

EC50s of GDC-0980 in TNBC Cells

TNBT Cell lines	EC50s GDC-0980	p53 Levels /Mutational status ² /p53 (IS) ⁴ /TP53 Amino Acid Mutations ¹³	PI3kinaseCA Mutation /PTEN Protein/pten Mutation ¹³ / Ras (KRAS, HRAS) Mutation	BRCA1 Mutation status	Epithelial / Mesenchymal Phenotype
HCC70*	0.46 μ M	++M ² /+++ ⁴ / TP53 WT ¹³	PI3KCA.WT ¹³ / PTEN mutation ¹ PTEN-Null ^{8,13} / PTEN WT ¹³ /RAS WT ¹³		
HCC1143*	1.2 μ M	++M ² /+++ ⁴ /TP53 WT ¹³	PI3KCA.WT ¹³ / PTEN.WT ^{8,13} / RAS WT ¹³		
HCC1937*	3.75 μ M	[² / ⁴ TP53 R306X ¹³	PI3KCA.WT ¹³ / PTEN-Null ^{8,13} /PTEN WT ¹³ / RAS WT ¹³	Mutated ³ 5382insC ⁹	Epithelial ⁵
MDA-MB231*	5 μ M	++M ² / TP53 R280K ¹³	PI3KCA.WT ¹³ /PTEN WT ^{8,10,13} / [KRas(G13D)] ^{11,12} /BRAF(G464V) ¹³	WT ⁹	Mesenchymal ⁵
MDA-MB468*	0.9 μ M	[² / TP53 R273H ¹³	PI3KCA.WT ¹³ / PTEN mutation ¹ PTEN-Null ^{8,10,13} /PTEN WT ¹³ /RAS WT ¹³	WT ⁹	Epithelial
BT20*	0.2 μ M	++WT ²	PIK3CA H1047R/ P539R ¹ /PTEN-WT ^{8,10}	WT ⁹	Epithelial ⁵

* From ATCC; †, Provided by Steve Ethier; Asterand (http://www.cancer.med.umich.edu/breast_cell/Production/index.html)
P53 protein levels and mutational status (M, mutant protein; WT, wild-type protein)
P53 Levels / Mutational status of the tumors used to derive the cell lines. Square brackets indicate mRNA levels (without any available protein data)² P53 (IS), P53 immuno-staining⁴
¹. Gordon Mills 2008. ². Joe Gray 2006. ³. C. Perou 2001. ⁴. Adi Gazdar 1998. ⁵. Lipkowitz 2008. ⁶. Berkeley National lab. ⁷. Steve Ethier, Asterand; ⁸. Hoefflich et al. 2009; ⁹. Elstrodt et al. 2006; ¹⁰. Saal et al. 2006, 2008. ¹¹. Kozma SC, Bogaard ME, Buser K, et al The human c-Kirsten ras gene is activated by a novel mutation in codon 13 in the breast carcinoma cell line MDA-MB231. Nucleic Acids Res. 15: 5963-71, 1987 [[Abstract/Free Full Text](#)] ¹². Kraus MH, Yuasa Y, Aaronson SA. A position 12-activated H-ras oncogene in all HSS78T mammary carcinosarcoma cells but not normal mammary cells of the same patient. Proc Natl Acad Sci USA, 81: 5384-8, 1984. [[Abstract/Free Full Text](#)] ¹³. Hu et al Mol. Can. Res. 2009;7, 511-522 ¹⁴. Lynn B. Eckert... Channing J. Der, Cancer Research 64, 4585-4592, July 1, 2004; ¹⁵ Chen et. al., 2009

Figure W1. EC₅₀ of GDC-0980 in TNBC cell lines. Genetic backgrounds of the cells were tabulated.

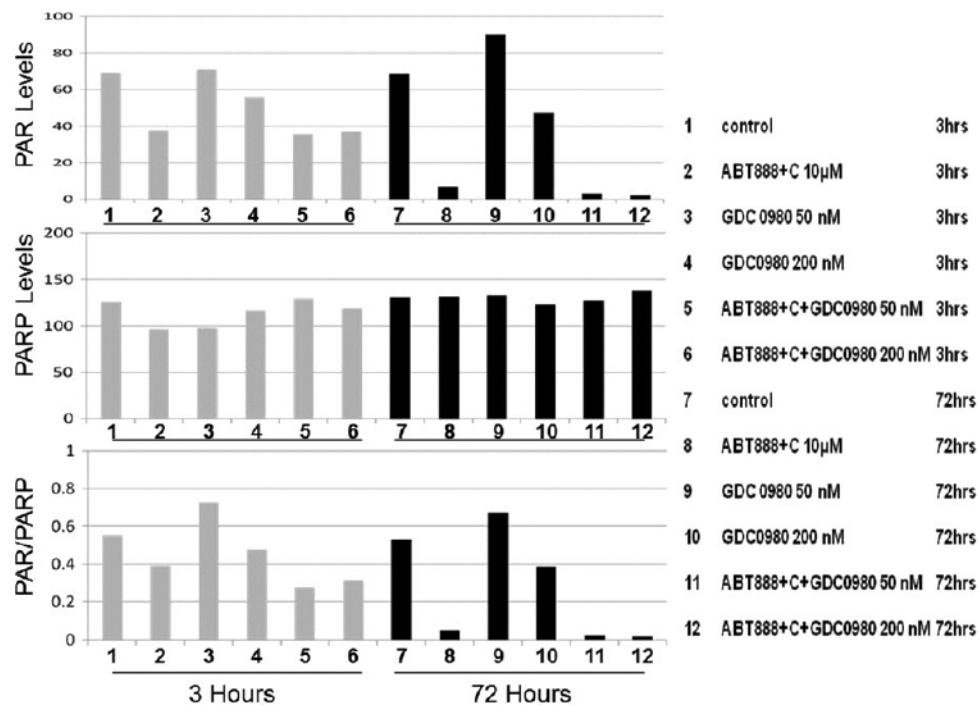


Figure W2. Effect of GDC-0980 alone and in combination with ABT888 plus carboplatin on ratios of PAR/PARP levels in MDA-MB231 at different time points. The semi-quantification of expression levels (of ImageJ intensities of the protein expression) of cellular PAR (upper panel), total PARP (middle panel), and ratio of PAR to total PARP (lower panel) in MDA-MB231 cells before and after treatments at different time points (3, 24, and 72 hours in successive darker shades) was shown as bar diagrams.

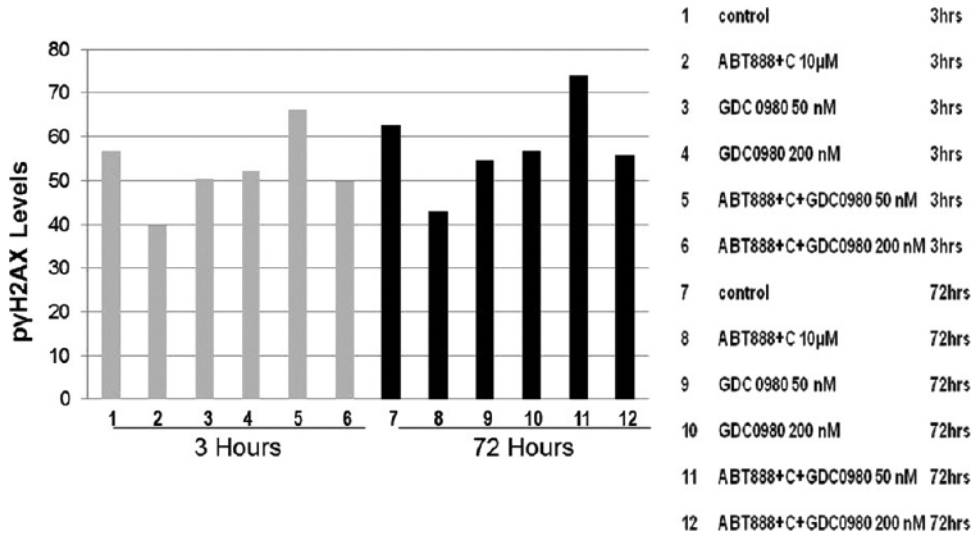


Figure W3. Effect of GDC-0980 alone and in combination with ABT888 plus carboplatin on pyH2AX^{S139} levels in MDA-MB231 at different time points. The semi-quantification of expression levels (of ImageJ intensities of the protein expression) of cellular pyH2AX^{S139} levels in MDA-MB231 cells before and after treatments at different time points (3 and 72 hours in successive darker shades) was shown as bar diagrams.

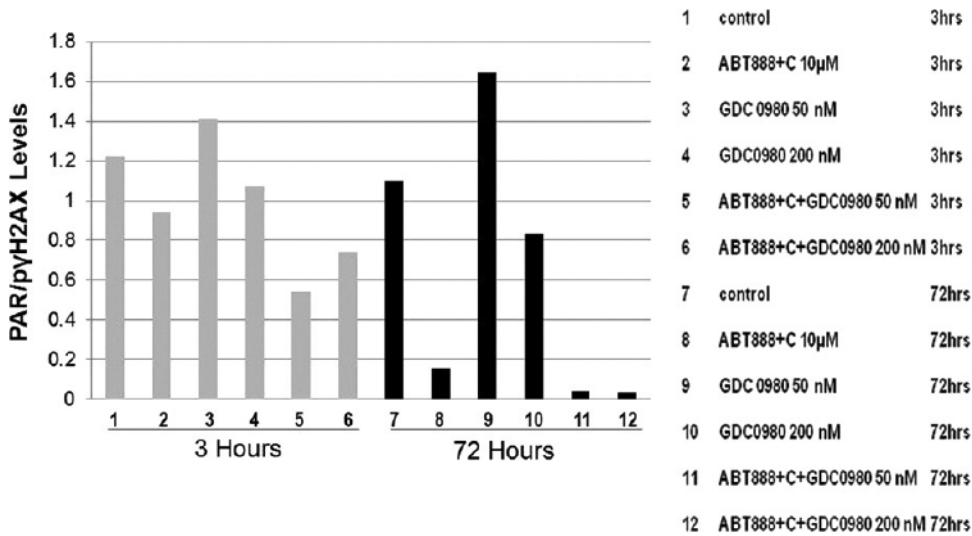
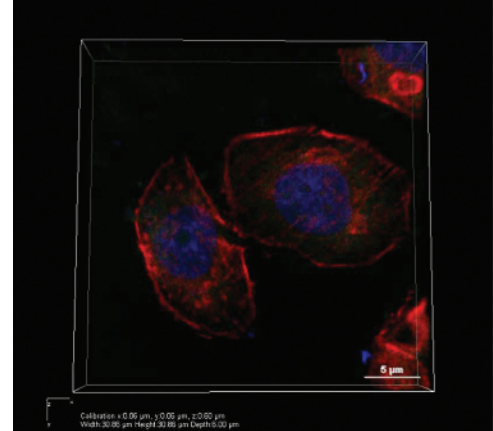
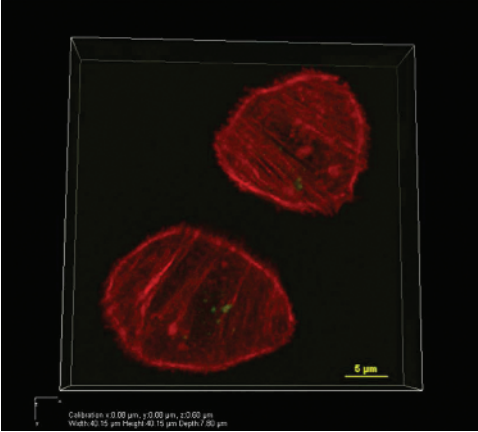
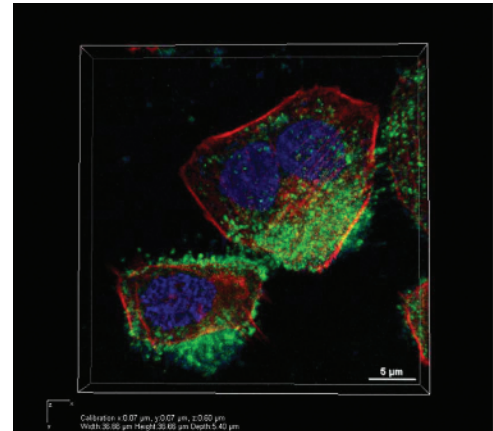
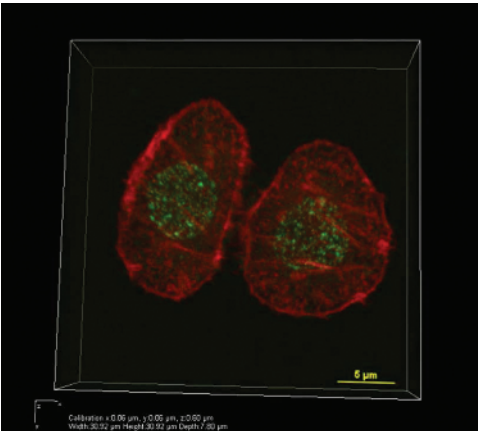


Figure W4. Effect of GDC-0980 alone and in combination with ABT888 plus carboplatin on ratios of PAR/pyH2AX^{S139} levels in MDA-MB231 at different time points. The semi-quantification of expression levels (of the ImageJ intensities of protein expression) of ratios of cellular PAR/pyH2AX^{S139} levels in MDA-MB231 cells before and after treatments at different time points (3 and 72 hours in successive darker shades) was shown as bar diagrams.



Movie W1. Three-dimensional projection movie showing nuclear $\text{pyH2AX}^{\text{S139}}$ foci in vehicle-treated MDA-MB468 cells at 24 hours.

Movie W3. Three-dimensional projection movie showing the absence of cytoplasmic cleaved caspase 3 in vehicle-treated MDA-MB468 cells at 72 hours.



Movie W2. Three-dimensional projection movie showing the effect of GDC-0980 alone on nuclear $\text{pyH2AX}^{\text{S139}}$ foci in MDA-MB468 cells at 24 hours.

Movie W4. Three-dimensional projection movie showing abundance of cytoplasmic cleaved caspase 3 in GDC-0980 + ABT888 + carboplatin-treated MDA-MB468 cells at 72 hours.

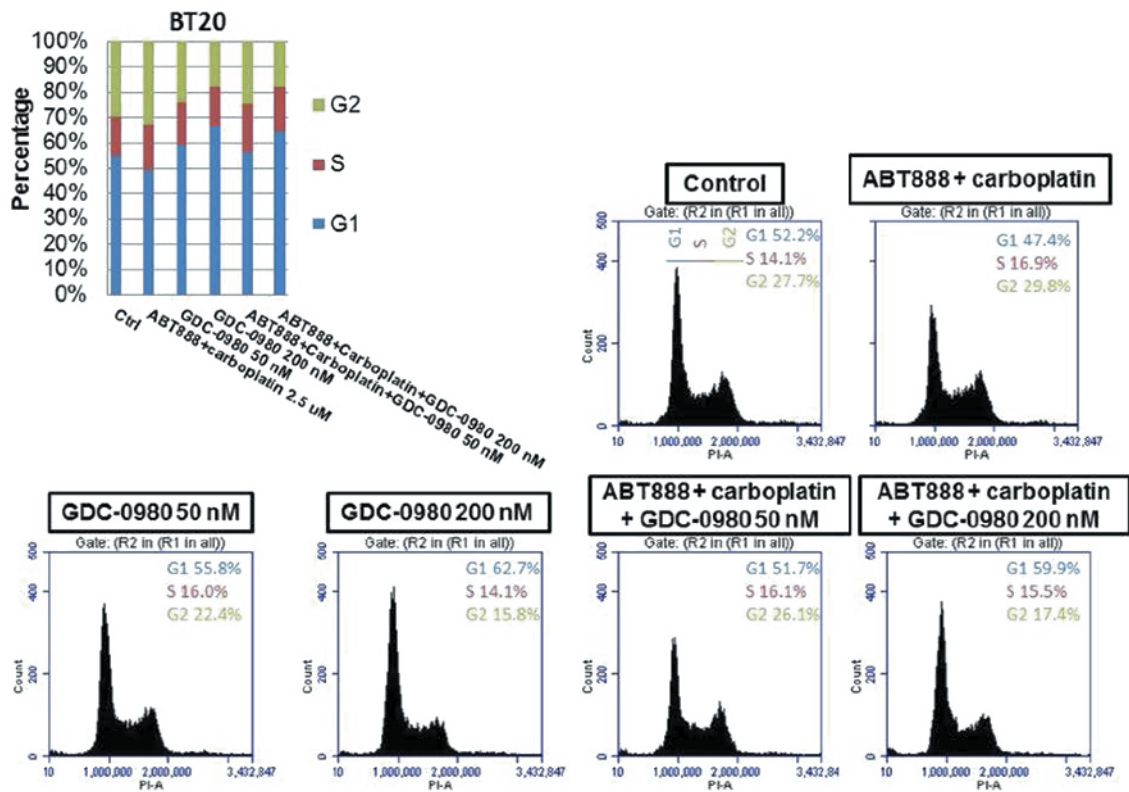


Figure W5. Effect of GDC-0980 alone and in combination with ABT888 plus carboplatin on cell cycle progression in BT20. Effect of two doses of GDC-0980 (50 and 200 nM) alone or in combination with ABT888 plus carboplatin (2.5 μ M) on cell cycle progression after 24 hours in BT20 cells.