

ADDITIONAL FILE 5. Dose adjustment algorithms based on plasma 5-fluorouracil measurement in colorectal cancer patients

Gamelin et al. (1996)[24] : 8 hour 5-fluorouracil infusion regimen + FA; initial dose 1,500 mg/m²						
<i>Plasma 5-fluorouracil (µg/L)</i>	AUC mg*H/L	Dose change § (%)	<i>Plasma 5-fluorouracil (µg/L)</i>	AUC mg*H/L	Dose change§ (%)	In case of toxicity
<500	<4	+50%	1800-2000	14.4-16	+5%	Grade 2 toxicity: 200mg dose decrease Grade 3 toxicity: 1 week break then 300mg dose decrease
500-1000	4-8	+40%	2000-3000	16-24	None	
1000-1300	8-10.4	+30%	3000-3200	24-25.6	-5%	
1300-1500	10.4-12	+20%	3200-3500	25.6-28	-10%	
1500-1800	12-14.4	+10%	>3500	>28	-30%	

§ percentage change from previous cycle dose; H = hours of 5-fluorouracil infusion

Kaldate et al. (2012)^[40] : 46 hour 5-fluorouracil infusion + oxaloplatin + FA; initial dose 2,400 to 3,000 mg/m² after a 400 mg/m² bolus					
<i>Plasma 5-fluorouracil (µg/L) ¥</i>	AUC §§ mg*H/L	Change in dose (mg/m²)	<i>Plasma 5-fluorouracil (µg/L) ¥</i>	AUC §§ mg*H/L	Change in dose (mg/m²)
174-217	8-10	↑727			
239-283	11-13	↑582	672-717	31-33	↓291
304-348	14-16	↑436	739-783	34-36	↓436
370-413	17-19	↑291	804-848	37-39	↓582
435-652	20-30	None	870	≥40	↓727

¥ Calculated assuming infusion of 46 hours; §§ area under the curve of previous cycle; H = hours of 5-fluorouracil infusion

Ychou et al. (1999)[32] 400 mg/ m² bolus 5-fluorouracil; then a 22 hour infusion of 600 mg/ m² 5-fluorouracil repeated the next day; +FA	
AUC §§§ mg*H/L*m²	Dose increase § (%)
≤5	150%
5<AUC≤10	100%
10<AUC≤15	50%
15<AUC≤20	25%
>20	No increase
§§§ note differently reported pharmacokinetic units and calculation for area under the curve relative to the other algorithms	