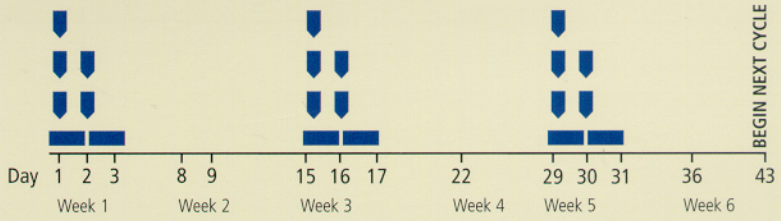
CAMPTOSAR+5-FU/LV*:

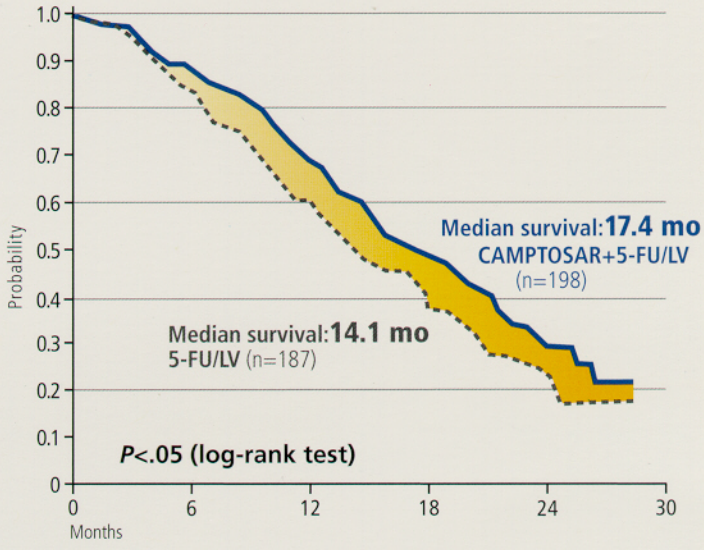
Proven survival benefit with a choice of 2 dosing regimens

CAMPTOSAR+INFUSIONAL 5-FU/LV vs INFUSIONAL 5-FU/LV

	STARTING DOSE
CAMPTOSAR	180 mg/m² IV over 90 min
LV	200 mg/m² IV over 2 h
5-FU bolus	400 mg/m² IV bolus
5-FU infusion†	600 mg/m² IV over 22 h



NOTE: Outside of a well-designed clinical study, CAMPTOSAR should not be used in combination with the "Mayo Clinic" regimen of 5-FU/LV (administration for 4 to 5 consecutive days every 4 weeks) because of reports of increased toxicity.



	CAMPTOSAR +INFUSIONAL 5-FU/LV (n=198)		INFUSIONAL 5-FU/LV (n=187)
Confirmed Response Rate (%)‡	**35**	(P<.005§)	**22**
TTP‖ (median/mo)	**6.7**	(P<.001¶)	**4.4**
Overall Survival (median/mo)	**17.4**	(P<.05¶)	**14.1**

Adverse Events[1] (%)		CAMPTOSAR +INFUSIONAL 5-FU/LV (n=145)	INFUSIONAL 5-FU/LV (n=143)
Late Diarrhea	grade 3	10	4
	grade 4	4	2
Vomiting	grade 3	3	1
	grade 4	1	1
Mucositis	grade 3	4	3
	grade 4	0	0
Neutropenia	grade 3	36	13
	grade 4	10	1
Neutropenic Fever[2]	grade 3/4	3	1

*5-FU/LV=5-fluorouracil/leucovorin.
†Infusion follows bolus administration.
‡Responses confirmed ≥4 to 6 weeks after initial objective response.
§Chi-square test.
‖TTP=Time to tumor progression.
¶Log-rank test.

Please see the enclosed full prescribing information for CAMPTOSAR.

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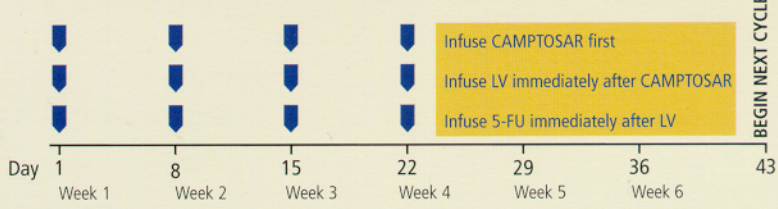
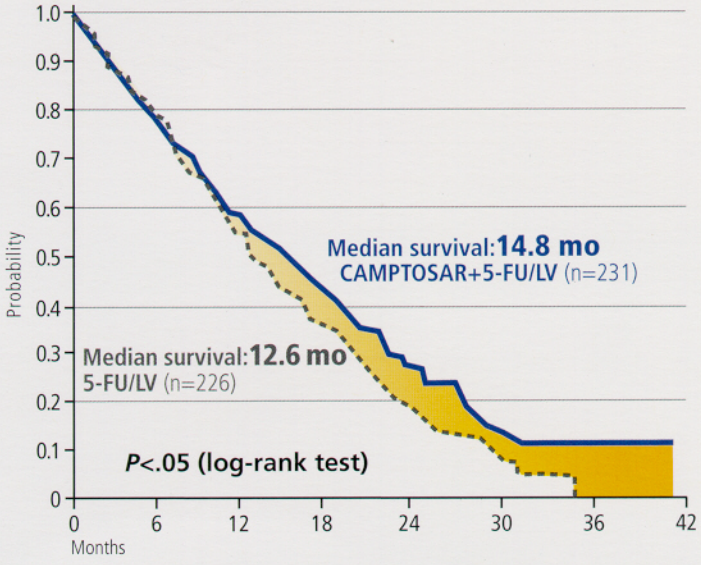
Base your dosing decision on the clinical data

CAMPTOSAR+BOLUS 5-FU/LV vs BOLUS 5-FU/LV

	STARTING DOSE
CAMPTOSAR	125 mg/m² IV over 90 min
LV	20 mg/m² IV
5-FU	500 mg/m² IV



NOTE: Outside of a well-designed clinical study, CAMPTOSAR should not be used in combination with the "Mayo Clinic" regimen of 5-FU/LV (administration for 4 to 5 consecutive days every 4 weeks) because of reports of increased toxicity.



	CAMPTOSAR +BOLUS 5-FU/LV (n=231)		BOLUS 5-FU/LV (n=226)
Confirmed Response Rate (%)*	**39**	(*P*<.0001†)	**21**
TTP‡ (median/mo)	**7.0**	(*P*=.004§)	**4.3**
Overall Survival (median/mo)	**14.8**	(*P*<.05§)	**12.6**

Adverse Events† (%)		CAMPTOSAR +BOLUS 5-FU/LV (n=225)	BOLUS 5-FU/LV (n=219)
Late Diarrhea	grade 3	15	6
	grade 4	8	7
Vomiting	grade 3	5	3
	grade 4	4	1
Mucositis	grade 3	2	15
	grade 4	0	2
Neutropenia	grade 3	30	24
	grade 4	24	43
Neutropenic Fever	grade 3/4	7	15

*Responses confirmed ≥4 to 6 weeks after initial objective response.
†Chi-square test.
‡TTP=Time to tumor progression.
§Log-rank test.

Recommended Dose Modifications for Combination Schedules of CAMPTOSAR

TOXICITY NCI CTC Grade[a] (Value)	DURING A COURSE OF THERAPY	AT THE START OF SUBSEQUENT COURSES OF THERAPY[b]
No toxicity	Maintain dose level	Maintain dose level
Neutropenia		
1 (1,500 to 1,999/mm^3)	Maintain dose level	Maintain dose level
2 (1,000 to 1,499/mm^3)	↓ 1 dose level	Maintain dose level
3 (500 to 999/mm^3)	Omit dose, then ↓ 1 dose level when resolved to ≤ grade 2	↓ 1 dose level
4 (< 500/mm^3)	Omit dose, then ↓ 2 dose levels when resolved to ≤ grade 2	↓ 2 dose levels
Neutropenic fever (grade 4 neutropenia & ≥ grade 2 fever)	Omit dose, then ↓ 2 dose levels when resolved	↓ 2 dose levels
Diarrhea		
1 (2-3 stools/day > pretx[c])	Maintain dose level	Maintain dose level
2 (4-6 stools/day > pretx)	↓ 1 dose level	Maintain dose level
3 (7-9 stools/day > pretx)	Omit dose, then ↓ 1 dose level when resolved to ≤ grade 2	↓ 1 dose level
4 (≥10 stools/day > pretx)	Omit dose, then ↓ 2 dose levels when resolved to ≤ grade 2	↓ 2 dose levels
Other nonhematologic toxicities		
1	Maintain dose level	Maintain dose level
2	↓ 1 dose level	Maintain dose level
3	Omit dose, then ↓ 1 dose level when resolved to ≤ grade 2	↓ 1 dose level
4	Omit dose, then ↓ 2 dose levels when resolved to ≤ grade 2	↓ 2 dose levels
	For mucositis/stomatitis decrease only 5-FU, not CAMPTOSAR	*For mucositis/stomatitis decrease only 5-FU, not CAMPTOSAR*

[a] National Cancer Institute Common Toxicity Criteria.
[b] Relative to the starting dose used in the previous course.
[c] Pretreatment.

	INFUSIONAL REGIMEN: STARTING DOSE AND MODIFIED DOSE LEVELS		
	Starting Dose	**Dose Level - 1**	**Dose Level - 2**
CAMPTOSAR	180 mg/m^2	150 mg/m^2	120 mg/m^2
LV	200 mg/m^2	200 mg/m^2	200 mg/m^2
5-FU bolus	400 mg/m^2	320 mg/m^2	240 mg/m^2
5-FU infusion*	600 mg/m^2	480 mg/m^2	360 mg/m^2

*Infusion follows bolus administration.

	BOLUS REGIMEN: STARTING DOSE AND MODIFIED DOSE LEVELS		
	Starting Dose	**Dose Level - 1**	**Dose Level - 2**
CAMPTOSAR	125 mg/m^2	100 mg/m^2	75 mg/m^2
LV	20 mg/m^2	20 mg/m^2	20 mg/m^2
5-FU	500 mg/m^2	400 mg/m^2	300 mg/m^2

For all first-line therapy

- In patients receiving either CAMPTOSAR + 5-FU/LV or 5FU-LV in clinical trials, higher rates of hospitalization, neutropenic fever, thromboembolism, first-cycle treatment discontinuation, and early deaths were observed in patients with a baseline performance status of 2 than in patients with a baseline performance status of 0 or 1
- Particular caution should be exercised in monitoring the effects of CAMPTOSAR in elderly patients with comorbid conditions and in patients who have previously received pelvic/abdominal irradiation
- Dosing recommendations for patients with bilirubin >2 mg/dL cannot be made as they were not included in the clinical trials
- It is recommended that patients receive premedication with antiemetic agents. Prophylactic or therapeutic administration of atropine should be considered in patients experiencing cholinergic symptoms

Please see the enclosed full prescribing information for CAMPTOSAR.

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CAMPTOSAR+5-FU/LV:

A standard of care in first-line metastatic colorectal cancer

Proven survival benefit with a choice of dosing regimens

- CAMPTOSAR+infusional 5-FU/LV: 6-week course
- CAMPTOSAR+bolus 5-FU/LV: 6-week course

Two regimens with significant survival advantage vs 5-FU/LV

CAMPTOSAR+INFUSIONAL 5-FU/LV				
Median Survival (mo)	17.4	vs	14.1	($P<.05$)
Response Rate (%)	35	vs	22	($P<.005$)
TTP (mo)	6.7	vs	4.4	($P<.001$)

CAMPTOSAR+BOLUS 5-FU/LV				
Median Survival (mo)	14.8	vs	12.6	($P<.05$)
Response Rate (%)	39	vs	21	($P<.0001$)
TTP (mo)	7.0	vs	4.3	($P=.004$)

Important safety considerations

- CAMPTOSAR can induce life threatening neutropenia and late diarrhea
- Toxicities are generally manageable with appropriate intervention
  - Diarrhea: high-dose loperamide therapy (see package insert for regimen), with antibiotic support, in some cases
  - Neutropenia: antibiotic support
  - Nausea/vomiting: prophylactic antiemetics

References: 1. Data on file. Oncologic Drug Advisory Committee Brochure, March 16, 2000. Pharmacia Corporation. **2.** Data on file. Final Study Report: Irinotecan V303, March 1999. Pharmacia Corporation.

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February 2003