

CODE: CISPFU/CISPCAPE-TRAST

[Regimen Name](#) | [Drug Regimen](#) | [Cycle Frequency](#) | [Premedication & Supportive Measures](#) | [Dose Modifications](#) | [Adverse Effects](#) | [Interactions](#) | [Drug Administration & Special Precautions](#) | [Clinical Monitoring](#) | [Administrative Information](#) | [Key References](#) | [Other Notes](#)

A	REGIMEN NAME	CISPLATIN-FLUOROURACIL / CAPECITABINE (Xeloda®)-TRASTUZUMAB Chemotherapy
Cancer	Advanced Gastric	Palliative Intent
Regimen Category	Emergent: A regimen which has not yet been accepted as a standard regimen but may become so based upon emergent Phase II & III clinical trial data. This is published on this website for your information, but it does not imply endorsement by the CCO Disease Site Group.	
Rationale and Uses	For the palliative treatment of HER2-positive locally advanced, recurrent, or metastatic gastric cancer.	

▲ [Back to Top](#)

B	DRUG REGIMEN		
LOADING DOSE			
<u>TRASTUZUMAB</u> (Round to nearest 1 mg)	8 mg/kg	IV	Day 1 (Loading dose – first cycle only)
MAINTENANCE DOSE			
<u>TRASTUZUMAB</u> (Round to nearest 1 mg)	6 mg/kg	IV	Day 1 (Cycle 2 and onwards)
<u>CISPLATIN</u> (Round to nearest 1mg)	80 mg/m ²	IV	Day 1
and <u>ONE</u> of:			
<u>FLUOROURACIL</u> (Round to nearest 50 mg)	800 mg/m ² /day	CIV for 5 days	Starting on Day 1
<u>OR</u>			
<u>CAPECITABINE</u> (Outpatient prescription in 150mg and 500mg tablets)	1000 mg/m ² *	PO	Q12H Days 1 to 14
(* Total dose 2000 mg/m ² /day)			

▲ [Back to Top](#)

C	CYCLE FREQUENCY
REPEAT EVERY 21 DAYS	<p><u>Cisplatin-Fluorouracil / Cisplatin-Capecitabine:</u> Up to 6 cycles, unless evidence of disease progression or unacceptable toxicity</p> <p><u>Trastuzumab:</u> Until evidence of disease progression or unacceptable toxicity</p>

▲ [Back to Top](#)

D	PREMEDICATION AND SUPPORTIVE MEASURES
<p>ANTIEMETIC REGIMEN: <u>HESKETH LEVEL 5</u> (On Cisplatin treatment days)</p>	<ul style="list-style-type: none"> • <i>Trastuzumab: Nausea and vomiting are usually symptoms that are related to infusion-associated reactions. To prevent recurrence of infusion-associated reactions, acetaminophen and diphenhydramine may be given as pre-medication. Refer to Trastuzumab drug monograph for full details.</i> • <i>Use standard regimens for cisplatin pre-medication and hydration. See Cisplatin monograph.</i> • <i>Capecitabine or Fluorouracil: Topical emollients (e.g. hand creams, udder balm) or oral pyridoxine therapy may ameliorate the manifestations of hand-foot syndrome in patients. Supportive care should be provided, including loperamide for diarrhea.</i>

▲ [Back to Top](#)

E

DOSE MODIFICATIONS

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations are in use at some centres.

Hematologic Toxicities

See [Appendix 6](#) for general recommendations.

Suggested dose modifications**:

<u>Toxicity / Counts (x 10⁹ /L)</u>		<u>Toxicity / Counts (x 10⁹ /L)</u>	<u>Cisplatin (% previous dose)</u>	<u>Fluorouracil (% previous dose)</u>	<u>Capecitabine (% previous dose)</u>	<u>Trastuzumab (% previous dose)</u>
Febrile Neutropenia	OR	ANC < 0.5 ≥ 7 days	75%	75%	See capecitabine dose modification table	No change
Thrombocytopenic bleeding	OR	Platelets < 25	75%	75%		No change
Platelets ≥ 100	AND	ANC ≥ 1.5	No change	No change		No change
Grade 2 Neurotoxicity			Consider dose reduction	No change	No change	No change
≥ grade 3 neurotoxicity			Discontinue	No change	No change	No change
≥ grade 3 diarrhea or mucositis			No change	Hold*, then 66%	See capecitabine dose modification table	No change
≥ grade 2 hand-foot syndrome			No change	66% (Hold* if ≥ grade 3)		No change
Other grade 3 non-hematological			Hold*, then 75%	Hold*, then 75%		Hold* if cardiovascular
Other grade 4 non-hematological			Discontinue			Discontinue

* Major organ toxicity must be ≤ grade 2, platelets ≥ 100 x 10⁹/L and ANC ≥ 1.5 x 10⁹/L before retreatment.

** Some content adapted from ECF clinical trials.

▲ [Back to Top](#)

E DOSE MODIFICATIONS (continued)

Dose Modifications: Capecitabine

	Action During a Course of Therapy	Dose Adjustment for Next Cycle (% of starting dose)
Grade 1	Maintain dose level	Maintain dose level
Grade 2 1 st appearance 2 nd appearance 3 rd appearance 4 th appearance	Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Discontinue treatment permanently	100% 75% 50%
Grade 3 1 st appearance 2 nd appearance 3 rd appearance	Interrupt until resolved to grade 0-1 Interrupt until resolved to grade 0-1 Discontinue treatment permanently	75% 50%
Grade 4 1 st appearance	Discontinue permanently or If physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	Discontinue or 50%
2 nd appearance	Discontinue permanently	

Renal Impairment

No adjustment required for trastuzumab.

Creatinine Clearance (mL/min)	Capecitabine (% previous dose)	Fluorouracil	Cisplatin (% previous dose)
>60-80	100%; monitor closely	No change	100 %
51-60			OMIT; or 50 % with caution
>40-50	75%; use with caution		OMIT*
30-40			
< 30mL/min	DISCONTINUE	May consider dose reduction	

*adapted from ECF clinical trials

E**DOSE MODIFICATIONS (continued)**Hepatic Impairment

No adjustment required for trastuzumab and cisplatin.

Capecitabine:

- Use dose modification table above for increases in bilirubin.
- In patients with mild to moderate hepatic impairment due to liver metastases exposure is increased, but no dose adjustment is necessary, although caution should be exercised.
- The use of capecitabine in patients with severe hepatic impairment has not been studied.

Fluorouracil: **OMIT** if bilirubin > 4 x ULN

Cardiac Toxicities

Trastuzumab should be held with a fall in LVEF of 10 or more points, or if LVEF falls to less than 50%. Repeat LVEF in 3 weeks and consider discontinuing. Trastuzumab should be discontinued if clinically significant cardiac dysfunction develops.

▲ [Back to Top](#)

F**ADVERSE EFFECTS**

Refer to the Cisplatin, 5FU, Capecitabine or Trastuzumab drug monographs for full details of adverse effects.

Prolonged 5FU regimens have more hand-foot syndrome but less myelosuppression and GI effects compared to bolus infusions

Most Frequently Occurring Adverse Effects

- Infusion-associated symptoms (chills and fever, nausea, vomiting, pain, rigors, headache, asthenia, etc)
- Nausea and vomiting
- Fatigue
- Hand-foot syndrome
- Nephrotoxicity
- Neurotoxicity (ototoxicity)
- Myelosuppression ± infection / bleeding
- Stomatitis and diarrhea
- Abdominal pain
- Weight loss

Less Common but may be Severe or Life-Threatening

- Cardiotoxicity
- Venous thromboembolism
- Leukemia

[▲ Back to Top](#)

G**INTERACTIONS**

Refer to the Cisplatin, 5FU, Capecitabine or Trastuzumab drug monographs for full details.

[▲ Back to Top](#)

H**DRUG ADMINISTRATION AND SPECIAL PRECAUTIONS**

Refer to the Cisplatin, 5FU, Capecitabine or Trastuzumab drug monographs for full details.

[▲ Back to Top](#)

I CLINICAL MONITORING

- Clinical toxicity assessment (including stomatitis, neurotoxicity, ototoxicity, cardiotoxicity, hand-foot syndrome, diarrhea). Grade toxicity using the current [NCI Common Toxicity Criteria Version](#).
- CBC before each cycle.
- Baseline and regular liver and renal function tests (including electrolytes and magnesium).
- Baseline and regular cardiac assessment, including evaluation of left ventricular function (Echocardiogram or MUGA scan); more frequent with asymptomatic reductions in LVEF.

▲ [Back to Top](#)

J ADMINISTRATIVE INFORMATION

Patient visit 4 to 5 hours

▲ [Back to Top](#)

K KEY REFERENCE(S)

Van Cutsem E, Kang Y, Chung H, et al. Efficacy results from the ToGA trial: A phase III study of trastuzumab added to standard chemotherapy (CT) in first-line human epidermal growth factor receptor 2 (HER2)-positive advanced gastric cancer (GC). J Clin Oncol 2009; 27(18s): abstract LBA4509.

▲ [Back to Top](#)

L OTHER NOTES

Schedule pump teaching session BEFORE first day of infusion.

▲ [Back to Top](#)