Group	N	Administration of test or control article				EBOLA Challenge (Day)
		Prime	Boost(s)	Dose	Schedule (Day)	
A	2	Neg Control (Ad26.empty)	Neg Control (MVA.empty)	$1.2x10^{11}$vp/ 5×10^{8} TCID50	0, 56	Day 84 Ebola Kikwit i.m. 100 pfu (approx 4 weeks after last immunization)
B	2	Ad26.ZEBOV	Ad35.ZEBOV	$1.2x10^{11}$vp	28, 56	
C	2	Ad26.MARVA Ad26.SEBOV Ad26.ZEBOV	MVA-Multi	$4x10^{10}$vp (each)/ 5×10^{8} TCID50	0, 56	
D	2	MVA-Multi	Ad26.MARVA Ad26.SEBOV Ad26.ZEBOV	5×10^{8} TCID50/ $4x10^{10}$vp(each)	0, 56	
E	2	Ad26.MARVA Ad26.SEBOV Ad26.ZEBOV	MVA-Multi	$4x10^{10}$vp (each)/ 5×10^{8} TCID50	0, 28, 56	

Figure 1

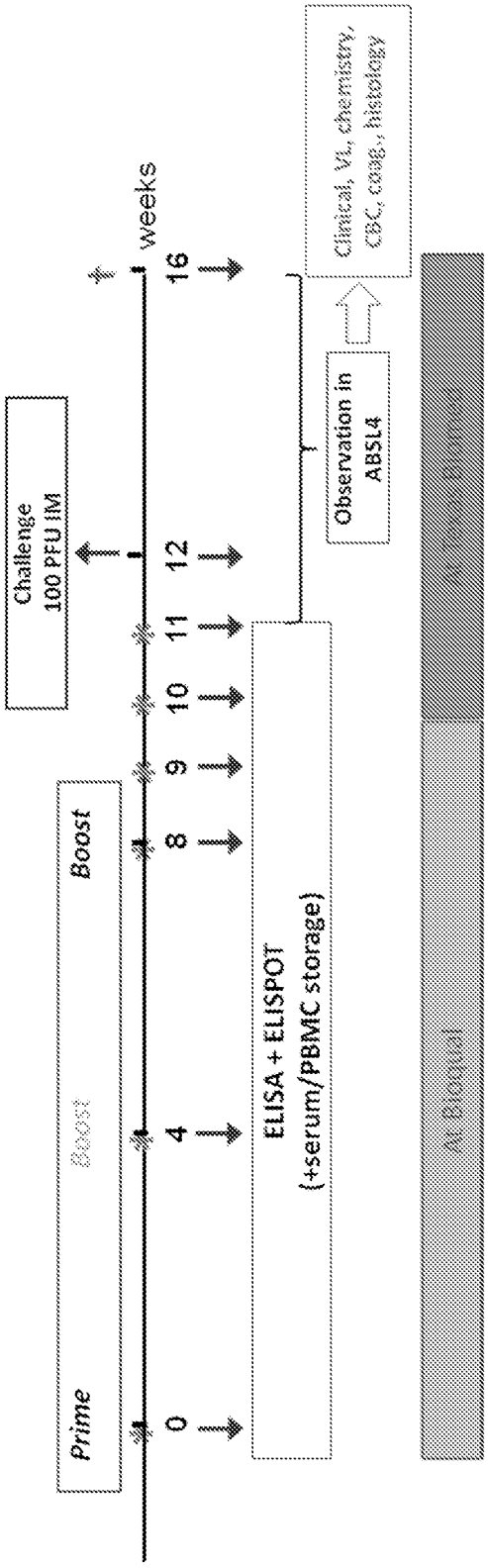

weeks
0
4
8
9
10
11
12
16
Prime
Boost
Boost
Challenge
100 PFU IM
ELISA + ELISPOT
(+serum/PBMC storage)
Observation in
ABSL4
Clinical, VL, chemistry,
CBC, cage., histology
At Biocad

Figure 2

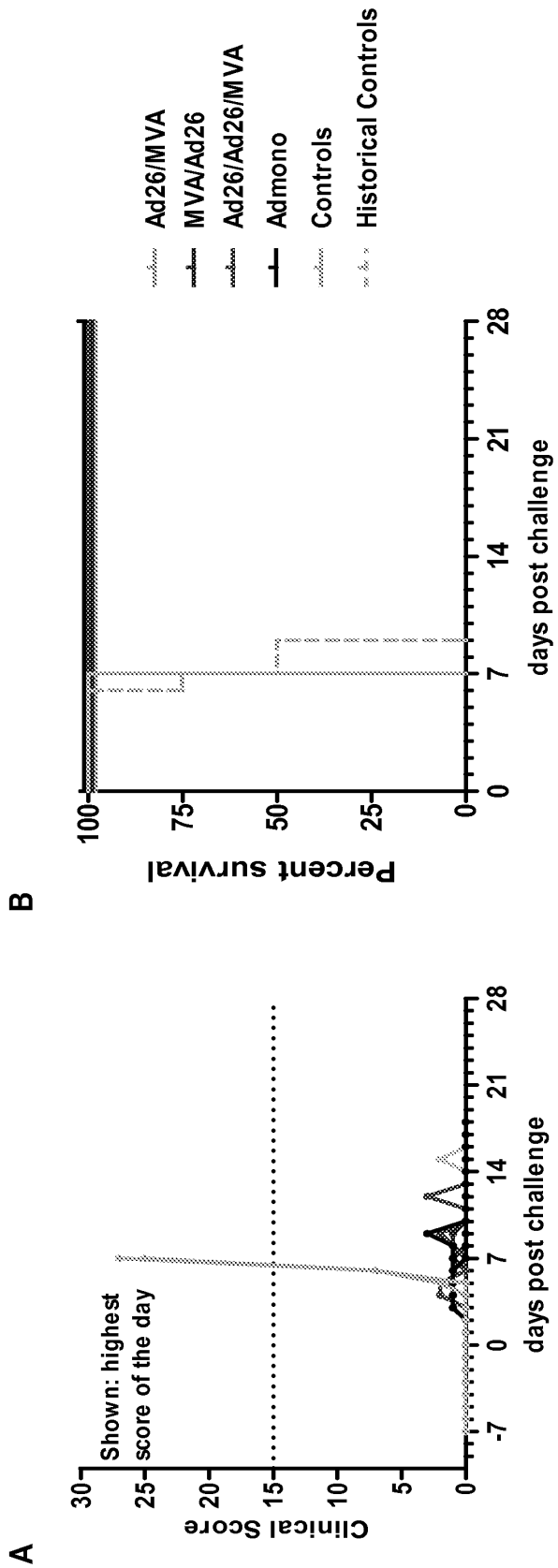

A
Clinical Score
30
25
20
15
10
5
0
Shown: highest score of the day
-7
0
7
14
21
28
days post challenge
B
Percent survival
100
75
50
25
0
0
7
14
21
28
days post challenge
Ad26/MVA
MVA/Ad26
Ad26/Ad26/MVA
Admono
Controls
Historical Controls

Figure 3

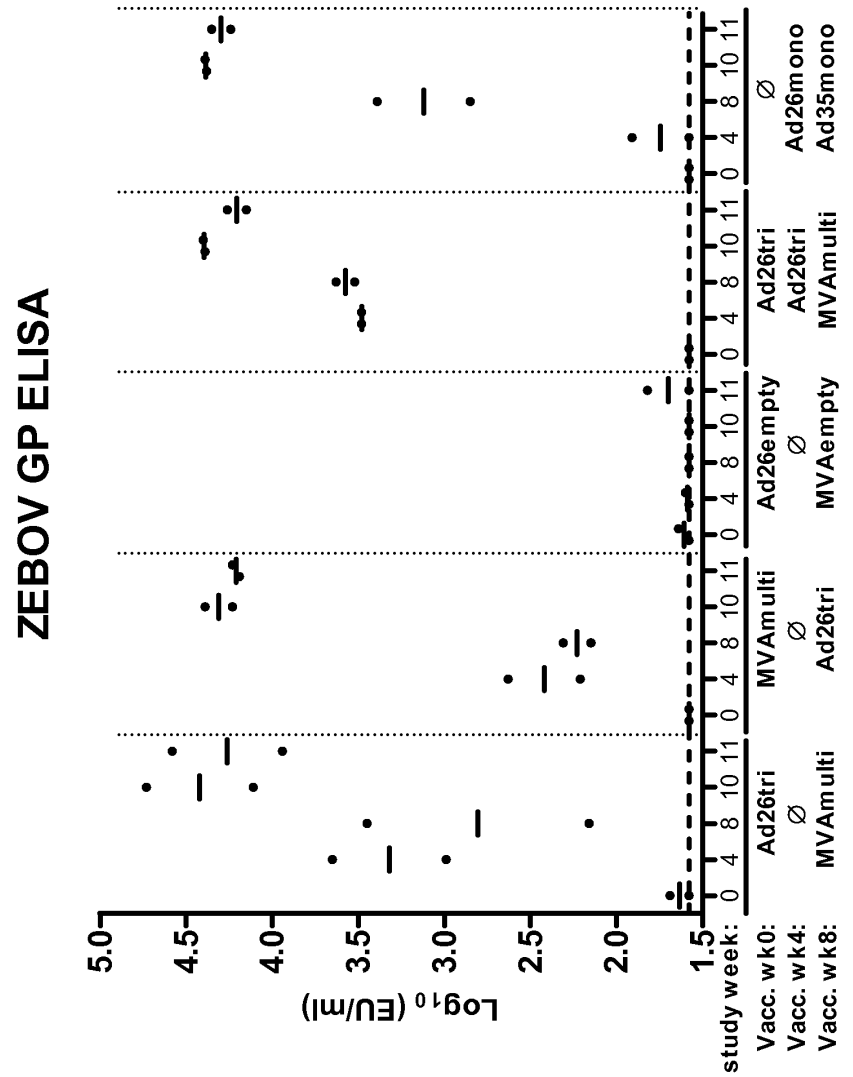

ZEBOV GP ELISA
Log10 (EU/ml)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
study week: 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11
Vacc. wk0: Ad26tri MVAmulti Ad26empty Ad26tri Ø
Vacc. wk4: Ø Ad26tri MVAempty Ad26tri Ad26mono
Vacc. wk8: MVAmulti Ø Ø MVAmulti Ad35mono

Figure 4

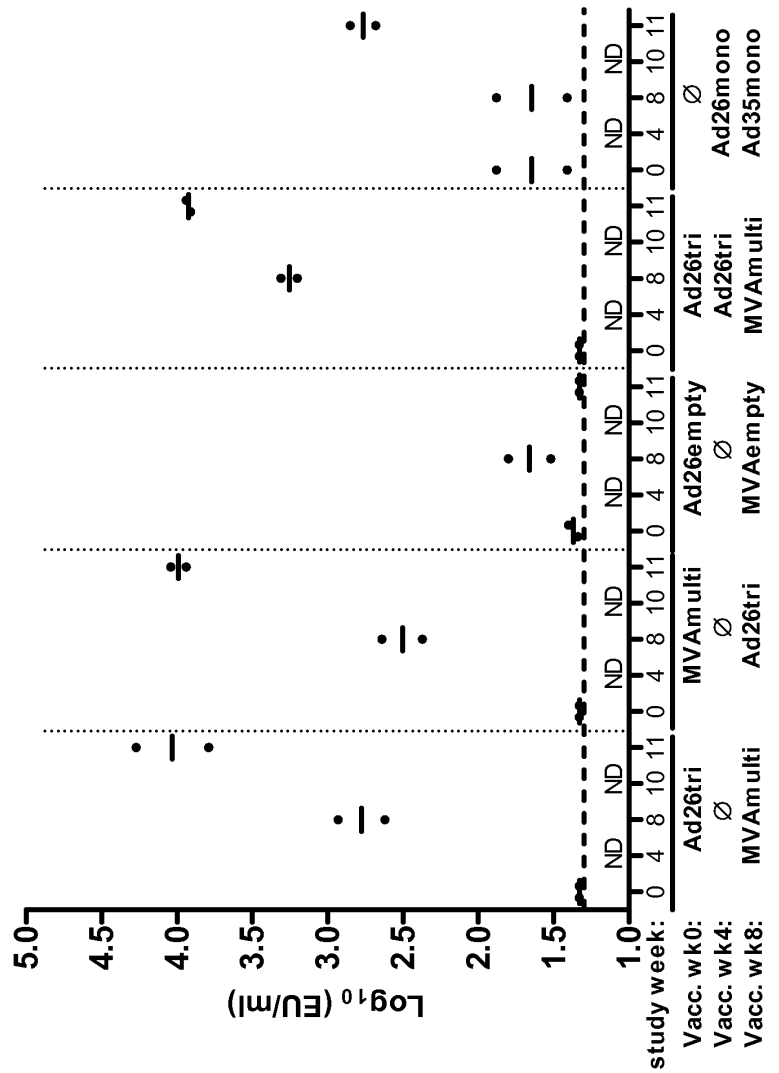

SEBOV GP ELISA
Log10 (EU/ml)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
study week: 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11
ND ND ND ND ND ND
Vacc. wk0: Ad26tri MVAmulti Ad26empty Ad26tri Ø
Vacc. wk4: Ø Ø Ø Ad26tri Ad26mono
Vacc. wk8: MVAmulti Ad26tri MVAempty MVAmulti Ad35mono

Figure 5

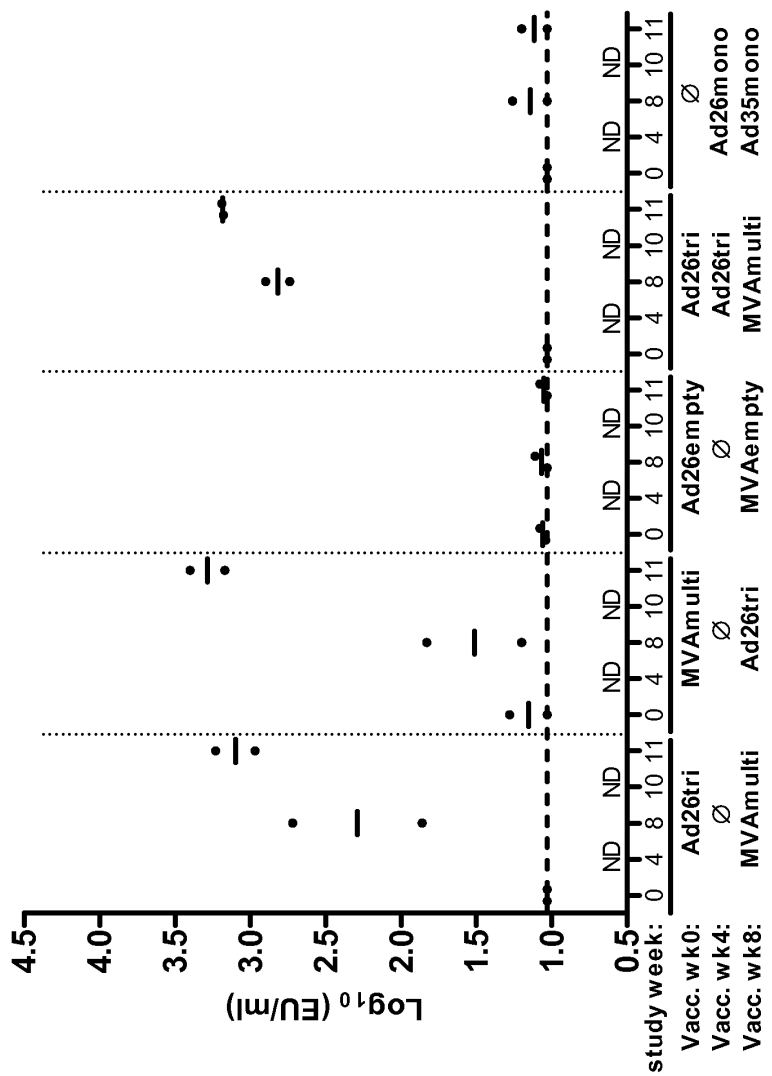

MARVA GP ELISA
Log10 (EU/ml)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
study week: 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11
ND ND ND ND ND ND
Vacc. wk0: Ad26tri MVAmulti Ad26empty Ad26tri Ø
Vacc. wk4: Ø Ø Ø Ad26tri Ad26mono
Vacc. wk8: MVAmulti Ad26tri MVAempty MVAmulti Ad35mono

Figure 6

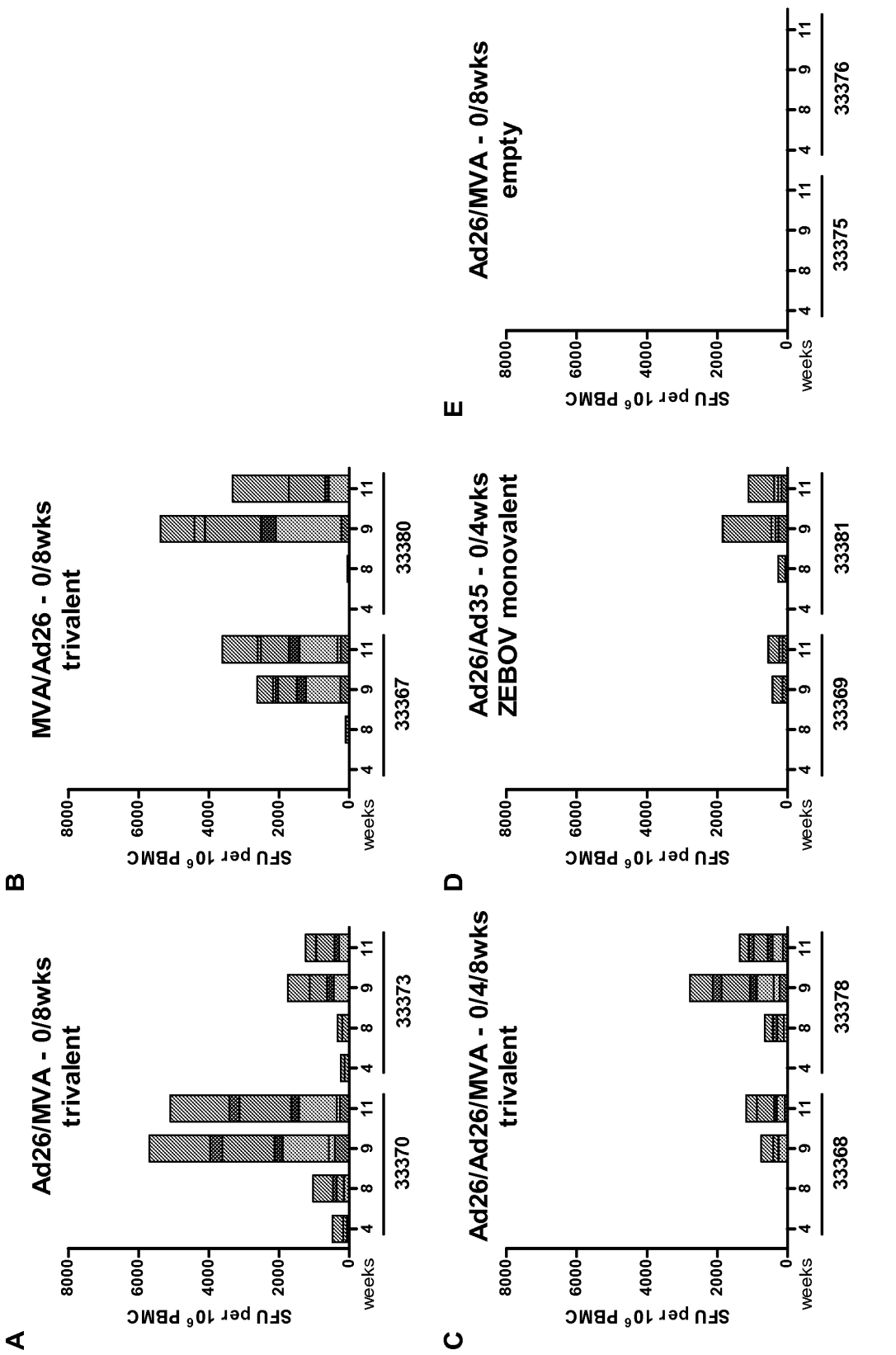

A
Ad26/MVA - 0/8wks
trivalent
B
MVA/Ad26 - 0/8wks
trivalent
C
Ad26/Ad26/MVA - 0/4/8wks
trivalent
D
Ad26/Ad35 - 0/4wks
ZEBOV monovalent
E
Ad26/MVA - 0/8wks
empty
SFU per 10^6 PBMC
weeks
33370
33373
33367
33380
33368
33378
33369
33381
33375
33376

Figure 7

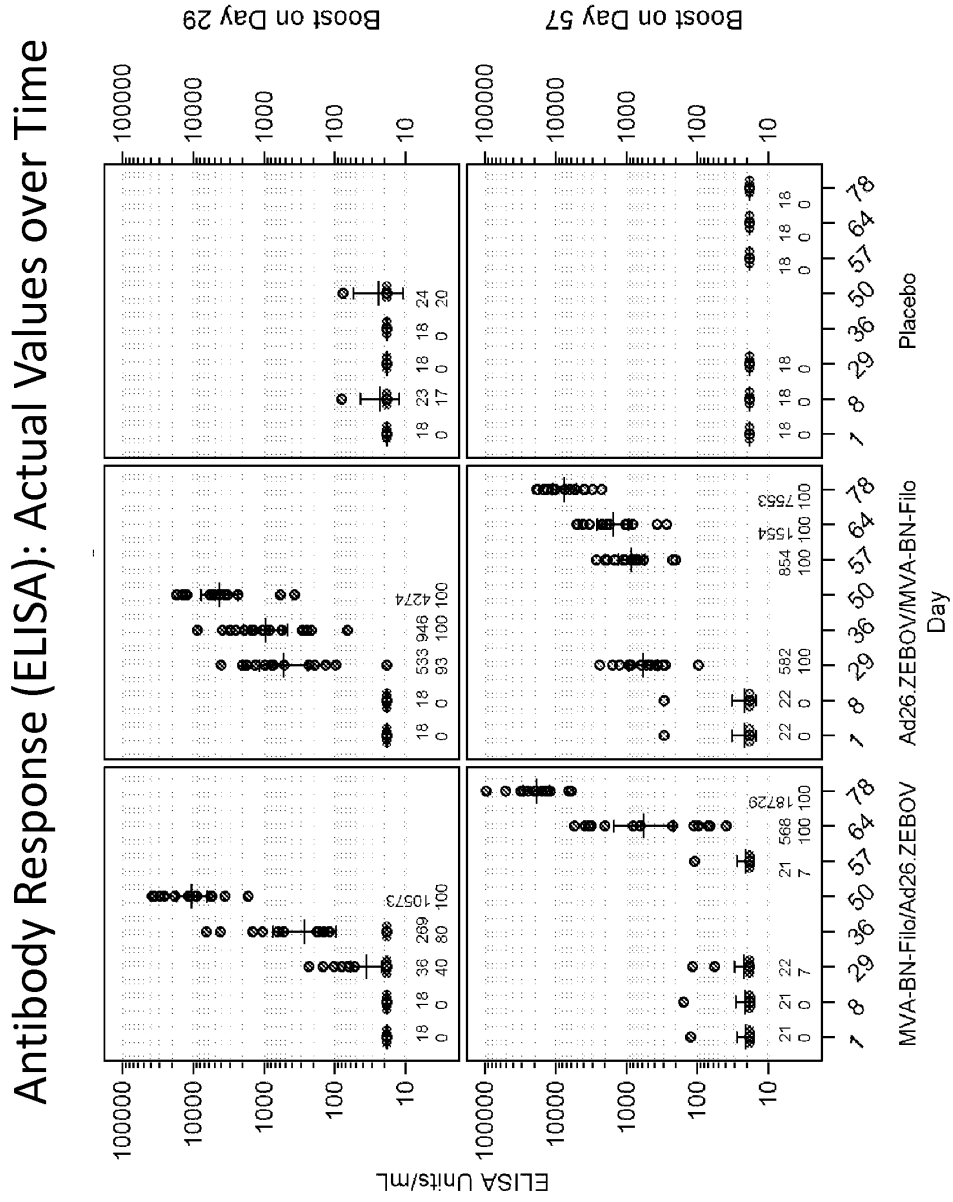

Antibody Response (ELISA): Actual Values over Time
Boost on Day 29
Boost on Day 57
ELISA Units/mL
100000
10000
1000
100
10
MVA-BN-Filo/Ad26.ZEBOV
Ad26.ZEBOV/MVA-BN-Filo
Placebo
Day

Figure 8

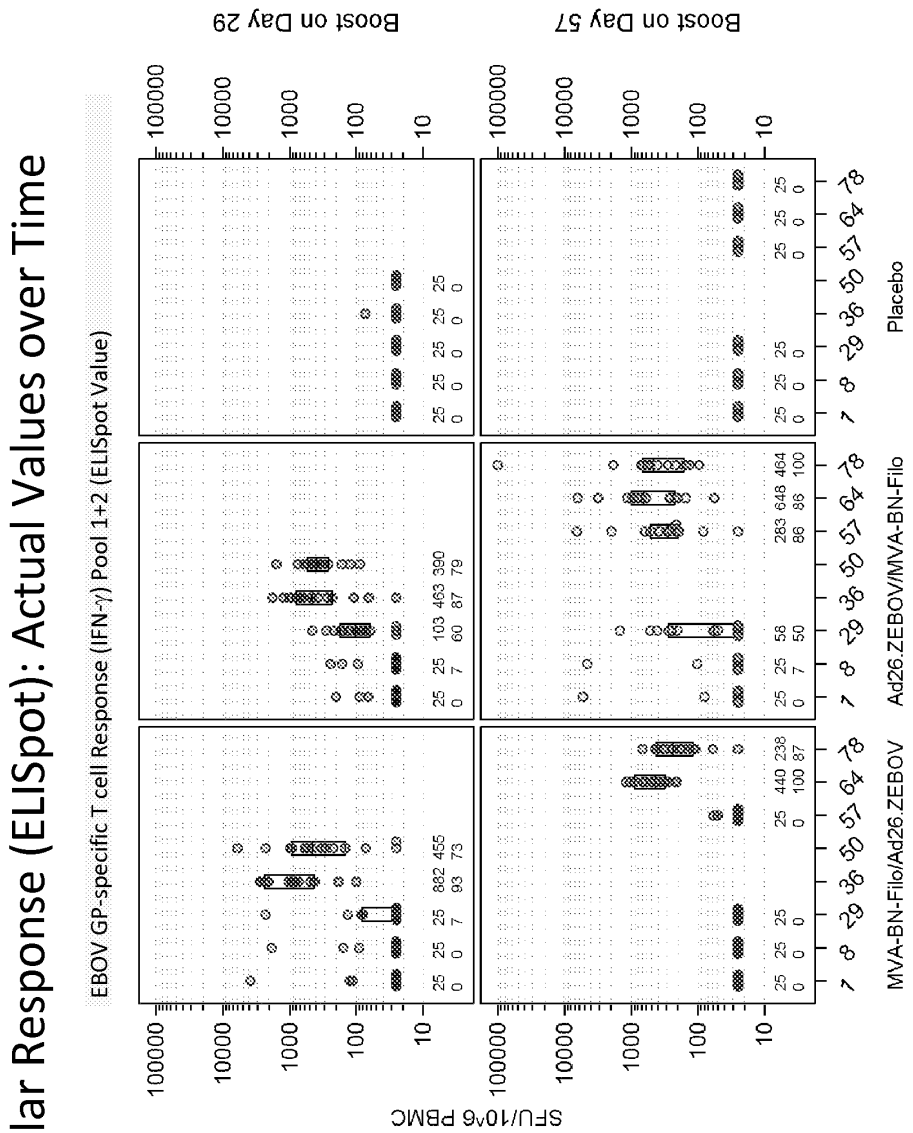

Cellular Response (ELISpot): Actual Values over Time
EBOV GP-specific T cell Response (IFN-γ) Pool 1+2 (ELISpot Value)
Boost on Day 29
Boost on Day 57
SFU/10^6 PBMC
100000
10000
1000
100
10
MVA-BN-Filo/Ad26.ZEBOV
Ad26.ZEBOV/MVA-BN-Filo
Placebo
Day
1 8 29 36 50 57 64 78
25 25 25 25 440 238
0 0 0 0 100 87
25 25 25 25 882 455
0 0 7 93 73
25 25 25 25 58
0 7 50
25 25 25 103 463 390
0 7 60 87 79
25 25 25 283 648 464
0 86 86 100
25 25 25 25 25 25
0 0 0 0 0 0
25 25 25 25 25 25
0 0 0 0 0 0

Figure 9

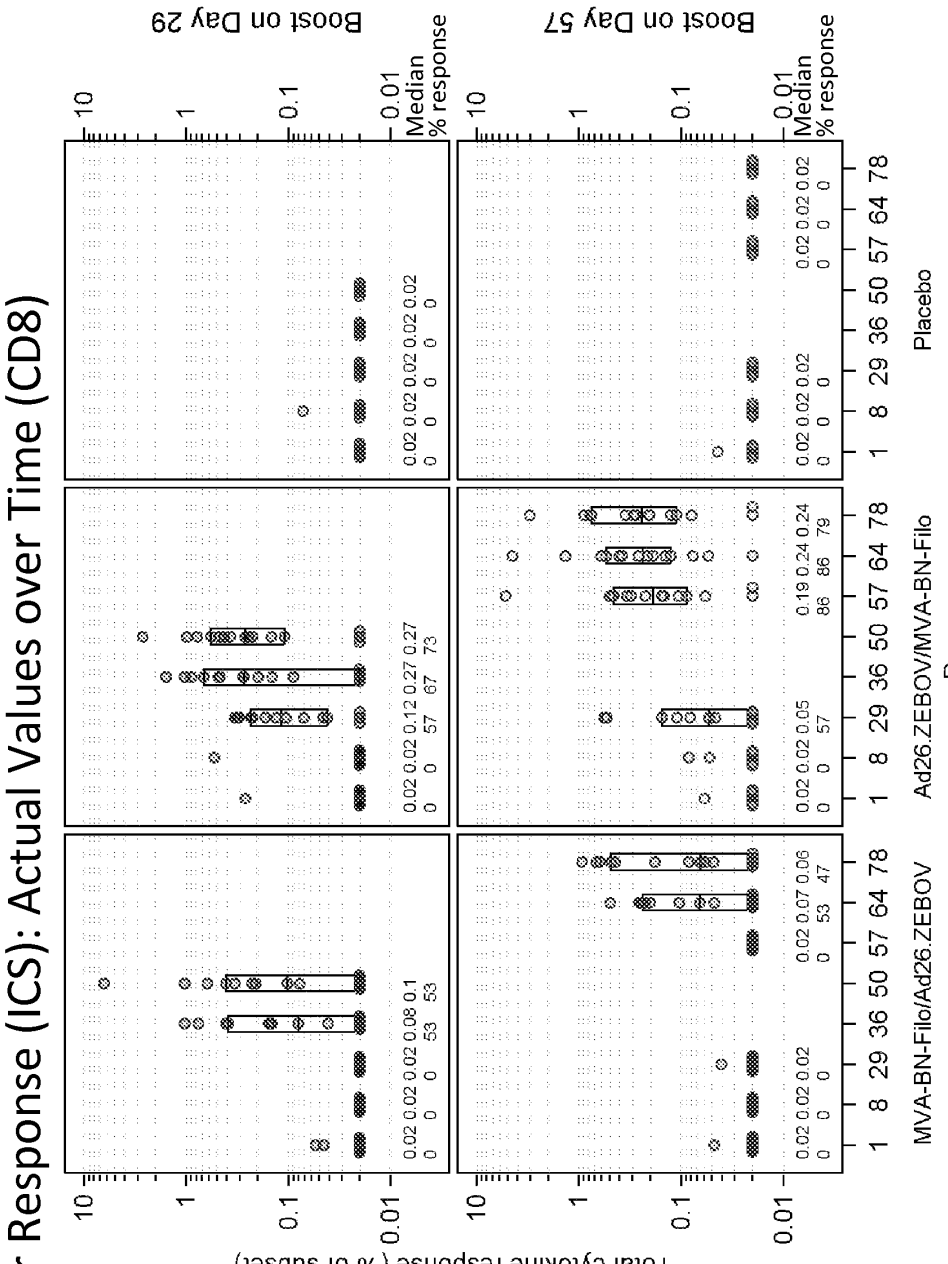

Cellular Response (ICS): Actual Values over Time (CD8)
Boost on Day 29
Boost on Day 57
Median % response
Total cytokine response (% of subset)
MVA-BN-Filo/Ad26.ZEBOV
Ad26.ZEBOV/MVA-BN-Filo
Placebo
Day

Figure 10

Cellular Response (ICS): Functionality of CD8 responses

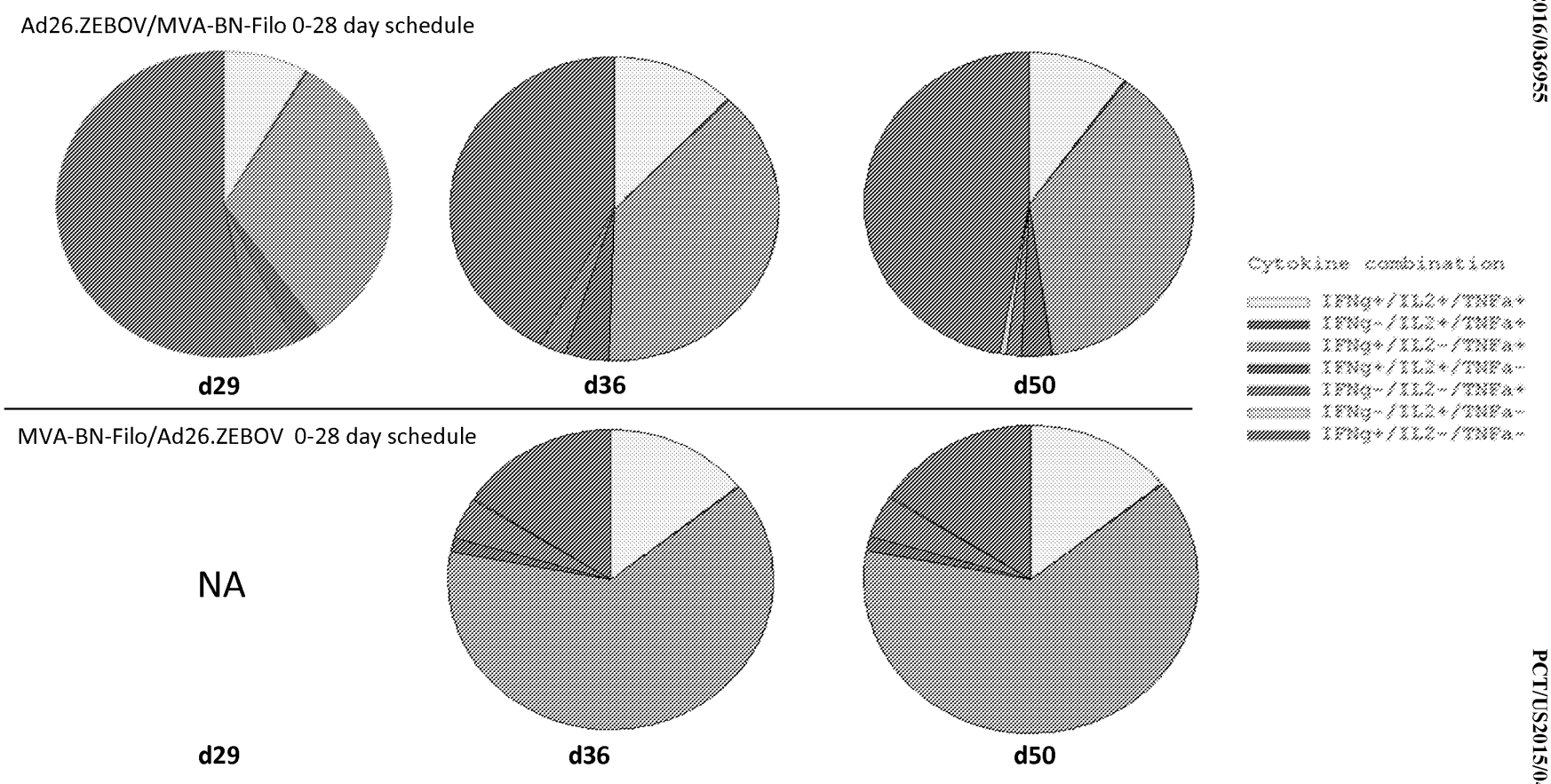


Figure 11

Cellular Response (ICS): Functionality of CD8 responses

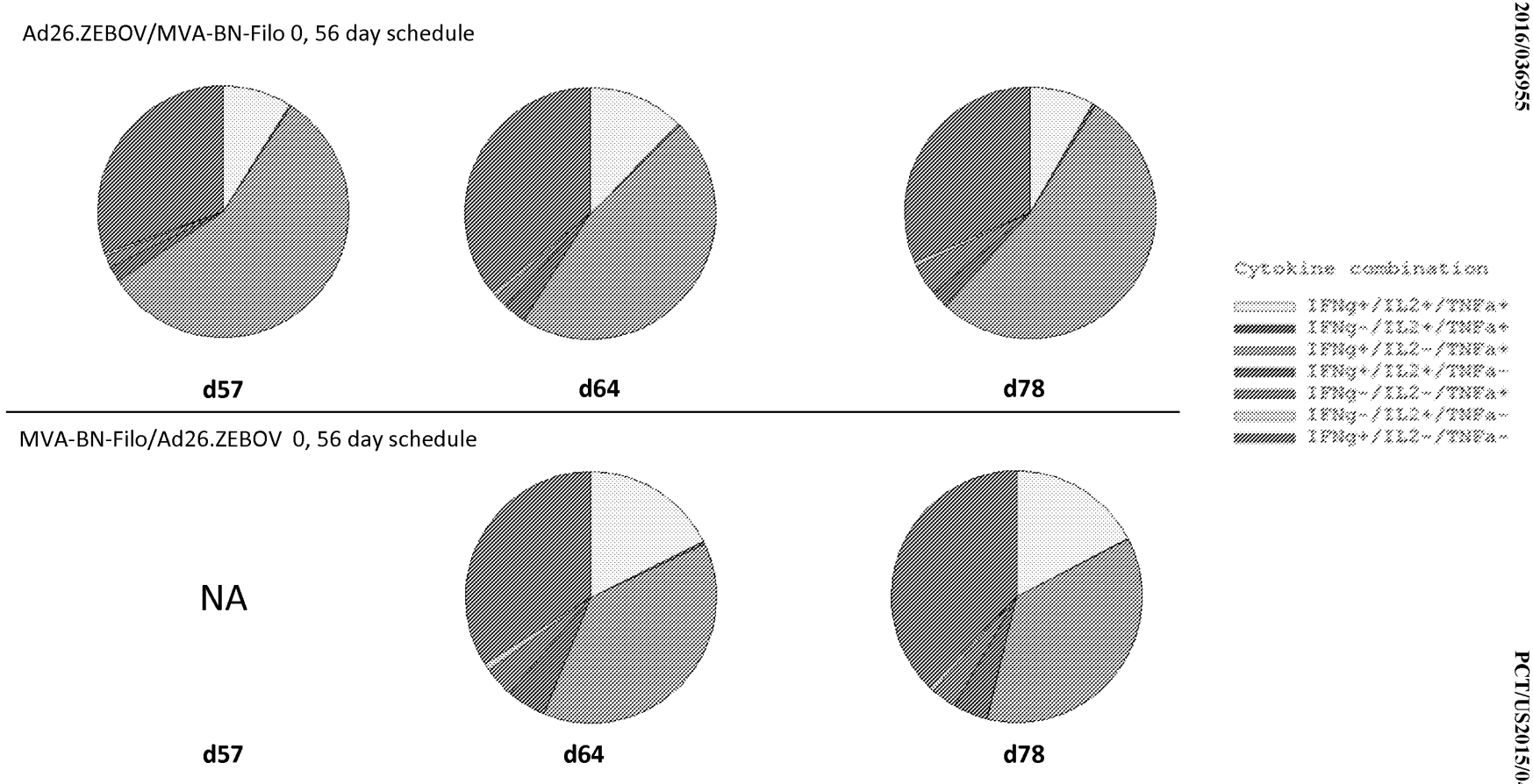


Figure 12

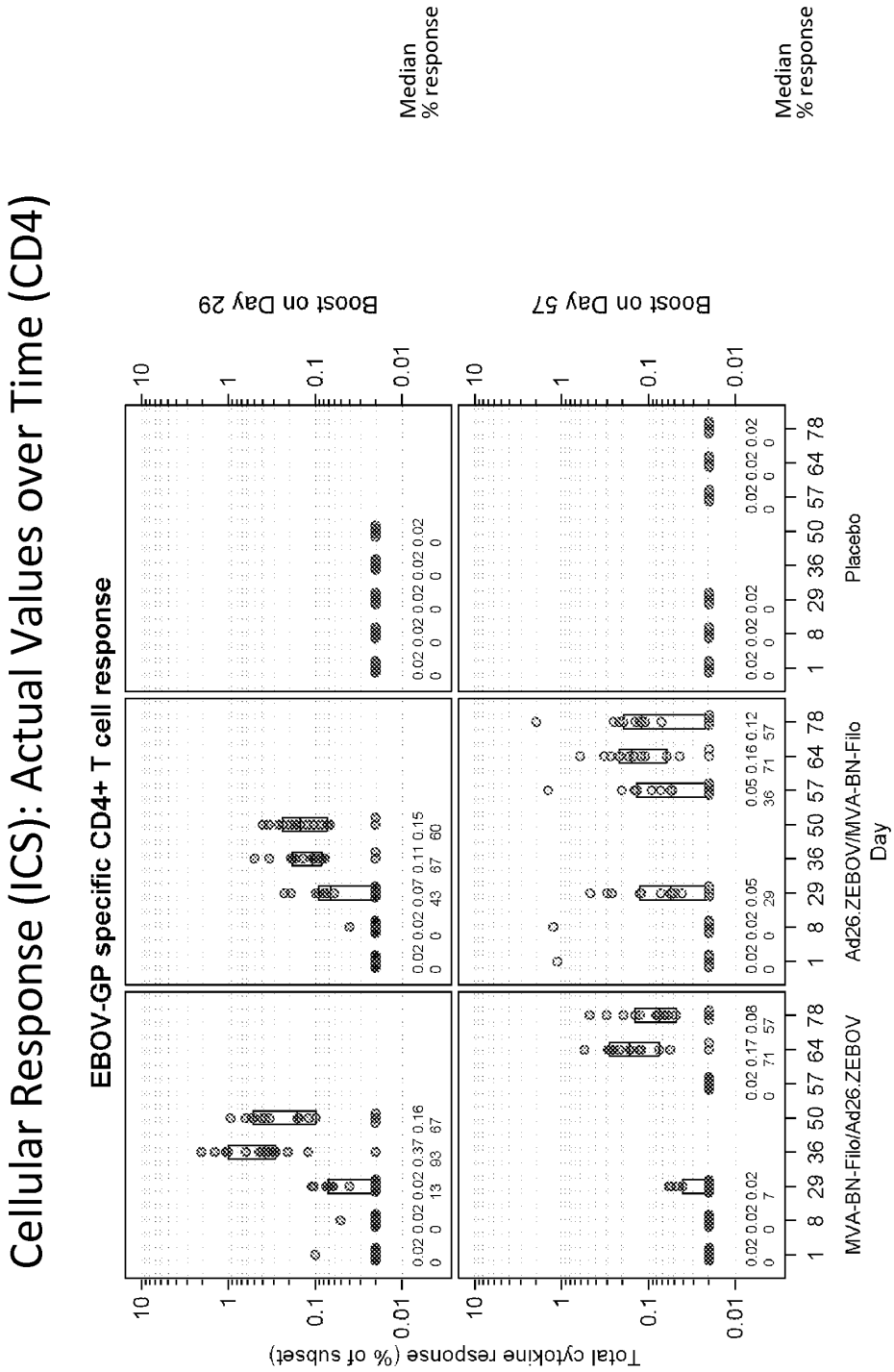

Cellular Response (ICS): Actual Values over Time (CD4)
EBOV-GP specific CD4+ T cell response
Boost on Day 29
Boost on Day 57
Median % response
Total cytokine response (% of subset)
MVA-BN-Filo/Ad26.ZEBOV
Ad26.ZEBOV/MVA-BN-Filo
Placebo
Day

Figure 13

Cellular Response (ICS): Functionality of CD4 responses

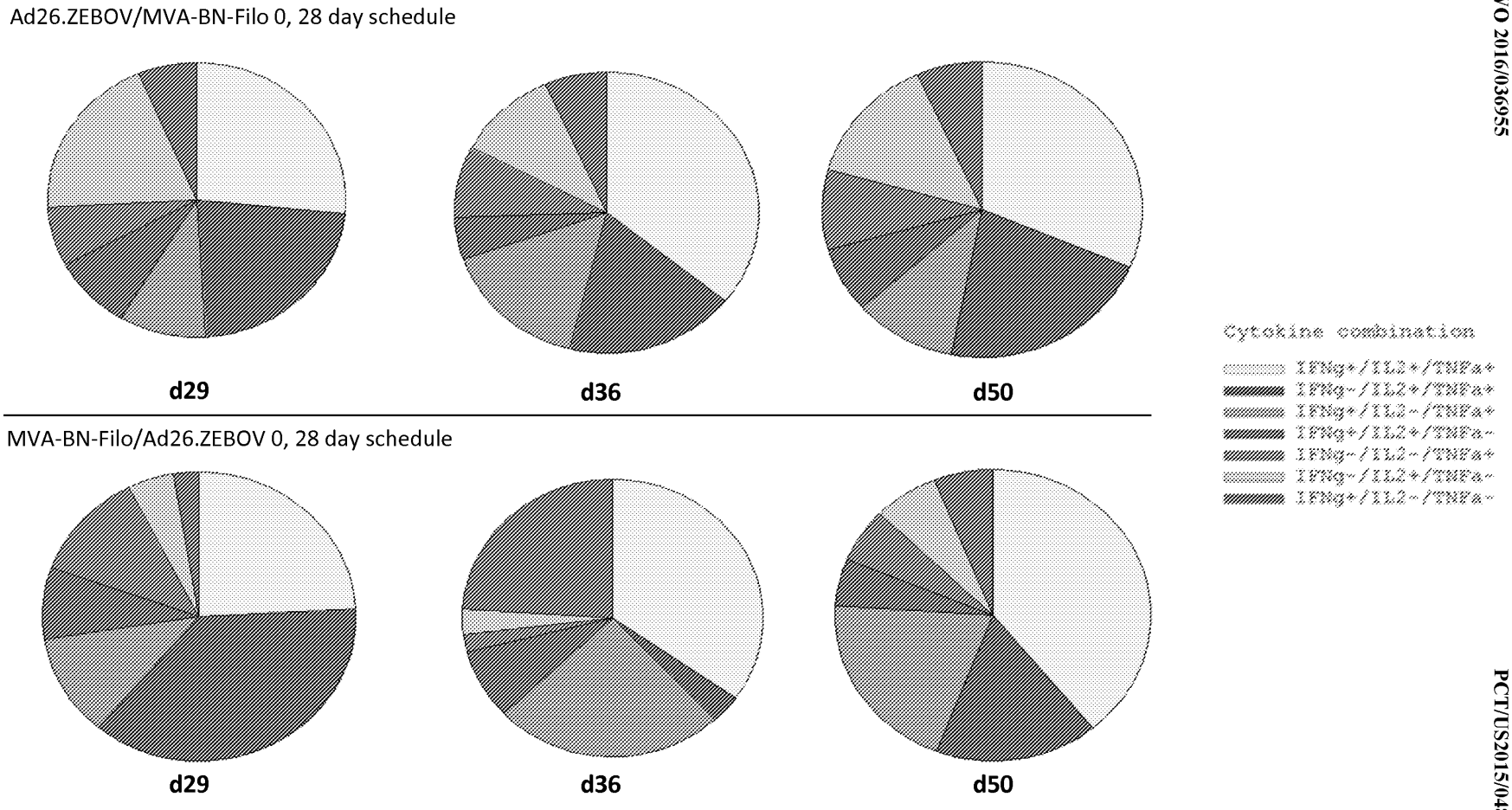
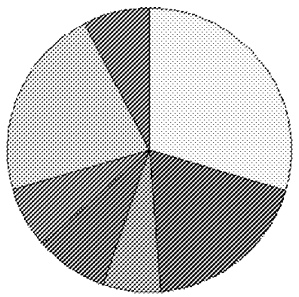


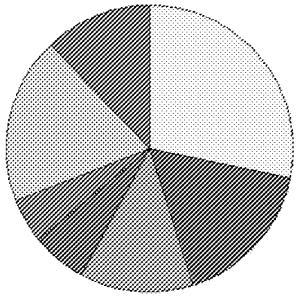
Figure 14

Cellular Response (ICS): Functionality of CD4 responses

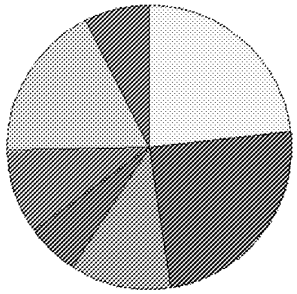
Ad26.ZEBOV/MVA-BN-Filo 0, 56 day schedule



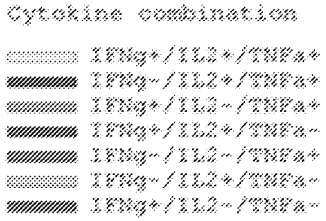
d57



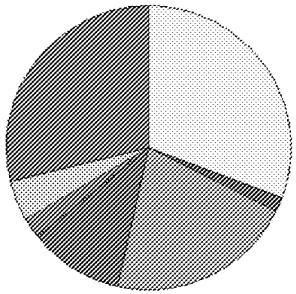
d64



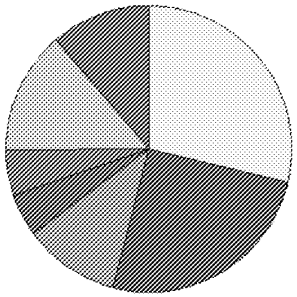
d78



MVA-BN-Filo/Ad26.ZEBOV 0, 56 day schedule



d57



d64

d78

Figure 15

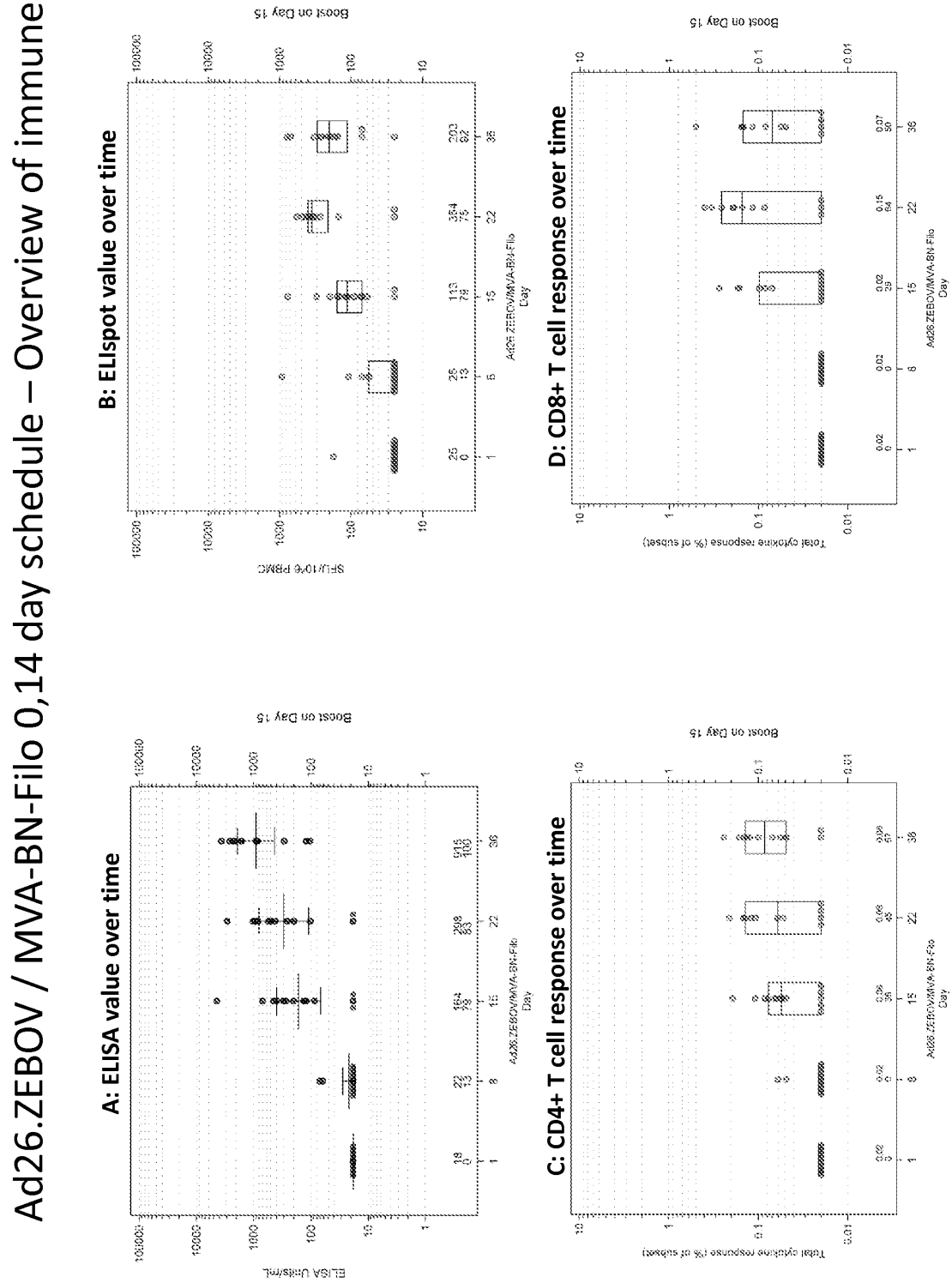

Ad26.ZEBOV / MVA-BN-Filo 0,14 day schedule – Overview of immune response
A: ELISA value over time
B: ELIspot value over time
C: CD4+ T cell response over time
D: CD8+ T cell response over time
Boost on Day 15
ELISA Units/mL
SFU/10^6 PBMC
Total cytokine response (% of subset)
Ad26.ZEBOV/MVA-BN-Filo
Day

Figure 16

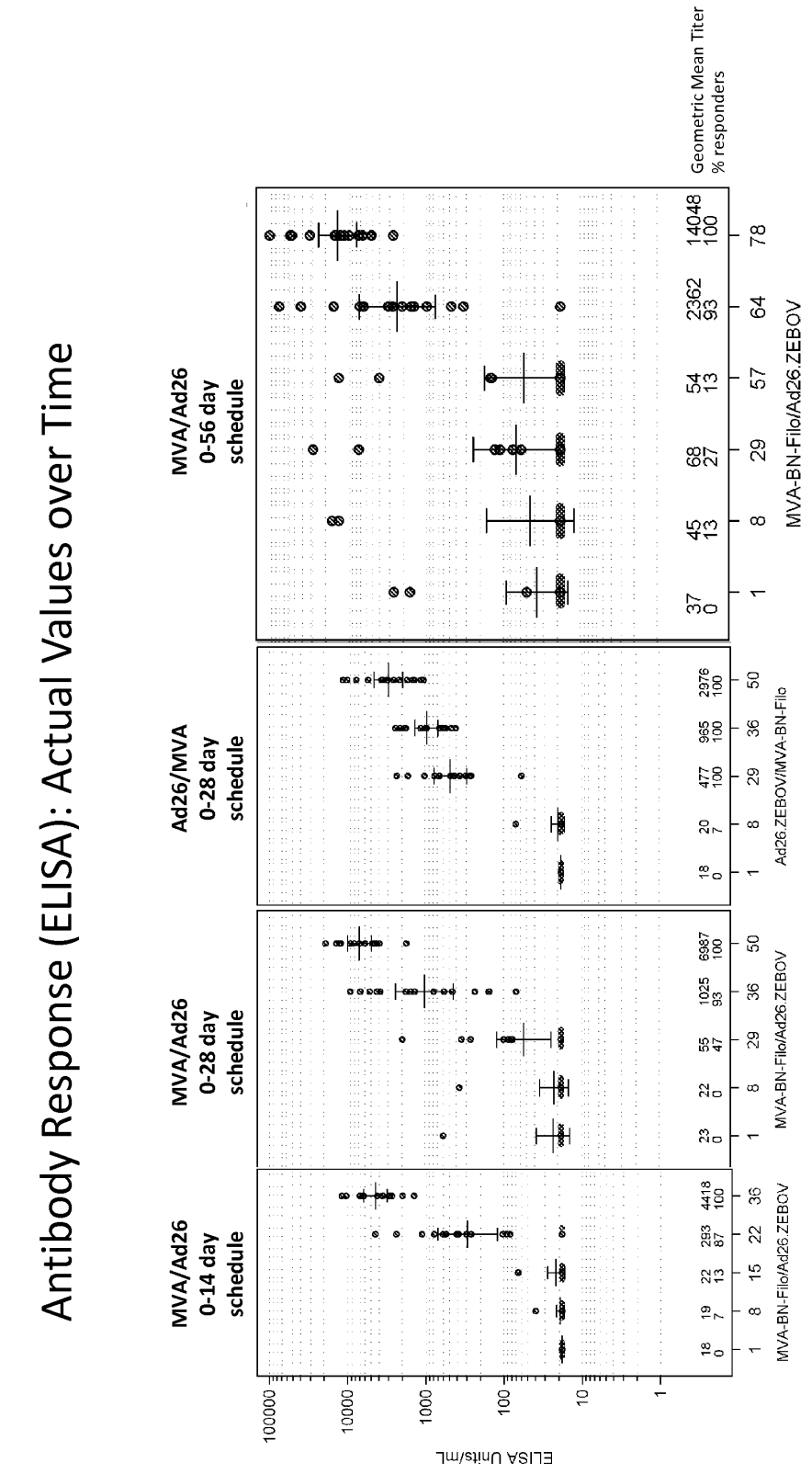

Antibody Response (ELISA): Actual Values over Time
MVA/Ad26 0-14 day schedule
MVA/Ad26 0-28 day schedule
Ad26/MVA 0-28 day schedule
MVA/Ad26 0-56 day schedule
ELISA Units/mL
100000
10000
1000
100
10
1
Geometric Mean Titer
% responders
MVA-BN-Filo/Ad26.ZEBOV
Ad26.ZEBOV/MVA-BN-Filo
MVA-BN-Filo/Ad26.ZEBOV

Figure 17

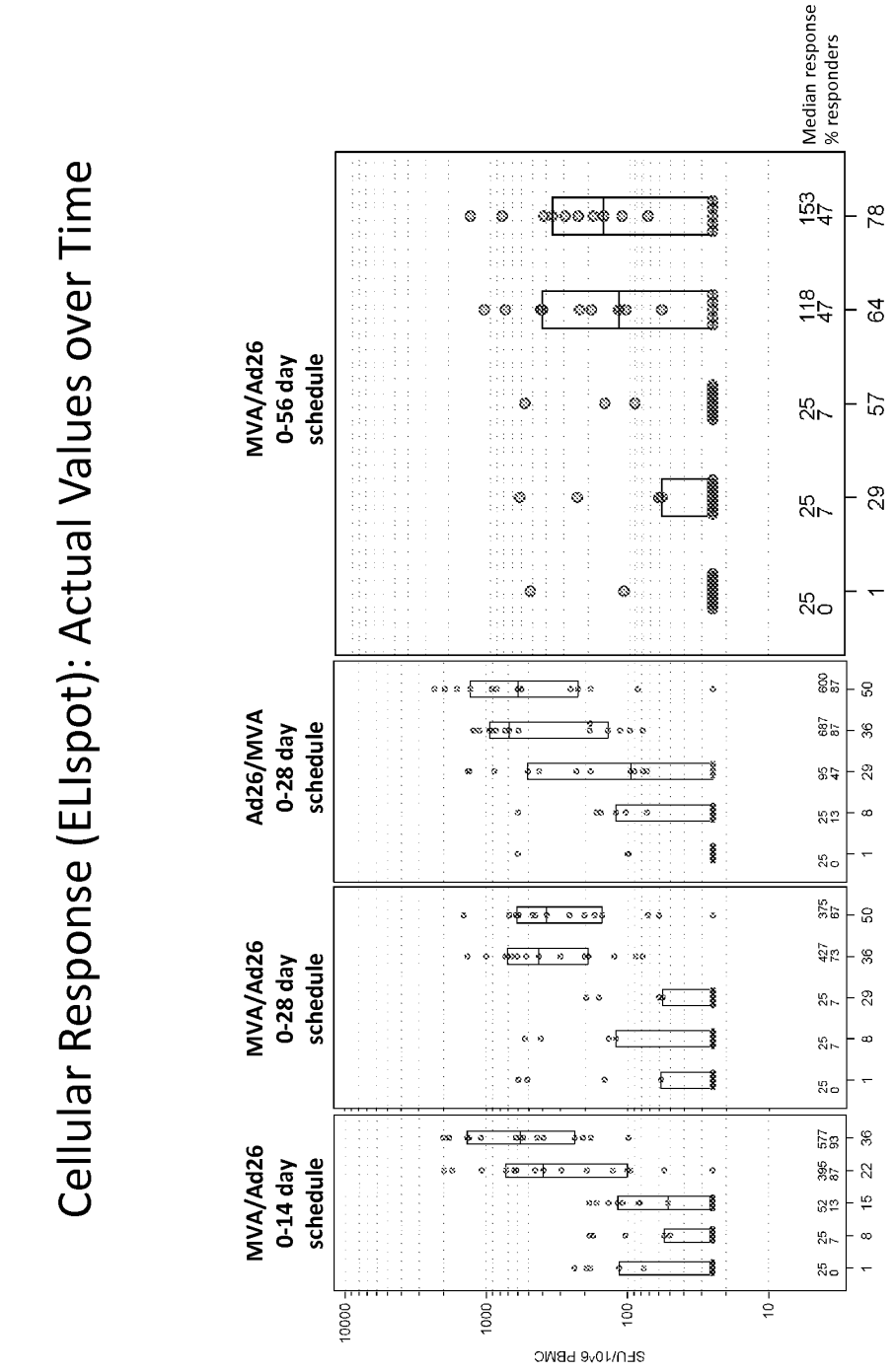

Cellular Response (ELIspot): Actual Values over Time
MVA/Ad26
0-14 day
schedule
MVA/Ad26
0-28 day
schedule
Ad26/MVA
0-28 day
schedule
MVA/Ad26
0-56 day
schedule
SFU/10^6 PBMC
10000
1000
100
10
Median response
% responders

Figure 18

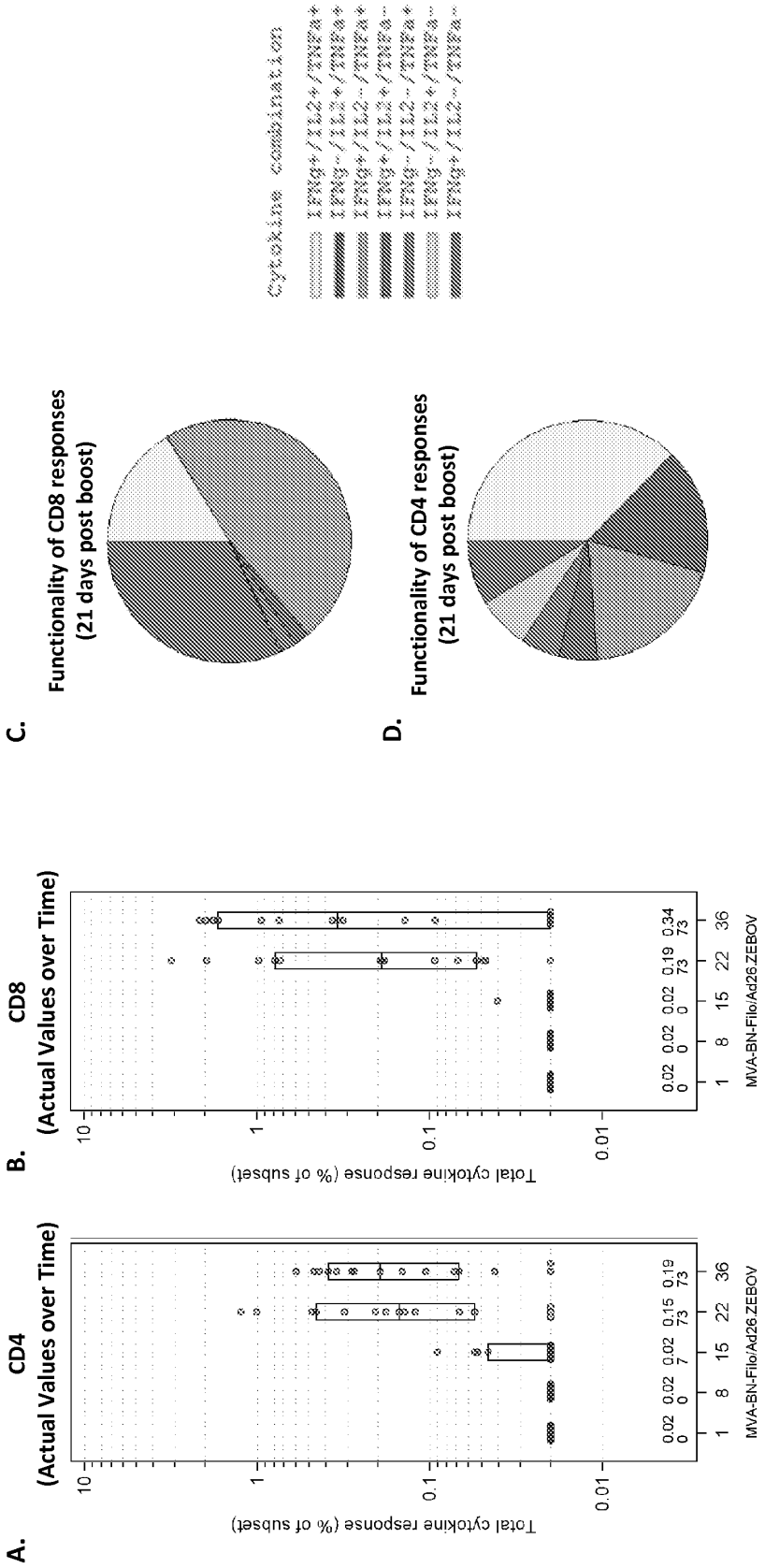

Cellular Response (ICS): MVA/Ad26 0, 14 days schedule
A.
CD4
(Actual Values over Time)
B.
CD8
(Actual Values over Time)
Total cytokine response (% of subset)
10
1
0.1
0.01
MVA-BN-Filo/Ad26.ZEBOV
C.
Functionality of CD8 responses
(21 days post boost)
D.
Functionality of CD4 responses
(21 days post boost)
Cytokine combination
IFNg+/IL2+/TNFa+
IFNg-/IL2+/TNFa+
IFNg+/IL2-/TNFa+
IFNg+/IL2+/TNFa-
IFNg-/IL2-/TNFa+
IFNg-/IL2+/TNFa-
IFNg+/IL2-/TNFa-

Figure 19

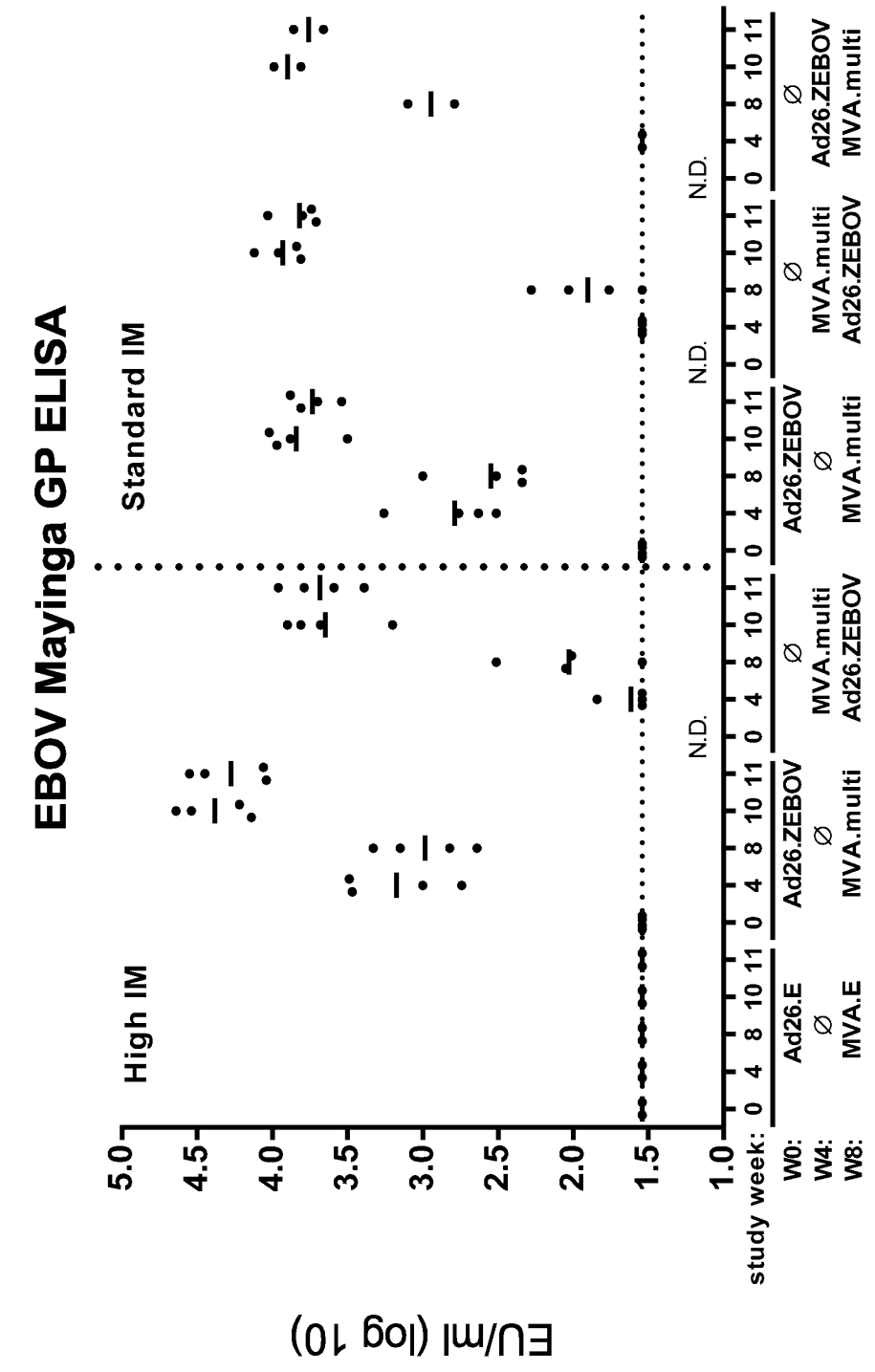

EBOV Mayinga GP ELISA
High IM
Standard IM
EU/ml (log 10)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
N.D.
N.D.
N.D.
study week: 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11 0 4 8 10 11
W0: Ad26.E Ad26.ZEBOV ∅ Ad26.ZEBOV ∅
W4: ∅ ∅ MVA.multi ∅ MVA.multi Ad26.ZEBOV
W8: MVA.E MVA.multi Ad26.ZEBOV MVA.multi Ad26.ZEBOV MVA.multi

Figure 20