

Figure 1

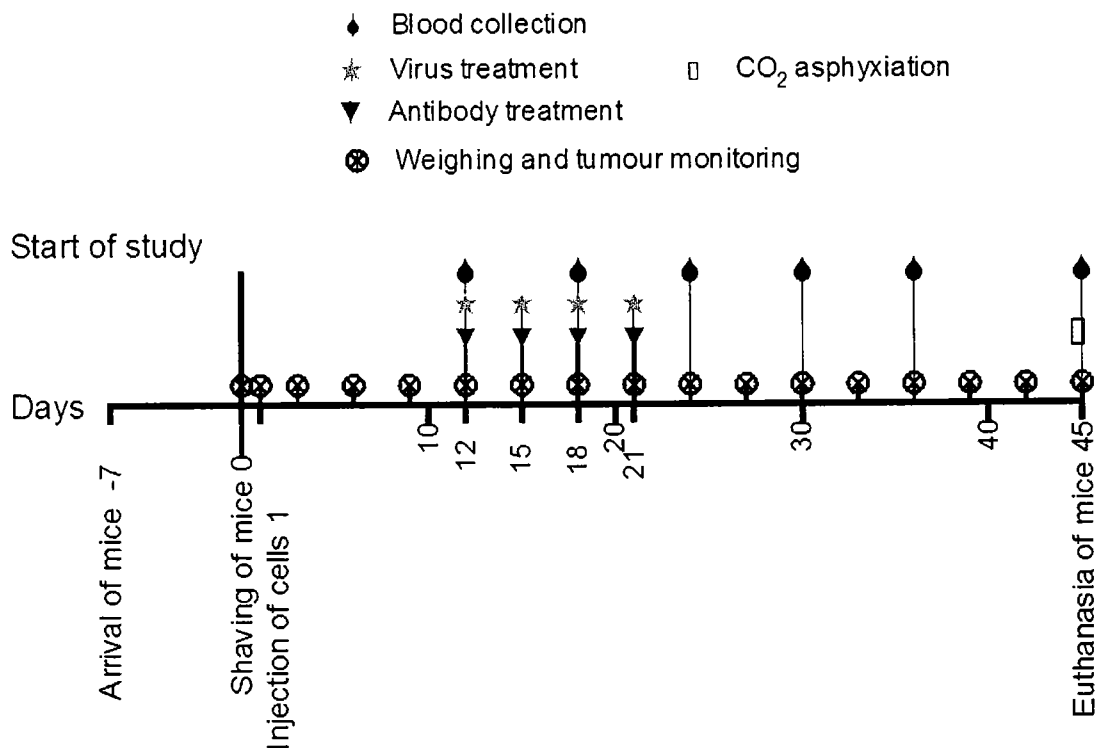
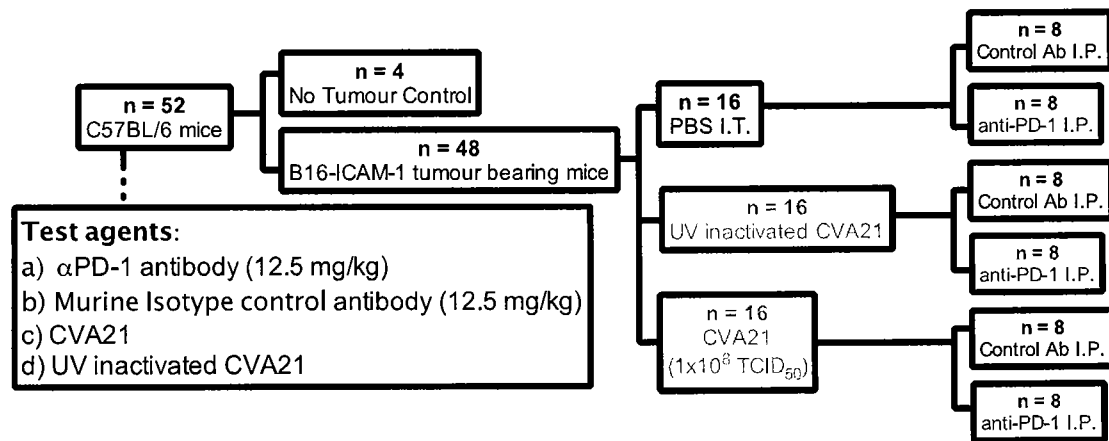


Figure 2

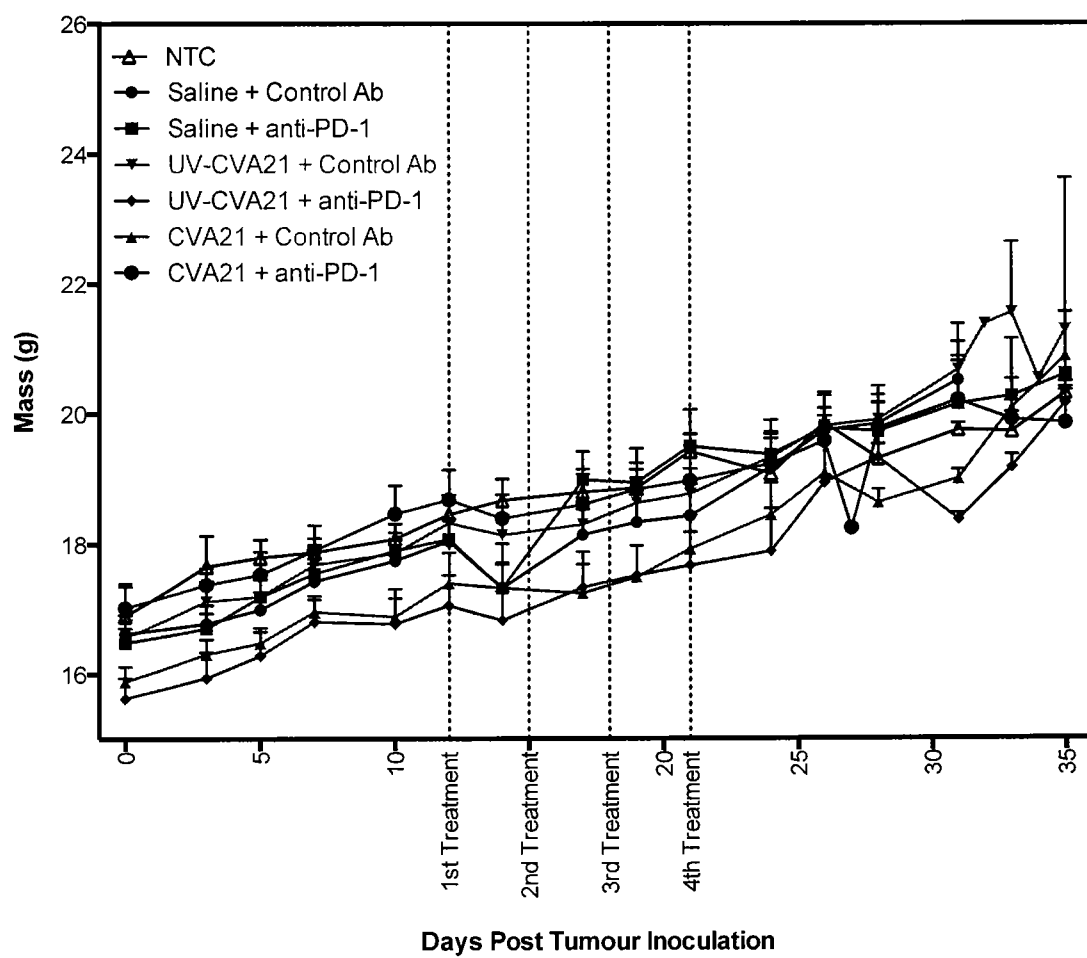


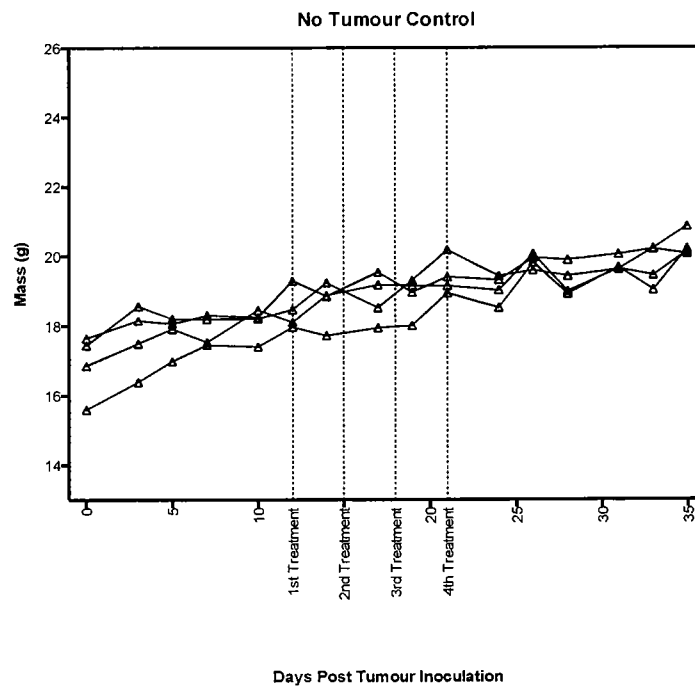
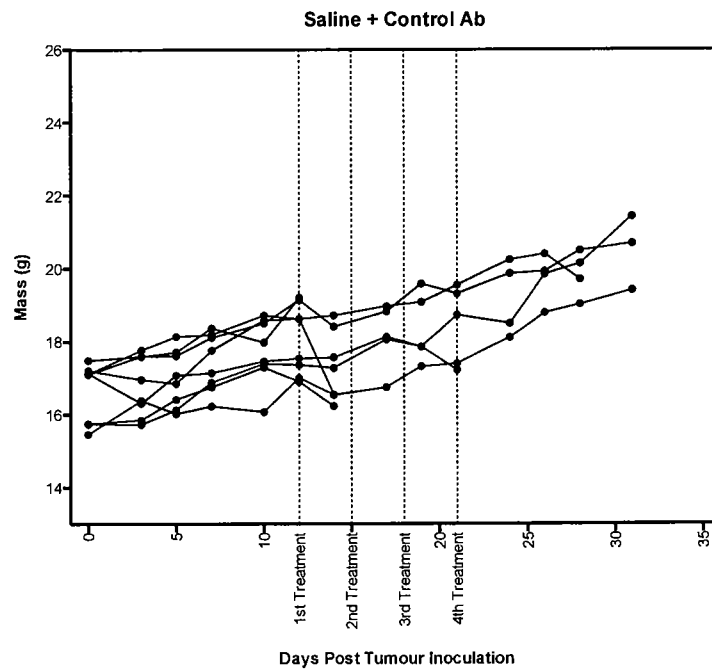
Figure 3**(A)****(B)**

Fig. 3C)

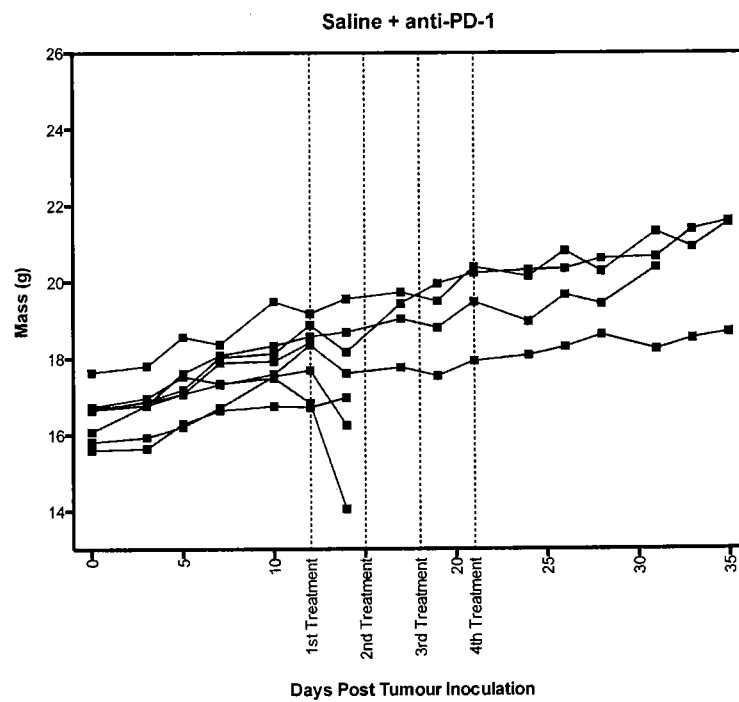


Fig.3D)

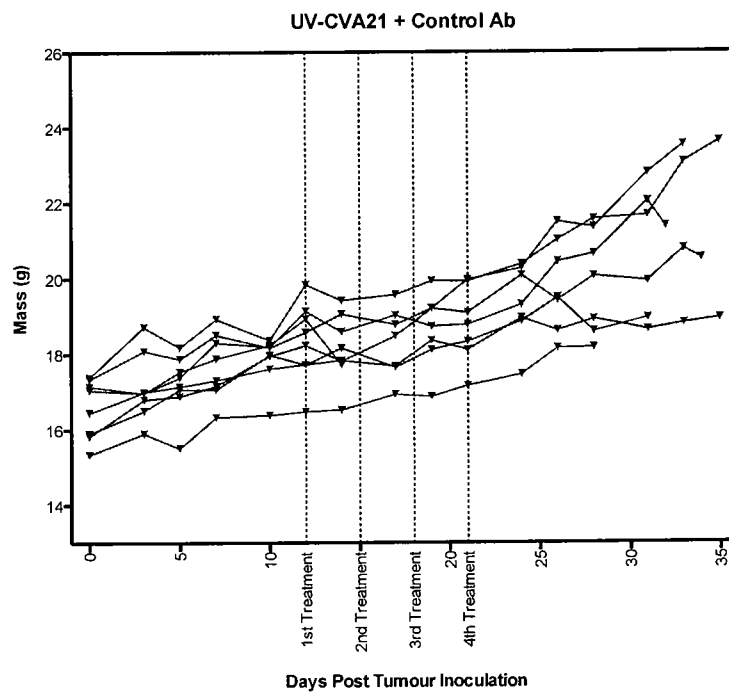


Fig. 3E)

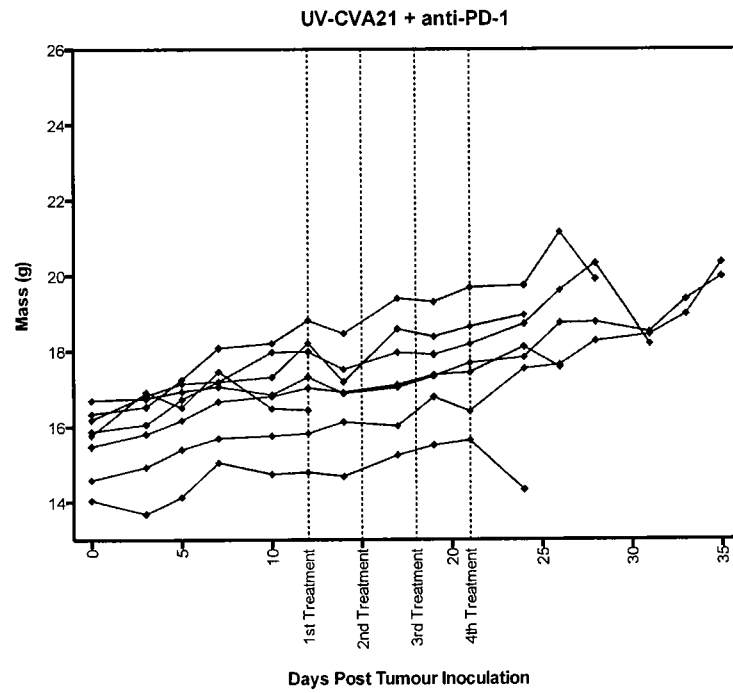


Fig. 3F)

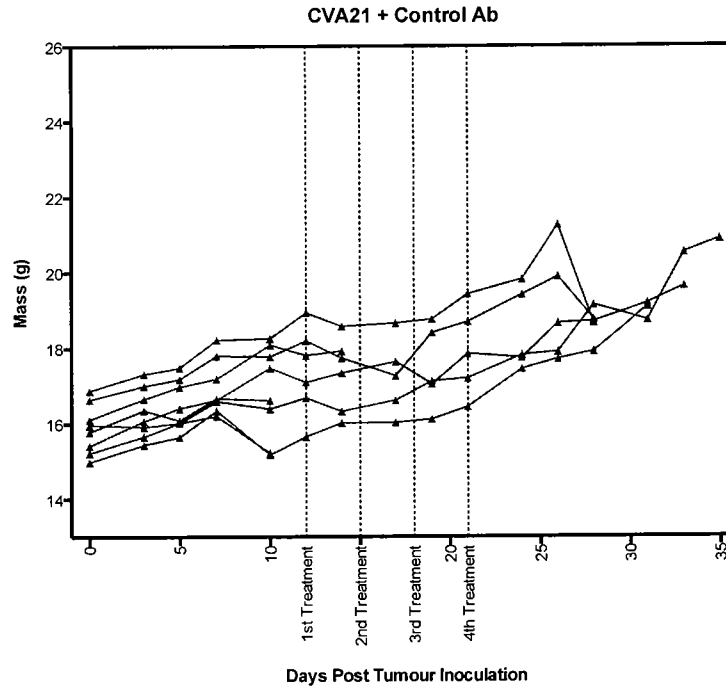


Fig 3G)

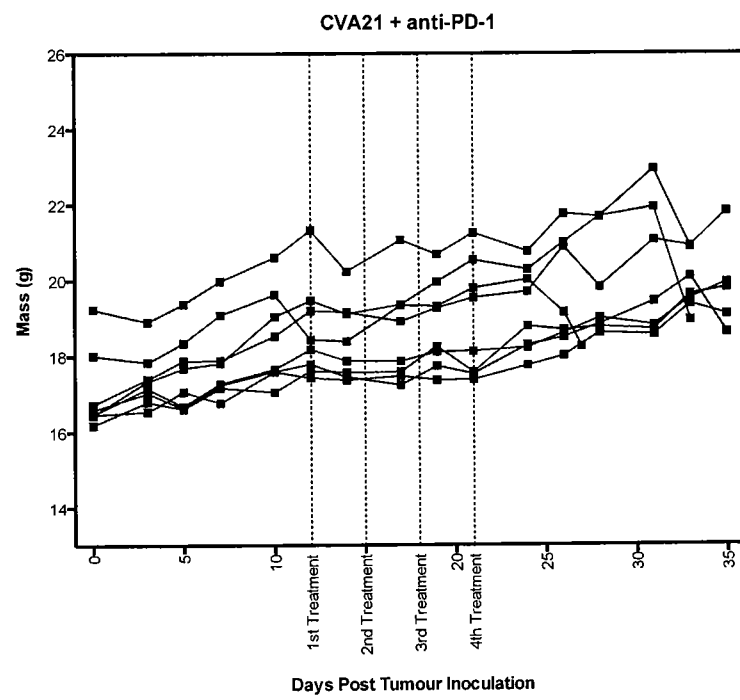


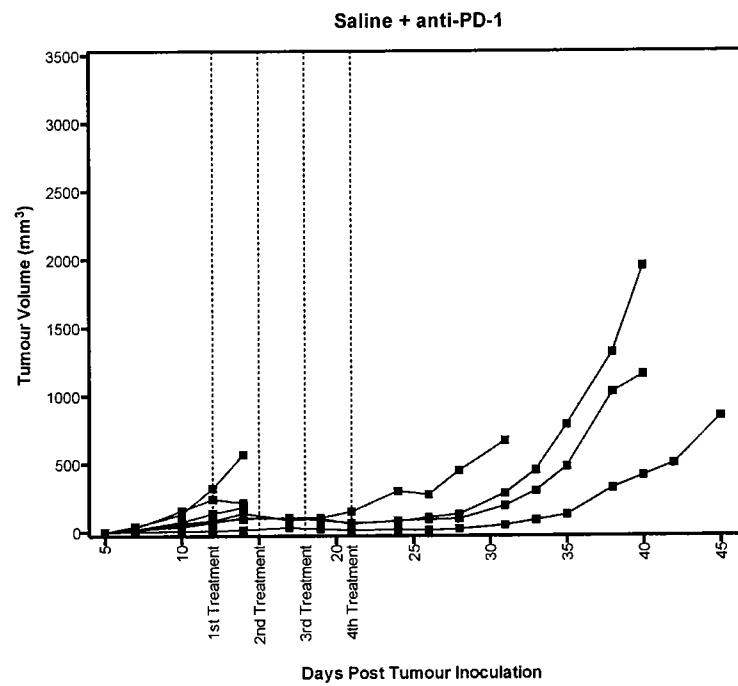
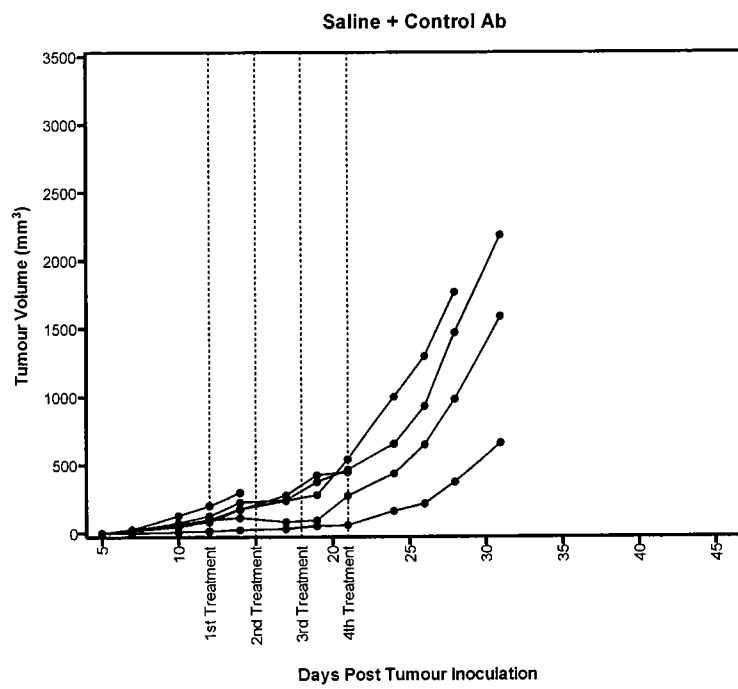
Figure 4

Fig. 4 (ctd)

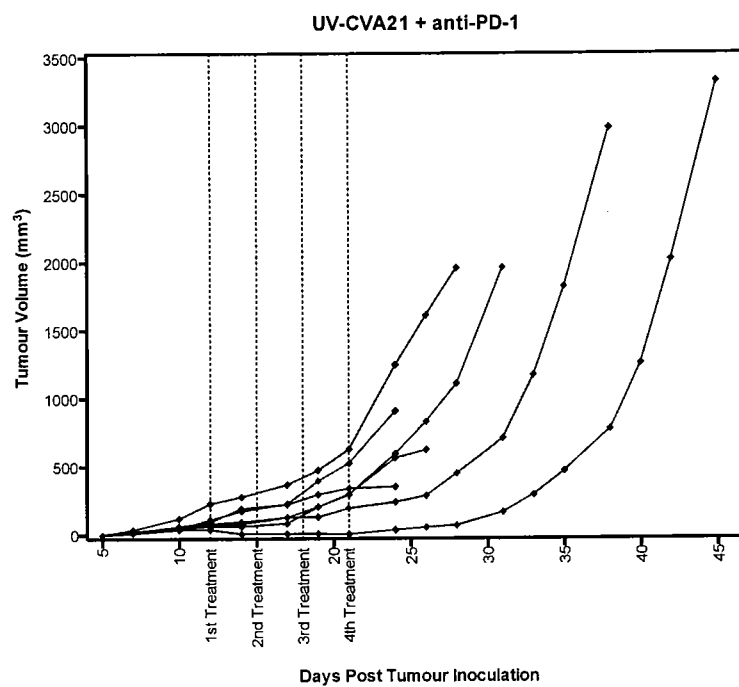
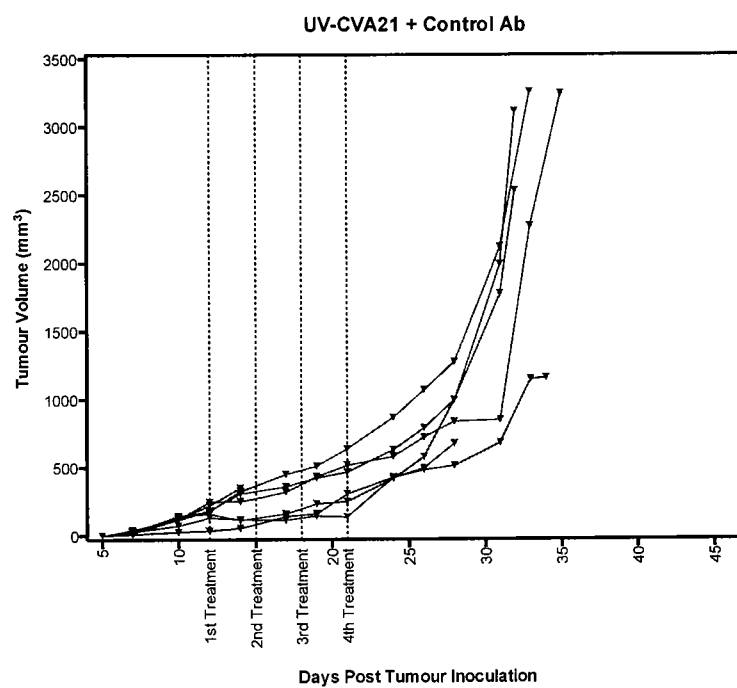


Fig. 4 (ctd)

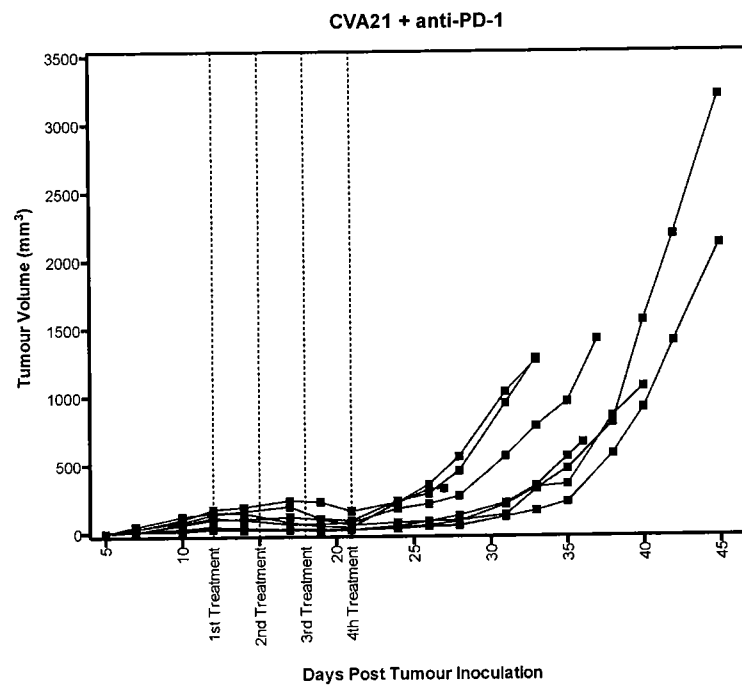
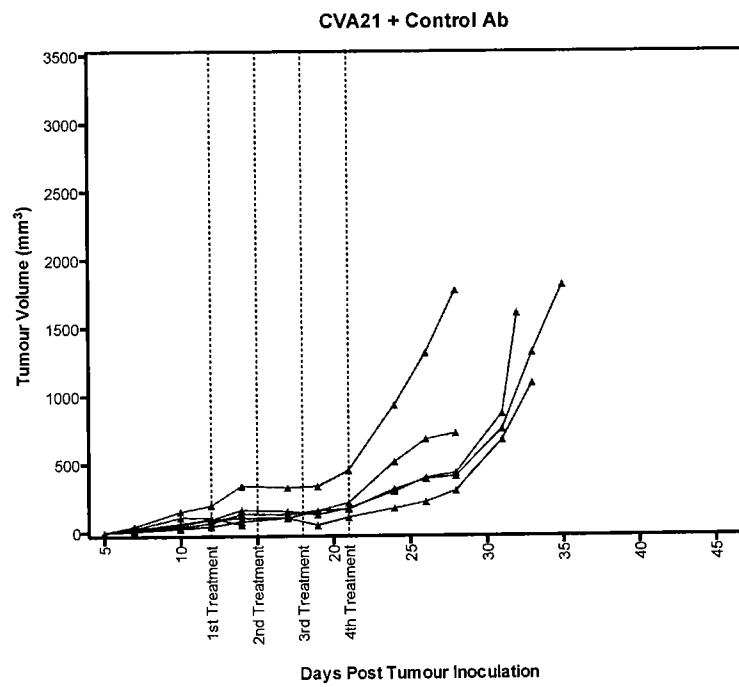
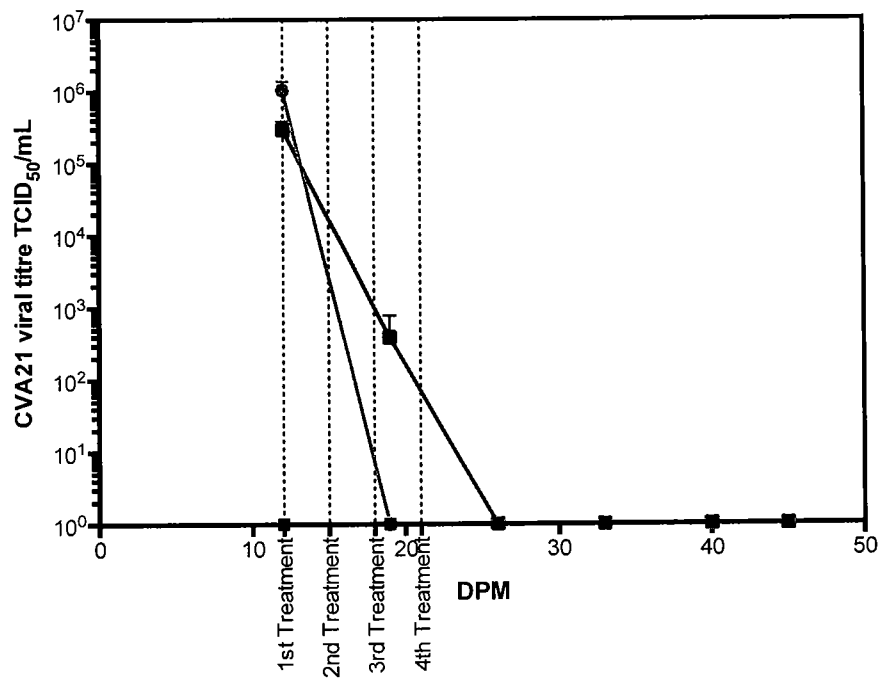
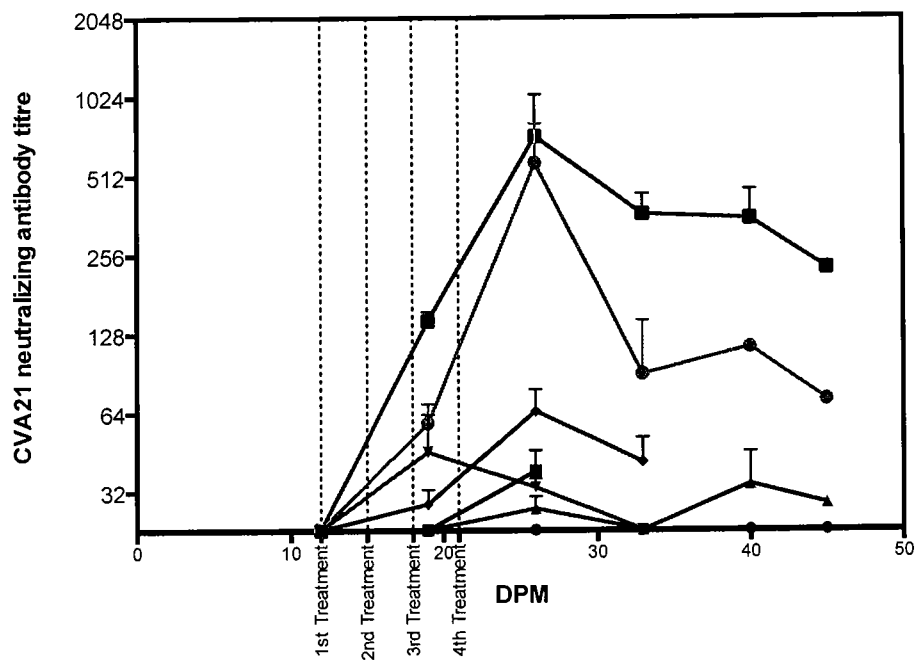


Figure 5

(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

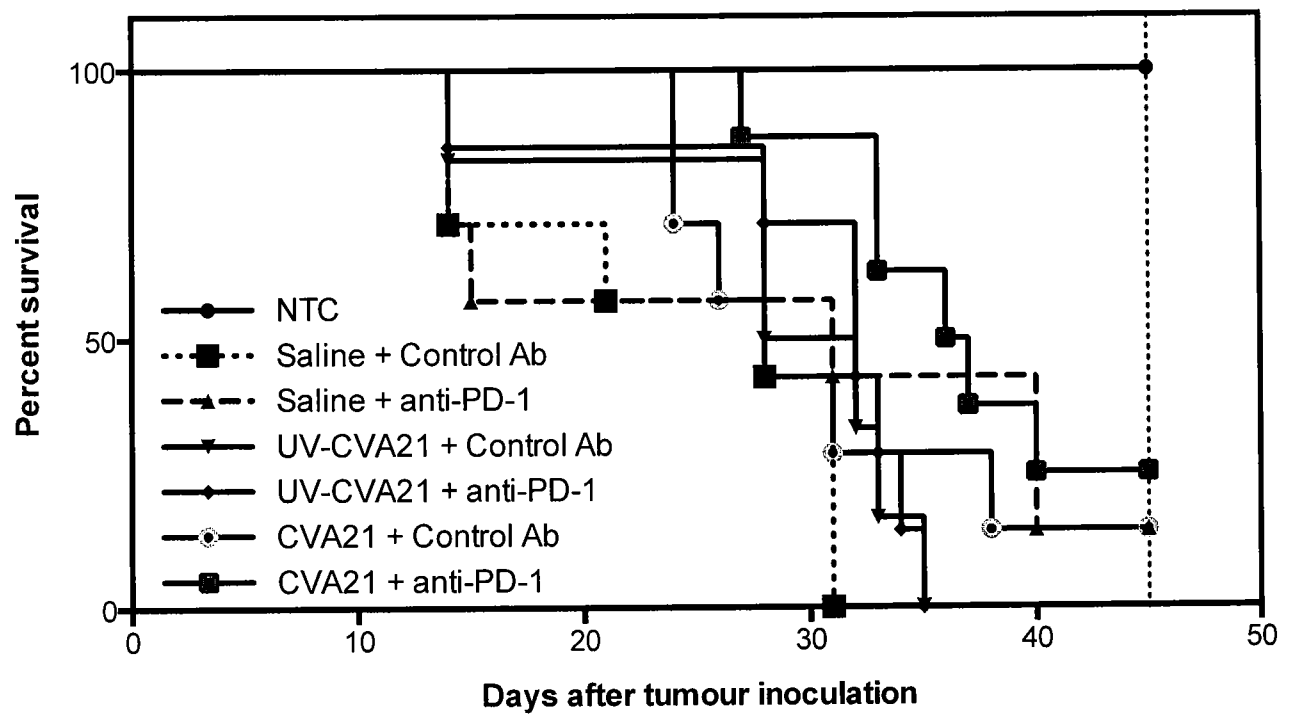
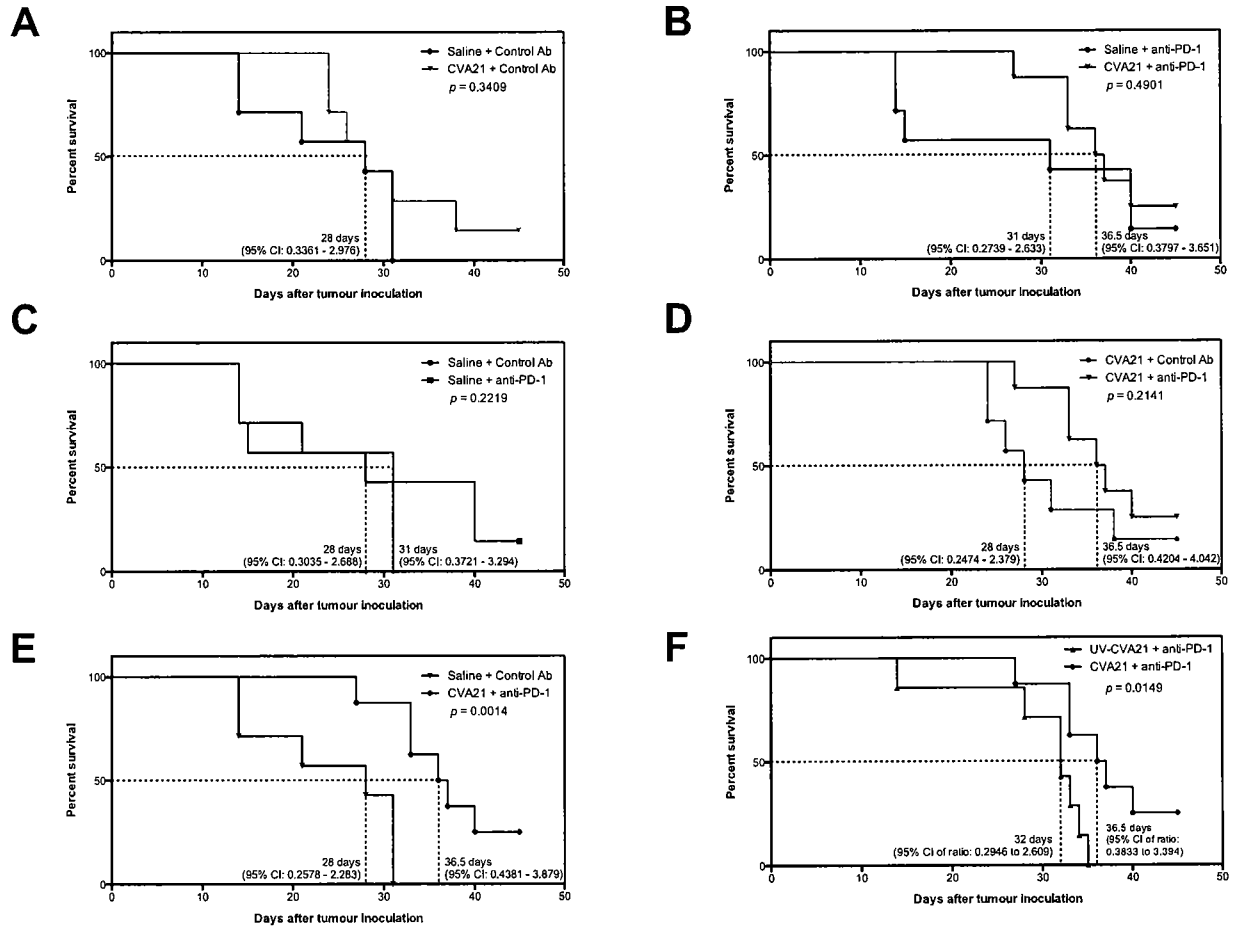


Figure 7



	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 CVA21 + Control Ab			Group 7 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

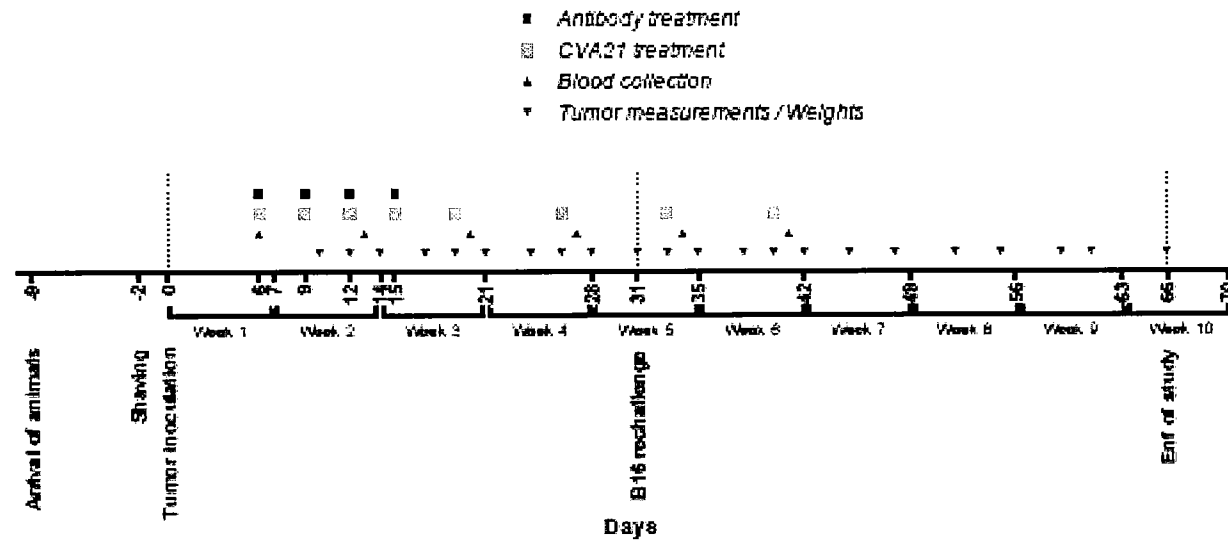


Figure 9

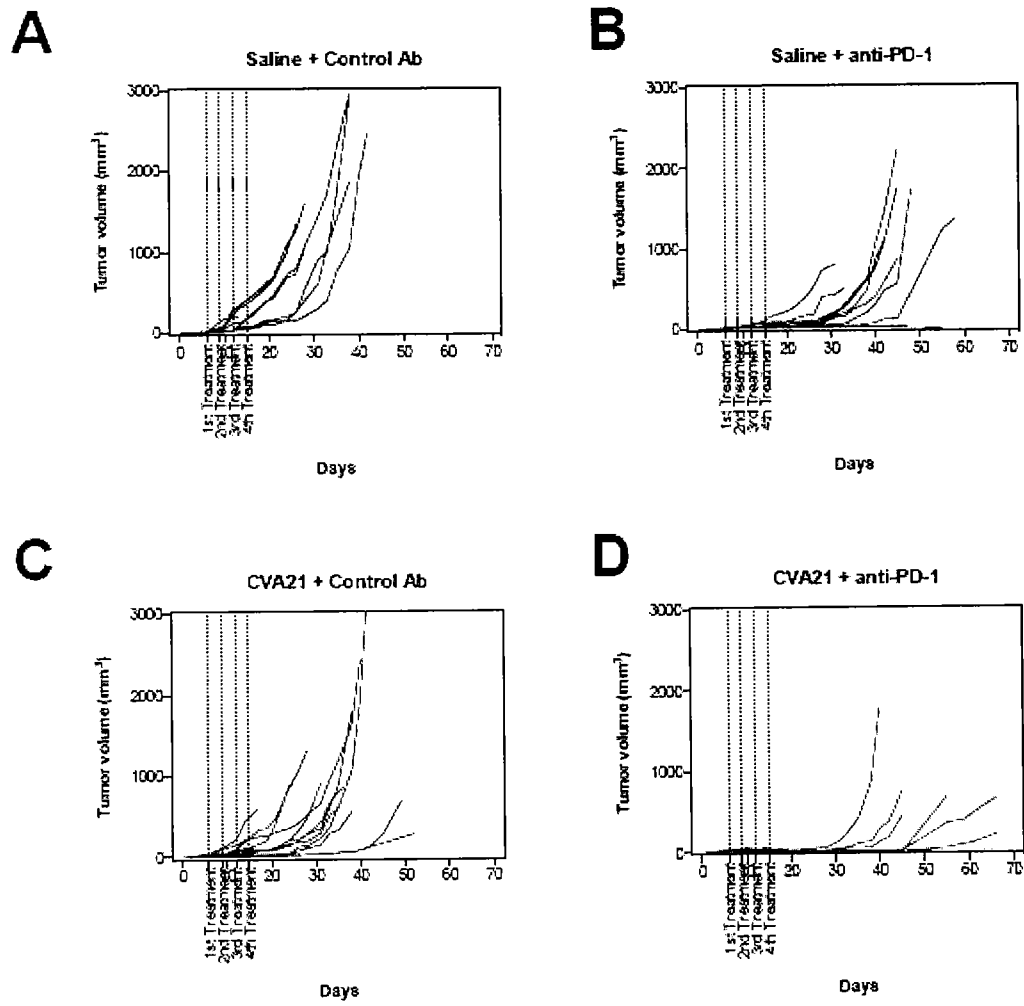


Figure 10

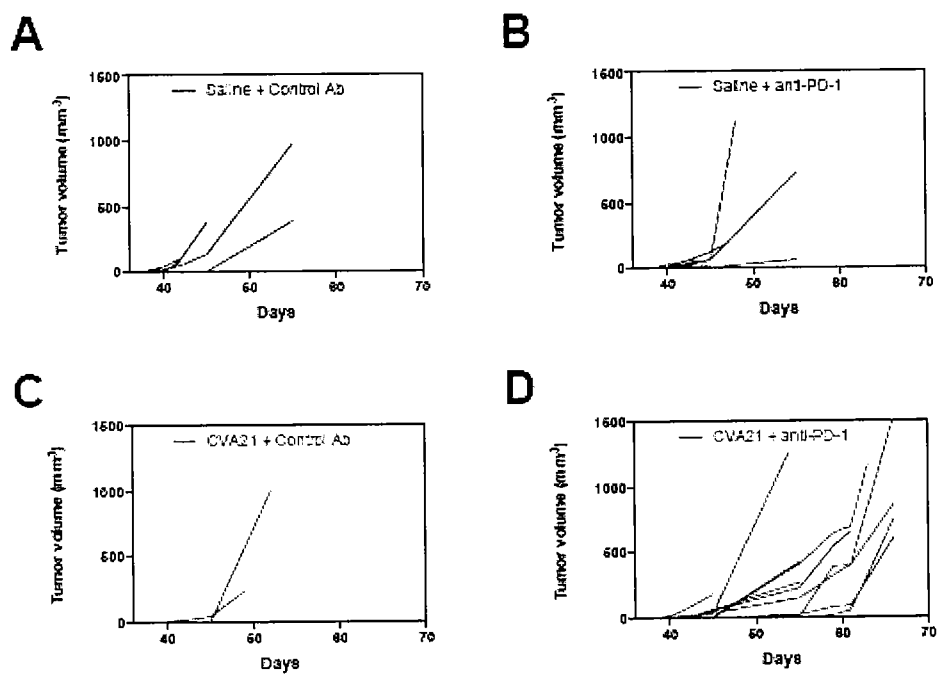


Figure 11

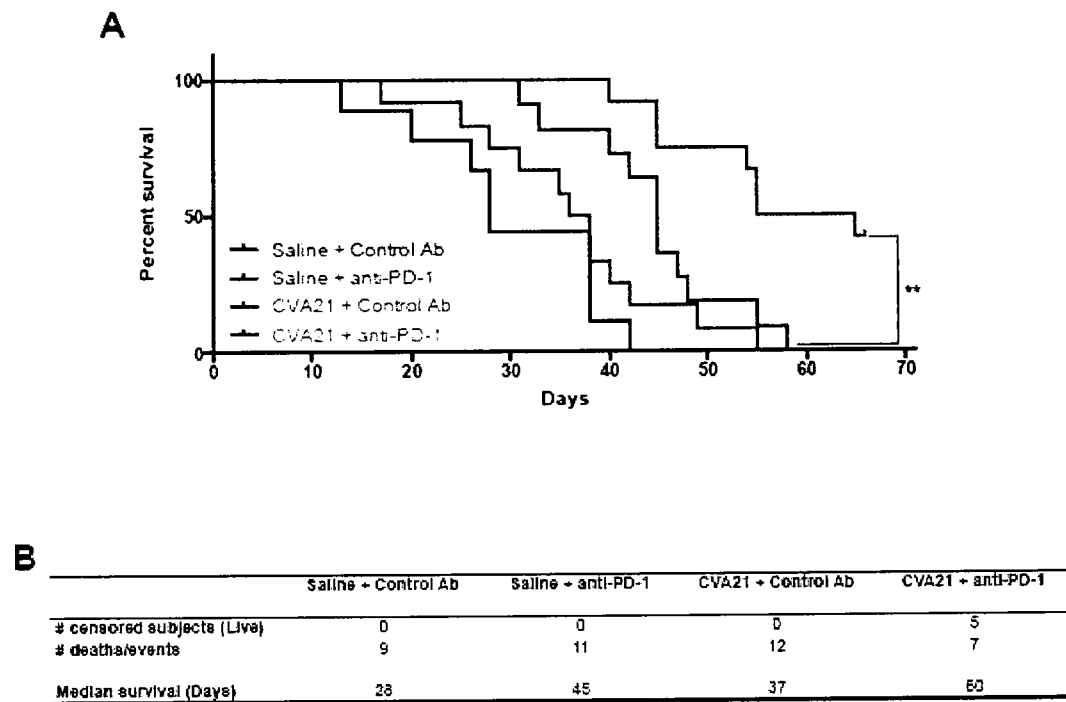


Figure 12

Timeline of Study

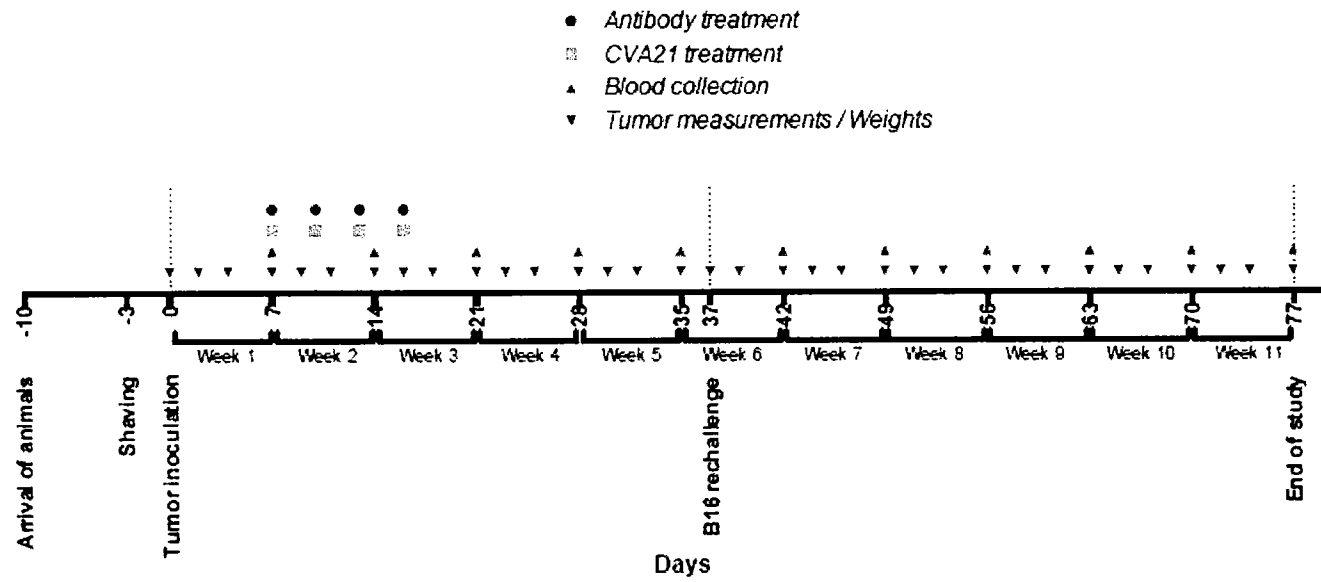


Figure 13

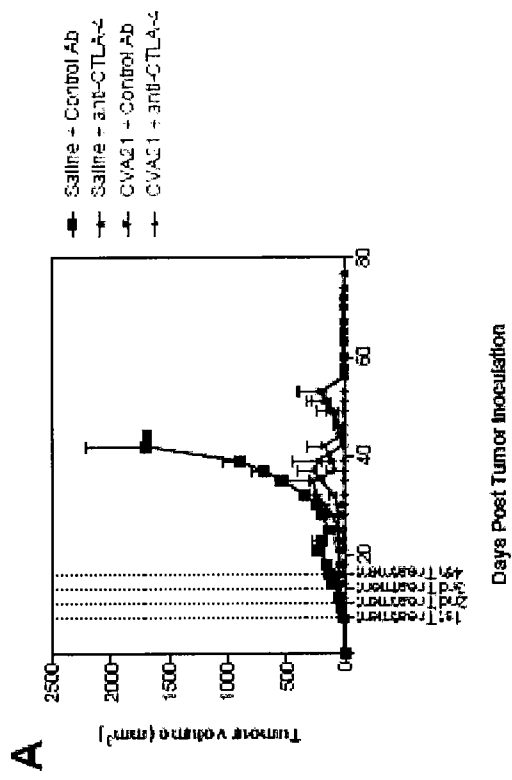


Figure 13 (ctd)

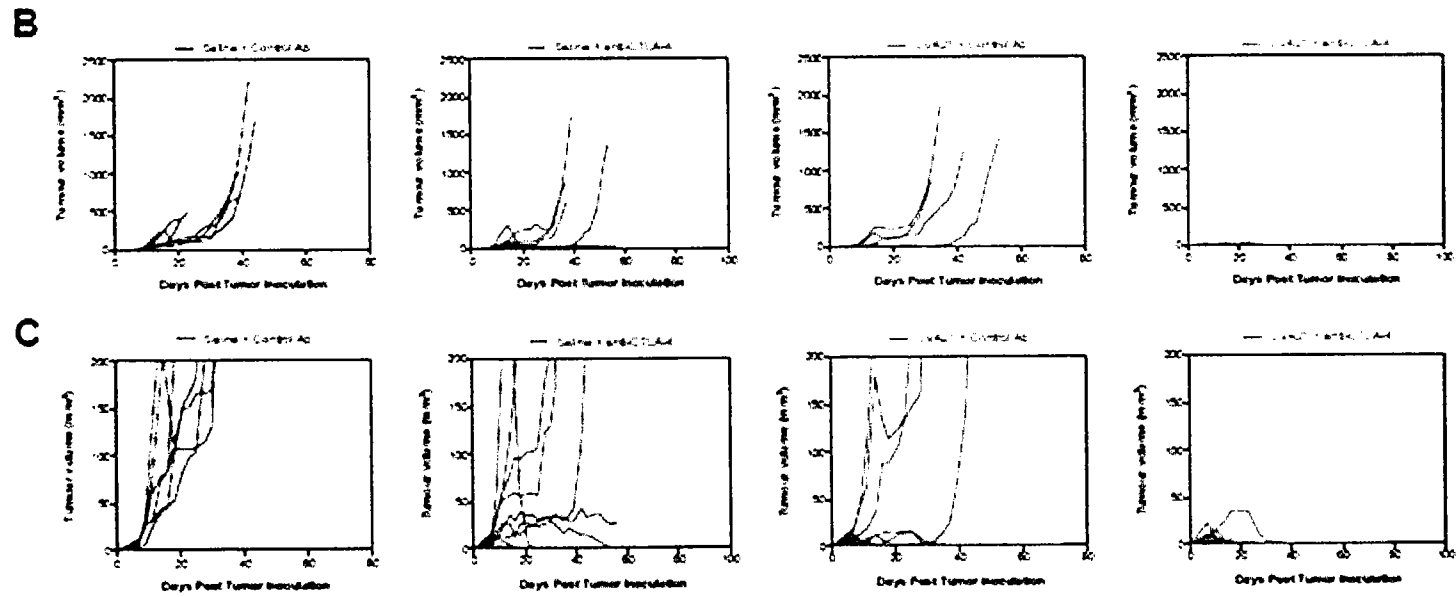
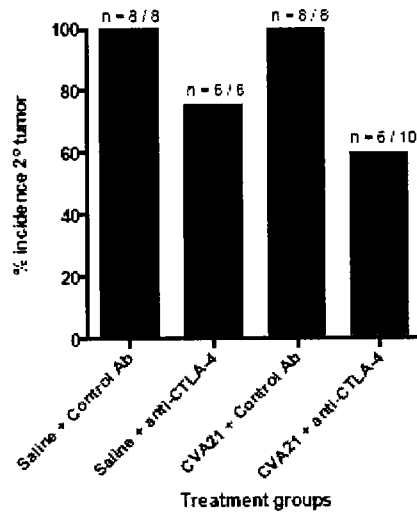
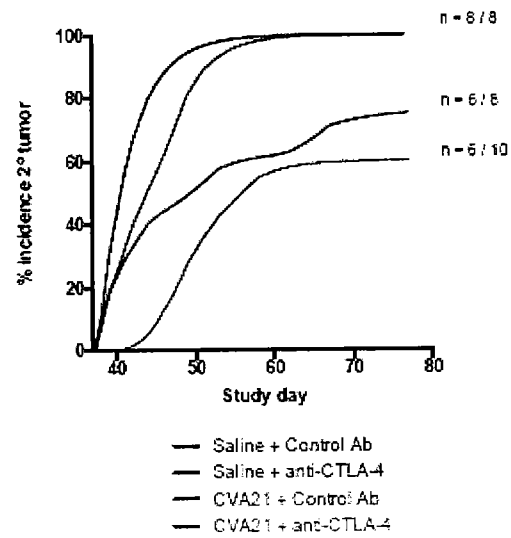


Figure 14

A



B



C

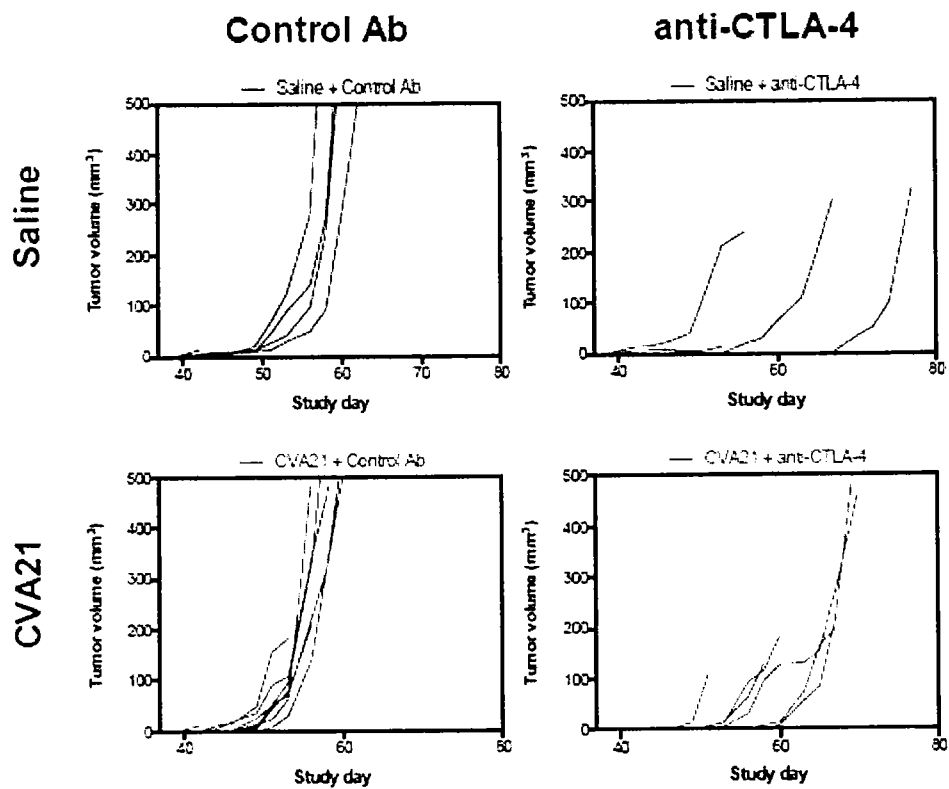
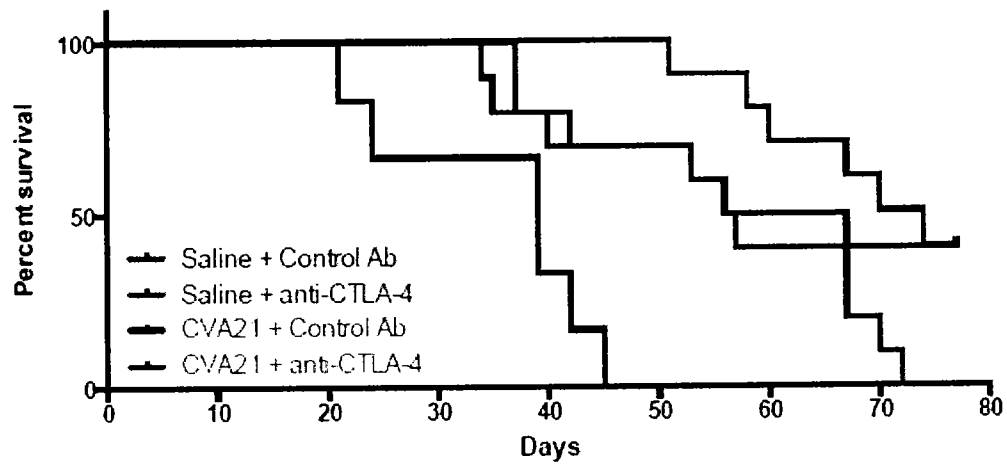


Figure 15

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

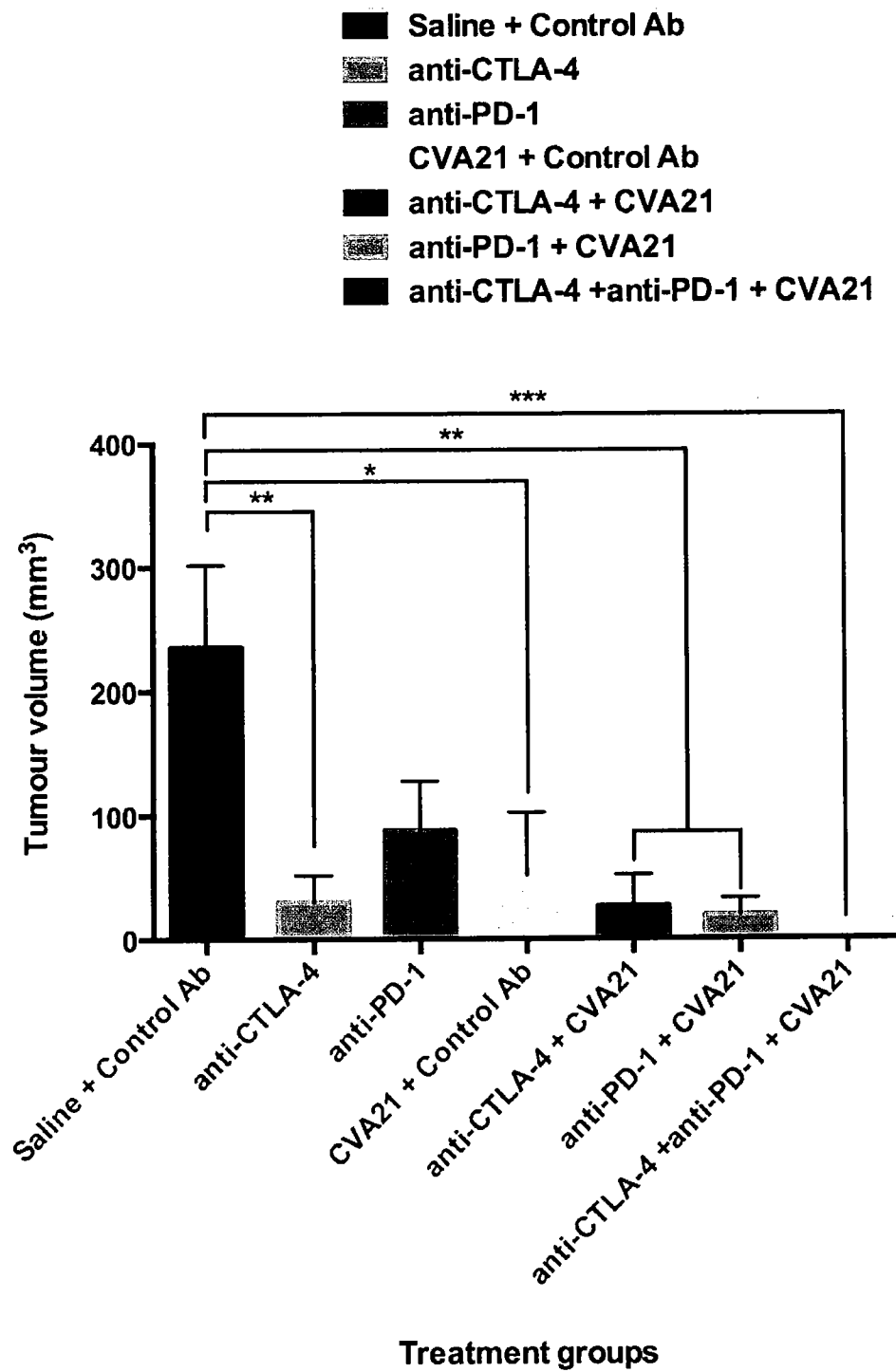


Figure 16B

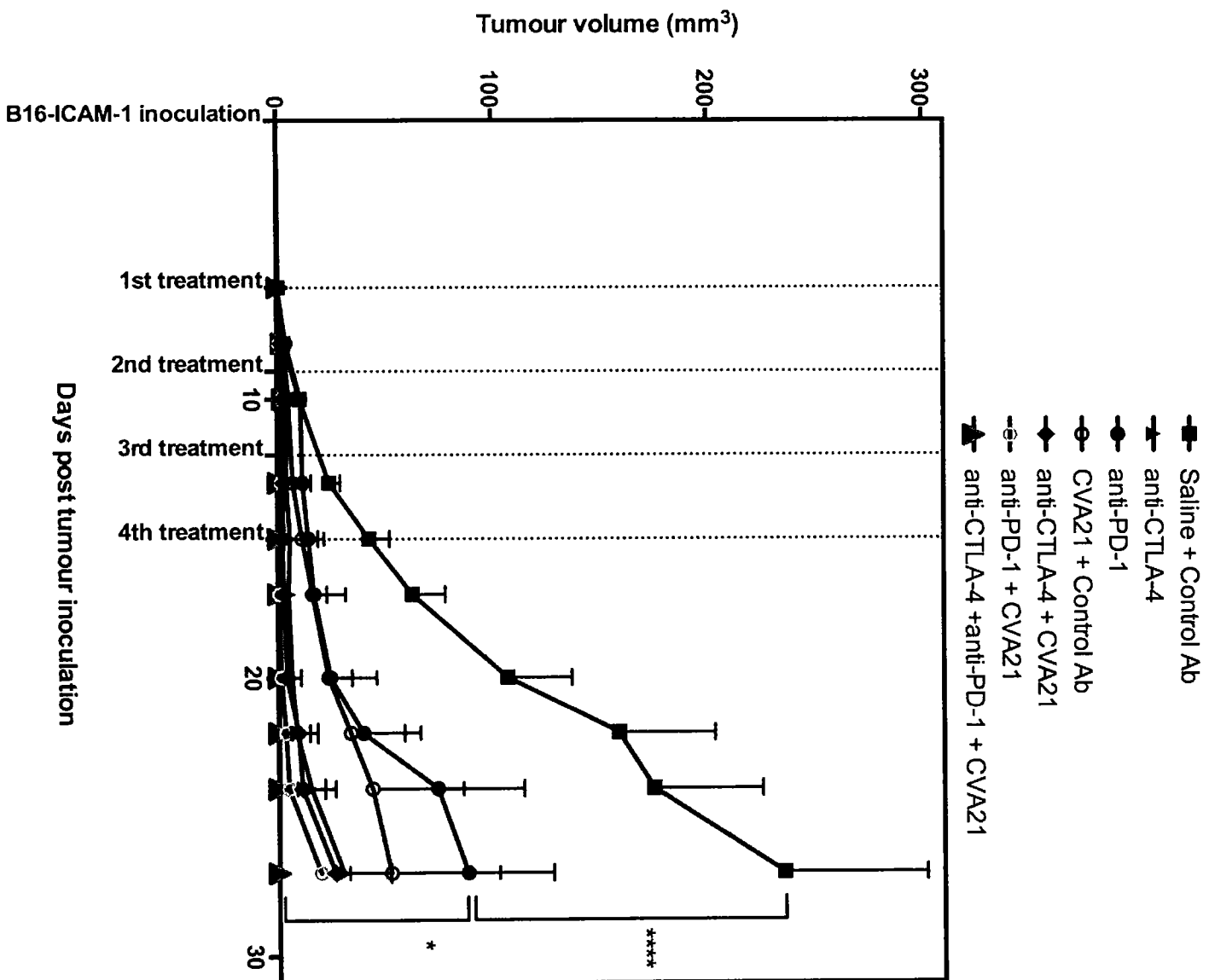


Figure 16C

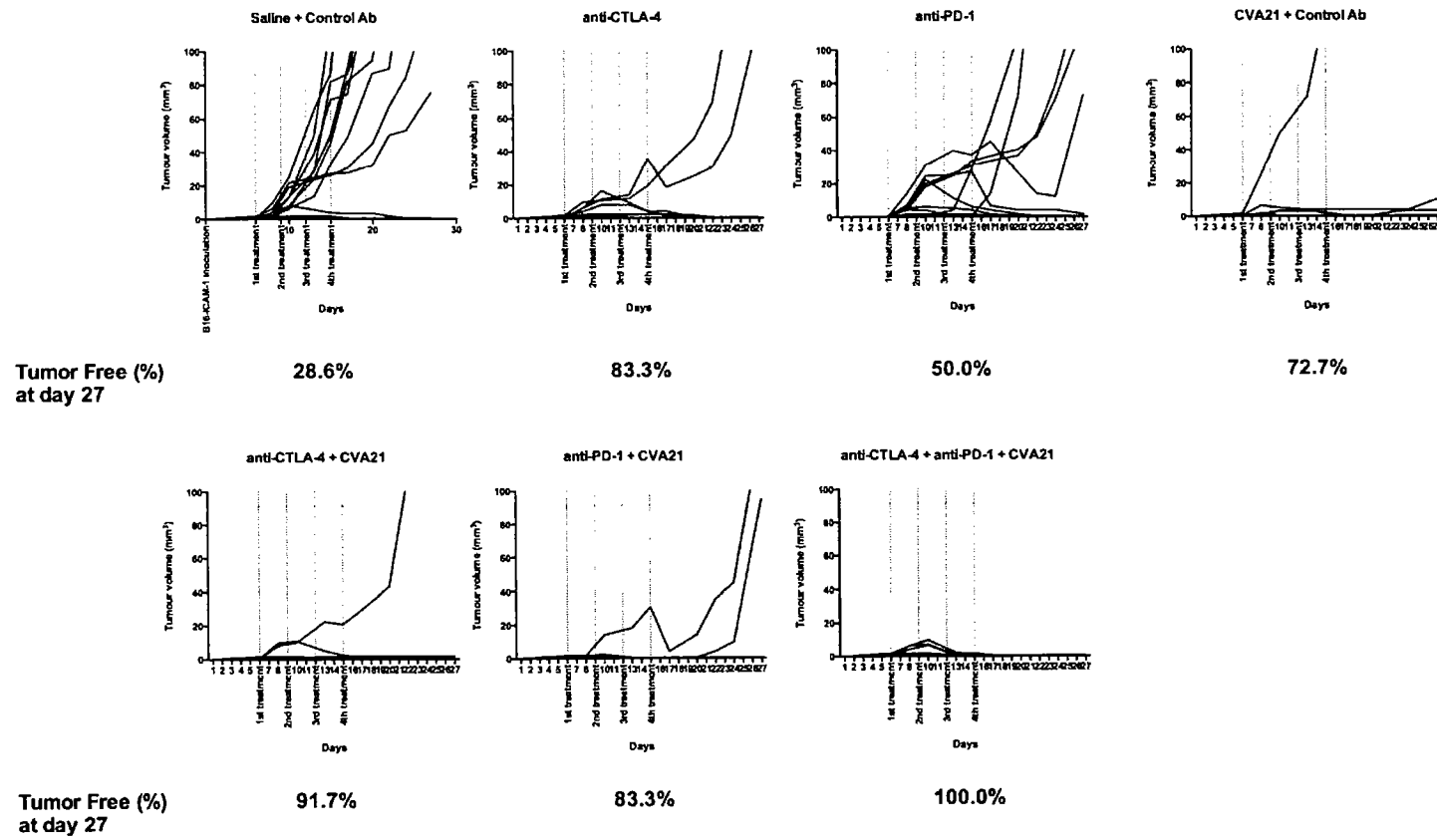
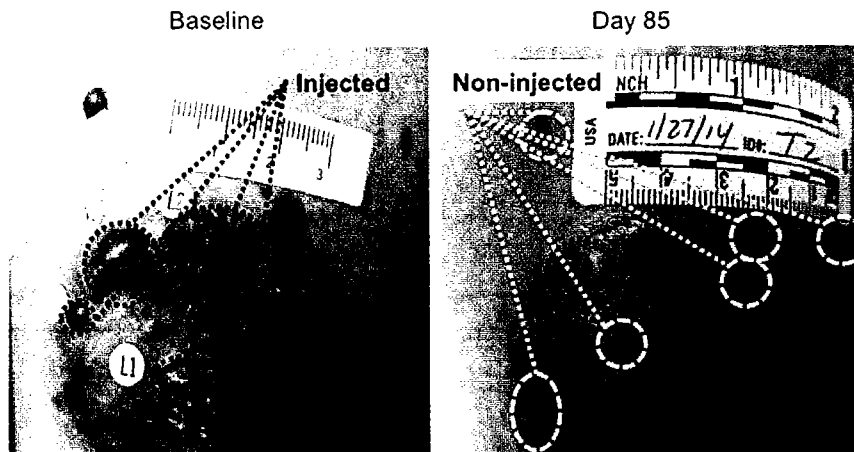


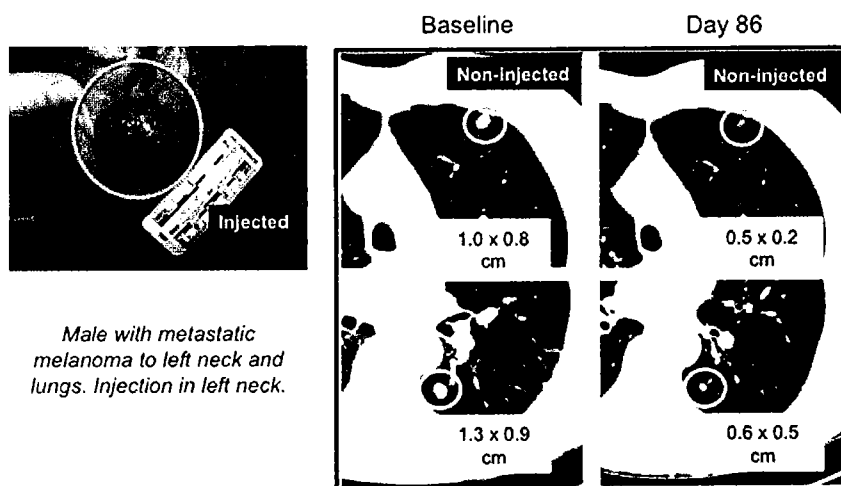
Figure 17

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

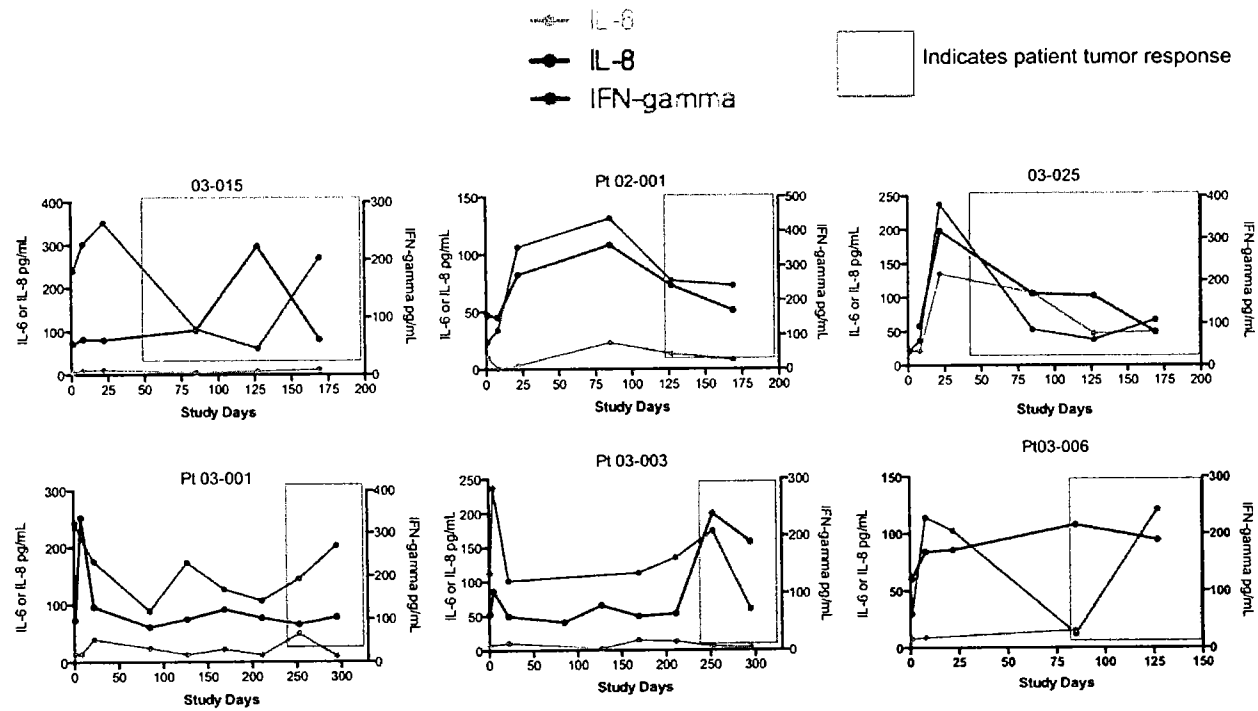


Figure 19

Tumor gene profiling

(HumanREF-8 v2 expression bead chips, illumina)

