

Figure 1

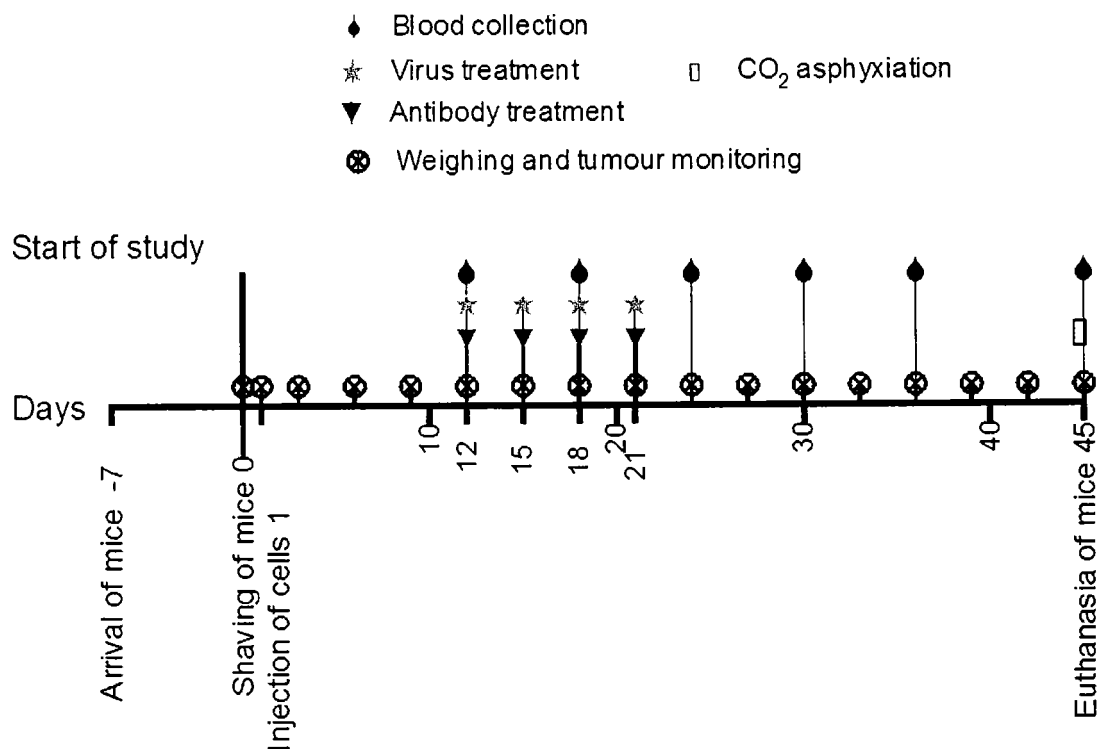
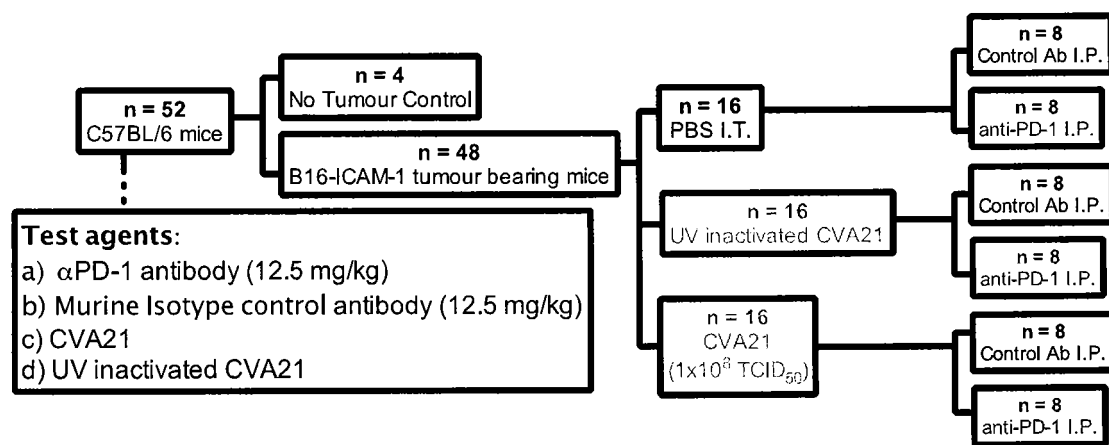


Figure 2

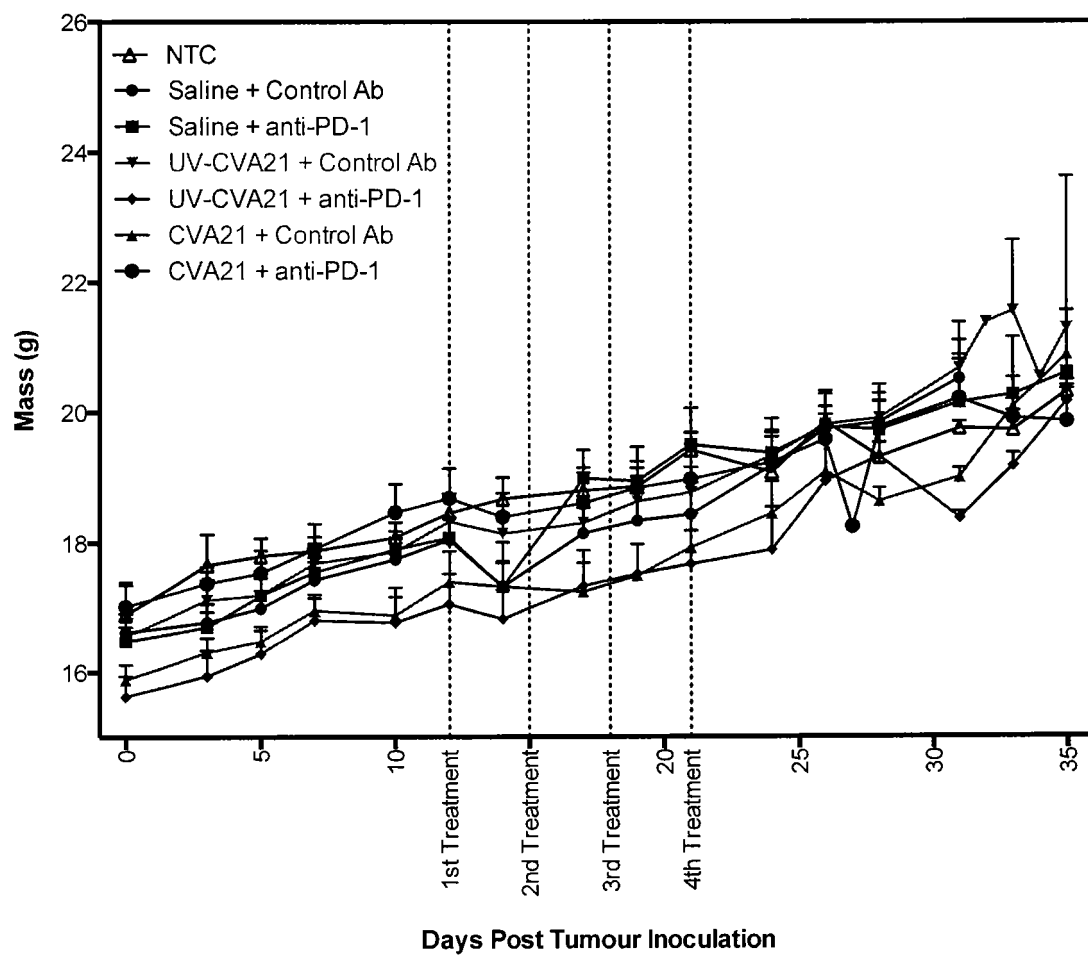


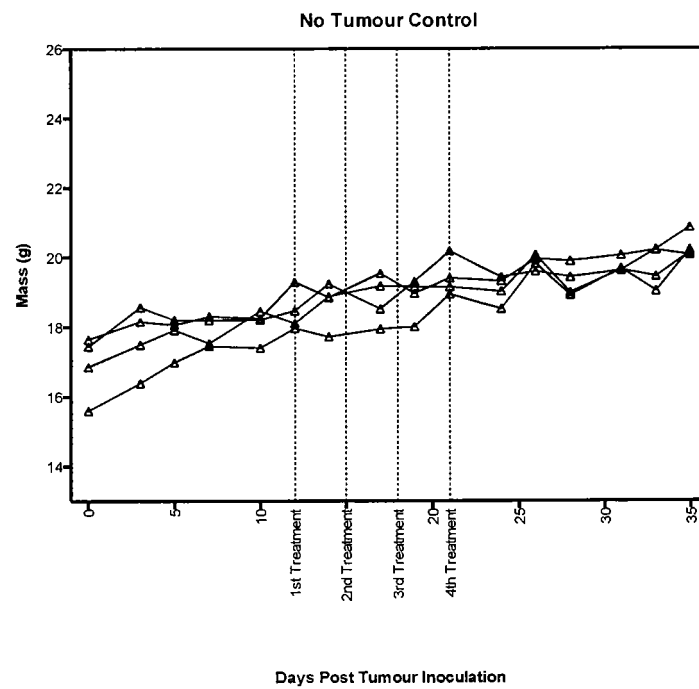
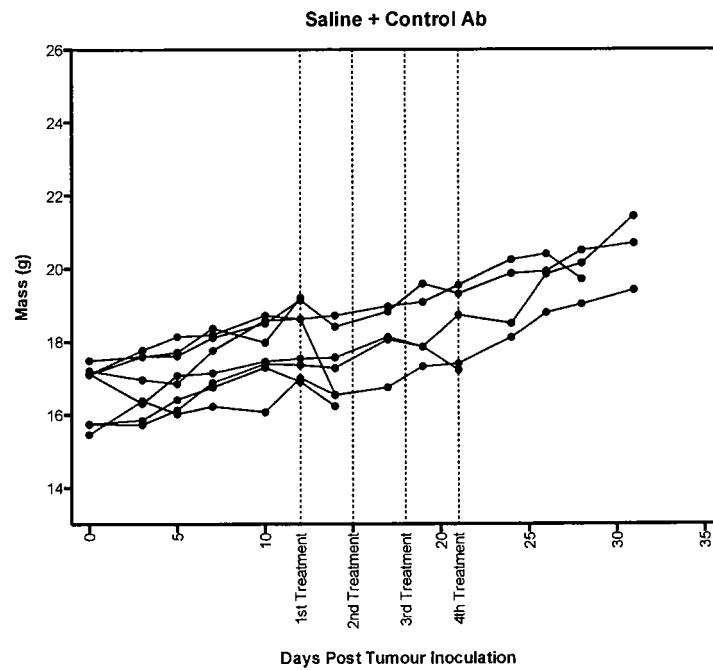
Figure 3**(A)****(B)**

Fig. 3C)

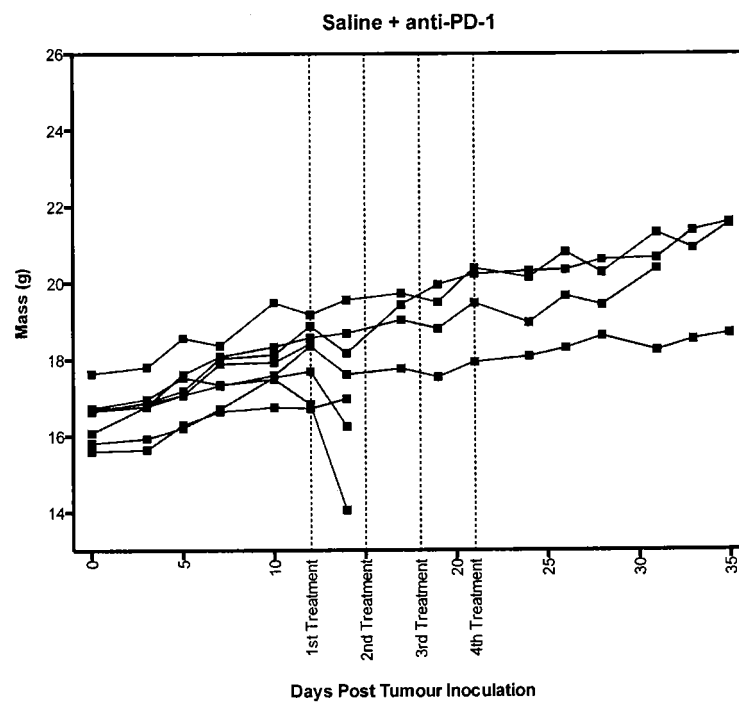


Fig.3D)

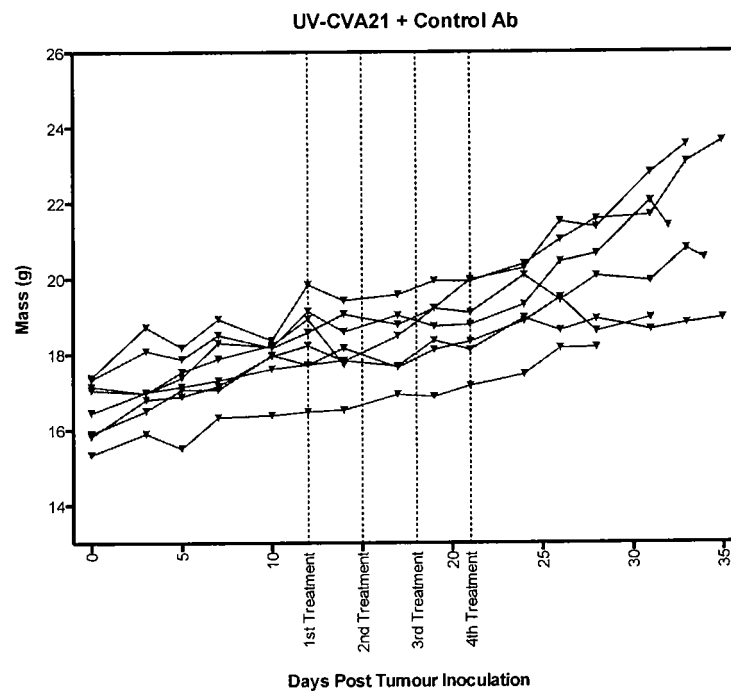


Fig. 3E)

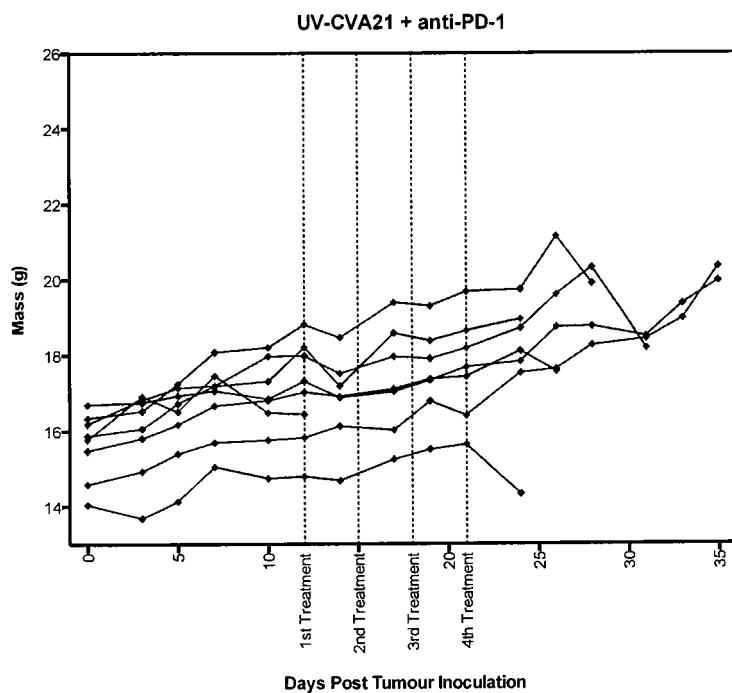


Fig. 3F)

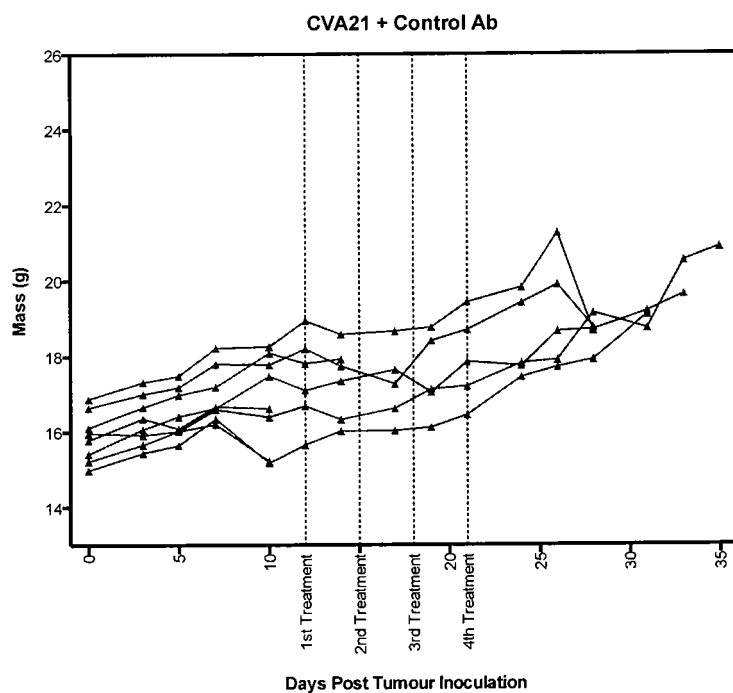


Fig 3G)

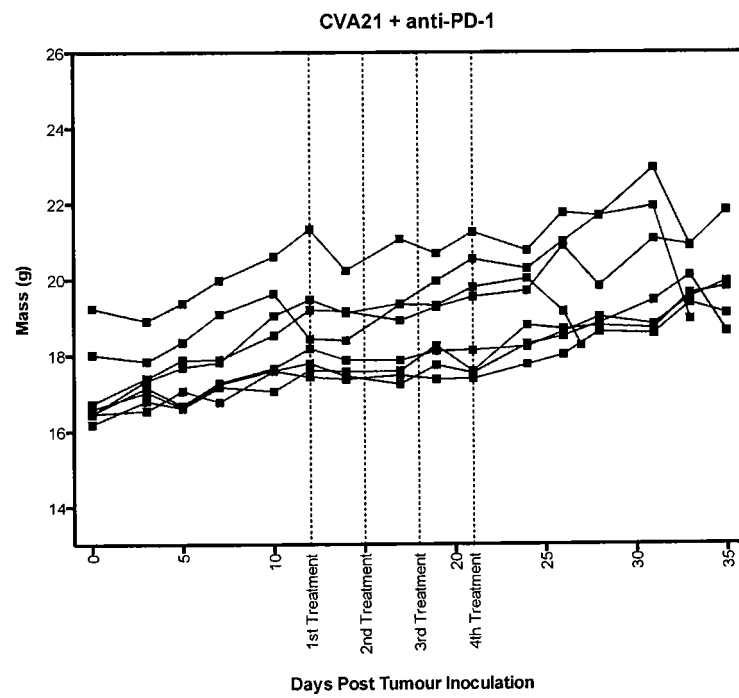


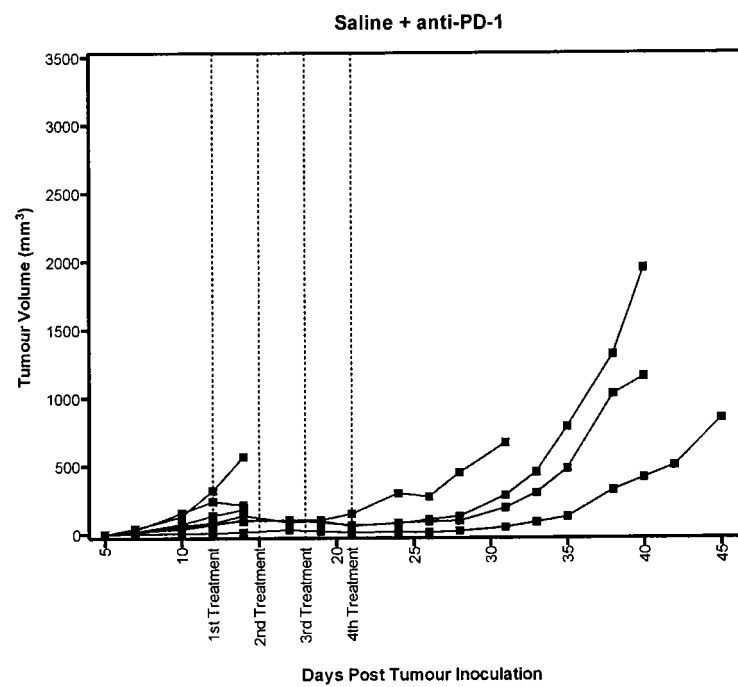
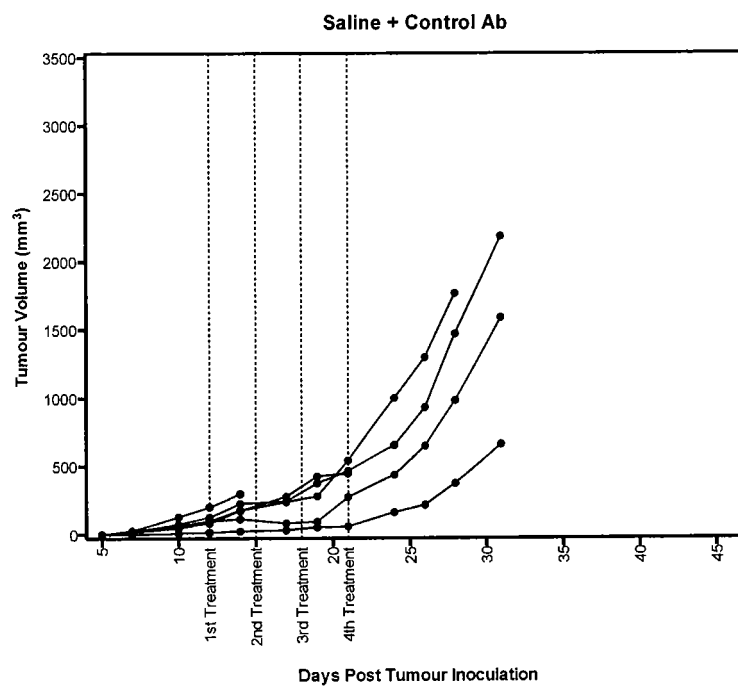
Figure 4

Fig. 4 (ctd)

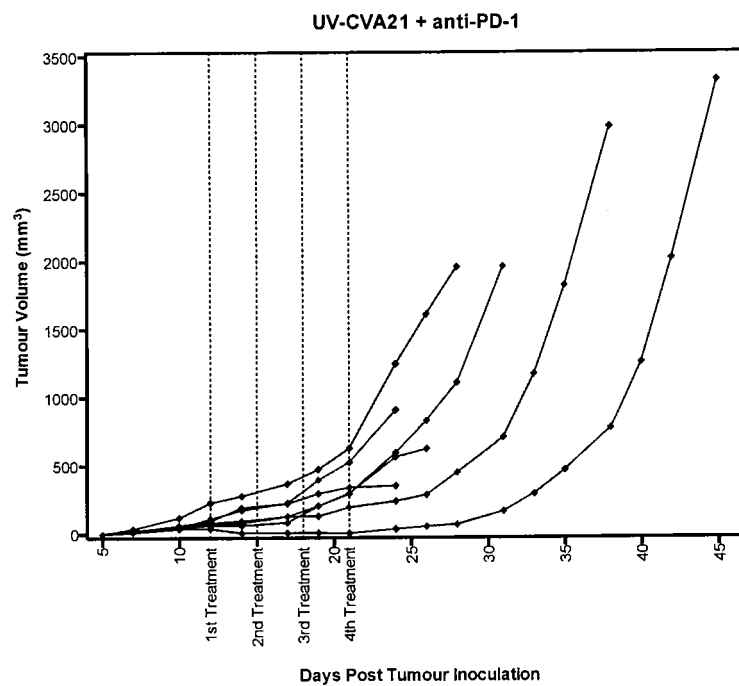
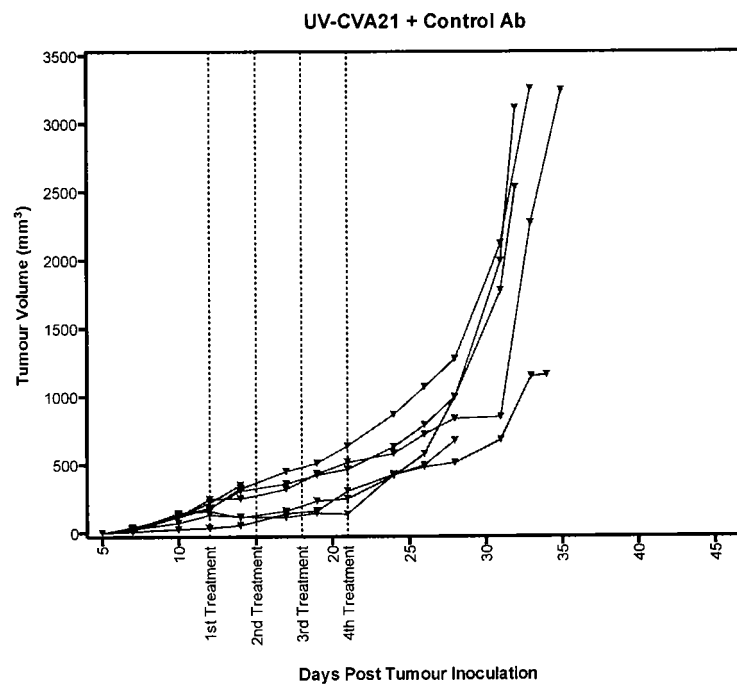


Fig. 4 (ctd)

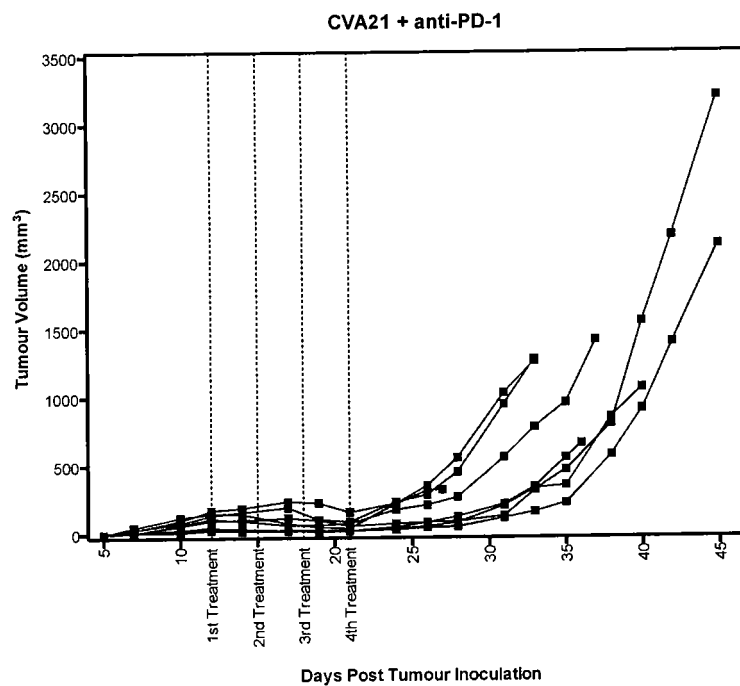
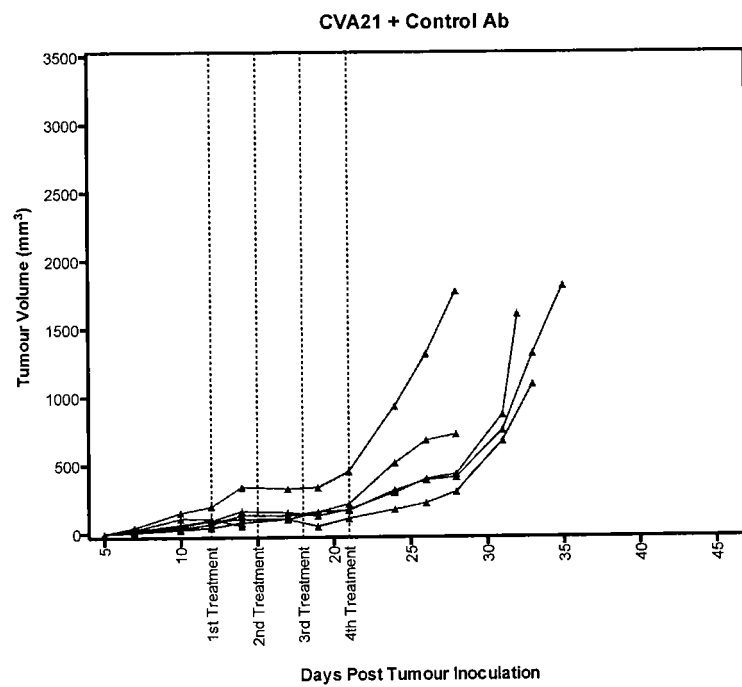
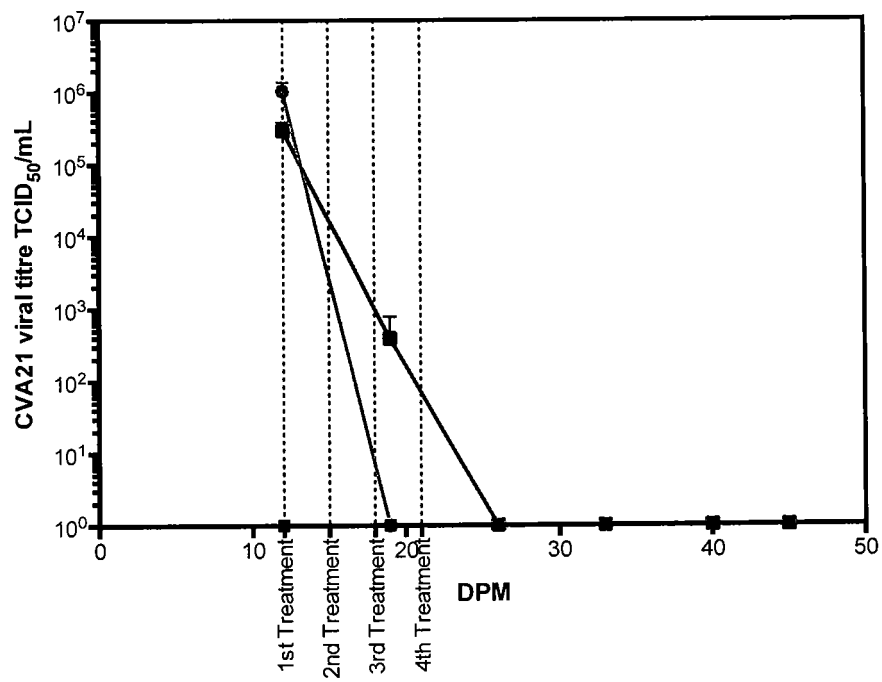
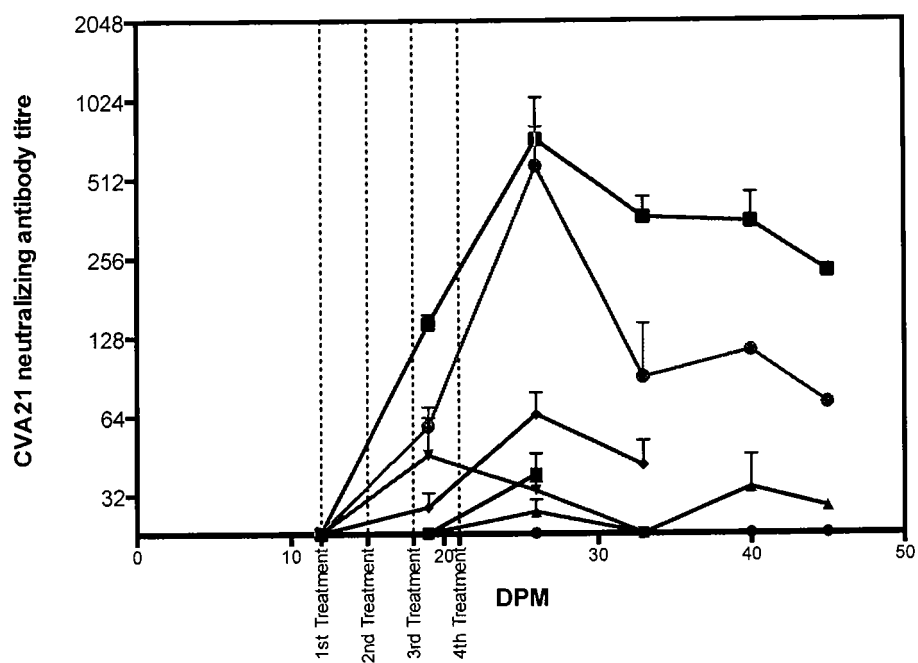


Figure 5

(A)



(B)



● NTC ■ Saline + Control AB ▲ UV-CVA21 + Control Ab ● CVA21 + Control Ab
 ▲ Saline + anti-PD-1 ● UV-CVA21 + anti-PD-1 ■ CVA21 + anti-PD-1

Figure 6

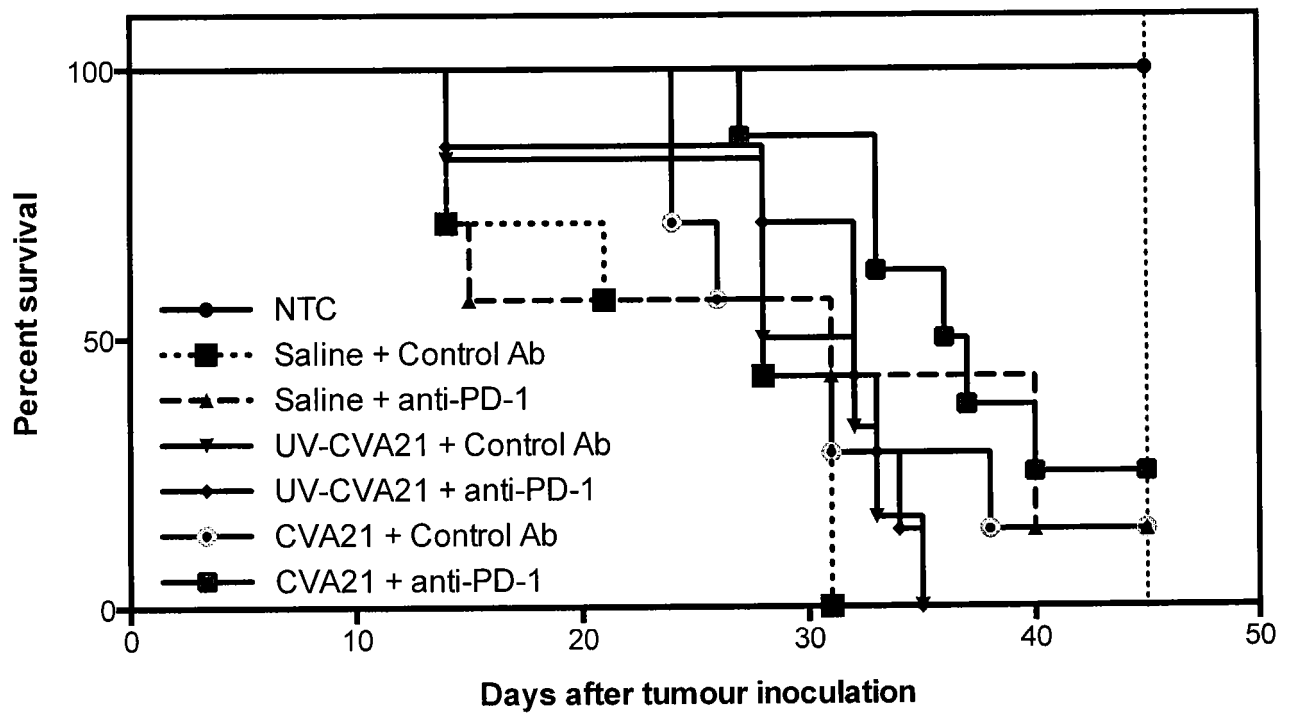
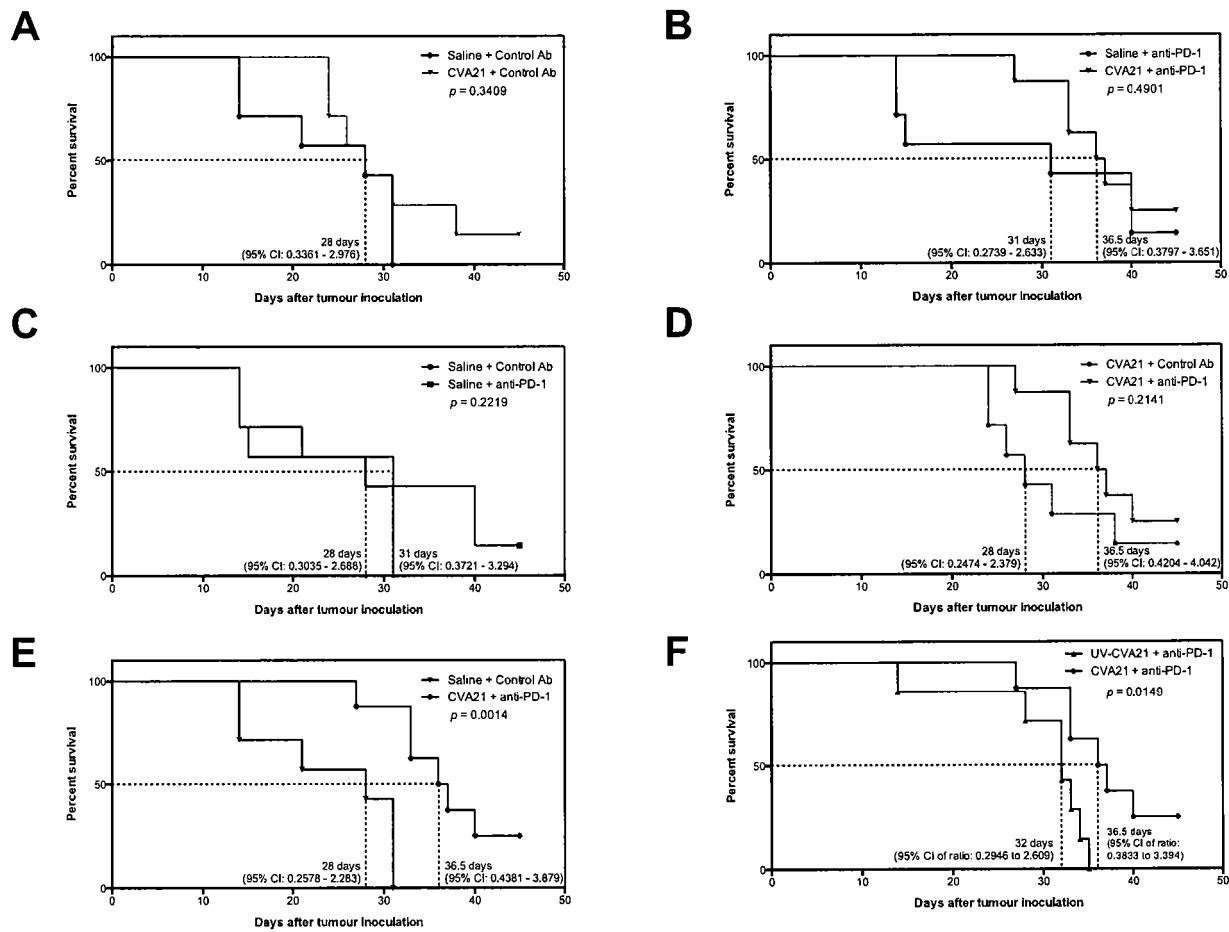


Figure 7



	NTC n = 4	Saline + Control Ab n = 7	Saline + anti-PD-1 n = 7	UV-CVA21 + Control Ab n = 7	UV-CVA21 + anti-PD-1 n = 8	CVA21 + Control Ab n = 8	CVA21 + anti-PD-1 n = 8
# deaths/events	0	7	6	6	7	6	6
Median survival	Undefined	28	31	30	32	28	36.5

Figure 7(a)

Table 9: Immune-competent animal model: Summary of mouse body weights (g) in each treatment group.

Study Day	Group 1 NTC			Group 2 Saline + Control Ab			Group 3 Saline + anti-PD-1			Group 4 UV CVA21 + Control Ab			Group 5 UV CVA21 + anti-PD-1		
	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.	n
-2	16.7	± 1.2	4	16.8	± 0.8	8	16.5	± 0.8	8	15.8	± 0.7	8	16.8	± 1.1	8
0	16.9	± 0.9	4	16.6	± 0.8	8	16.5	± 0.6	8	15.9	± 0.7	8	16.6	± 0.8	8
3	17.7	± 0.9	4	16.8	± 0.8	8	16.7	± 0.7	8	16.3	± 0.7	8	17.1	± 0.9	8
5	17.8	± 0.6	4	17.0	± 0.8	8	17.2	± 0.8	8	16.5	± 0.7	8	17.2	± 0.8	8
7	17.9	± 0.4	4	17.4	± 0.8	8	17.5	± 0.6	8	17.0	± 0.7	8	17.7	± 0.9	8
10	18.1	± 0.5	4	17.7	± 0.9	8	17.9	± 0.8	8	16.9	± 1.2	8	17.9	± 0.6	8
12	18.5	± 0.6	4	18.1	± 0.9	8	18.1	± 0.9	8	17.4	± 1.2	6	18.3	± 1.0	8
14	18.7	± 0.7	4	17.3	± 1.0	7	17.3	± 1.8	7	17.3	± 1.0	6	18.1	± 0.9	8
17	18.8	± 0.7	4	18.1	± 0.9	5	19.0	± 0.9	4	17.2	± 1.0	5	18.3	± 0.9	7
19	18.9	± 0.6	4	18.3	± 0.9	5	18.9	± 1.0	4	17.5	± 1.1	5	18.6	± 1.0	7
21	19.4	± 0.5	4	18.4	± 1.1	5	19.5	± 1.1	4	17.9	± 1.2	5	18.8	± 1.0	7
24	19.1	± 0.4	4	19.2	± 1.0	4	19.4	± 1.1	4	18.5	± 1.1	5	19.3	± 1.0	7
26	19.9	± 0.2	4	19.7	± 0.7	4	19.8	± 1.1	4	19.1	± 1.5	5	19.8	± 1.2	7
27	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
28	19.3	± 0.4	4	19.8	± 0.6	4	19.7	± 0.9	4	18.6	± 0.4	5	19.9	± 1.4	7
31	19.7	± 0.2	4	20.5	± 1.0	3	20.1	± 1.3	4	19.0	± 0.2	3	20.7	± 1.7	6
32	-	-	-	-	-	-	-	-	-	17.9	± 0.0	1	20.3	± 1.5	2
33	19.7	± 0.6	4	-	-	-	20.3	± 1.5	3	20.1	± 0.6	2	21.5	± 2.2	4
34	-	-	-	-	-	-	-	-	-	-	-	-	20.5	± 0.0	1
35	20.3	± 0.4	4	-	-	-	20.6	± 1.7	3	20.9	0.0	1	21.3	± 3.3	2
36	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
38	20.2	± 0.4	4	-	-	-	21.6	± 2.0	3	-	-	-	19.8	± 0.0	1
40	20.7	± 0.5	4	-	-	-	22.2	± 2.0	3	-	-	-	19.6	± 0.0	1

Figure 7(a) (ctd)

42	20.9	± 0.9	4	-	-	-	20.3	± 0.0	1	-	-	20.0	± 0.0	1
45	21.0	± 1.0	4	-	-	-	21.1	± 0.0	1	-	-	20.4	± 0.0	1

Figure 7(b)

Table 10: Immune-competent animal model: Summary of mouse body weights in each treatment group.

Study Day	Group 6			Group 7		
	CVA21 + Control Ab			CVA21 + anti-PD-1		
	Mean	S.D.	n	Mean	S.D.	n
-2	15.6	±0.9	8	17.0	±1.2	8
0	15.6	±0.9	8	17.0	±1.1	8
3	15.9	±1.1	8	17.4	±0.7	8
5	16.3	±1.1	8	17.5	±1.0	8
7	16.8	±1.0	8	17.9	±1.1	8
10	16.8	±1.1	8	18.5	±1.2	8
12	17.1	±1.3	8	18.7	±1.3	8
14	16.8	±1.2	7	18.4	±1.0	8
17	17.3	±1.4	7	18.6	±1.3	8
19	17.5	±1.2	7	18.8	±1.2	8
21	17.7	±1.4	7	19.0	±1.5	8
24	17.9	±1.7	7	19.2	±1.1	8
26	18.9	±1.5	5	19.6	±1.4	8
27	-	-	-	18.3	±0.0	1
28	19.3	±1.0	4	19.8	±1.4	7
31	18.4	±0.2	3	20.2	±1.8	7
32	-	-	-	-	-	-
33	19.2	±0.3	2	19.9	±0.8	7
34	-	-	-	-	-	-
35	20.2	±0.3	2	19.9	±1.2	5
36	-	-	-	16.2	±0.0	1
37	-	-	-	16.1	±0.0	1
38	21.0	±0.0	2	21.2	±0.8	3
40	21.7	±0.0	1	21.6	±2.6	3

Figure 7(b) (ctd)

42	22.4	± 0.0	1	22.2	± 2.7	2
45	24.7	± 0.0	1	21.6	± 2.3	2

Figure 7(c)

Table 11: Table showing significance values (p) following statistical analysis of survival curve comparisons. Values of $p < 0.05$ are shaded.

	Saline + Control Ab	Saline + anti-PD- 1	UV-CVA21 + Control Ab	UV-CVA21 + anti-PD- 1	CVA21 + Control Ab	CVA21 + anti-PD- 1
Saline + Control Ab	-	0.2219	0.2472	0.0475	0.3409	0.0014
Saline + anti-PD-1	0.2219	-	0.7745	0.9488	0.847	0.4901
UV-CVA21 + Control Ab	0.2472	0.7745	-	0.7555	0.8866	0.0269
UV-CVA21 + anti-PD-1	0.0475	0.9488	0.7555	-	0.6073	0.0149
CVA21 + Control Ab	0.3409	0.847	0.8866	0.6073	-	0.2141
CVA21 + anti-PD-1	0.0014	0.4901	0.0269	0.0149	0.2141	-

Figure 8

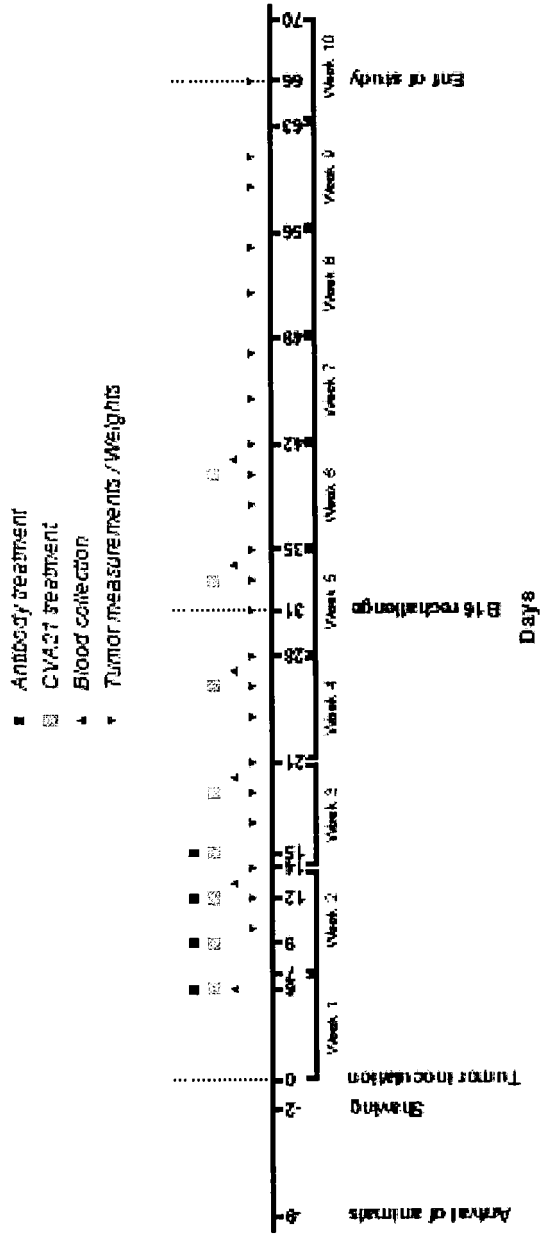


Figure 9

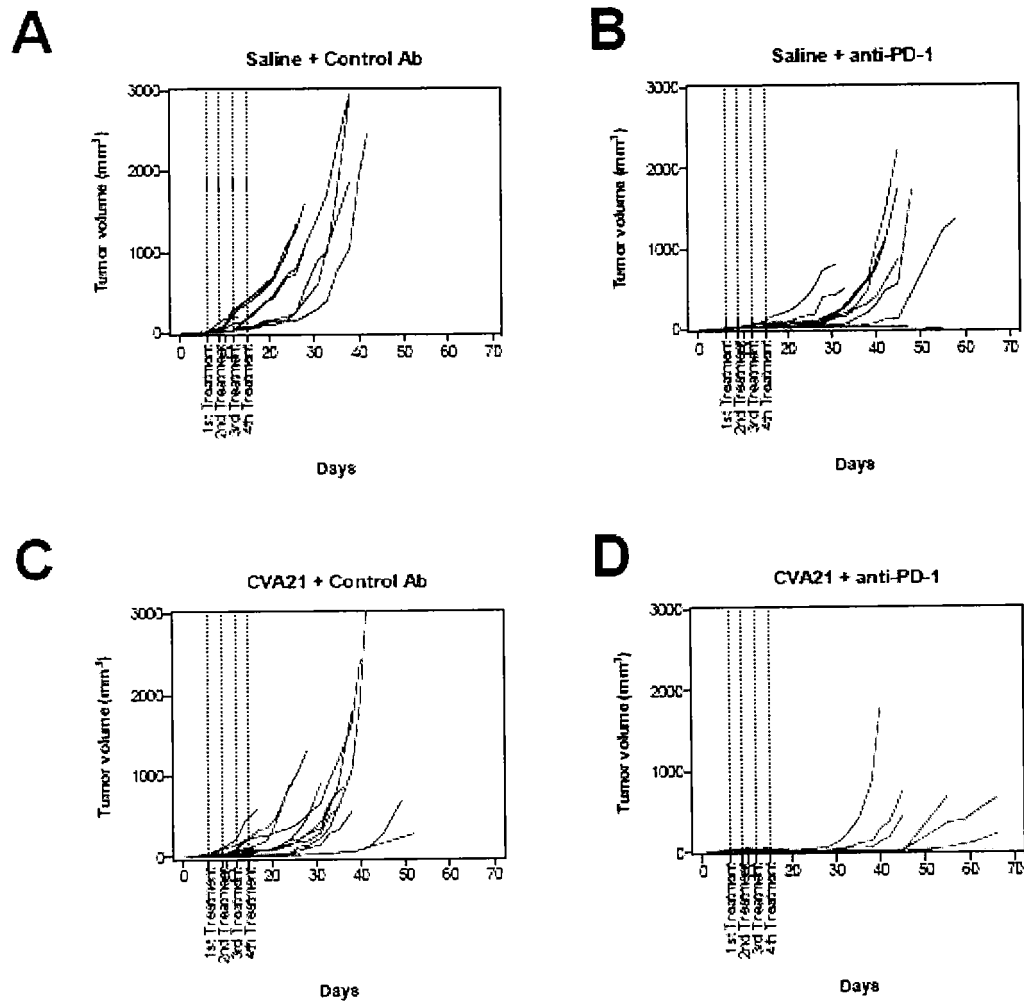


Figure 10

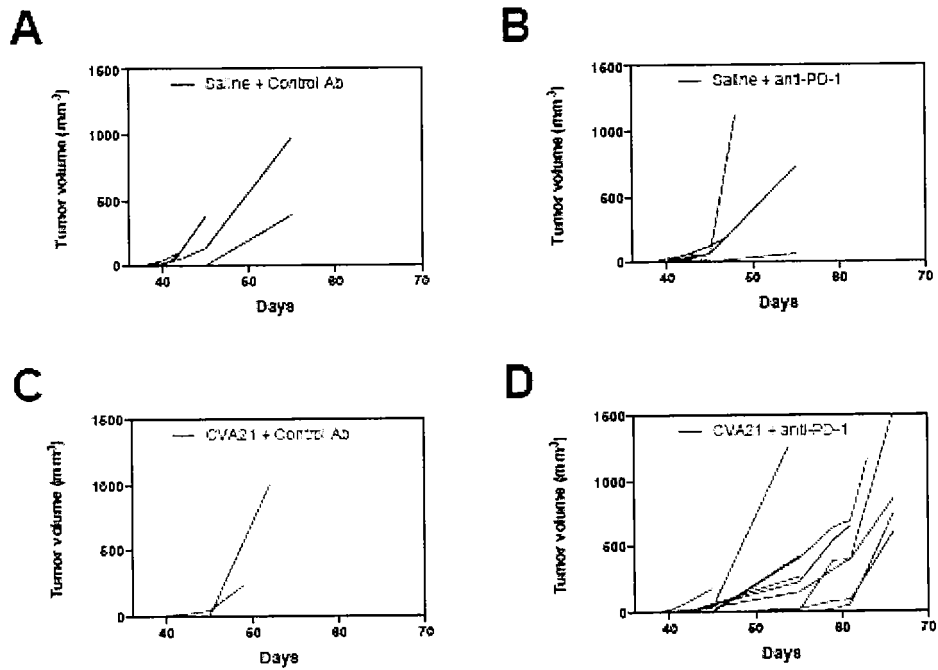


Figure 11

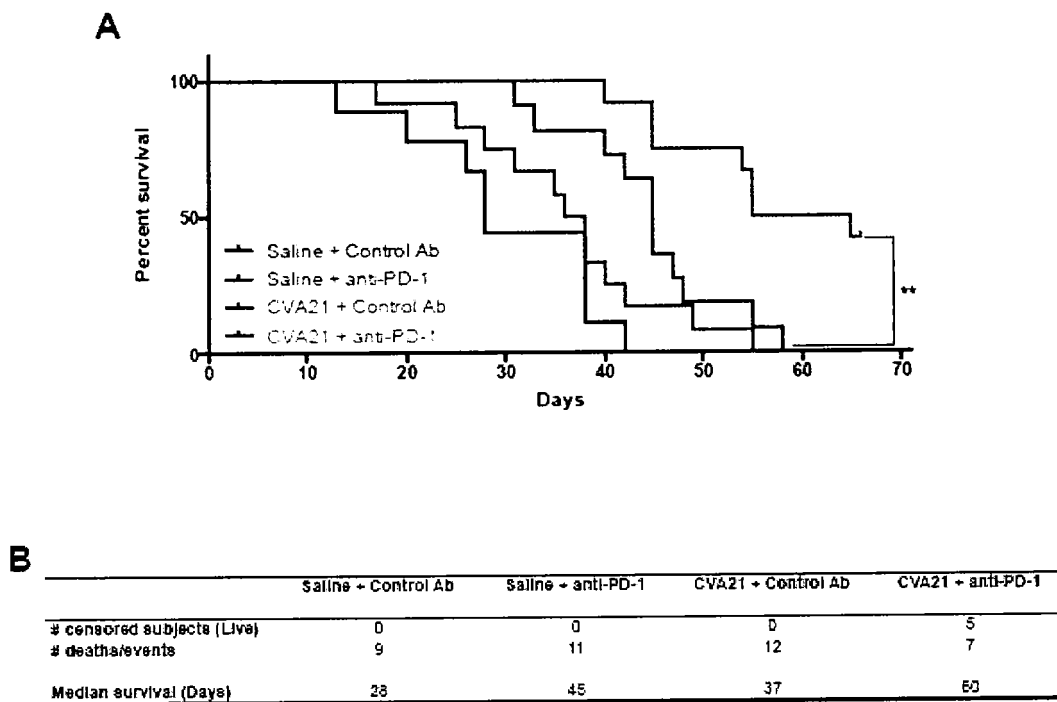


Figure 12

Timeline of Study

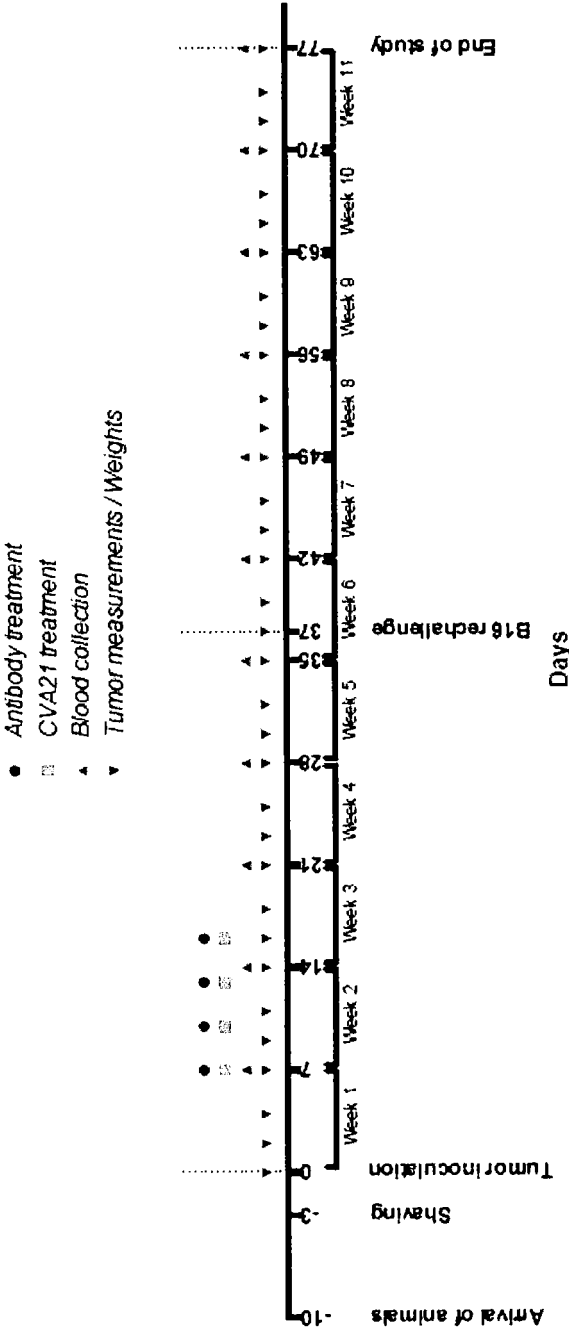


Figure 13

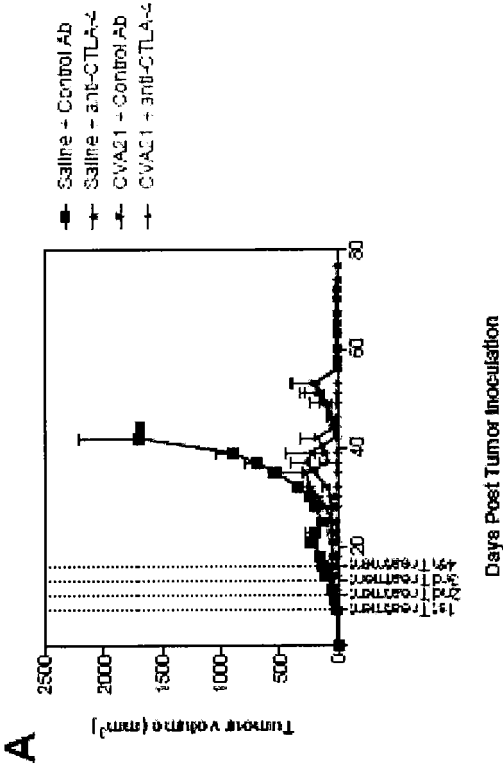


Figure 13 (ctd)

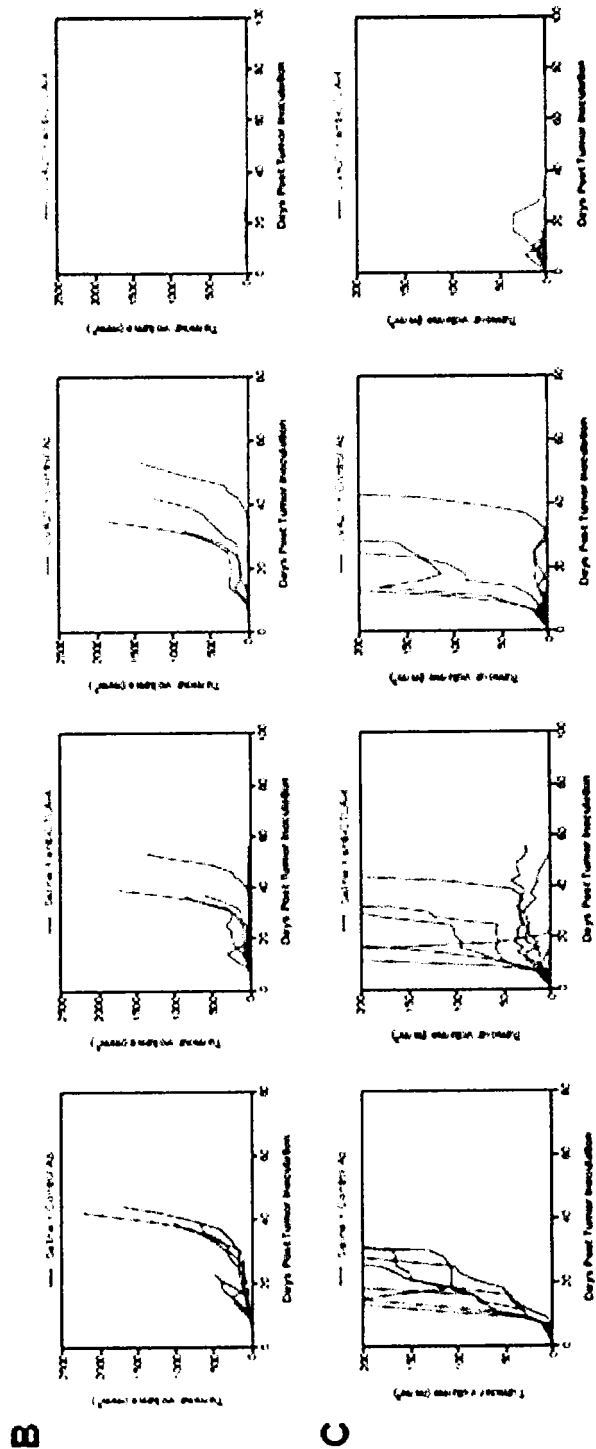
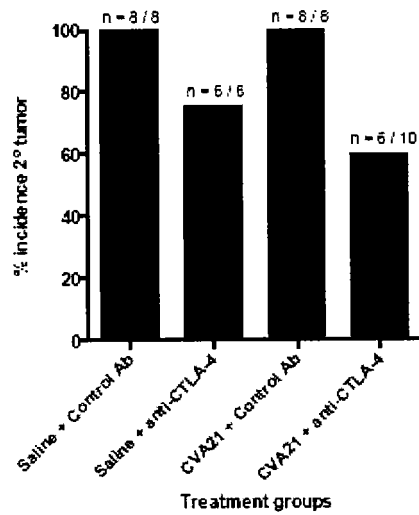
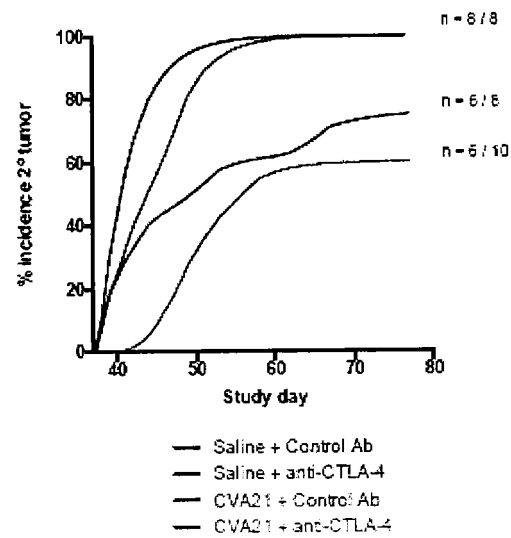


Figure 14

A



B



C

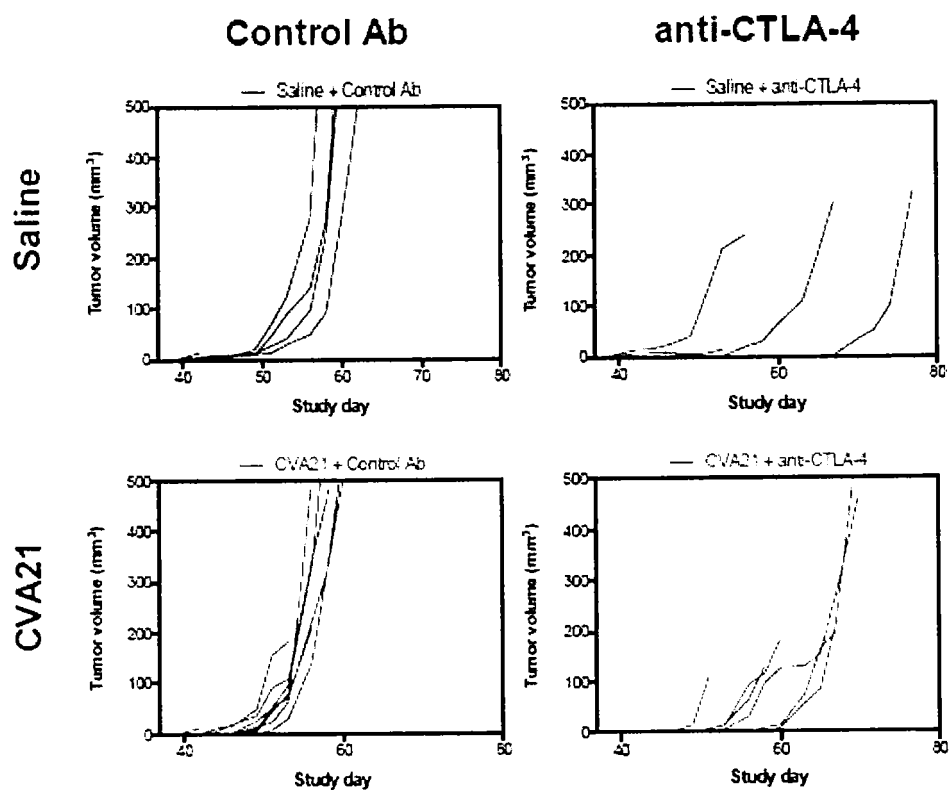
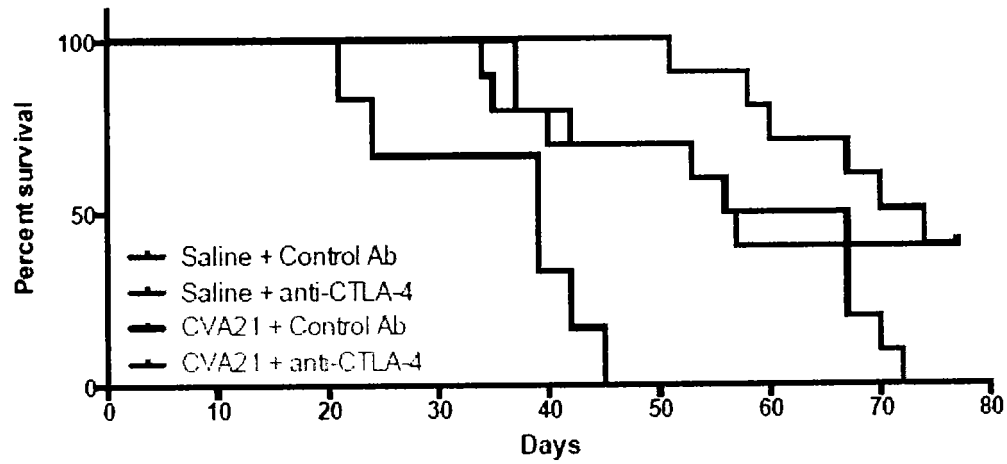


Figure 15

A



B

	Saline + Control Ab	Saline + anti-CTLA-4	CVA21 + Control Ab	CVA21 + anti-CTLA-4
# censored subjects	0	4	0	4
# deaths/events	6	6	10	6
Median survival	39	61.5	56.5	72

Figure 16A

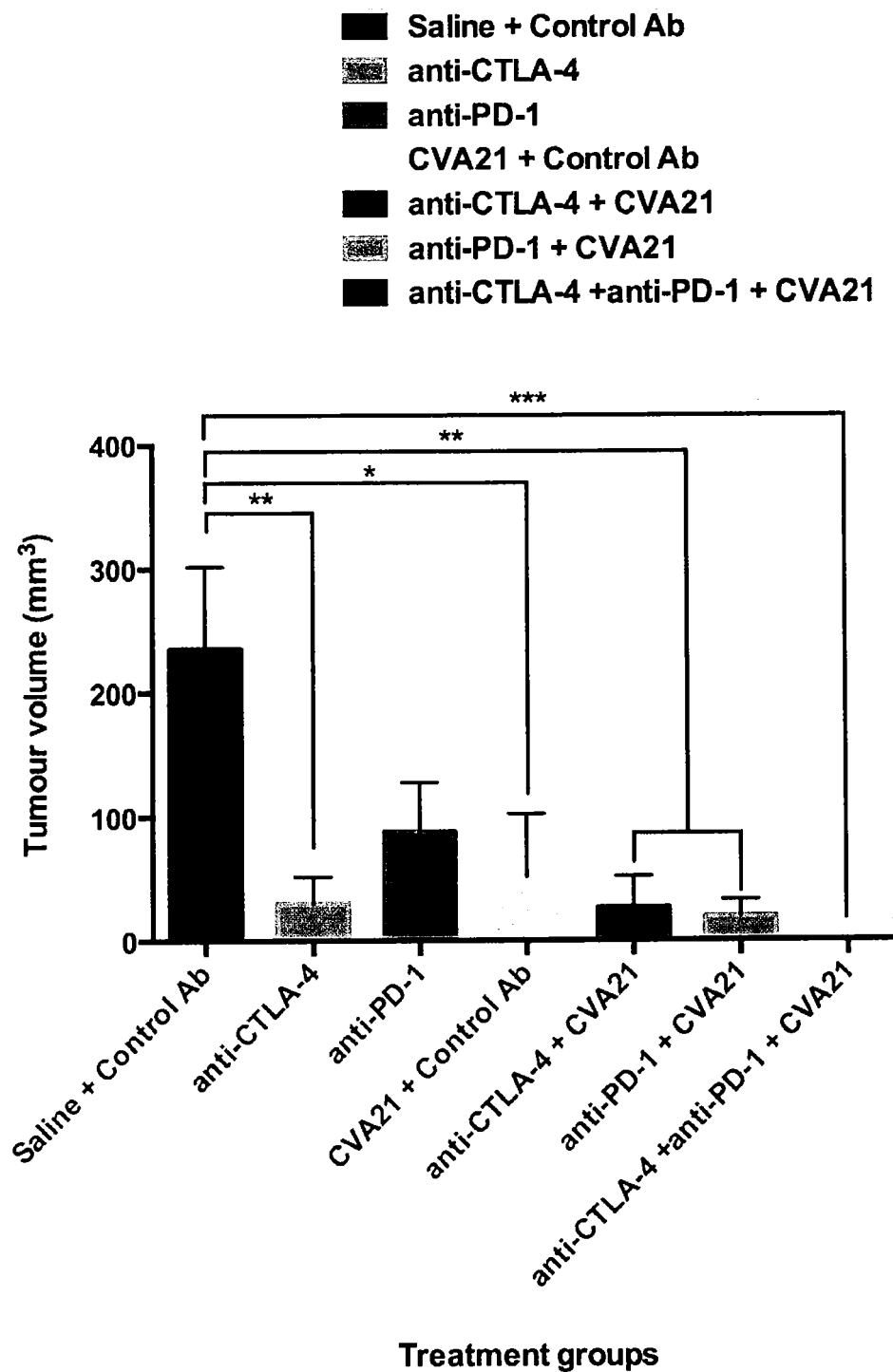


Figure 16B

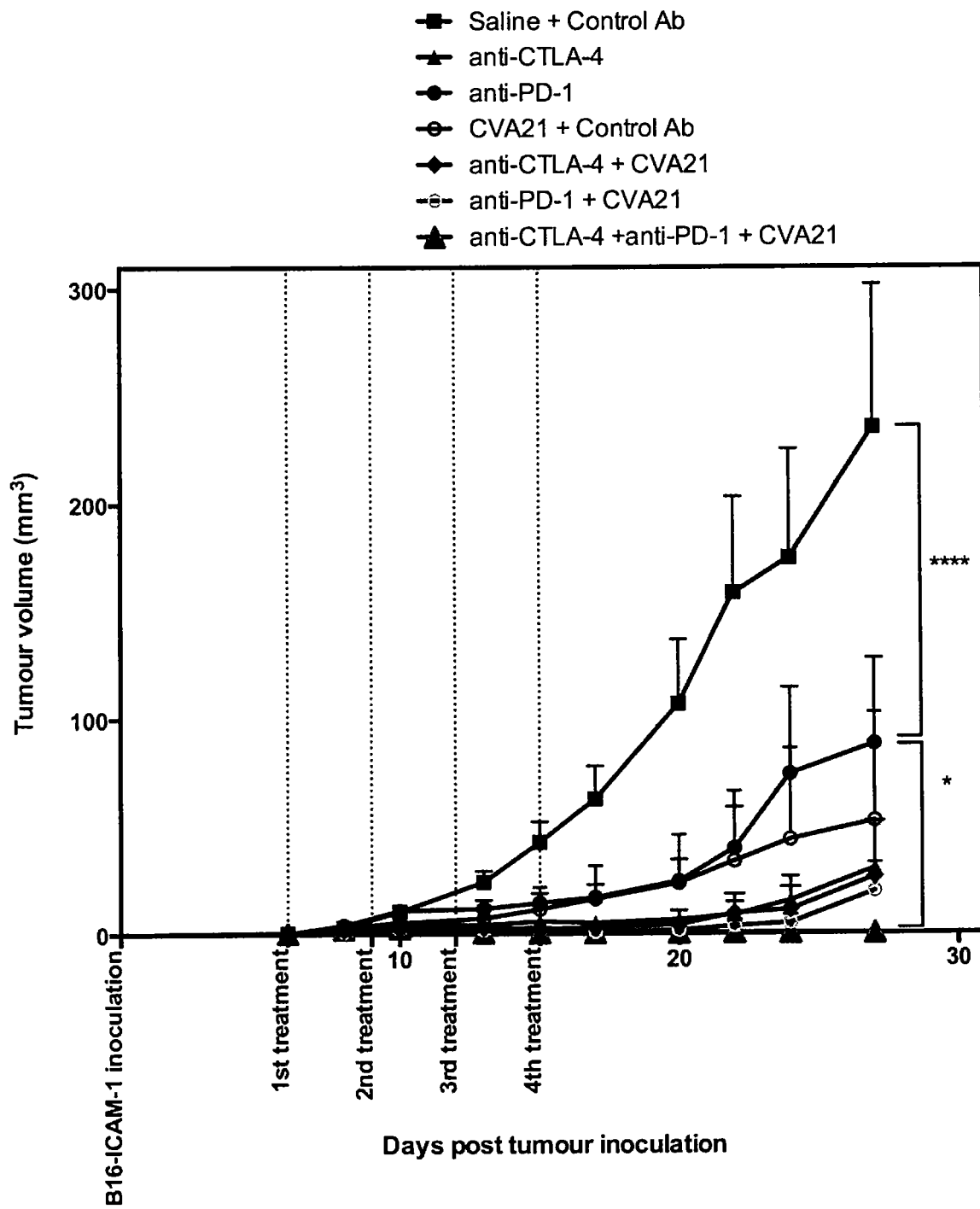


Figure 16C

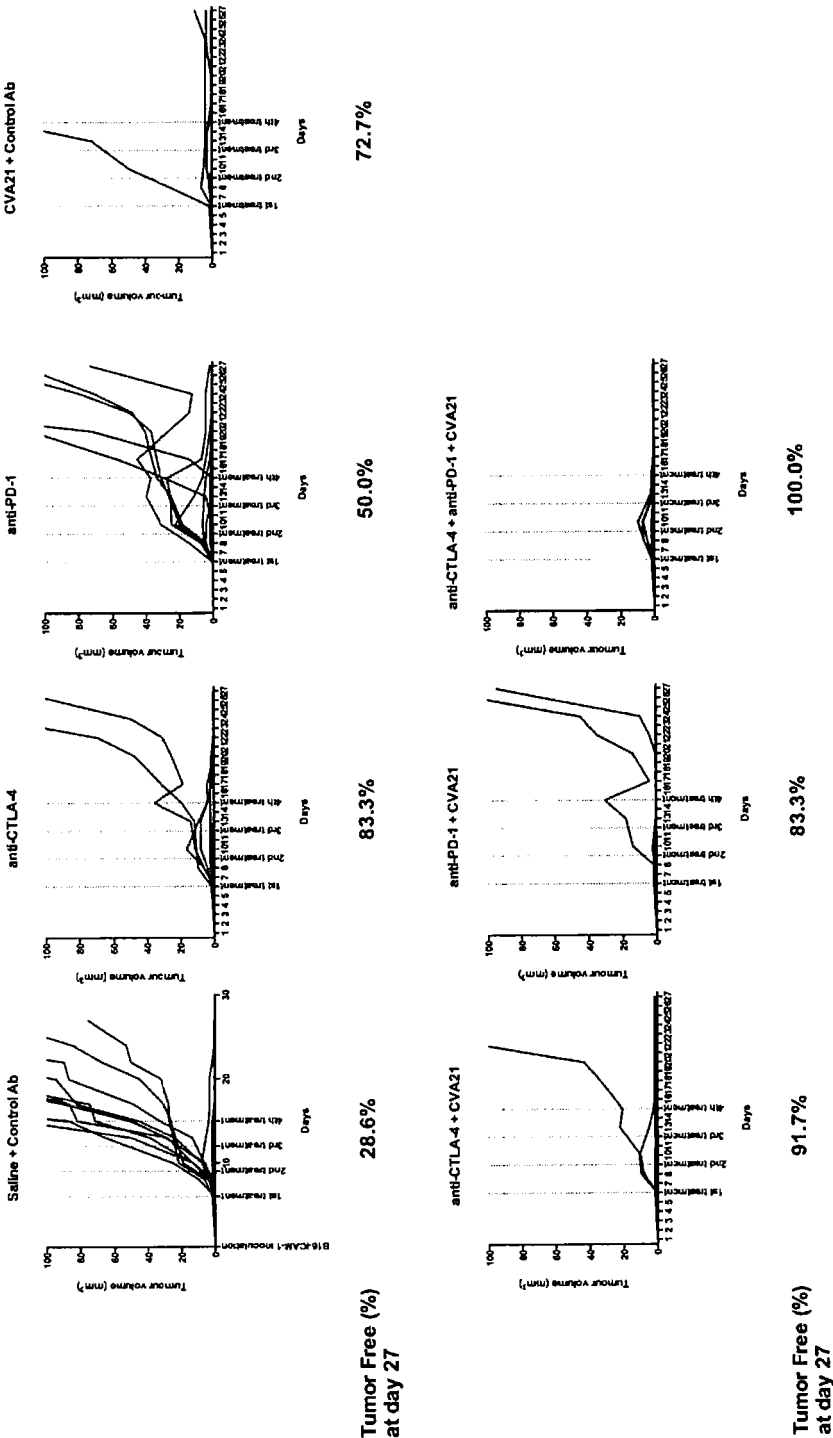
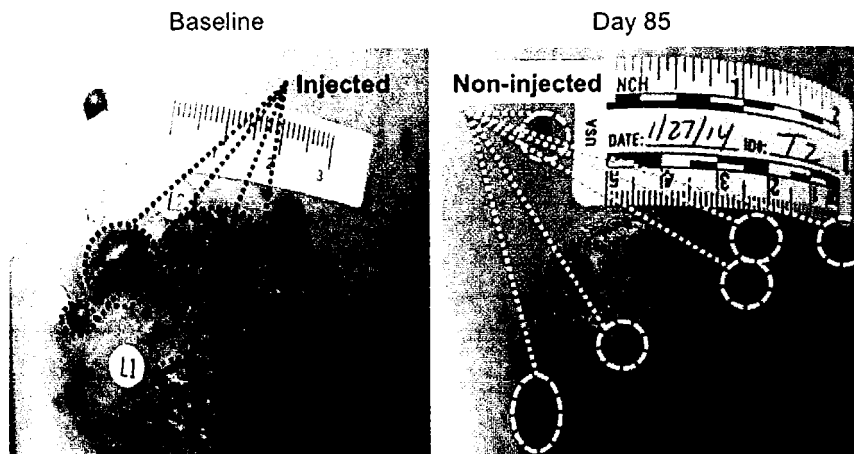


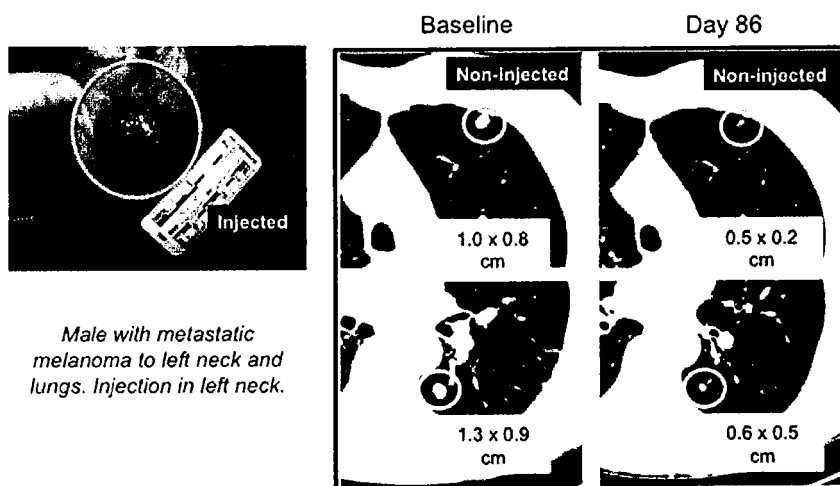
Figure 17

Pt 12-002: Local injected and non-injected lesion responses



Male with metastatic melanoma to the leg. Injection in leg lesions .

Pt 03-032: Non-injected distant visceral lesion response



Male with metastatic melanoma to left neck and lungs. Injection in left neck.

Figure 18

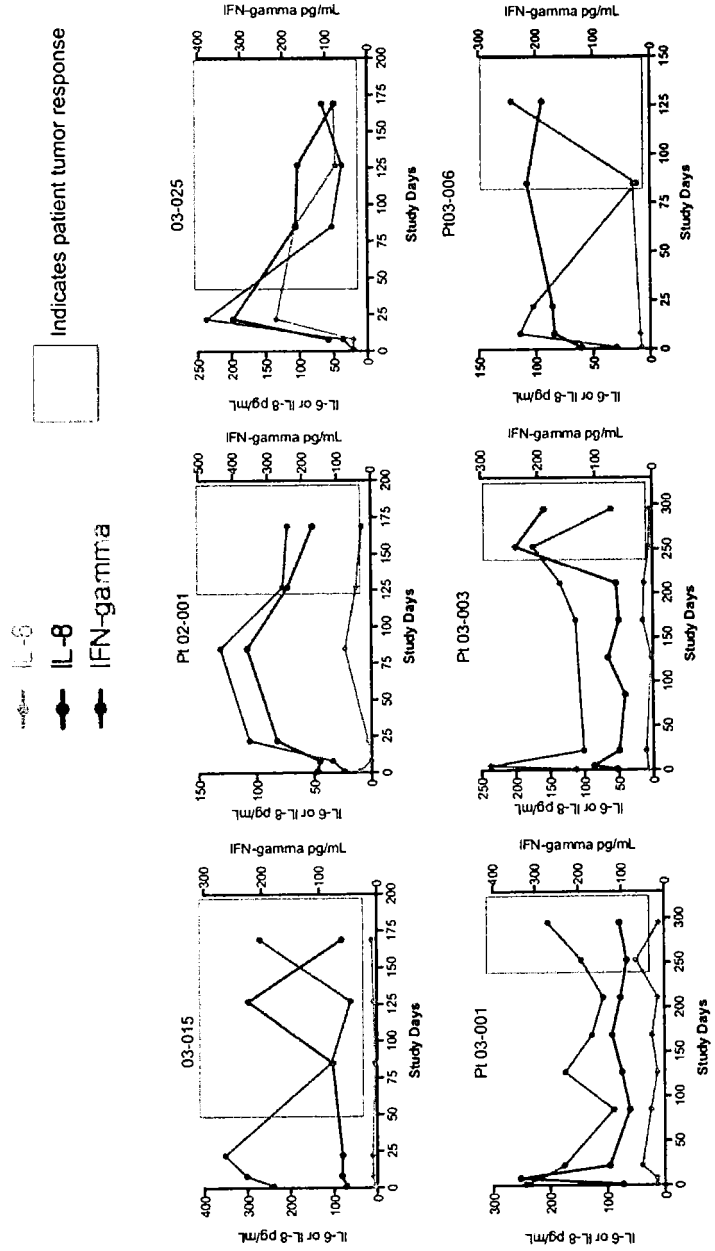


Figure 19

Tumor gene profiling
(HumanREF8 v2 expression bead chips, illumina)

