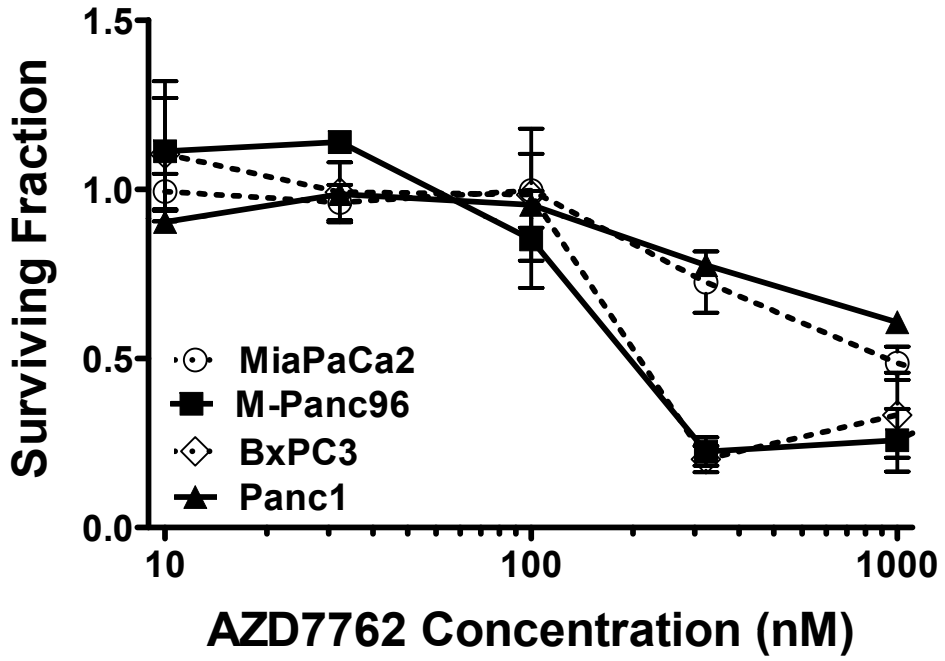
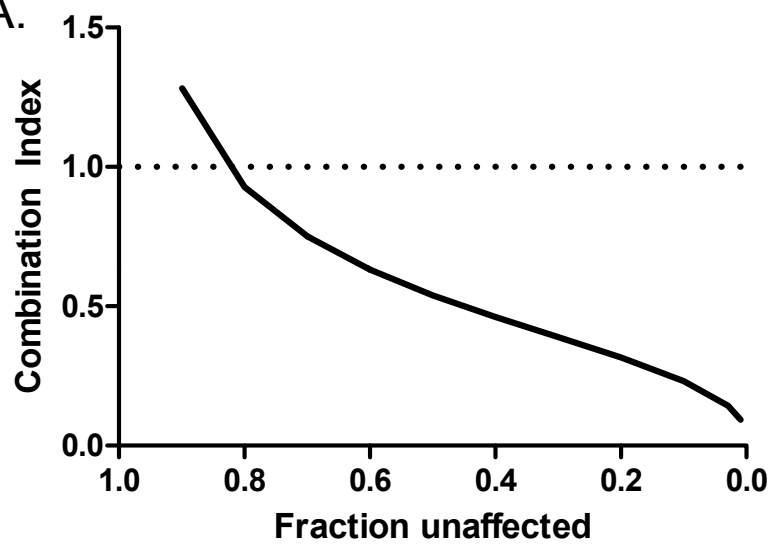
Supplementary Figure 1



Supplementary Figure 1. AZD7762 dose response. The indicated pancreatic cancer cell lines were treated for 24 hours with AZD7762 and then processed for clonogenic survival. Data are the mean of 2-6 independent experiments.

Supplementary Figure 2

A.



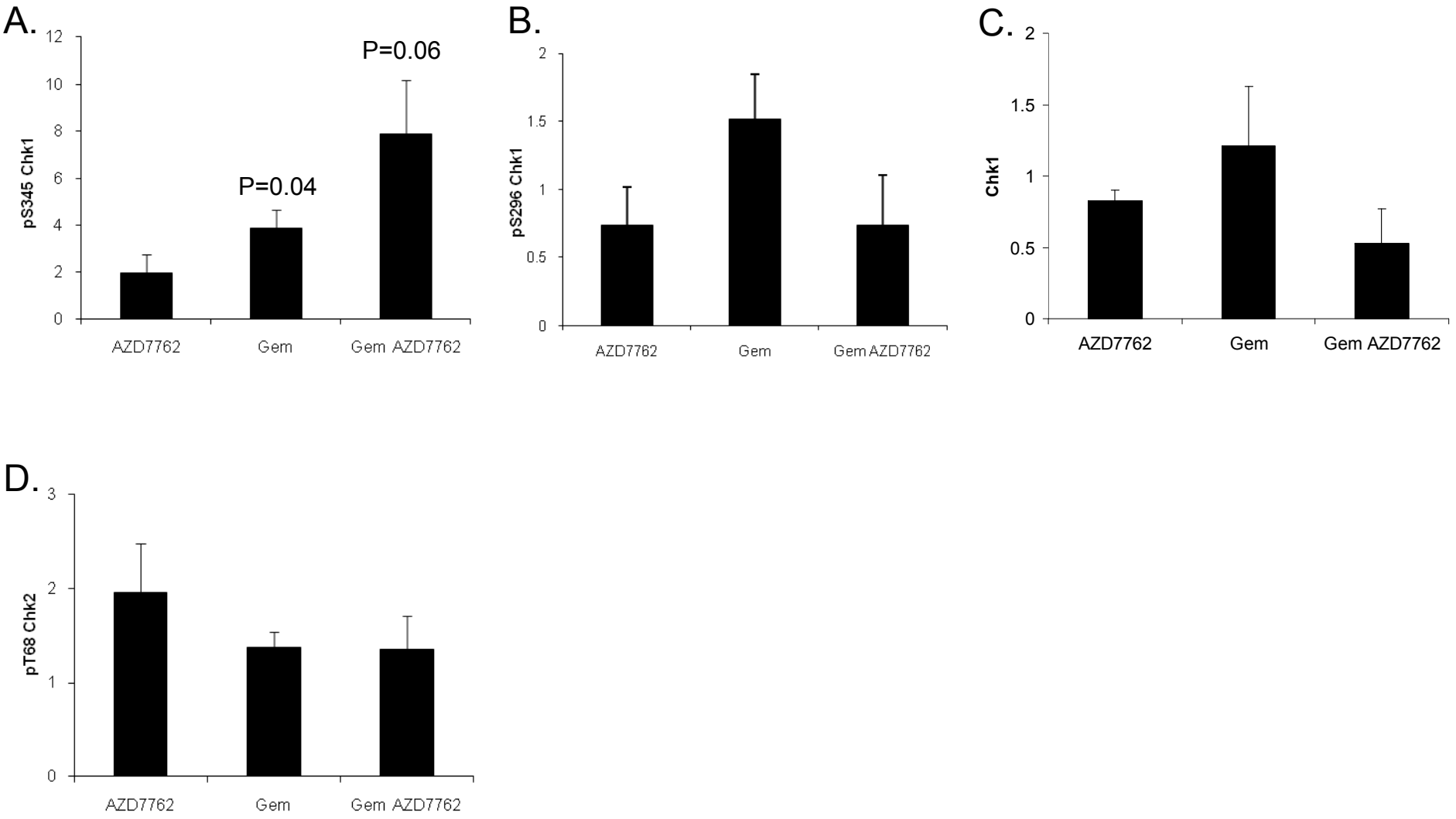
B.

Combination indices for gemcitabine and AZD7762

Fraction unaffected	Combination Index
0.5	0.5 ± 0.3
0.3	0.2 ± 0.1*
0.1	0.09 ± 0.02*
0.01	0.02 ± 0.01*

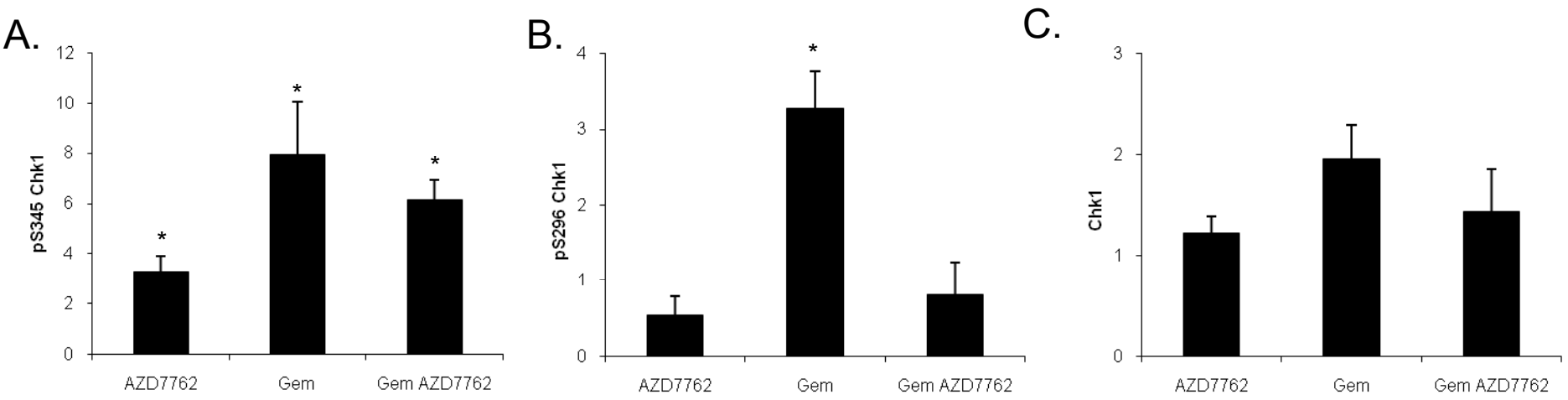
Supplementary Figure 2. Combination indices for gemcitabine and AZD7762. MiaPaCa-2 cells were treated with a fixed ratio of AZD7762:gemcitabine (1:2.5) under schedule 2 at drug concentrations of 20-400nM (AZD7762) and 50-500nM (gemcitabine). Data are from a single representative experiment (A) or are the mean of 3 independent experiments ± standard error (B). A combination index less than 1 indicates synergy and statistically significant differences are indicated (*P<0.05). Combination indices were calculated as previously described (22-23).

Supplementary Figure 3



Supplementary Figure 3. Quantification of cell cycle checkpoint proteins in MiaPaCa-2 tumors. MiaPaCa-2 tumor immunoblots, presented in Fig. 4A were quantitated by film densitometry. Data are the mean of n = 3 tumors per treatment condition. Statistically significant differences from control tumors are indicated (*P<0.05) and were determined by a Student's t-test.

Supplementary Figure 4



Supplementary Figure 4. Quantification of cell cycle checkpoint proteins in Patient-J tumors. Patient-J tumor immunoblots, presented in Fig. 4B were quantitated by film densitometry. Data are the mean of n = 3 tumors per treatment condition. Statistically significant differences from control tumors are indicated (*P<0.05) and were determined by a Stundent's t-test.

Supplementary Table 1

Suppl. Table 1. Relative weight loss during and after therapy

Treatment	Day 7	Day 14	Day 21
MiaPaca-2			
Control	1.06±0.02	1.09±0.02	1.13±0.01
Gem	1.04±0.01	1.09±0.03	1.09±0.02
AZD7762	1.03±0.02	1.06±0.01	1.10±0.00
Gem AZD7762	0.93±0.01	0.96±0.00	0.95±0.05
Patient-J			
Control	1.00±0.02	1.00±0.02	1.05±0.02
Gem	1.00±0.02	0.95±0.02	0.95±0.02
AZD7762	0.95±0.02	0.95±0.03	0.95±0.03
Gem AZD7762	1.00±0.02	0.93±0.02	0.93±0.02

Weights are relative to the first day of therapy (day 0).

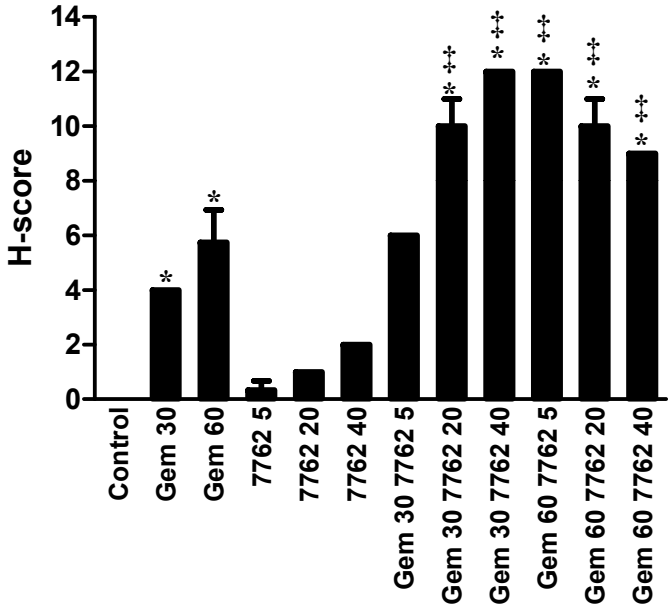
Supplementary Table 2

Suppl. Table 2. pS345 Chk1 and γ-H2AX immunohistochemistry

Treatment	pS345 Chk1	γ-H2AX
MiaPaca-2		
Control	-	-
Gem	- / + (<2%)	-
AZD7762	+ (<5%)	-
Gem AZD7762	++	++
Patient-J		
Control	-	-
Gem	++	+++
AZD7762	++	+++
Gem AZD7762	++/+++	+++

Data are an average score of 3 – 4 tumors per treatment group.

Supplementary Figure 5



Supplementary Figure 5. Quantification of S345 immunohistochemical staining in H460 tumor xenografts in response to gemcitabine and AZD7762. Mice bearing H460 tumors were treated with gemcitabine (30 - 60 mg/kg) and three hours later with AZD7762 (5 - 40 mg/kg). Three hours post-AZD7762, tissues were harvested and fixed for immunohistochemistry. H-score was determined as described in materials and methods. Data are the mean of 3 tumors per condition ± standard error. Statistically significant differences from control* or gemcitabine‡ are indicated ($P<0.05$) and were determined by one-way ANOVA.