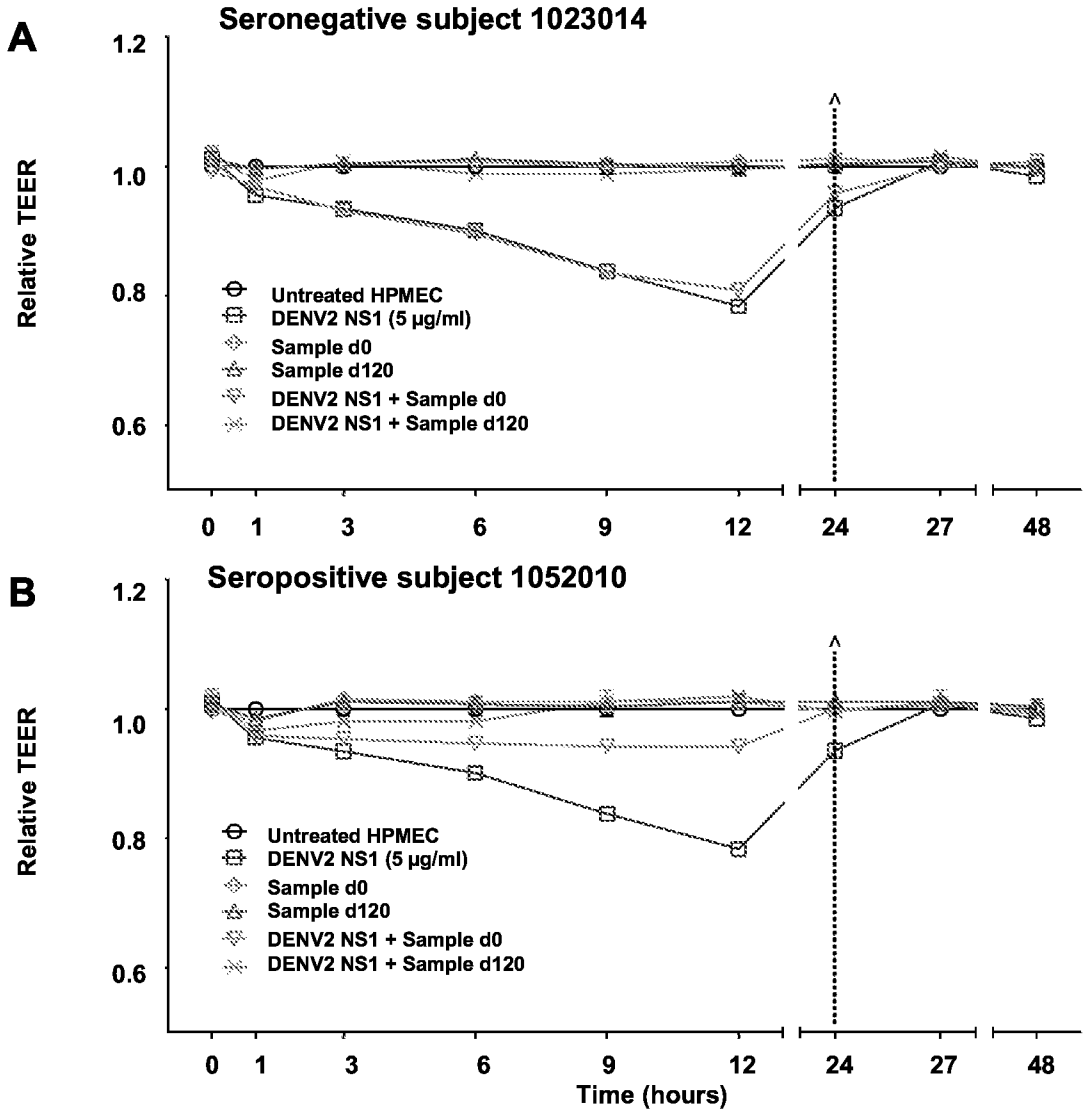
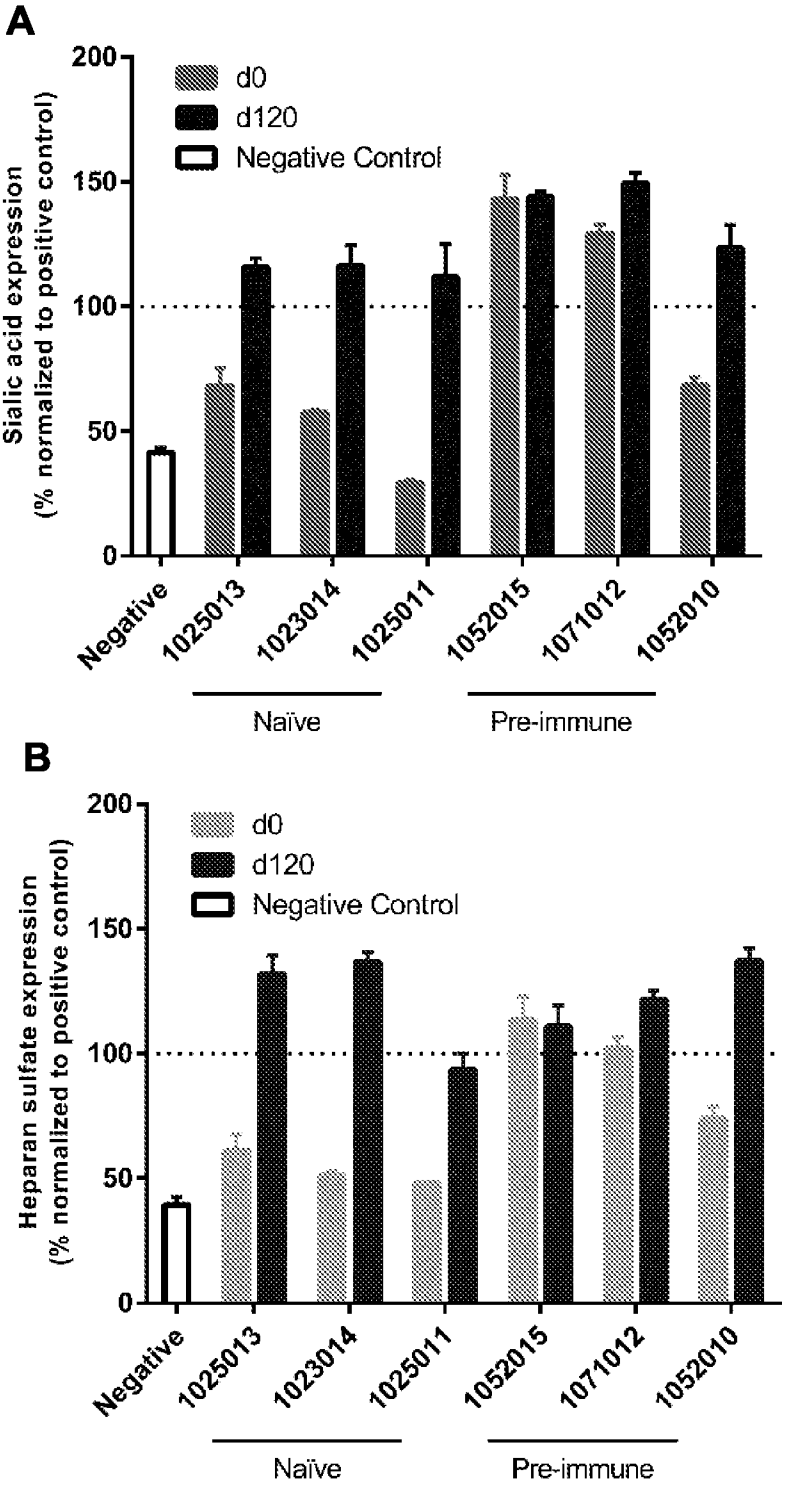

A
Seronegative subject 1023014
Relative TEER
1.2
1.0
0.8
0.6
Untreated HPMEC
DENV2 NS1 (5 µg/ml)
Sample d0
Sample d120
DENV2 NS1 + Sample d0
DENV2 NS1 + Sample d120
0 1 3 6 9 12 24 27 48
B
Seropositive subject 1052010
Relative TEER
1.2
1.0
0.8
0.6
Untreated HPMEC
DENV2 NS1 (5 µg/ml)
Sample d0
Sample d120
DENV2 NS1 + Sample d0
DENV2 NS1 + Sample d120
0 1 3 6 9 12 24 27 48
Time (hours)

Figure 8


A
Sialic acid expression
(% normalized to positive control)
200
150
100
50
0
d0
d120
Negative Control
Negative
1025013
1023014
1025011
1052015
1071012
1052010
Naïve
Pre-immune
B
Heparan sulfate expression
(% normalized to positive control)
200
150
100
50
0
d0
d120
Negative Control
Negative
1025013
1023014
1025011
1052015
1071012
1052010
Naïve
Pre-immune

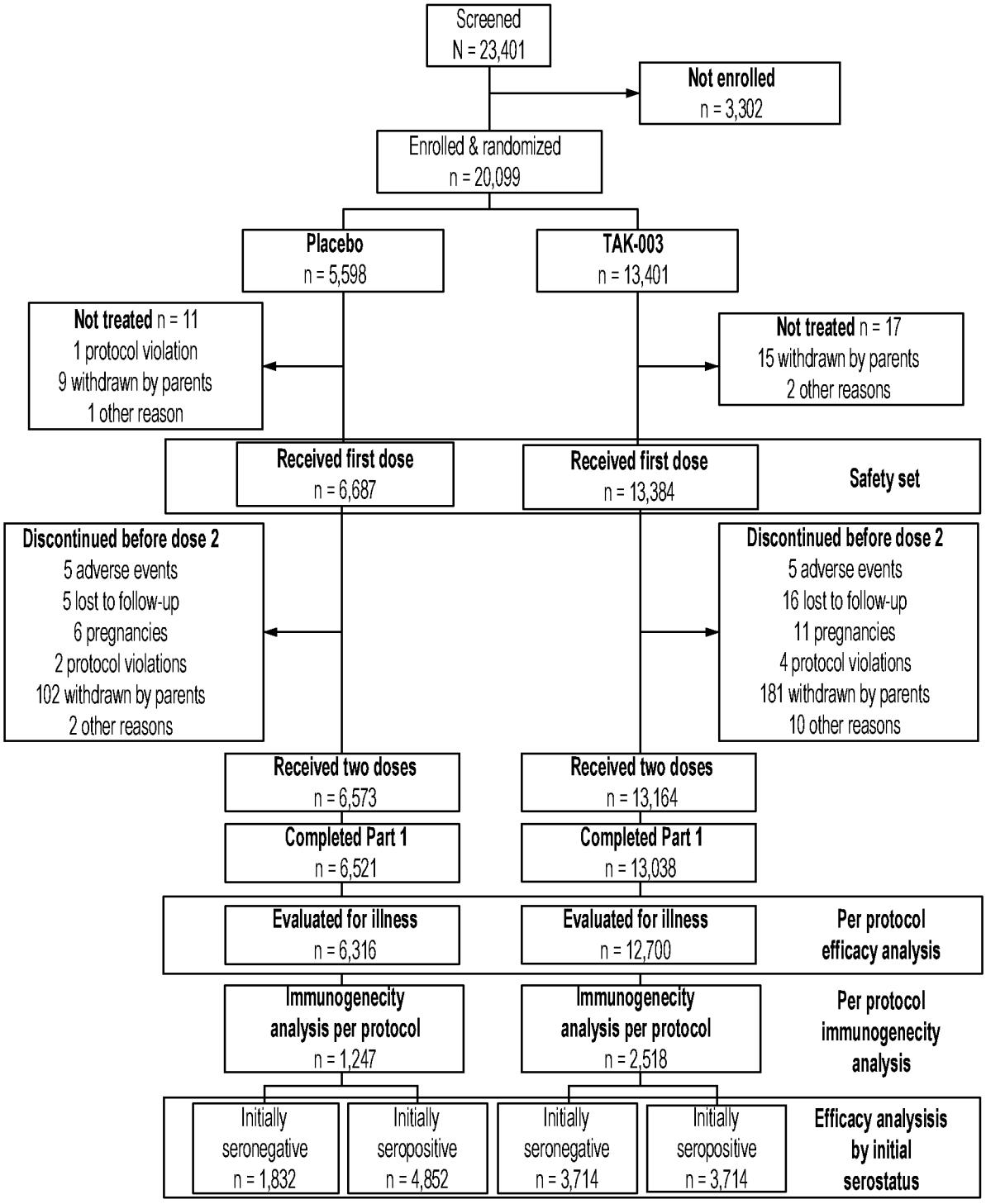
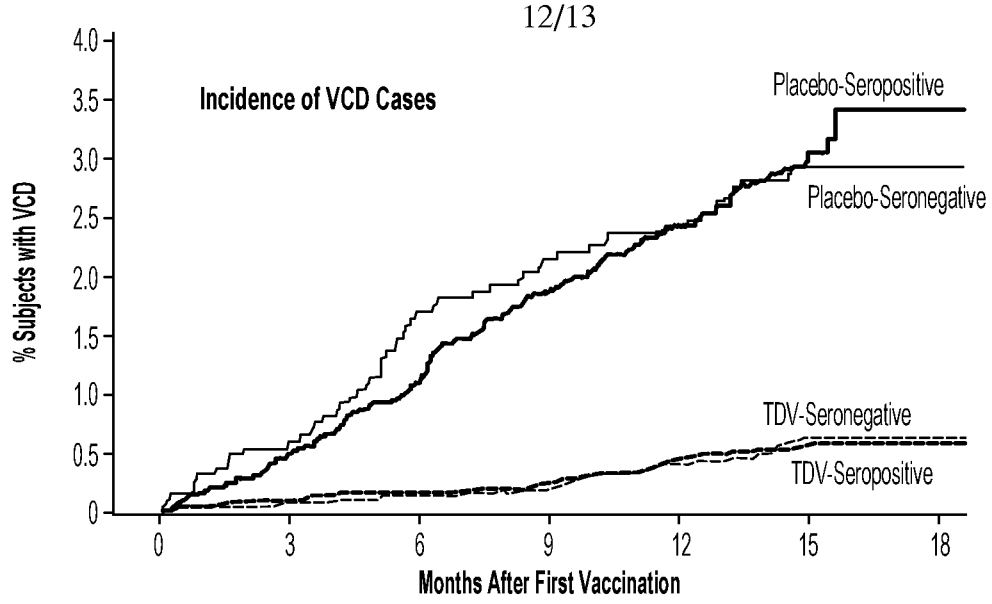
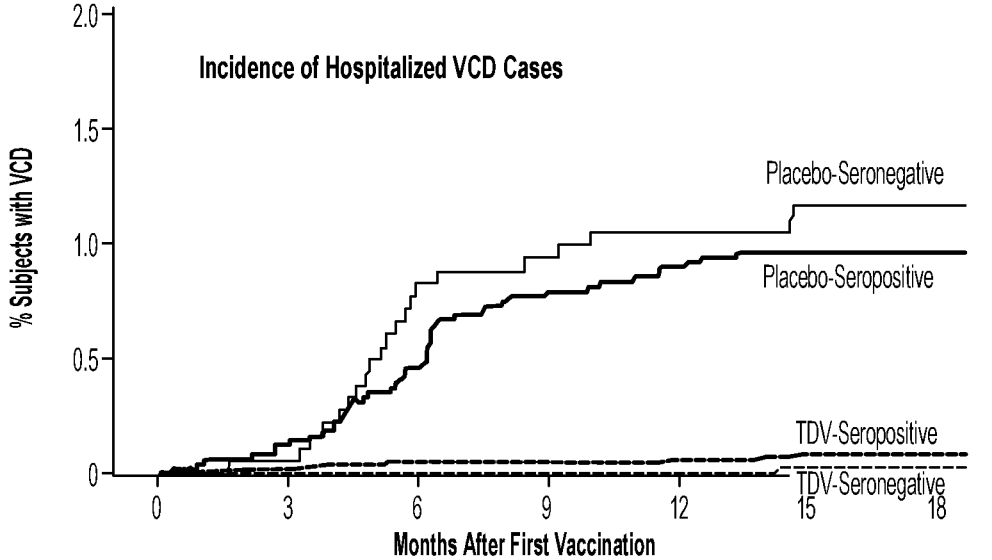

Screened
N = 23,401
Not enrolled
n = 3,302
Enrolled & randomized
n = 20,099
Placebo
n = 5,598
TAK-003
n = 13,401
Not treated n = 11
1 protocol violation
9 withdrawn by parents
1 other reason
Not treated n = 17
15 withdrawn by parents
2 other reasons
Received first dose
n = 6,687
Received first dose
n = 13,384
Safety set
Discontinued before dose 2
5 adverse events
5 lost to follow-up
6 pregnancies
2 protocol violations
102 withdrawn by parents
2 other reasons
Discontinued before dose 2
5 adverse events
16 lost to follow-up
11 pregnancies
4 protocol violations
181 withdrawn by parents
10 other reasons
Received two doses
n = 6,573
Received two doses
n = 13,164
Completed Part 1
n = 6,521
Completed Part 1
n = 13,038
Evaluated for illness
n = 6,316
Evaluated for illness
n = 12,700
Per protocol
efficacy analysis
Immunogenecity
analysis per protocol
n = 1,247
Immunogenecity
analysis per protocol
n = 2,518
Per protocol
immunogenecity
analysis
Initially
seronegative
n = 1,832
Initially
seropositive
n = 4,852
Initially
seronegative
n = 3,714
Initially
seropositive
n = 3,714
Efficacy analysisis
by initial
serostatus

Figure 9



	Month 0	Month 3.0	Month 14.5	Month 14.5	Month 18.0
Placebo-Seronegative	n = 1,832	n = 1,817	n = 1,744	n = 94	n = 7
Placebo-Seropositive	n = 4,852	n = 4,805	n = 4,607	n = 218	n = 6
TDV -Seronegative	n = 3,714	n = 3,690	n = 4,615	n = 157	n = 10
TDV -Seropositive	n = 9,661	n = 9,591	n = 9,391	n = 417	n = 10

Figure 10A



	Month 0	Month 3.0	Month 14.5	Month 15.9	Month 18.0
Placebo-Seronegative	n = 1,832	n = 1,827	n = 1,776	n = 94	n = 7
Placebo-Seropositive	n = 4,852	n = 4,823	n = 4,700	n = 220	n = 6
TDV -Seronegative	n = 3,714	n = 3,693	n = 3,635	n = 157	n = 6
TDV -Seropositive	n = 9,661	n = 9,599	n = 9,435	n = 417	n = 10

Figure 10B

Study Design

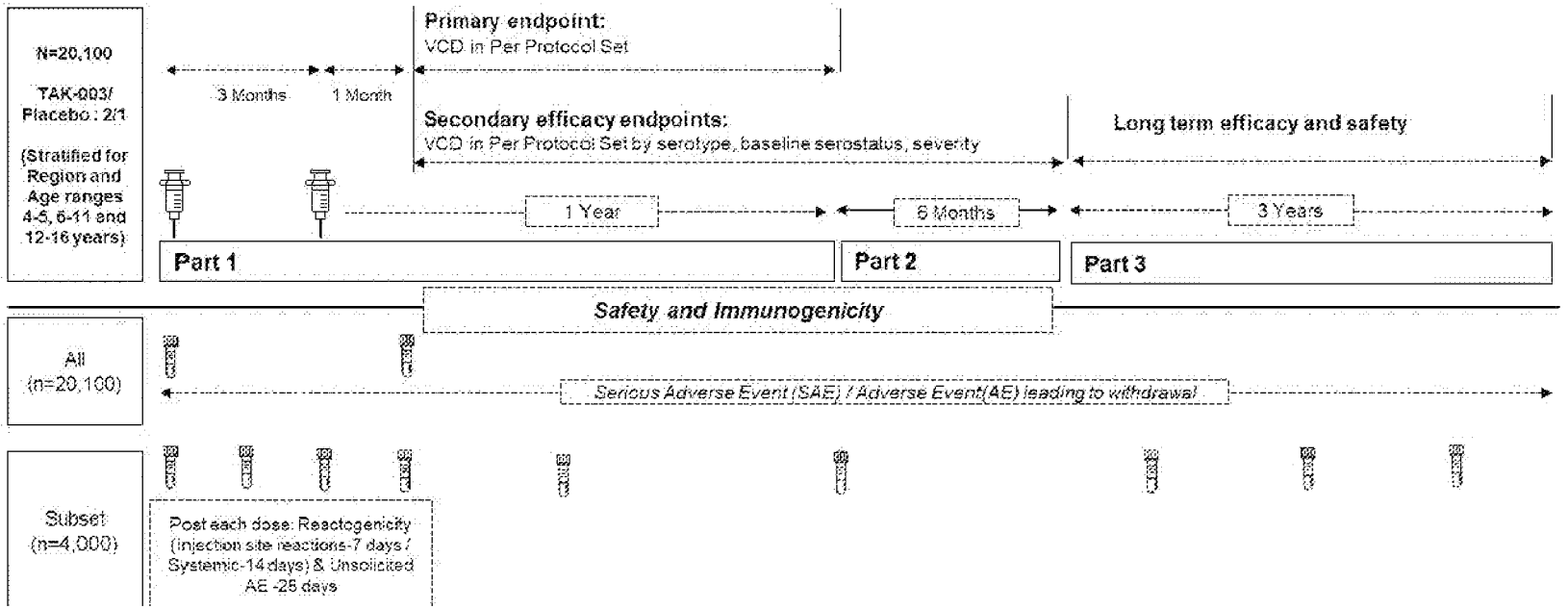


Figure 11