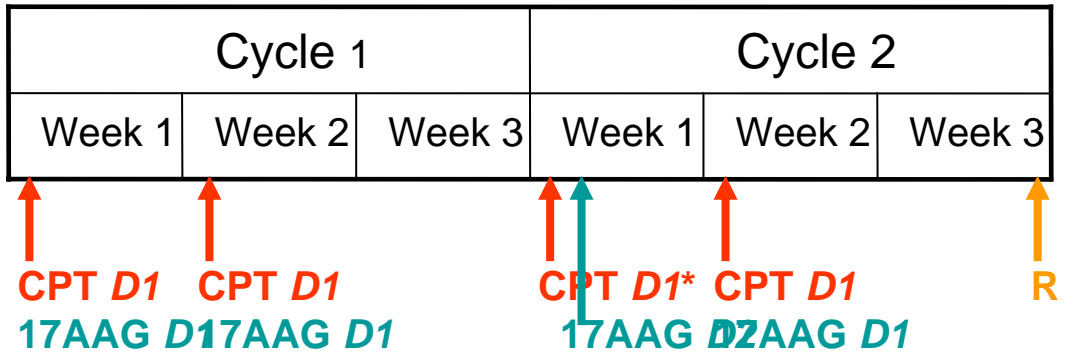
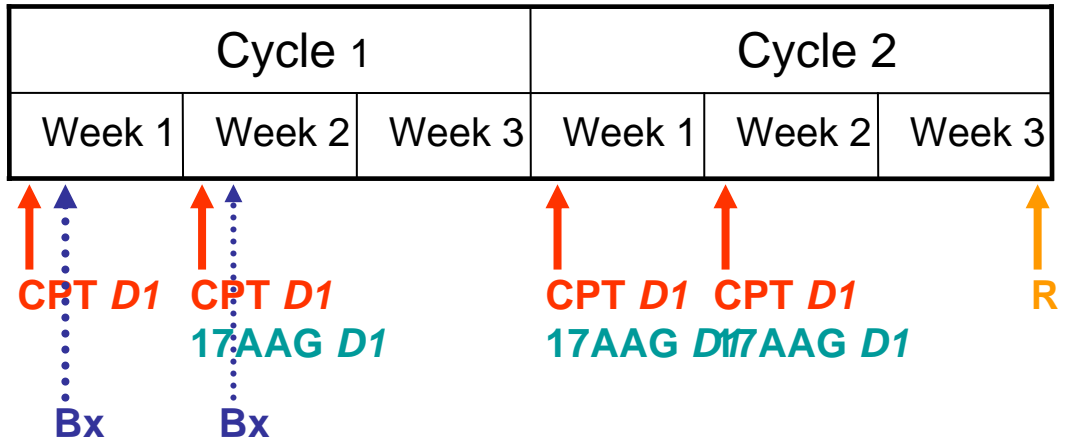


Supplemental Fig. 1

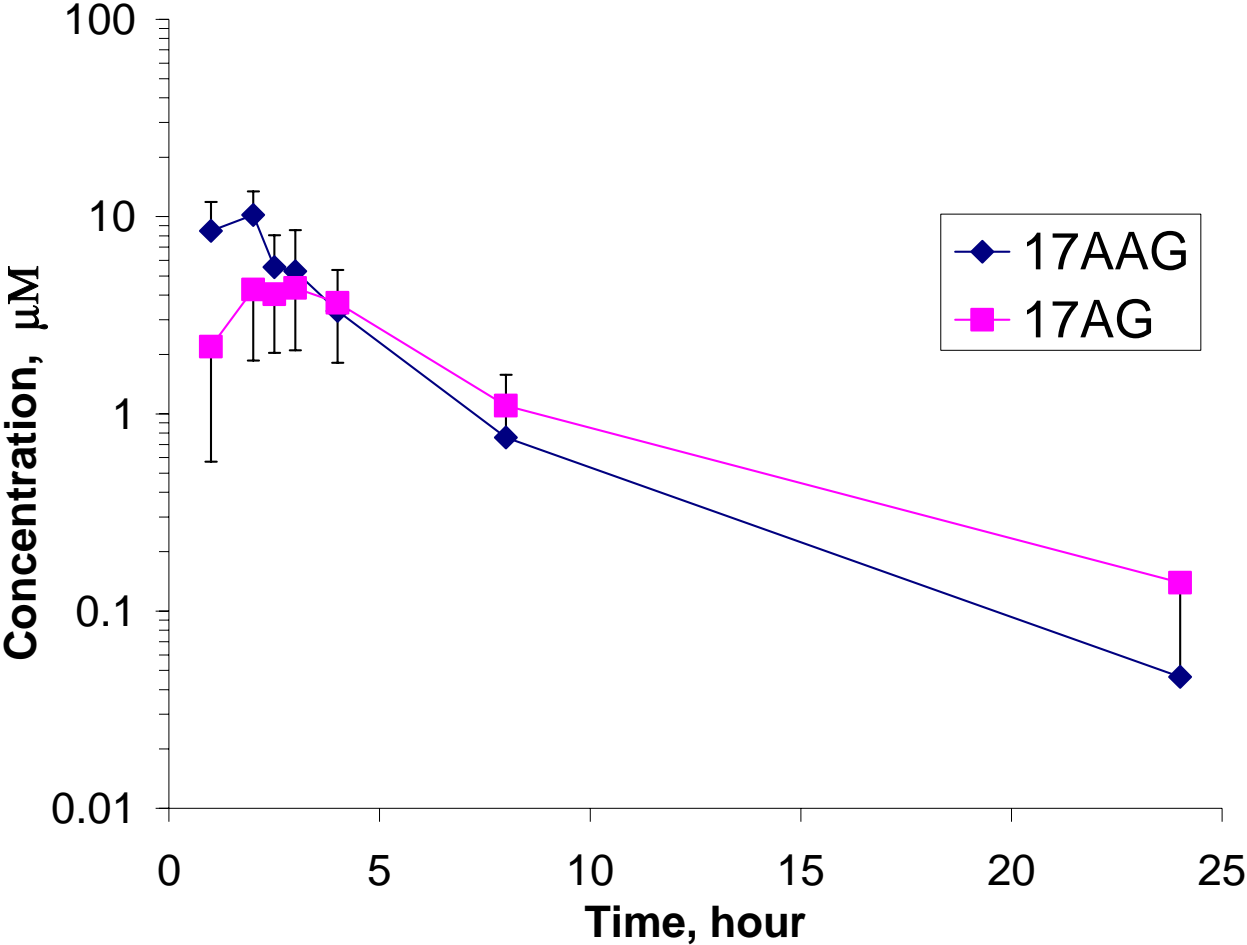
At non-MTD Doses (Dose Escalation Phase)



At MTD (Expansion Cohort)



Supplemental Fig. 2



Supplemental Figure Legends

Supplemental Figure 1. Study design schema. *During cycle 2 week 1 of dose escalation phase, irinotecan was given on day 1 and 17AAG on day 2 for pharmacokinetic interaction study purpose. CPT, irinotecan; D, day; Bx, tumor biopsy; R, radiological evaluation.

Supplemental Figure 2. Time versus mean plasma concentration curves of 17AAG and 17AG given at the MTD (300 mg/m² 17AAG and 100 mg/m² irinotecan).

Supplemental Table 1. Pair-wise comparison of PK parameters of 17AAG and 17AG obtained during Cycle 1 and Cycle 2				
PK parameters	# of Patients	C1	C2	<i>p</i> -value
		Median value	Median value	
17AAG				
AUC, $\mu\text{M}\cdot\text{h}$	11	31.1	26.2	0.12
$T_{1/2}$, h	11	2.4	2.5	0.64
Cl, L/h/m ²	11	13.1	15.0	0.067
17AG				
AUC, $\mu\text{M}\cdot\text{h}$	9	37.1	33.2	1.0
$T_{1/2}$, h	9	4.8	6.6	0.16

The differences between the pharmacokinetic (PK) parameters of 17AAG and 17AG obtained during Cycle 1 (C1) and Cycle 2 (C2) were compared using a paired Wilcoxon test. AUC, area under the curve; $T_{1/2}$, half-life; Cl, clearance.

Supplemental Table 2. Pair-wise comparison of PK parameters of irinotecan, SN38, and SN38G obtained during Cycle 1 and Cycle 2				
PK parameters	# of Patients	C1	C2	<i>p</i> -value
		Median value	Median value	
Irinotecan				
AUC, $\mu\text{M}\cdot\text{h}$	9	8500	5520	0.42
$T_{1/2}$, h	9	1.9	1.9	1.0
Cl, L/h/m ²	9	21.3	27.1	0.43
SN38				
AUC, $\mu\text{M}\cdot\text{h}$	9	753	1830	0.30
$T_{1/2}$, h	9	24	27	0.50
Cl, L/h/m ²	9	241	273	0.73
SN38G				
AUC, $\mu\text{M}\cdot\text{h}$	8	2540	3400	1.0
$T_{1/2}$, h	8	35	25	0.82
Cl, L/h/m ²	8	68.9	32.2	0.43

The differences between the pharmacokinetic (PK) parameters of irinotecan, SN38, and SN38G obtained during Cycle 1 (C1) and Cycle 2 (C2) were compared using a paired Wilcoxon test. AUC, area under the curve; $T_{1/2}$, half-life; Cl, clearance.