

BCCA Protocol Summary for Continuation of Palliative Treatment of Metastatic or Inoperable, Locally Advanced Gastric or Gastroesophageal Junction Adenocarcinoma Using Trastuzumab

Protocol Code: GIGAVTR

Tumour Group: Gastrointestinal

ELIGIBILITY:

- Metastatic or inoperable locally advanced gastric or gastroesophageal junction adenocarcinoma responding to UGIGAVCFT or UGIGAVCCT
- ECOG performance status 0-2,
- HER-2 overexpression defined as either IHC3+, or FISH amplification ratio of greater than or equal to 2 per BCCA central laboratory
- No signs or symptoms of cardiac disease. For patients with cardiac risk factors or history of cardiac disease, a MUGA or ECHO should be done to document normal left ventricular ejection fraction (LVEF).
- A "Class II Drug Registration Form" must be submitted at the time of initiation of treatment.

NOTE: A BCCA "Compassionate Access Program" form with appropriate clinical information re ongoing response must be submitted and approved prior to the fourth cycle of maintenance treatment.

EXCLUSIONS:

- Clinically significant cardiac disease (history of symptomatic ventricular arrhythmias, congestive heart failure or myocardial infarction within previous 12 months)

TESTS:

- Baseline: CBC and differential, platelets
- (ECG, Echocardiogram or MUGA scan)
- If clinically indicated anytime: cardiac function (ECG, Echocardiogram or MUGA scan), LFTs, creatinine, tumour markers,

PREMEDICATIONS:

- Not usually required for trastuzumab

TREATMENT: Patients to have received previous cycles of treatment with Trastuzumab

Drug	Dose	BCCA Administration Guideline
Trastuzumab	6 mg/kg	IV in 250 mL NS over 30 min for all. (Observe for 60 minutes post-infusion*)

*Observation period not required after 3 consecutive treatments with no reaction

Repeat every 21 days until disease progression or unacceptable toxicities. NOTE: A BCCA "Compassionate Access Program" form with appropriate clinical information re ongoing response must be submitted and approved prior to the fourth cycle of maintenance treatment.

DOSE MODIFICATIONS:

- None required. Discontinued if unacceptable toxicity occurs.
- NOTE: Weight will be measured at each scheduled physician visit. Consider change in trastuzumab dose for weight change greater than 10%.
- NOTE: If an interruption in treatment of greater than 6 weeks occurs, consider repeating the loading dose of 8 mg/kg (see protocol UGIGAVCFT or UGIGAVCCT) then resume usual dosing.

PRECAUTIONS:

1. **Cardiac toxicity:** Trastuzumab can produce ventricular dysfunction and congestive heart failure in less than 2% of patients. The majority of patients who develop cardiac dysfunction are symptomatic. Regular monitoring of asymptomatic patients is not routinely necessary but can be considered after 6 months of treatment with trastuzumab. If no significant decline in cardiac function, repeated testing is not generally necessary, unless clinically indicated. Discontinue treatment for symptomatic congestive heart failure or serious cardiac arrhythmias.
2. **Trastuzumab infusion-associated symptoms**, usually chills and fever, can occur in some patients during the first trastuzumab infusion. Symptoms may be treated with acetaminophen, diphenhydramine and meperidine with or without an infusion rate reduction. Rarely, serious infusion-related reactions have been reported. For serious reactions, discontinue the trastuzumab infusion and provide supportive therapy such as oxygen, beta-agonists and corticosteroids.
3. **Neutropenia (uncommon):** Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **A possible interaction with warfarin has been reported.** An increased INR and bleeding may occur in patients previously stabilized on warfarin. The interaction was noted in two patients after 8-10 doses of trastuzumab. Patients will have had routine INR monitoring while receiving chemotherapy. If stable, monthly INR's should be continued and patient should be informed to watch for any bleeding.

Call the GI Systemic Therapy physician at your regional cancer centre or Dr. Sanjay Rao at (250) 712-3900 or 1-888-563-7773 with any problems or questions regarding this treatment program.

Date activated: February 1, 2010

Date revised:

Reference:

1. 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(15s): Abstract LBA4509.
2. Bang YJ, Chung HC, Xu JM, et al. Pathological features of advanced gastric cancer: relationship to human epidermal growth factor receptor 2 positivity in the global screening programme of the ToGA trial. J Clin Oncol 2009; 27(15s): Abstract 4556.