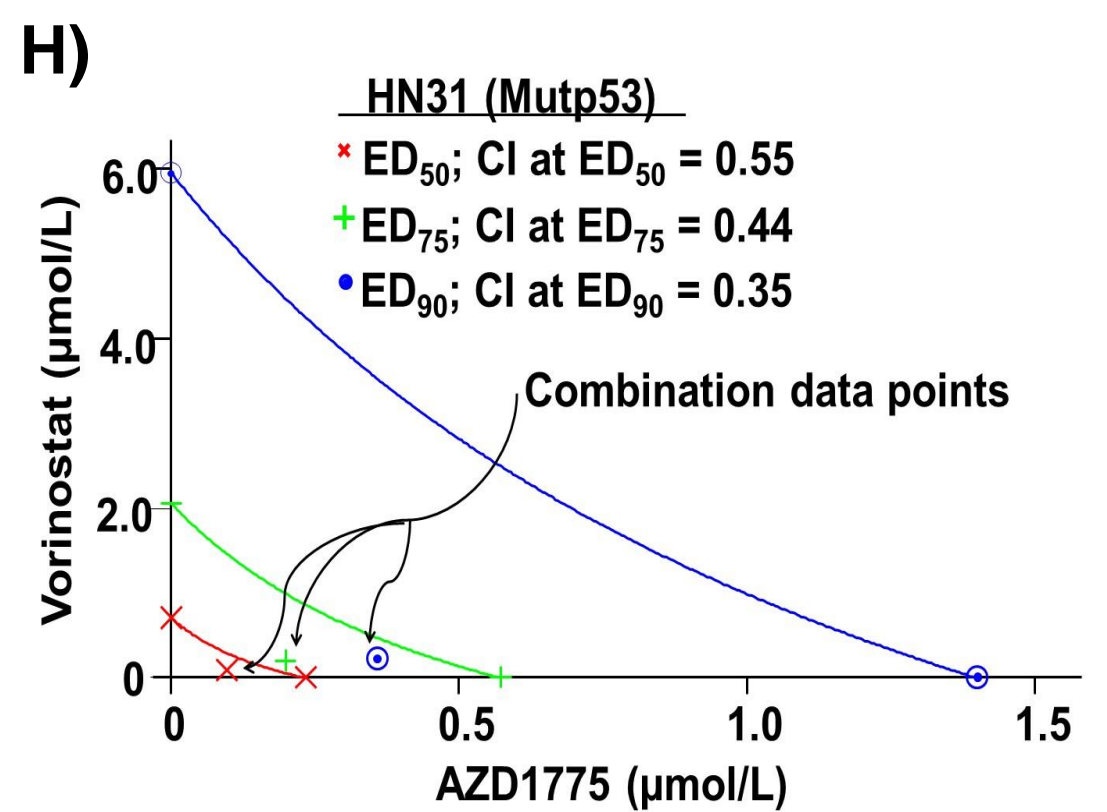
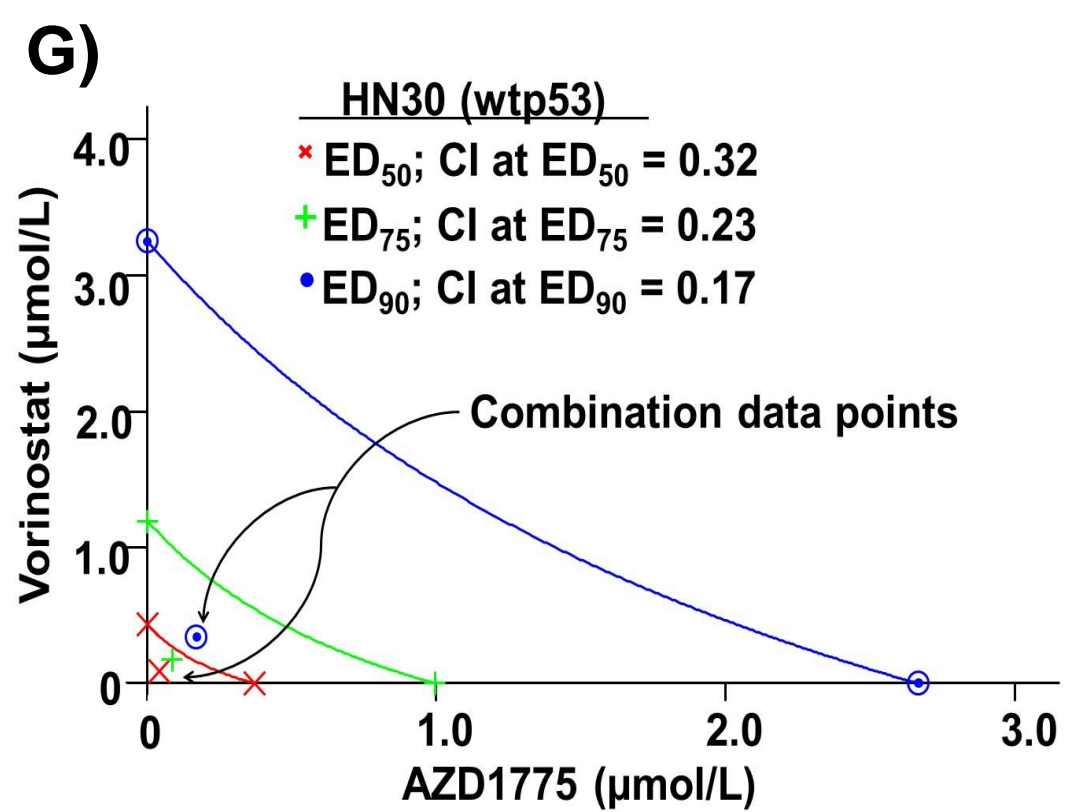
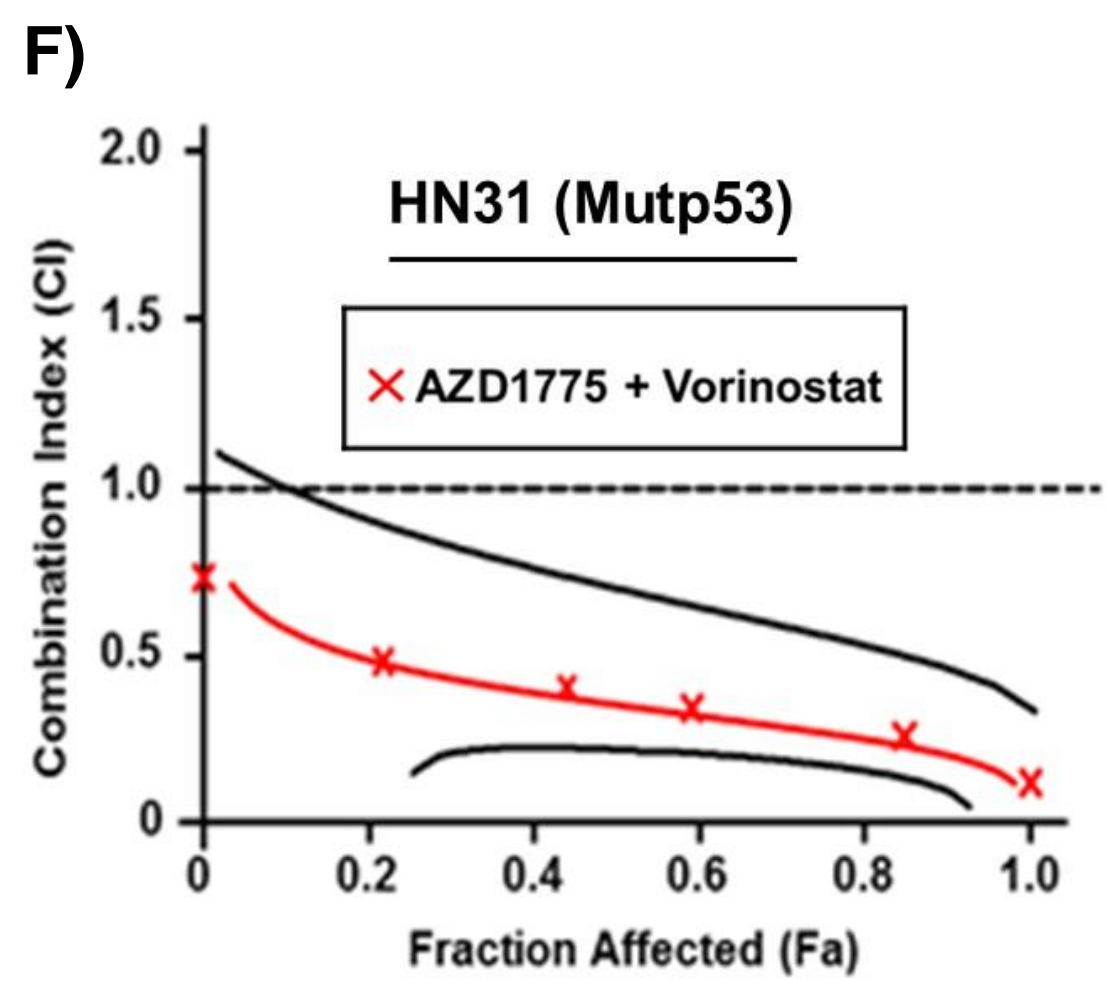
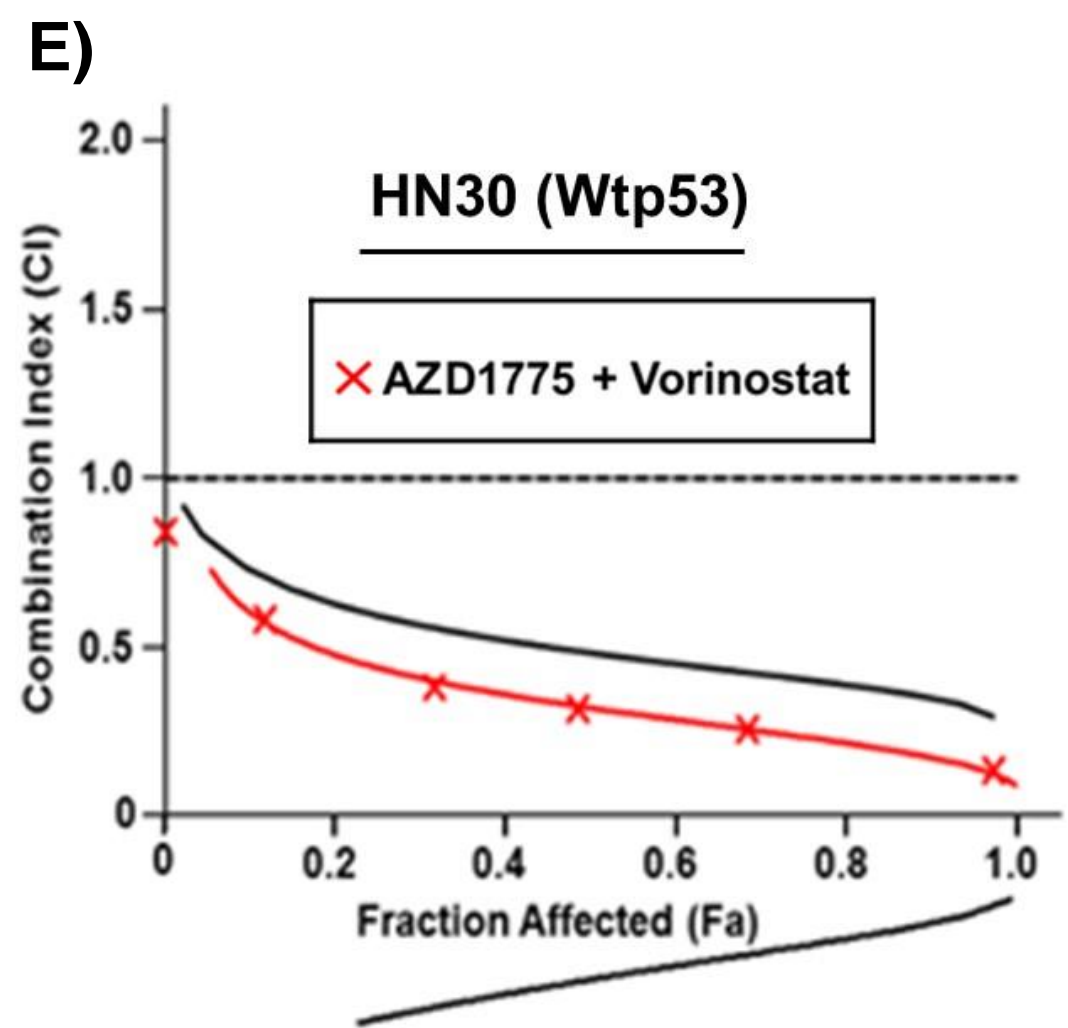
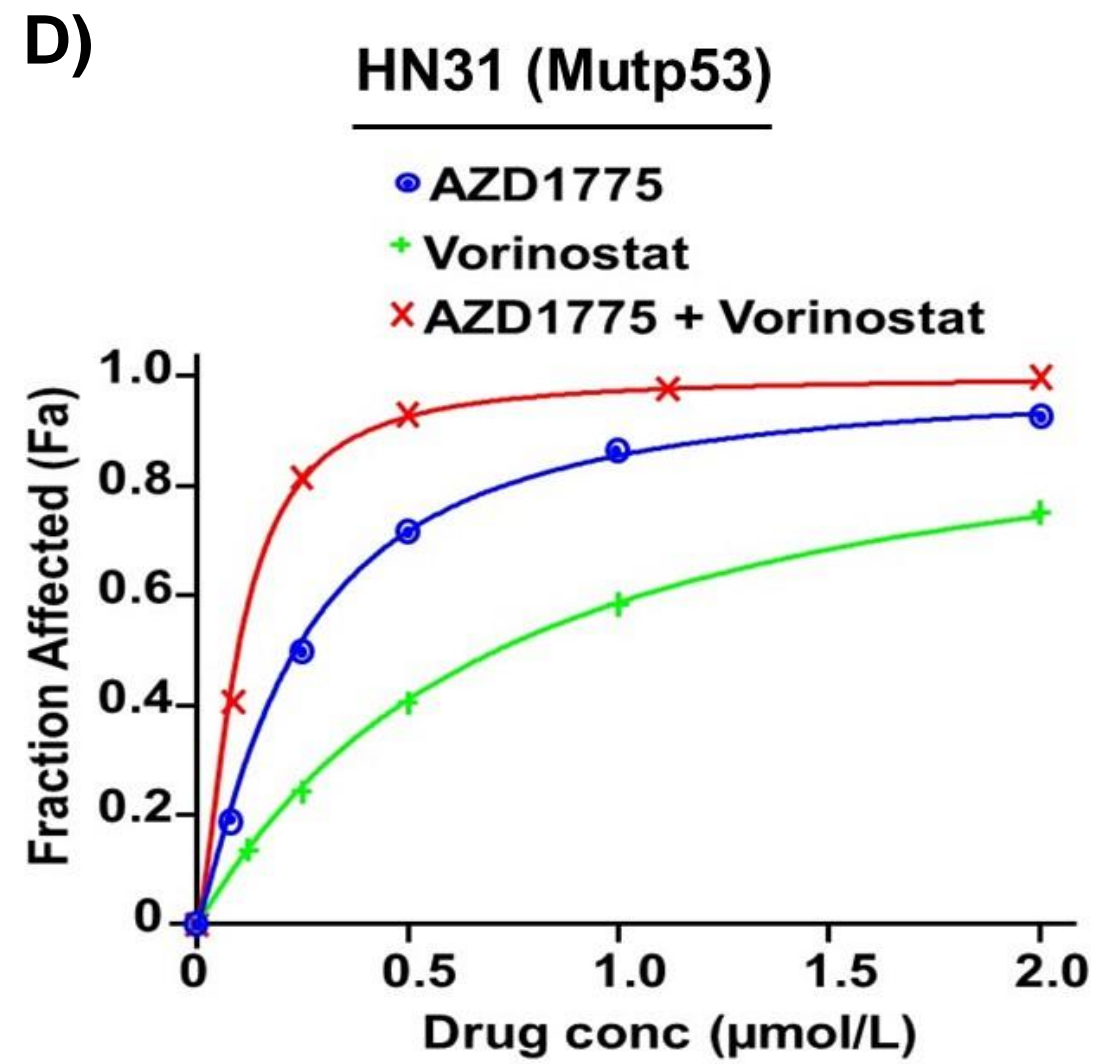
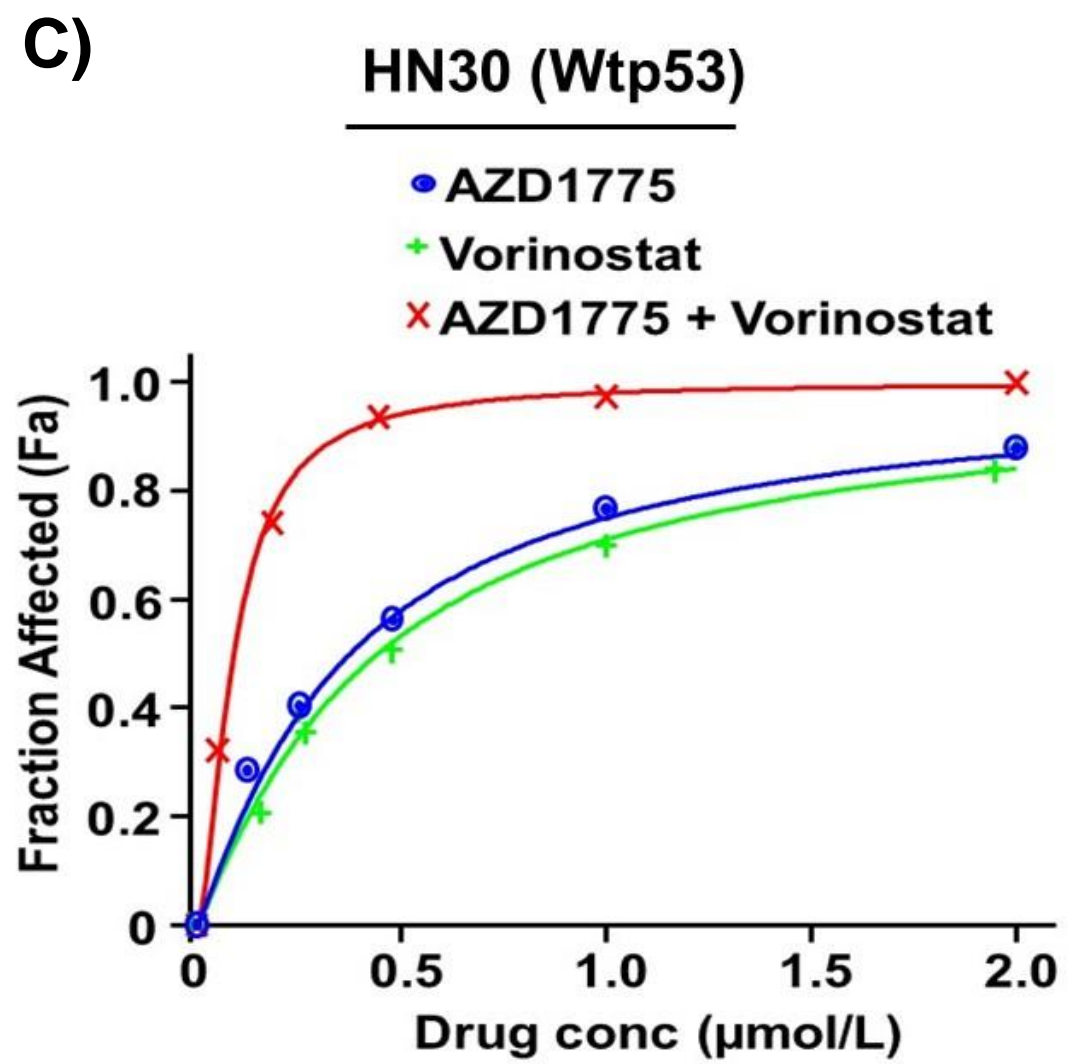
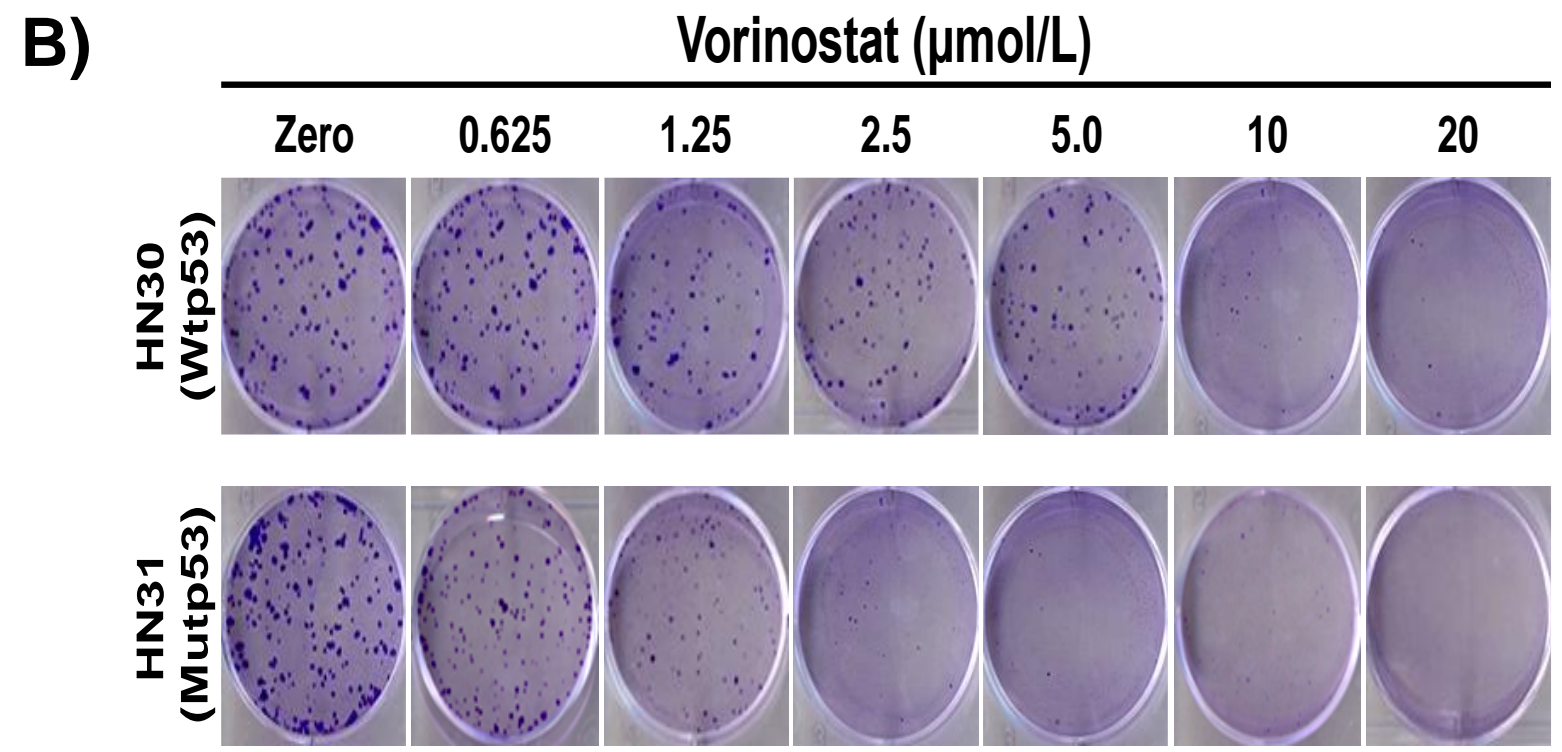
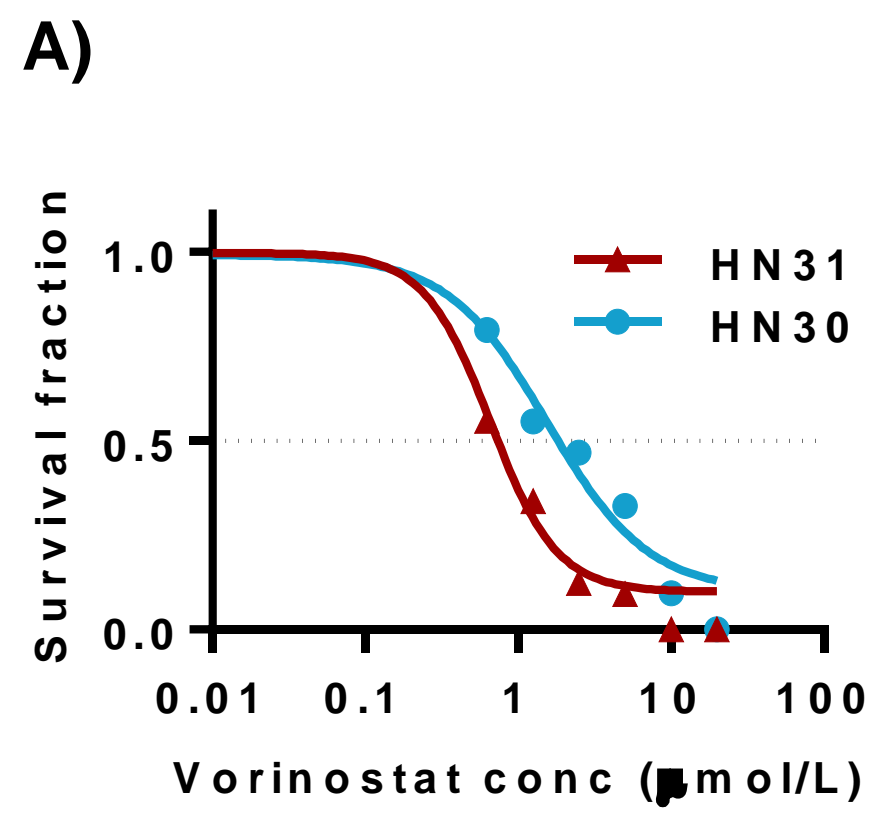
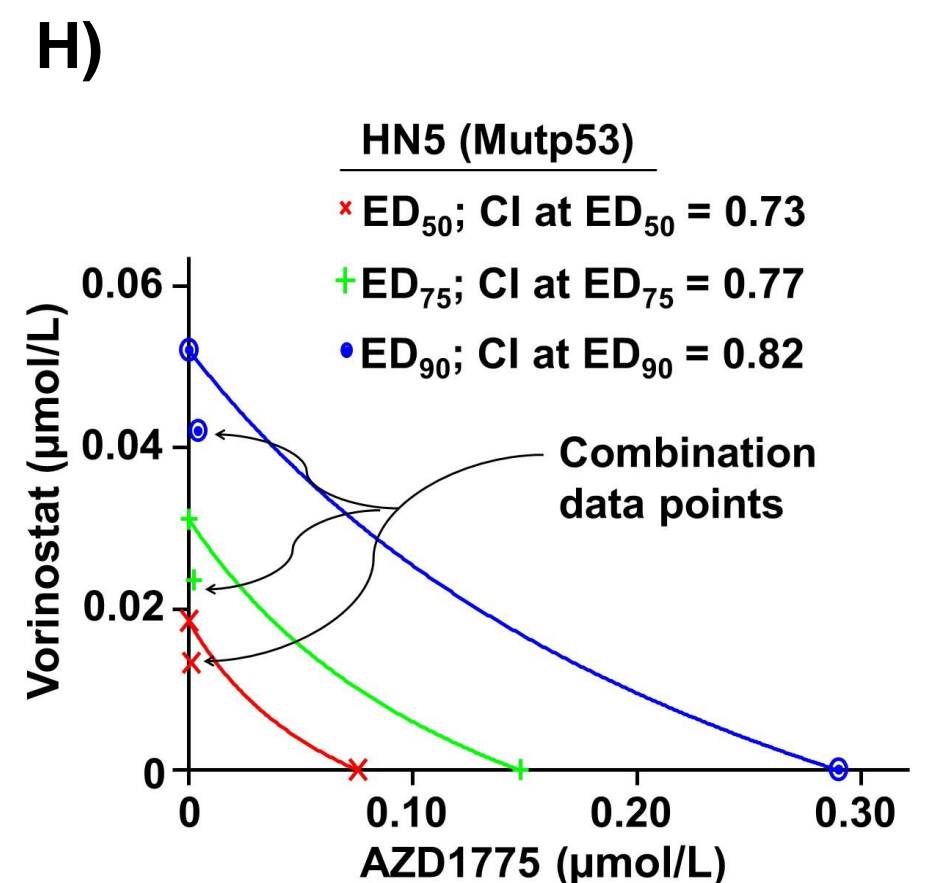
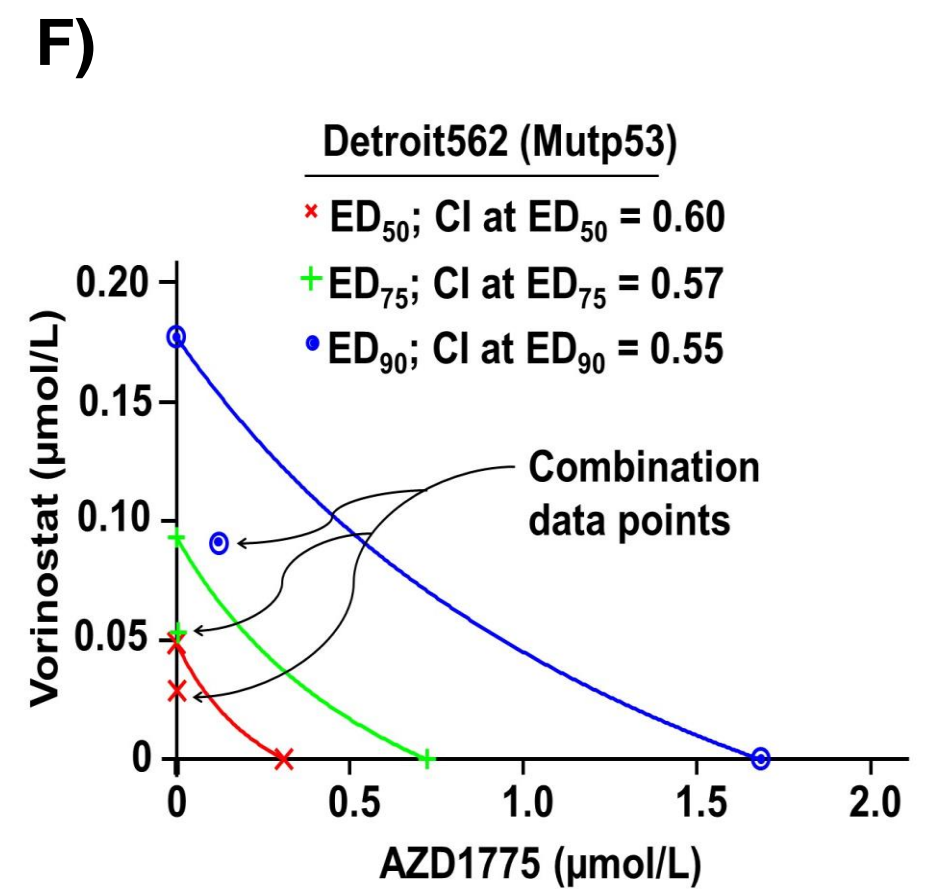
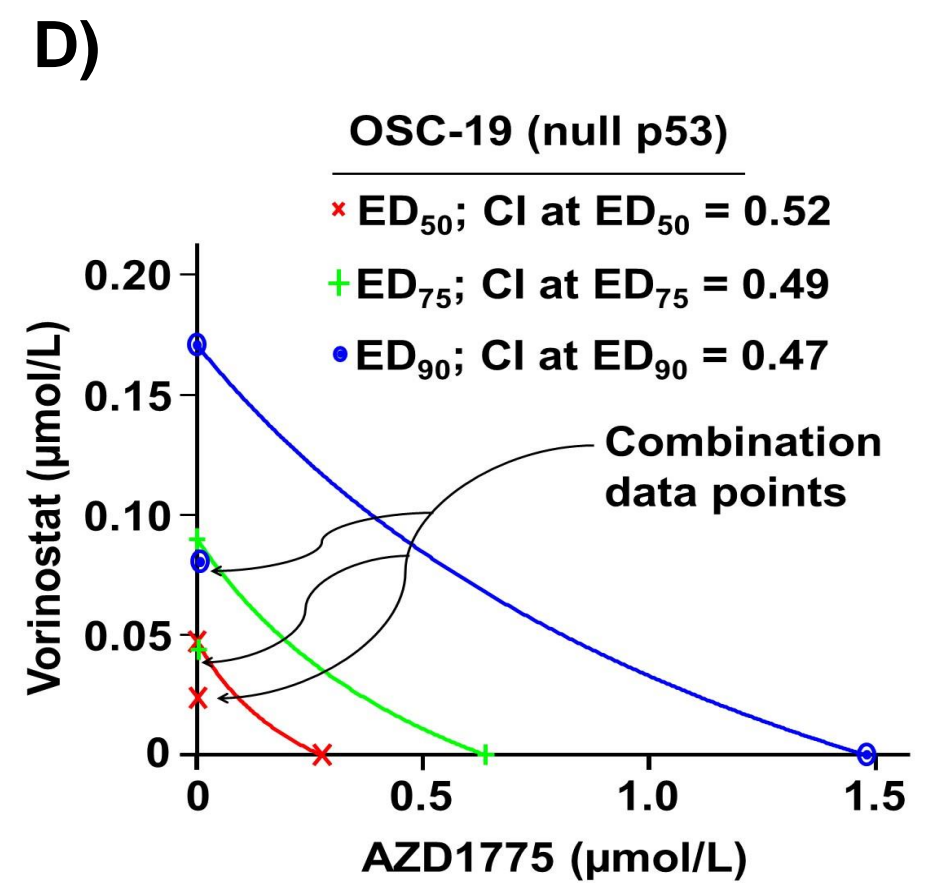
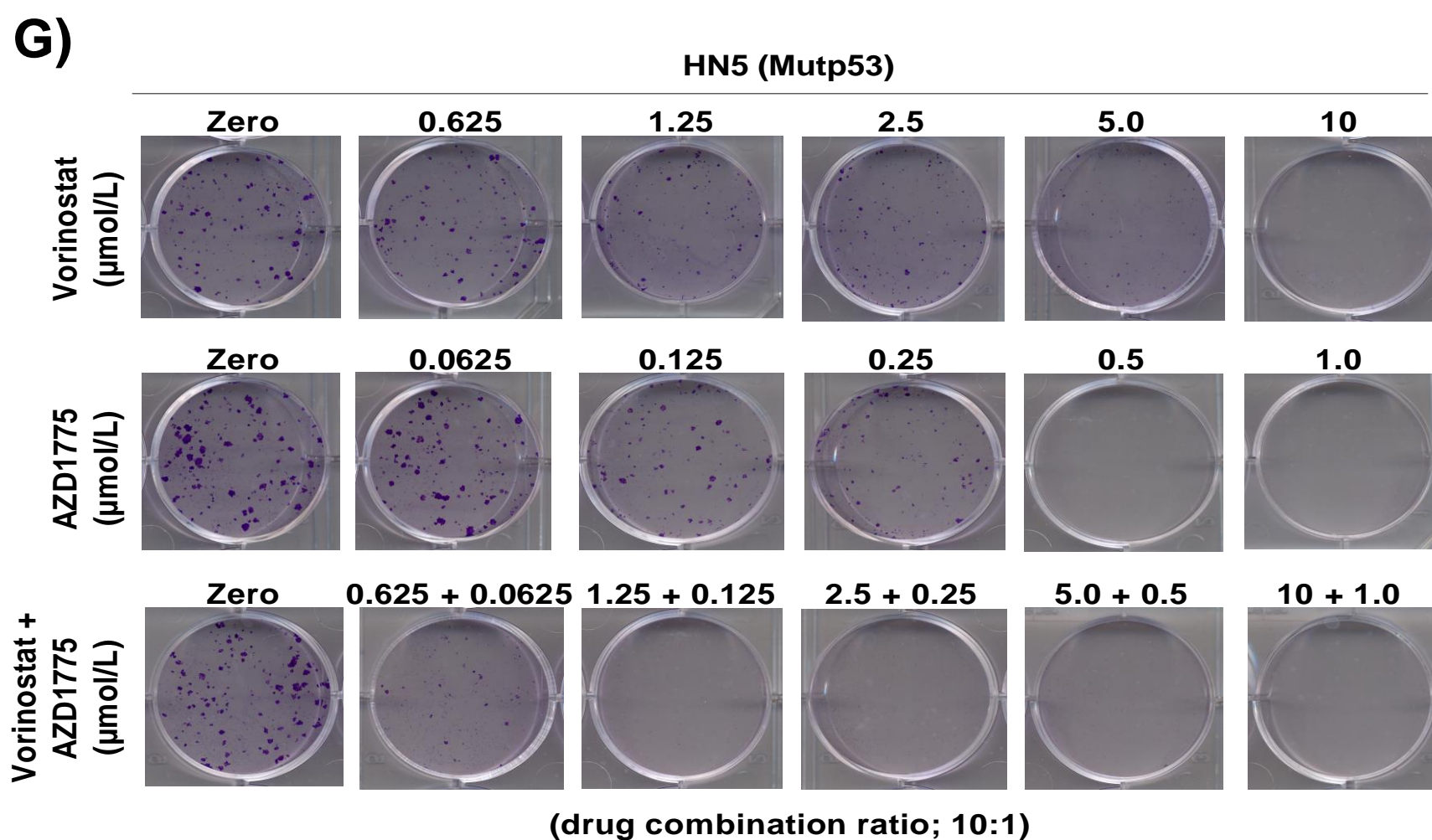
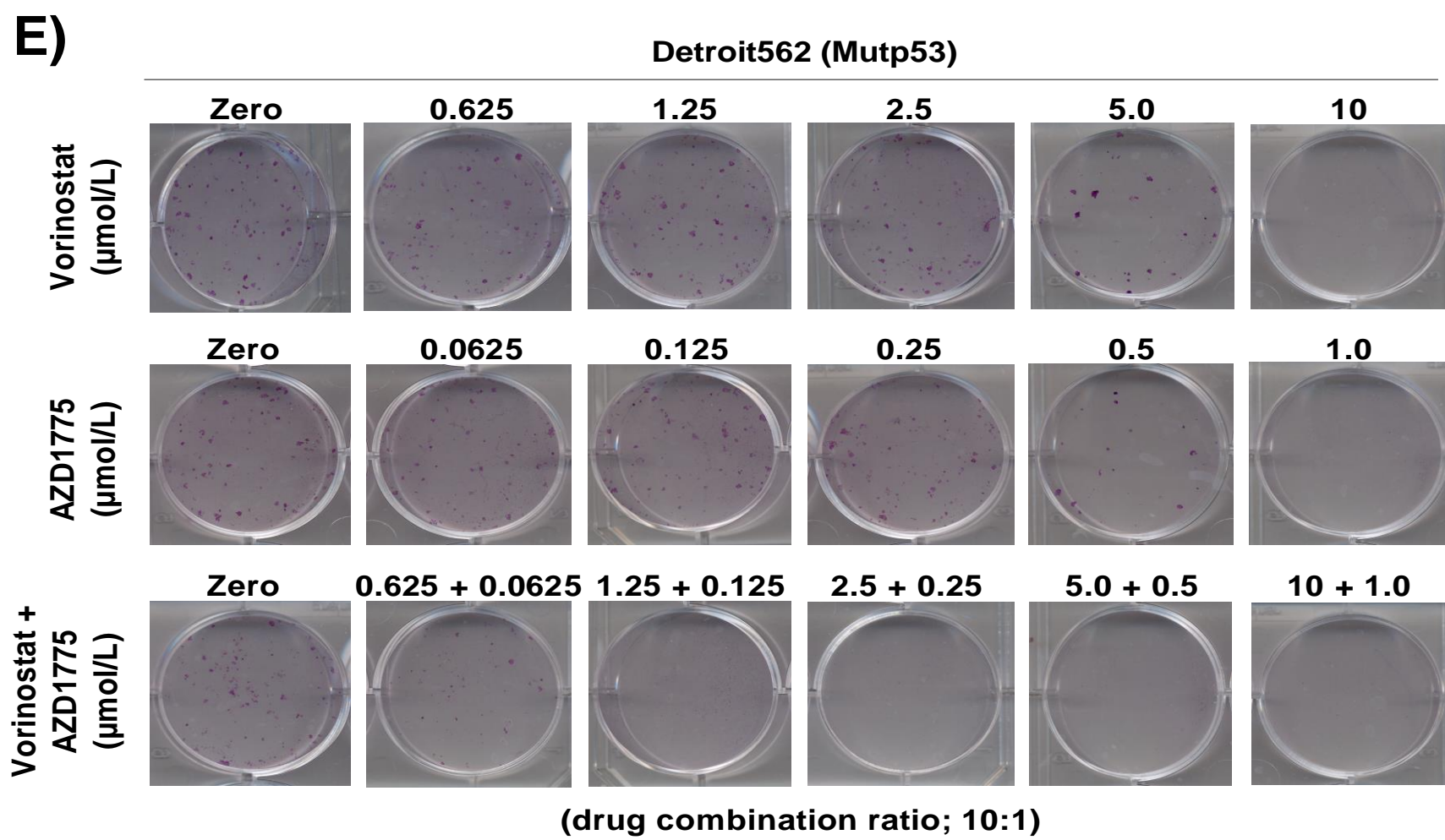
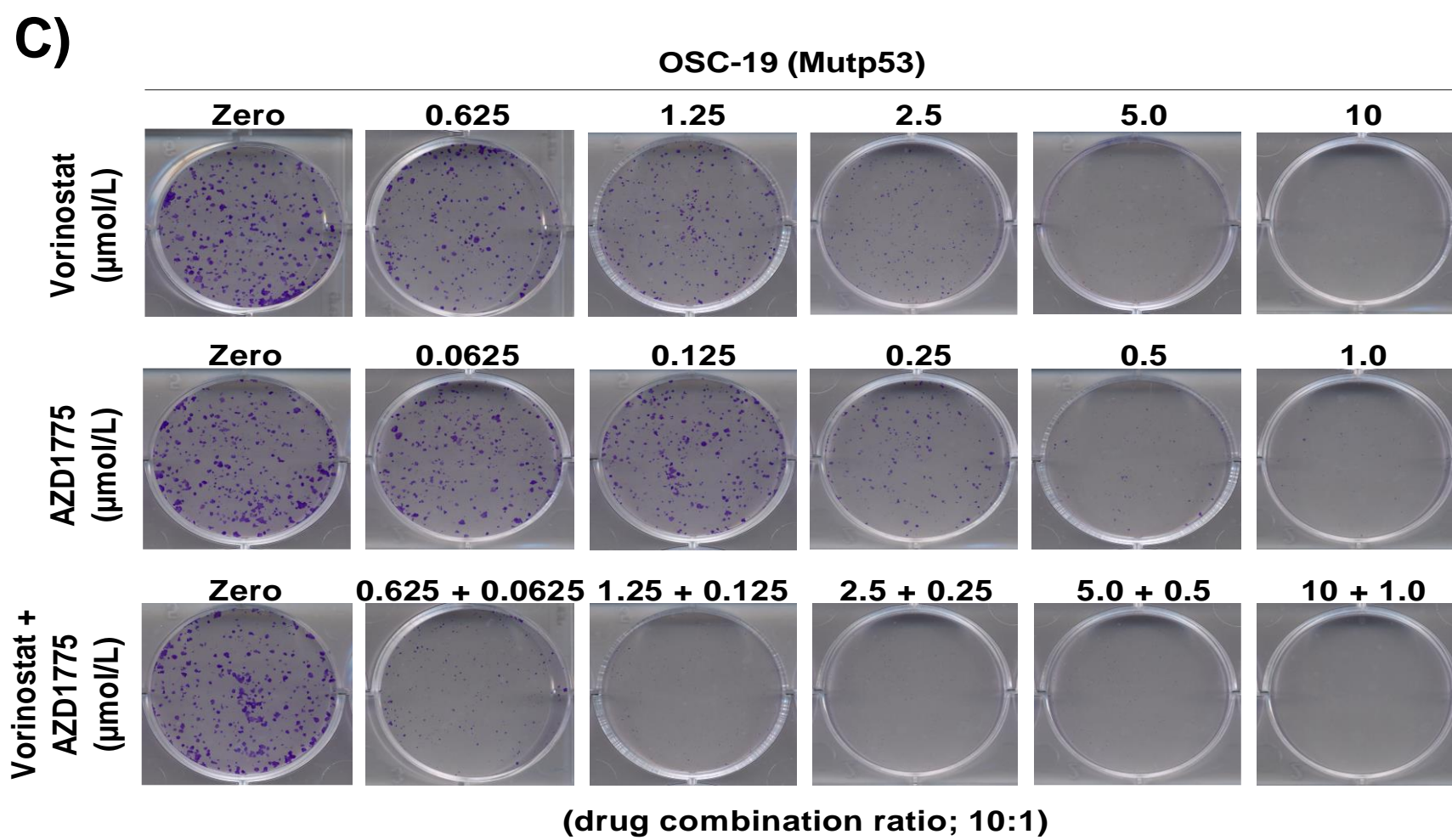
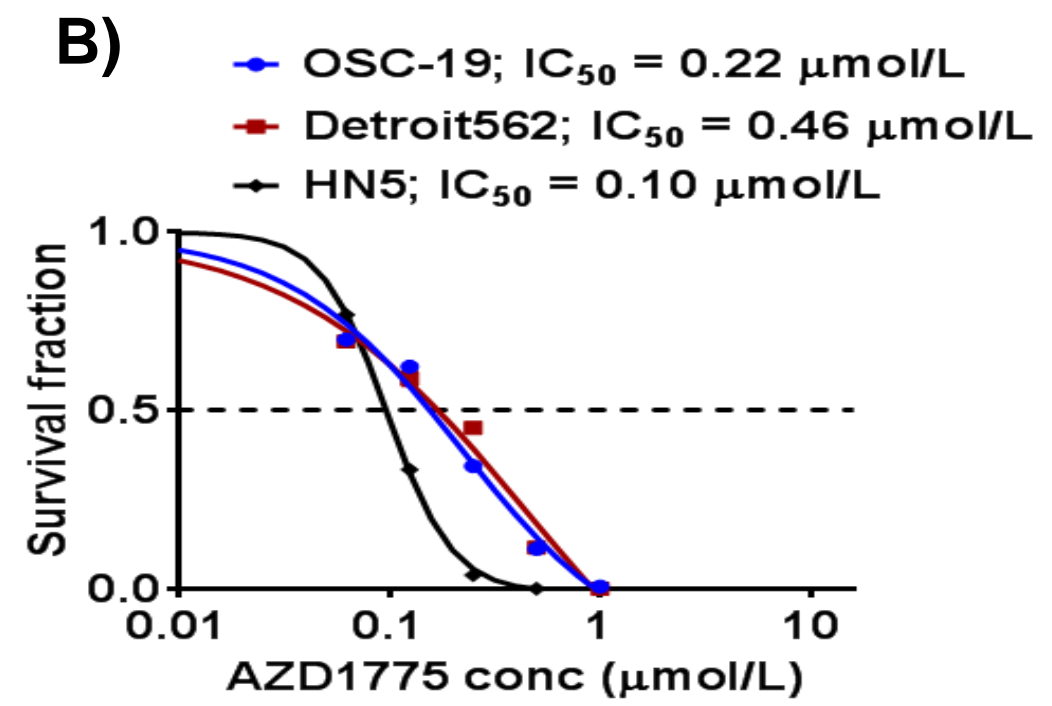
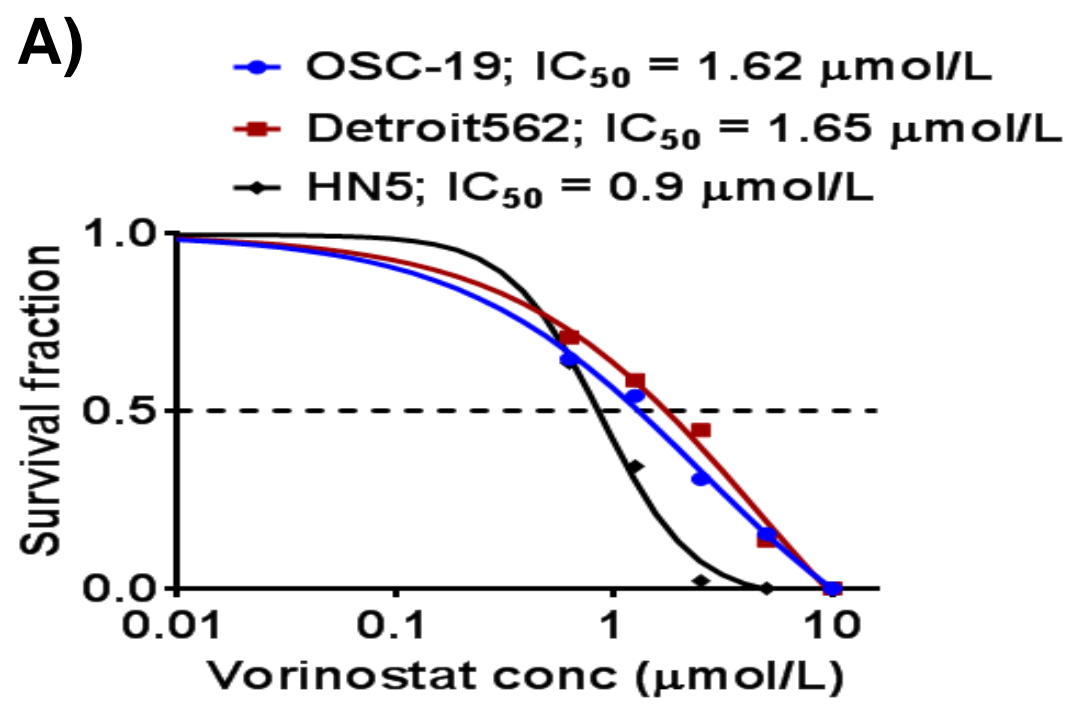


Supplementary Figure S1



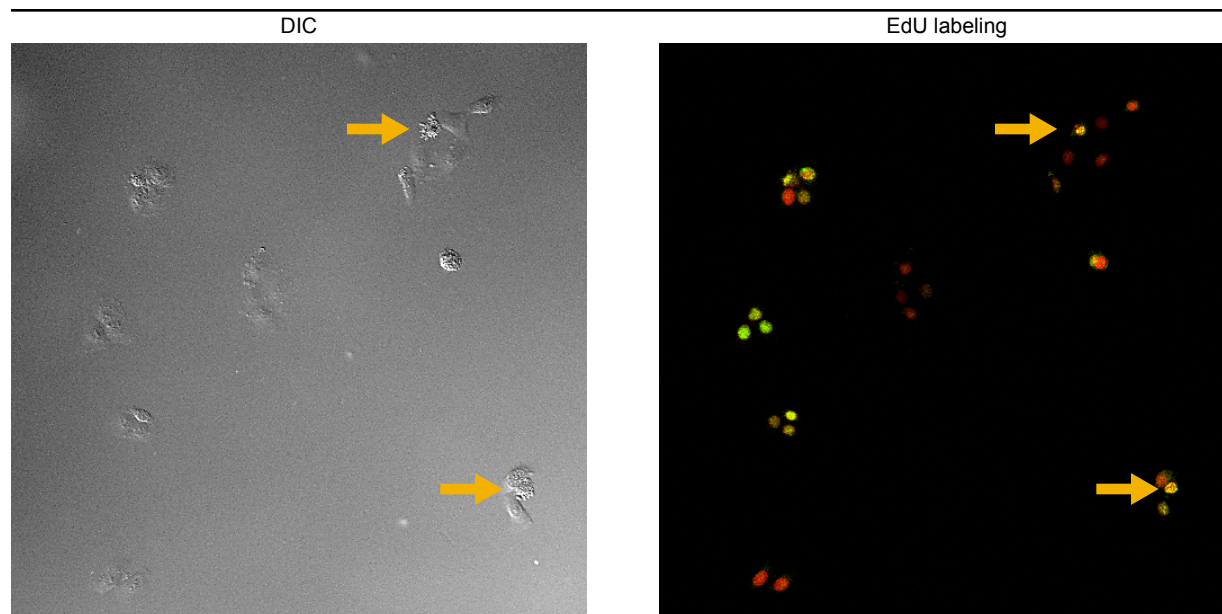
Supplementary Figure S2



Supplementary Figure S3.

A)

Vorinostat + AZD1775



B)

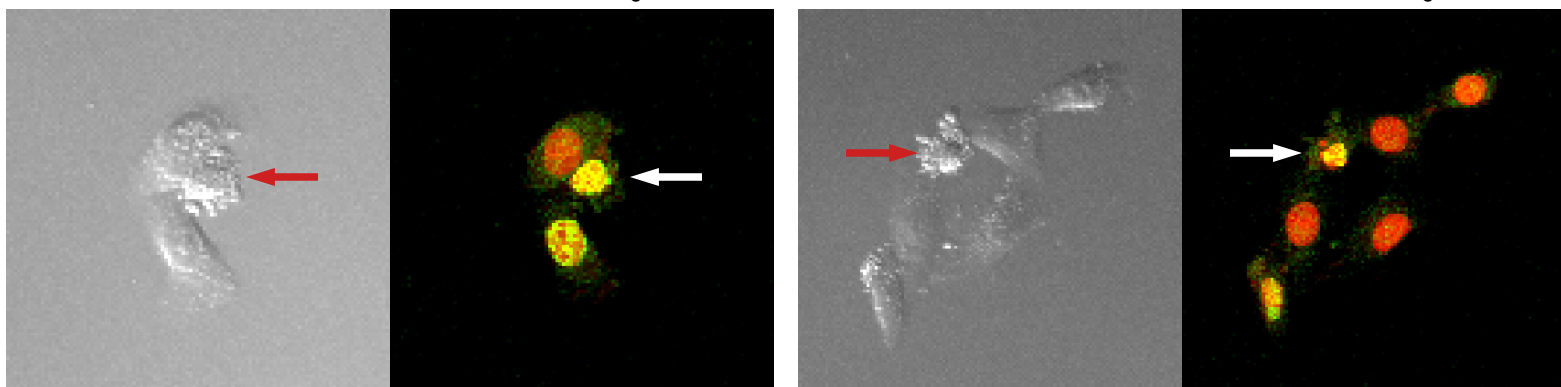
Vorinostat + AZD1775

DIC

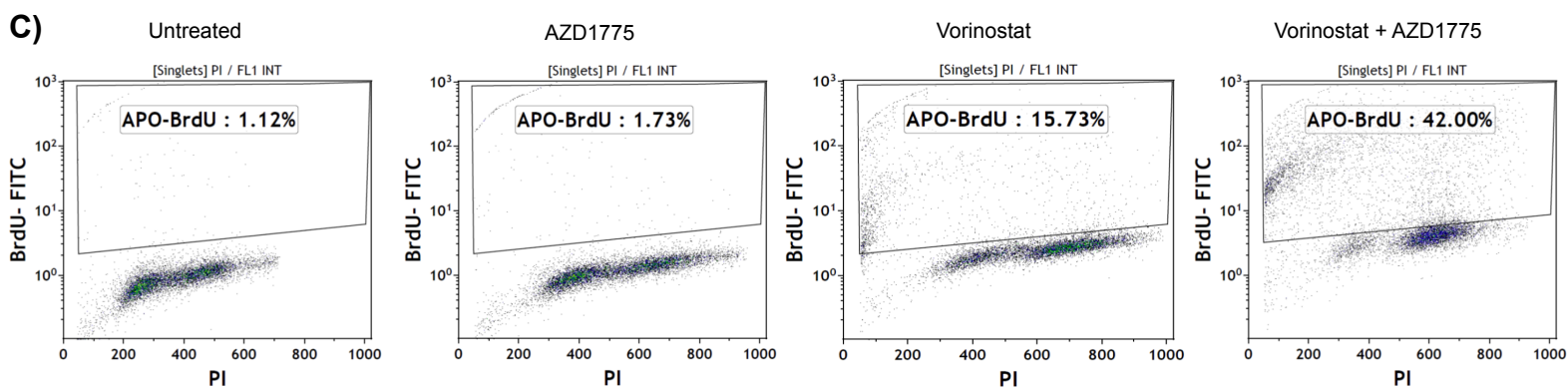
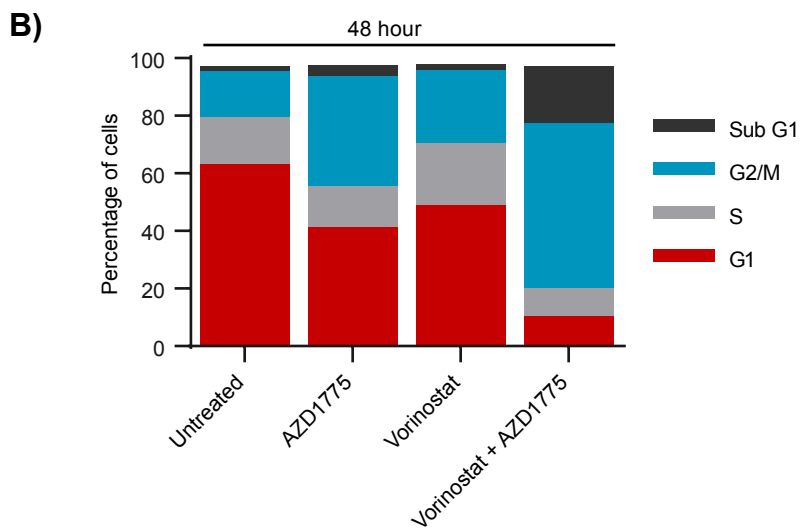
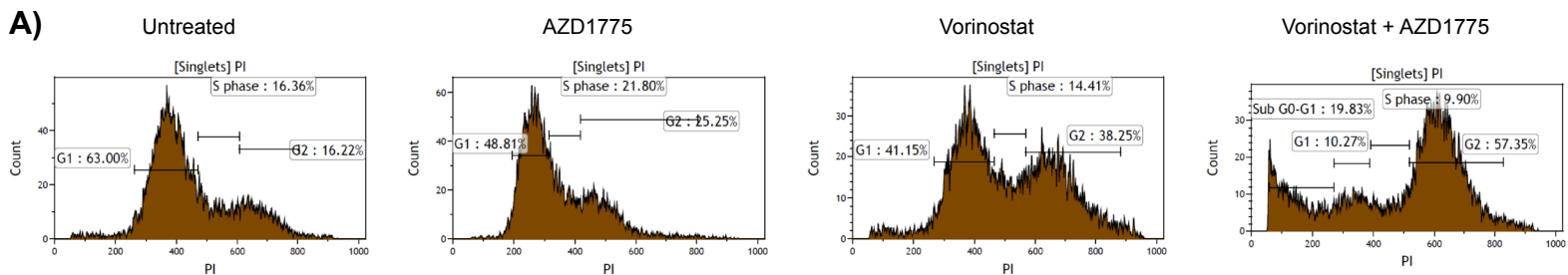
EdU labeling

DIC

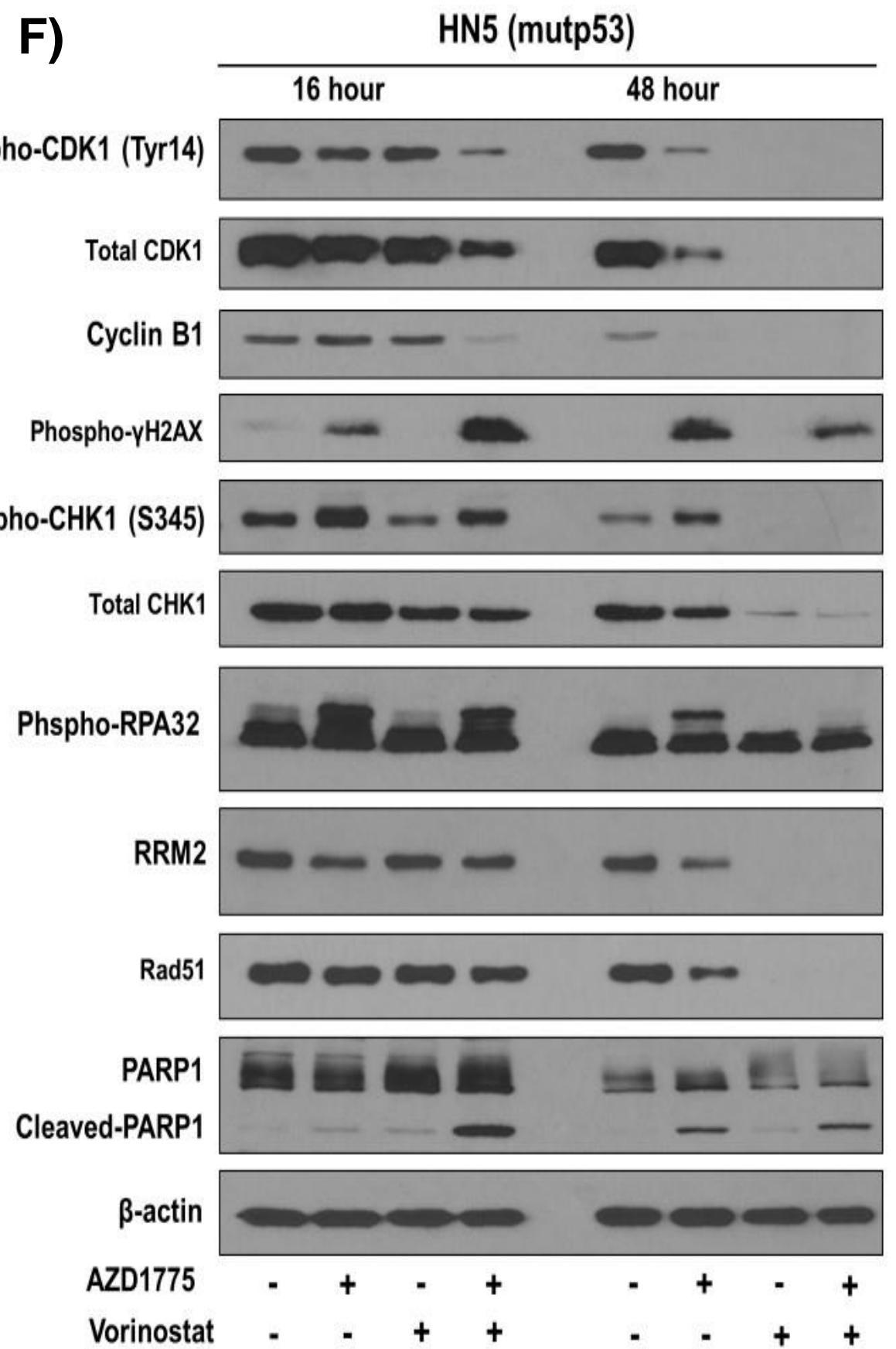
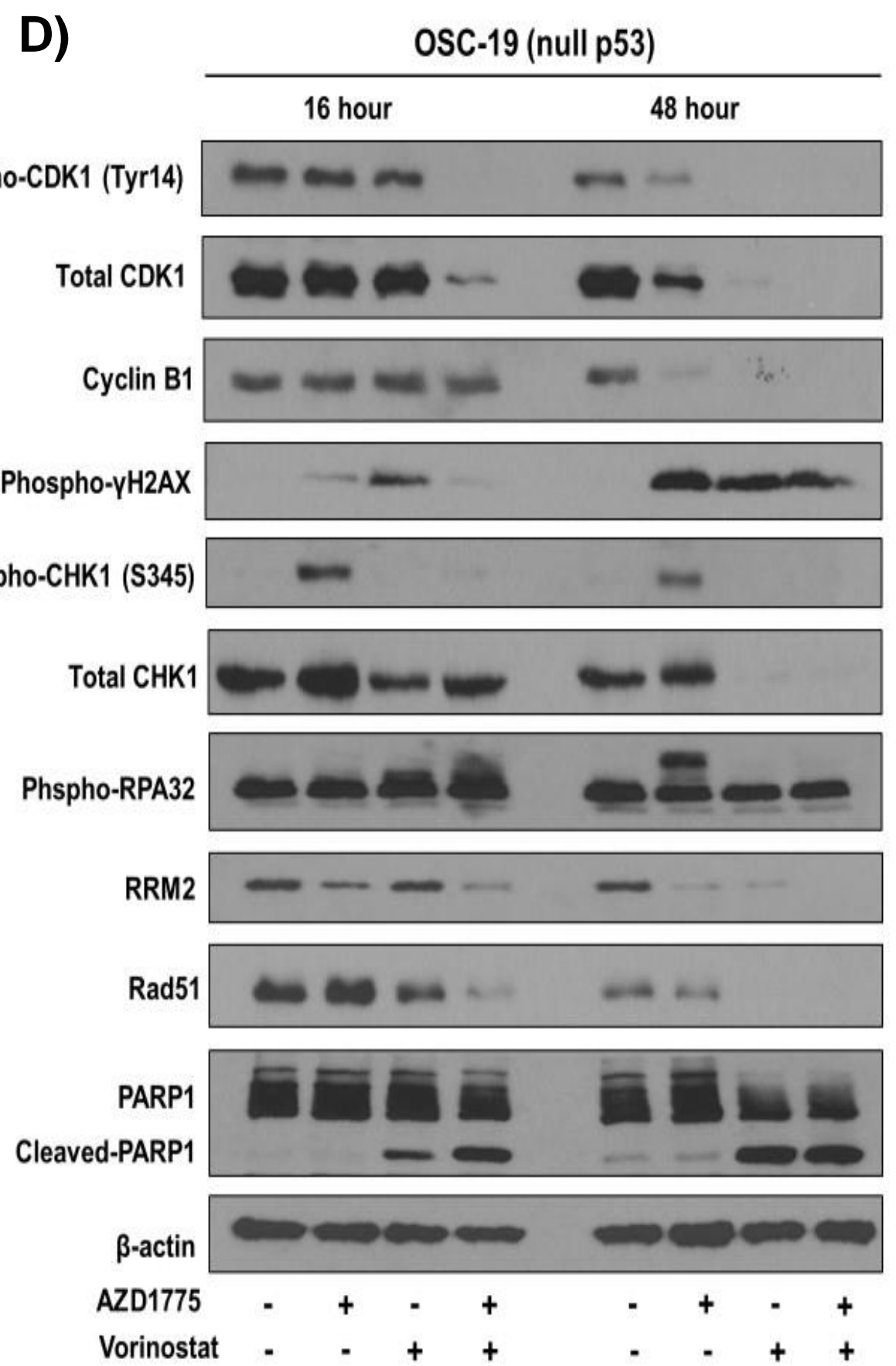
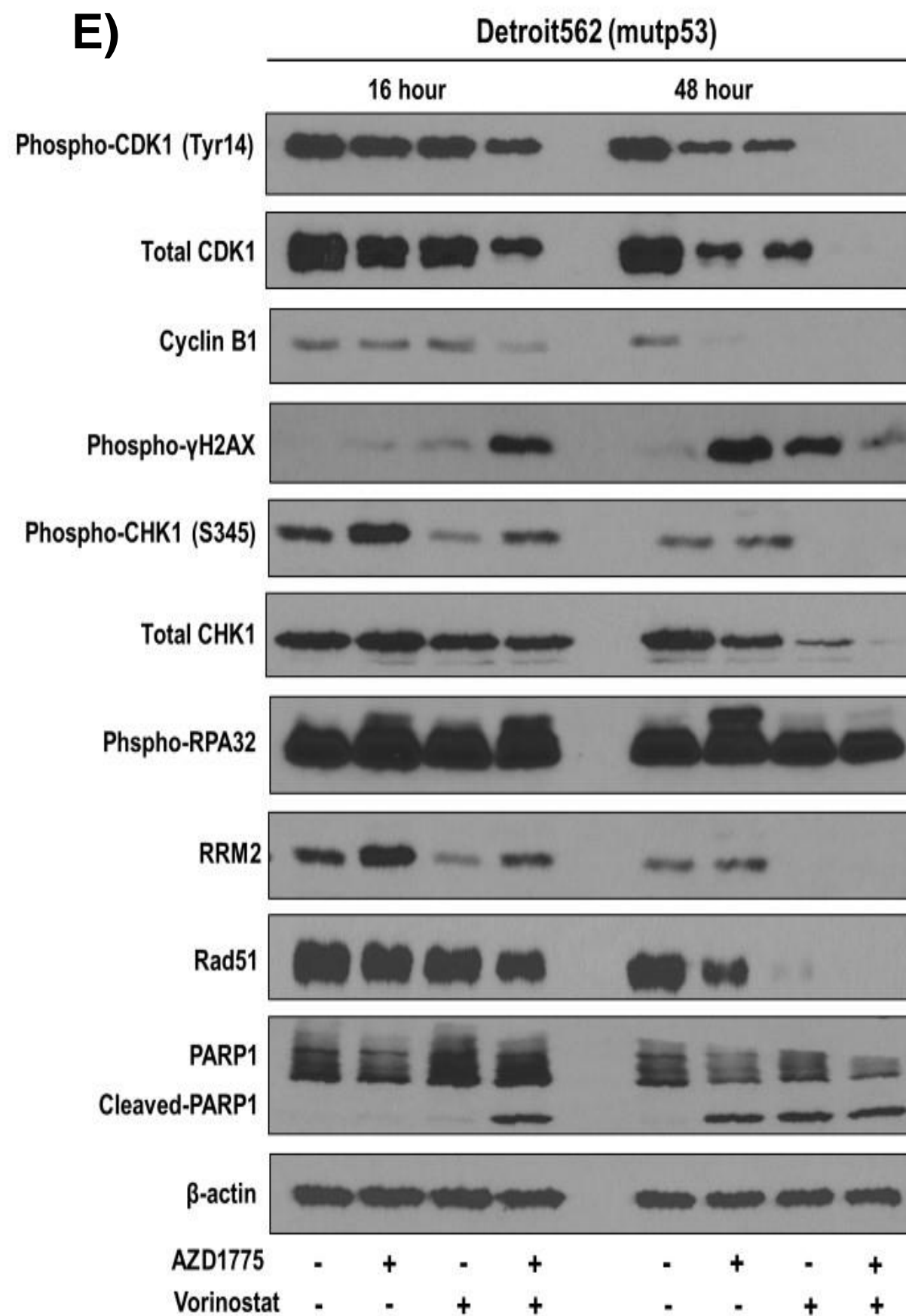
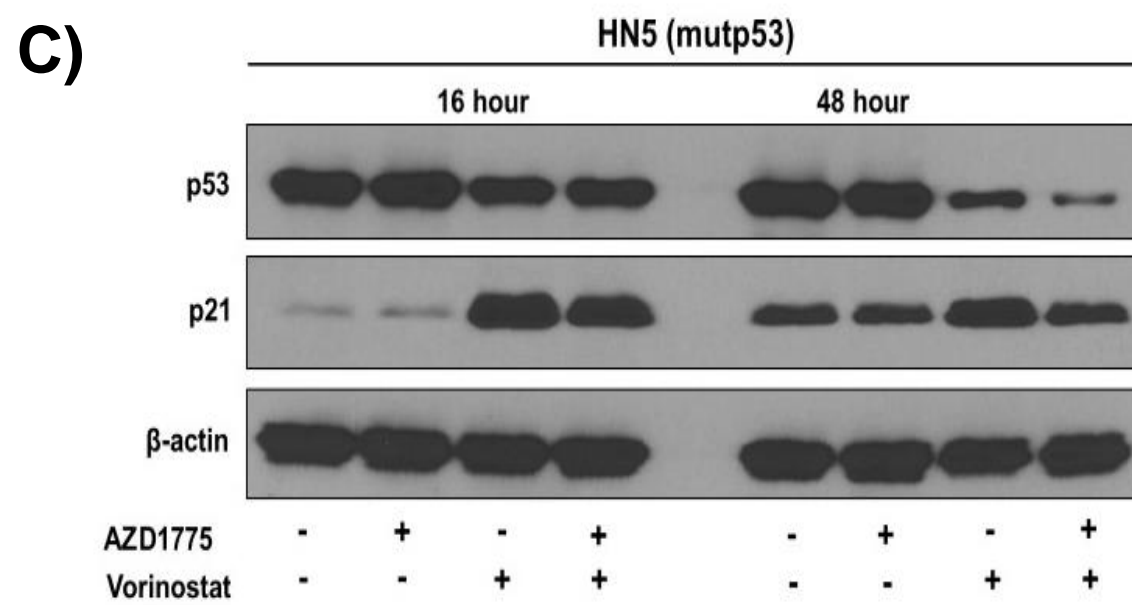
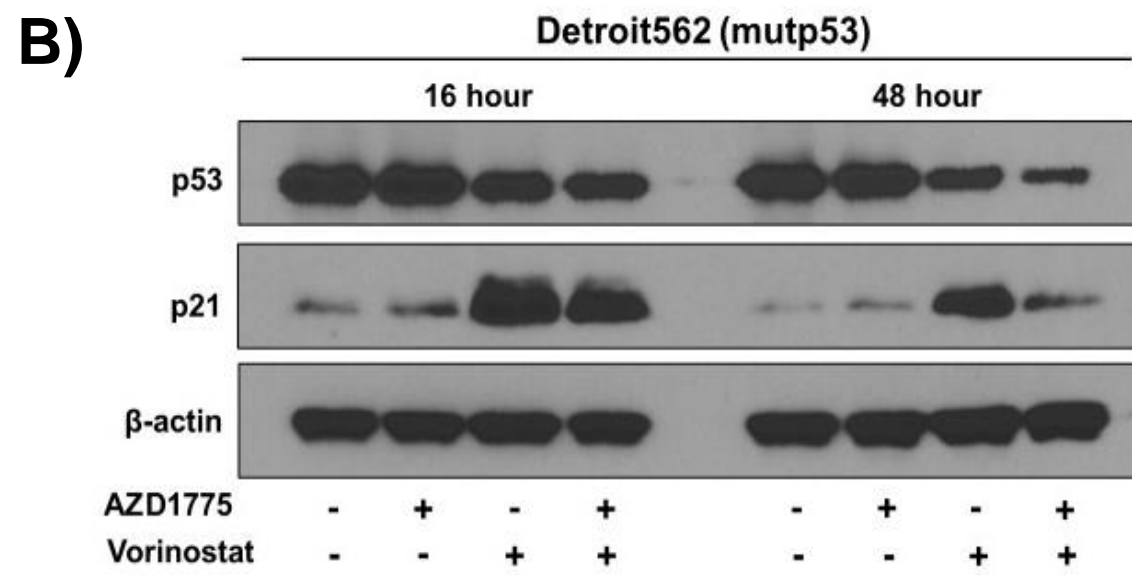
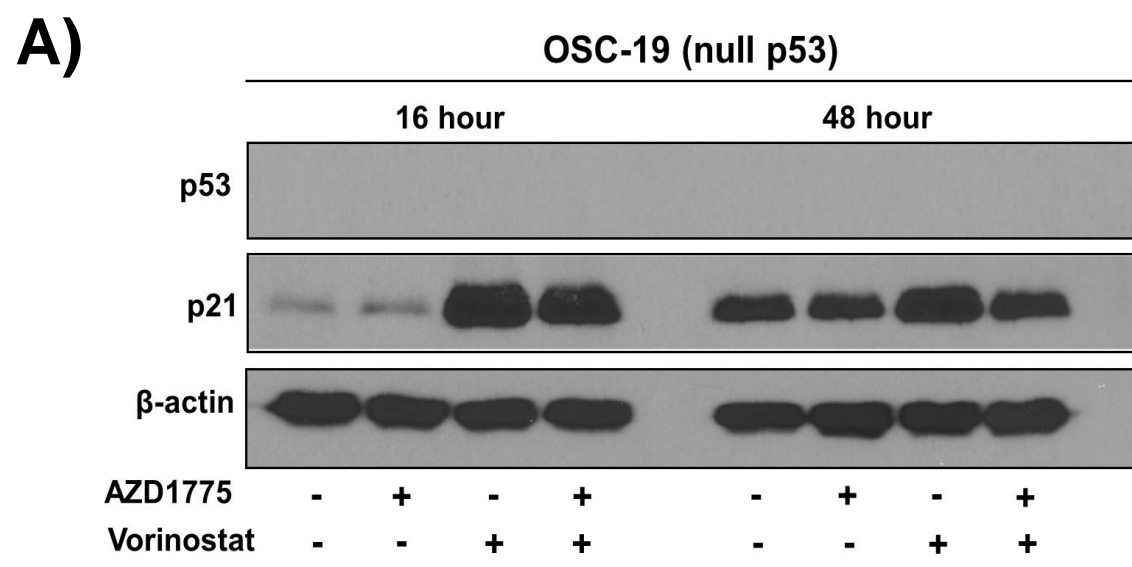
EdU labeling



Supplementary Figure S4

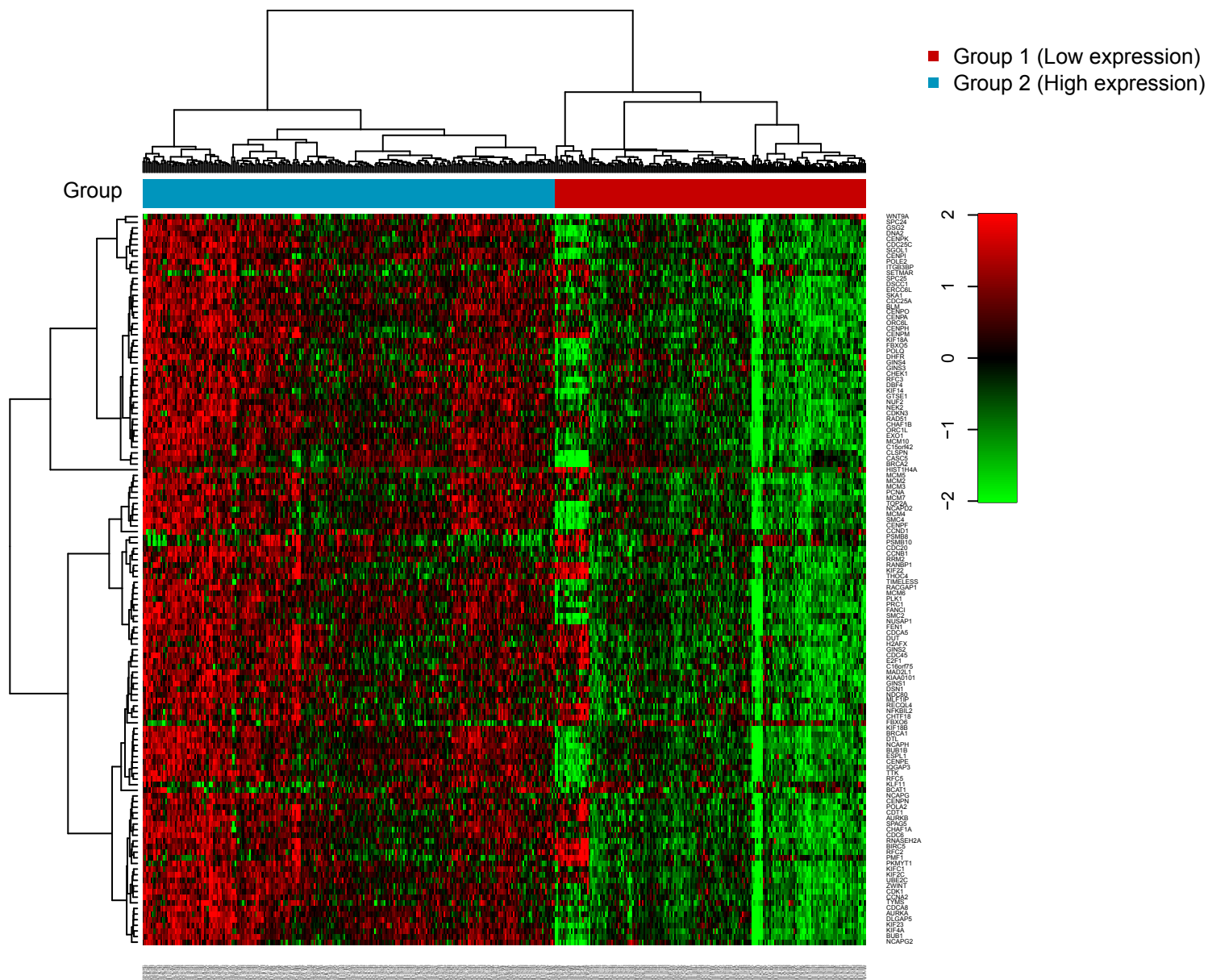


Supplementary Figure S5

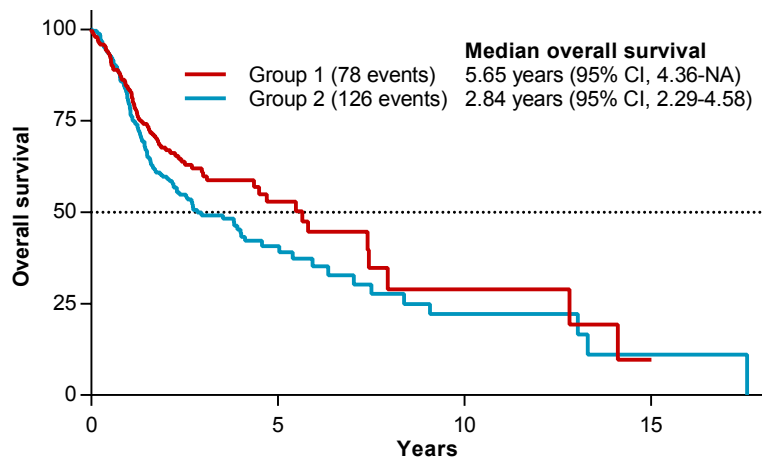


Supplementary Figure S6.

A



B



No. at risk

Group 1	193	22	4	1
Group 2	255	25	7	1

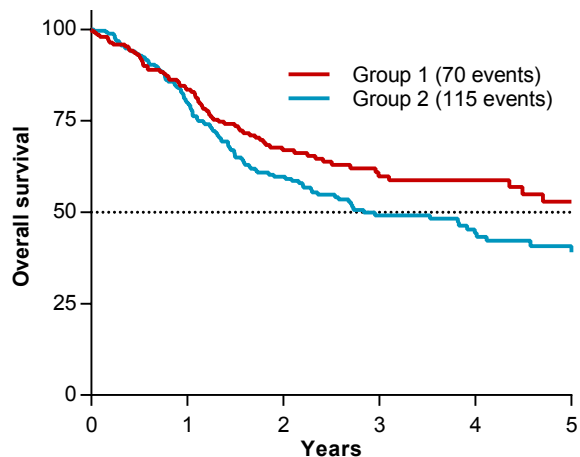
Univariate analysis

Hazard ratio, 1.32 (95% CI, 0.99-1.75)
 P = 0.057

Multivariate analysis

Hazard ratio, 1.30 (95% CI, 0.96-1.76)
 P = 0.094

C



No. at risk

Group 1	193	153	92	54	36	22
Group 2	255	187	104	64	43	25

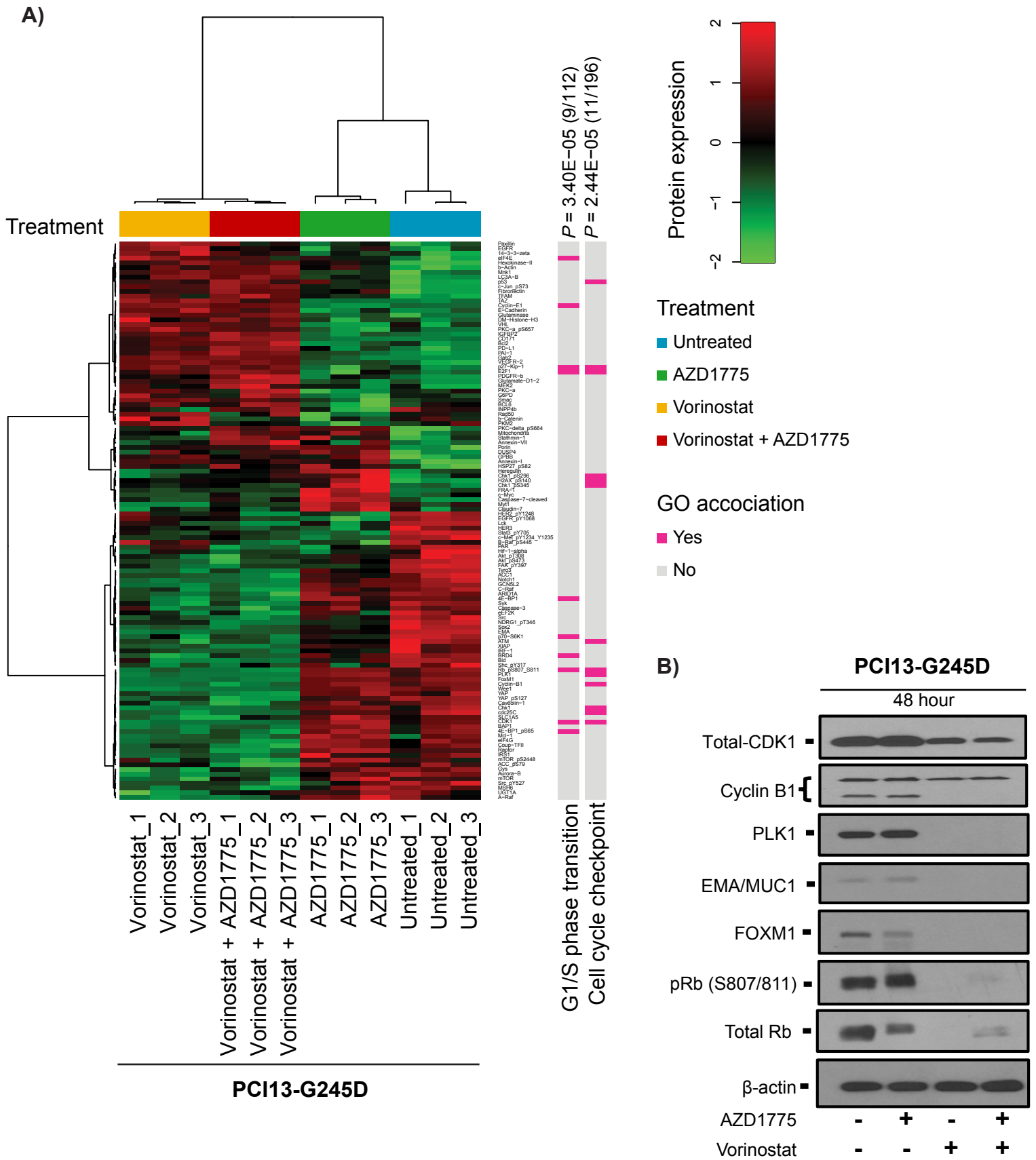
Univariate analysis

Hazard ratio, 1.36 (95% CI, 1.01-1.84)
 P = 0.040

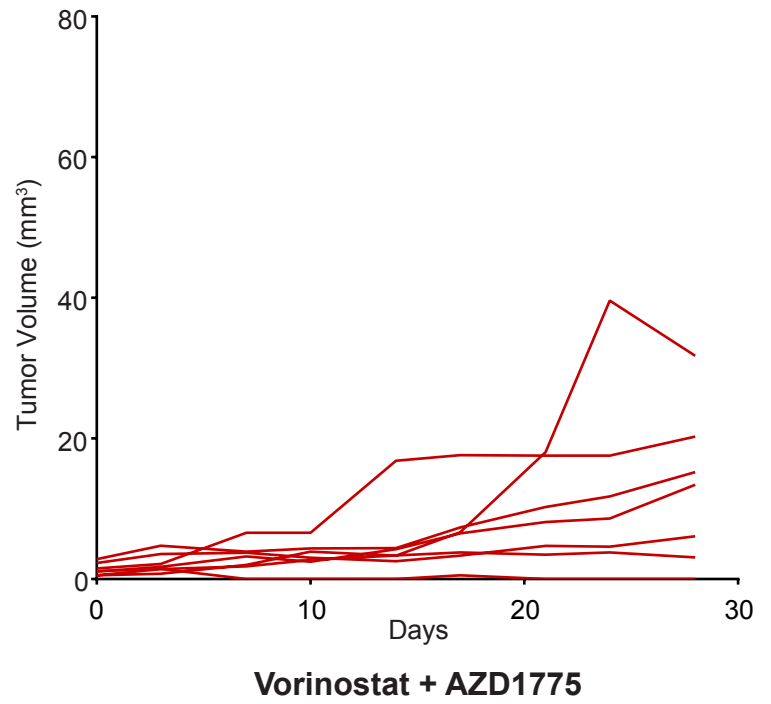
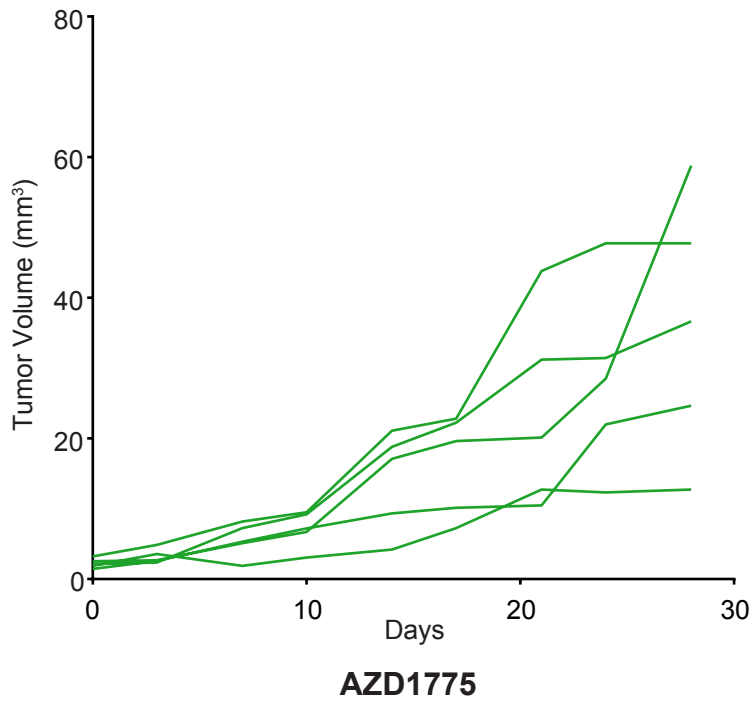
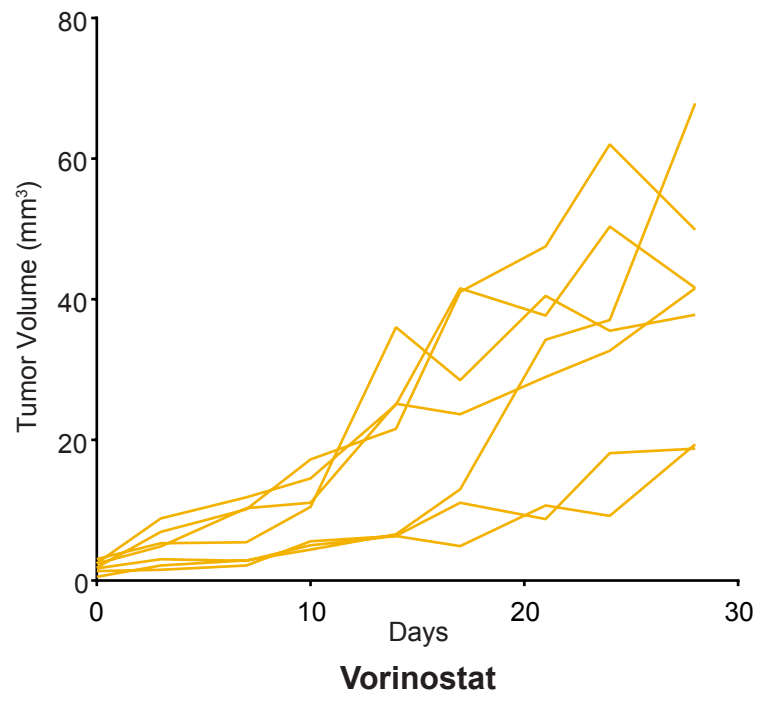
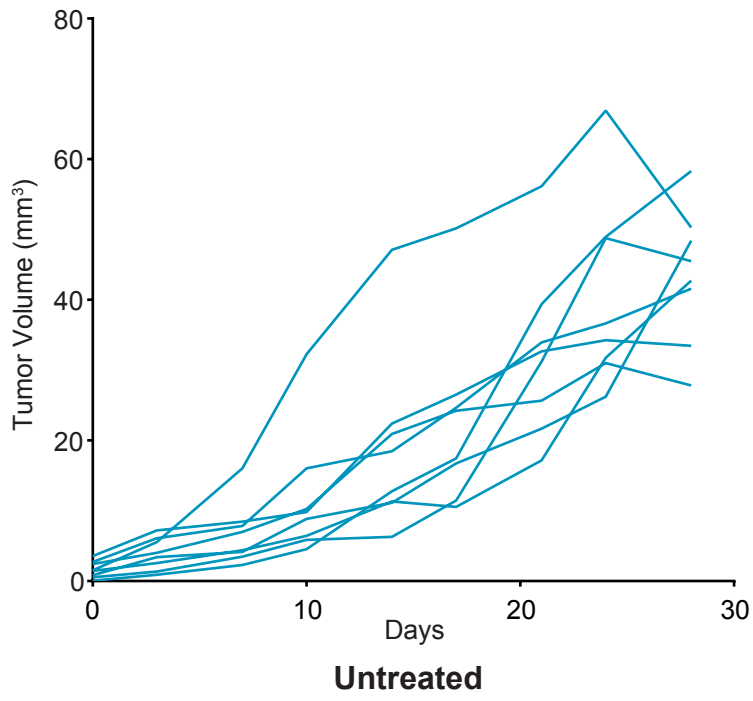
Multivariate analysis

Hazard ratio, 1.30 (95% CI, 0.95-1.79)
 P = 0.104

Supplementary Figure S7.



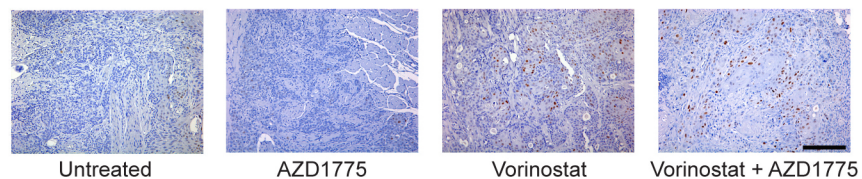
Supplementary Figure S8.



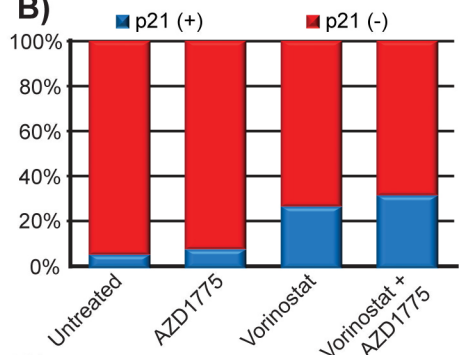
Supplementary Figure S9

A)

PCI13-G245D p21

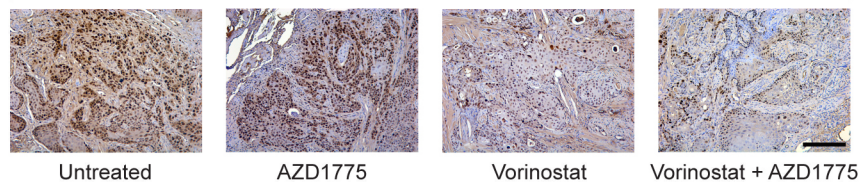


B)

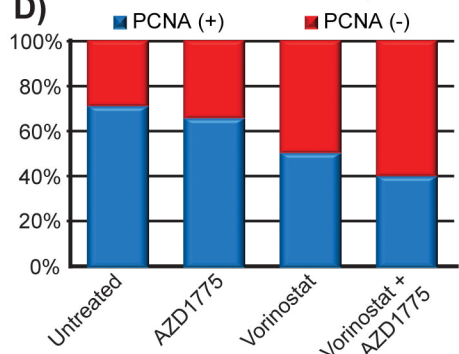


C)

PCI13-G245D PCNA

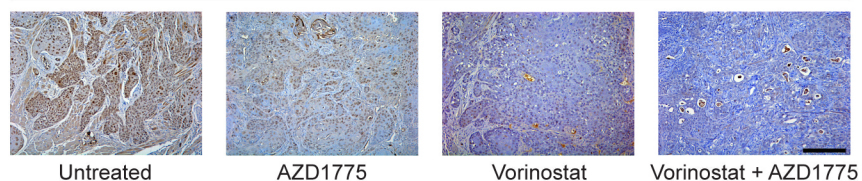


D)

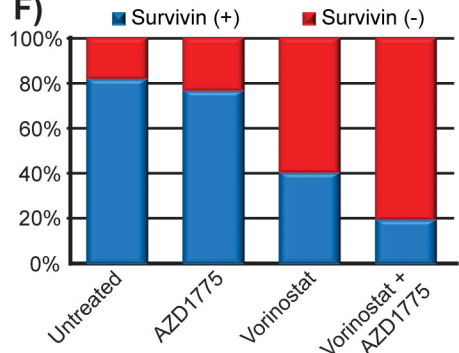


E)

PCI13-G245D Survivin

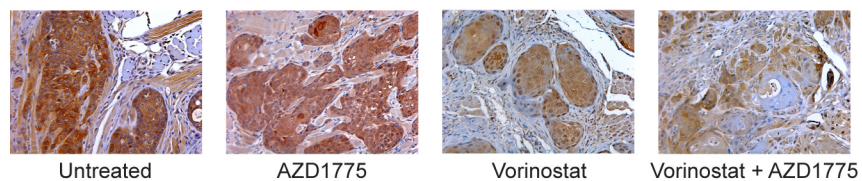


F)



G)

PCI13-G245D RRM2



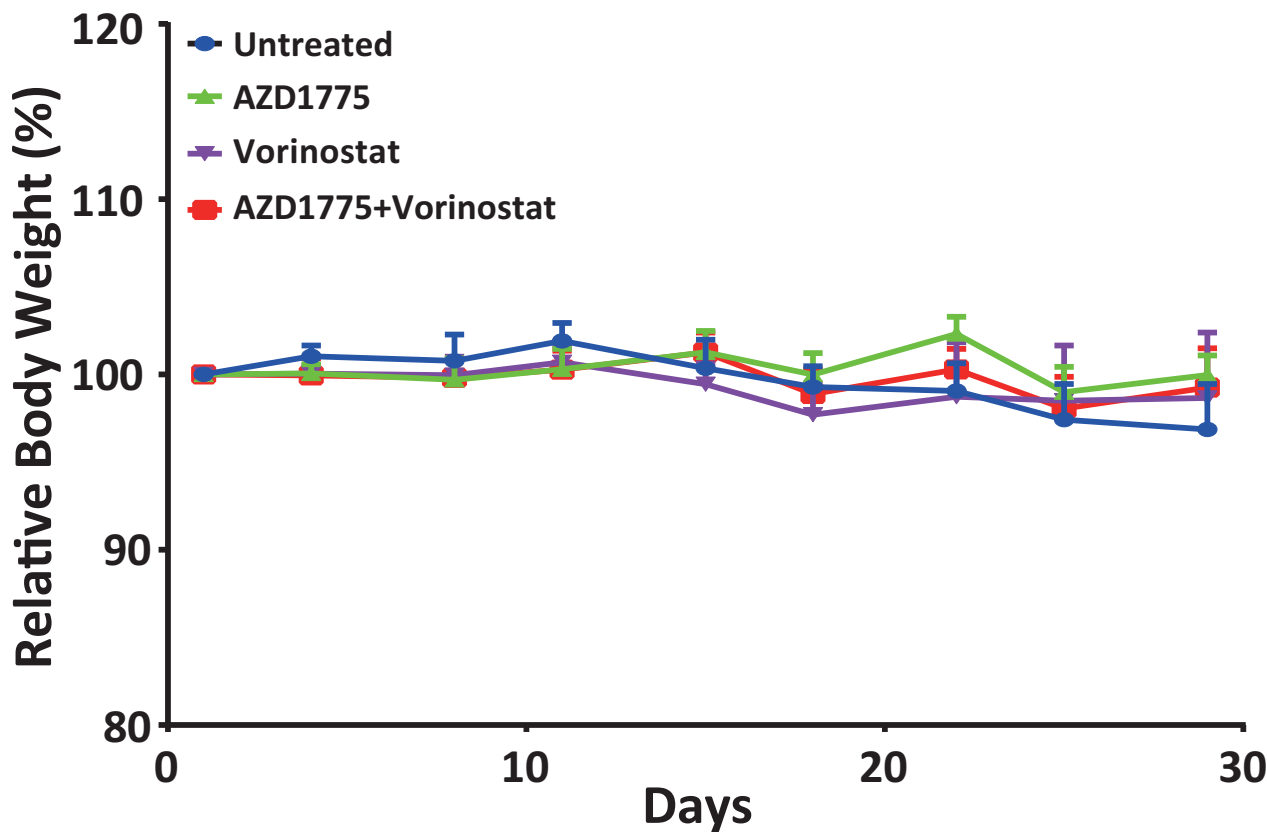
A)

Treatment Schedule

Day	1	2	3	4	5	6	7
AZD1775 (45mg/kg)		↓			↓		
Vorinostat (65mg/kg)	↓	↓	↓	↓	↓		

Repeat 4 weeks

B)



Supplementary Table S1. CI at Fa of 0.5, 0.75 and 0.9 of vorinostat in combination with AZD1775 in various HNSCC cell lines

Cell line	Drug combination	Drug conc (μM)	Drug ratio	Fa	CI an Fa 0.5 (ED50), 0.75 (ED75) and 0.90 (ED90) respectively	Effect
PCI13-Wtp53	Vorinostat + AZD1775	0.11 + 0.052	2:1	0.50 (50%)	0.34	Synergistic
		0.19 + 0.095	2:1	0.75 (75%)	0.22	Synergistic
		0.34 + 0.17	2:1	0.90 (90%)	0.14	Synergistic
PCI13-pBabe (null p53)	Vorinostat + AZD1775	0.21 + 0.21	1:1	0.50 (50%)	0.90	Synergistic
		0.42 + 0.42	1:1	0.75 (75%)	0.66	Synergistic
		0.84 + 0.84	1:1	0.90 (90%)	0.49	Synergistic
PCI13-C238F	Vorinostat + AZD1775	0.07 + 0.07	1:1	0.50 (50%)	0.30	Synergistic
		0.15 + 0.15	1:1	0.75 (75%)	0.23	Synergistic
		0.30 + 0.30	1:1	0.90 (90%)	0.19	Synergistic
PCI13-G245D	Vorinostat + AZD1775	0.08 + 0.08	1:1	0.50 (50%)	0.38	Synergistic
		0.16 + 0.16	1:1	0.75 (75%)	0.29	Synergistic
		0.32 + 0.32	1:1	0.90 (90%)	0.23	Synergistic
HN30-Wtp53	Vorinostat + AZD1775	0.08 + 0.04	2:1	0.50 (50%)	0.32	Synergistic
		0.18 + 0.09	2:1	0.75 (75%)	0.23	Synergistic
		0.34 + 0.17	2:1	0.90 (90%)	0.17	Synergistic
HN31-Mutp53	Vorinostat + AZD1775	0.09 + 0.09	1:1	0.50 (50%)	0.55	Synergistic
		0.19 + 0.19	1:1	0.75 (75%)	0.44	Synergistic
		0.40 + 0.40	1:1	0.90 (90%)	0.35	Synergistic
OSC-19 (null p53)	Vorinostat + AZD1775	0.024 + 0.0024	10:1	0.50 (50%)	0.52	Synergistic
		0.044 + 0.0044	10:1	0.75 (75%)	0.49	Synergistic
		0.080 + 0.0080	10:1	0.90 (90%)	0.47	Synergistic
Detroit562-Mutp53	Vorinostat + AZD1775	0.028 + 0.0028	10:1	0.50 (50%)	0.60	Synergistic
		0.052 + 0.0052	10:1	0.75 (75%)	0.57	Synergistic
		0.096 + 0.0096	10:1	0.90 (90%)	0.55	Synergistic
HN5-Mutp53	Vorinostat + AZD1775	0.013 + 0.0013	10:1	0.50 (50%)	0.73	Synergistic
		0.023 + 0.0023	10:1	0.75 (75%)	0.77	Synergistic
		0.042 + 0.0042	10:1	0.90 (90%)	0.82	Synergistic

CI = Combination indexes; Fa = fraction affected. CI value < 1.0 indicates synergistic interaction.