

BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Trastuzumab and Vinorelbine

Protocol Code

BRAVTRNAV

Tumour Group

Breast

Contact Physician

Dr. Karen Gelmon

ELIGIBILITY:

- Overexpression of HER-2 neu
- HER-2 overexpression defined as either IHC3+, or FISH amplification ratio greater than or equal to 2 per BCCA central laboratory
- Previous taxane as adjuvant therapy
- Contraindication to trastuzumab-paclitaxel (BRAVTRAP) or trastuzumab-paclitaxel-carboplatin (BRAVTPC)
- Grade 2 or higher myalgia/arthralgia (moderate pain that interferes with function or worse) not responsive to symptomatic measures in a patient responding to trastuzumab-paclitaxel (BRAVTRAP)
- Patient ineligible for, or unwilling to participate in, a clinical trial
- Life expectancy greater than 3 months
- ECOG status 0-2
- No signs or symptoms of cardiac disease. For patients with equivocal cardiac status, a MUGA scan or ECHO should be done and reveal a normal left ventricular ejection fraction.
- A "Class II Drug Registration Form" must be submitted at the time of initiation of treatment.

EXCLUSIONS:

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

TESTS:

- Baseline: CBC & diff, platelets, total bilirubin
- Baseline if clinically indicated: cardiac function (ECG, echocardiogram or MUGA scan)
- Before each treatment: CBC & diff, platelets
- If clinically indicated: total bilirubin, cardiac function

PREMEDICATIONS:

- Antiemetic protocol for low emetogenic chemotherapy (see protocol SCNAUSEA)

TREATMENT:

Loading Dose (Week 1 only)

Day 1

Drug	Dose	BCCA Administration Guideline
Trastuzumab (HERCEPTIN®)	4 mg/kg	IV in 250 mL NS over 1 hour Observe for 30 minutes post-infusion* then start vinorelbine
Vinorelbine	25 mg/m ²	IV in 50 mL NS over 6 minutes, then flush line with 75 to 125 mL NS prior to removing/capping IV access

Maintenance Dose (Week 2 on)

Day 1

Drug	Dose	BCCA Administration Guideline
Trastuzumab (HERCEPTIN®)	2 mg/kg	IV in 250 mL NS over 30 minutes Observe for 30 minutes post-infusion* then start vinorelbine
Vinorelbine	25 mg/m ²	IV in 50 mL NS over 6 minutes, then flush line with 75 to 125 mL NS prior to removing/capping IV access

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

Repeat maintenance dose once weekly until disease progression, stable disease, best response or toxicity. To continue single-agent trastuzumab, see protocol BRAVTR

DOSE MODIFICATIONS:

1. Trastuzumab:

None required. Discontinue if unacceptable toxicity occurs.

2. Vinorelbine:

2a. Hematological

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose
greater than 1.25	and	greater than or equal to 100	25 mg/m ²
0.75 - 1.25	or	50-99	15 mg/m ²
less than 0.75	or	less than 50	omit dose and reassess in 1 week*

*Continue trastuzumab once weekly. If greater than 3 week delay, discontinue vinorelbine. To continue single agent trastuzumab, see protocol BRAVTR

2b. Hepatic Dysfunction

Bilirubin (micromol/L)	Dose
less than 36	25 mg/m ²
36 - 50	12.5 mg/m ²
greater than 50	omit*

*Continue trastuzumab once weekly. If greater than 3 week delay, discontinue vinorelbine. To continue single agent trastuzumab, see protocol BRAVTR

2c. **Neuropathy:** Discontinue vinorelbine if moderate or severe. To continue single agent trastuzumab, see protocol BRAVTR

PRECAUTIONS:

- 1. Cardiac toxicity:** Trastuzumab can produce ventricular dysfunction and congestive heart failure in about 2-4% of patients. The majority of patients who develop cardiac dysfunction are symptomatic. Regular monitoring of asymptomatic patients is not routinely necessary but may be ordered within 4-6 months of treatment with trastuzumab. If no significant decline in cardiac function is apparent, repeated testing is not generally necessary, unless the patient's medical condition changes. Discontinue treatment for symptomatic congestive heart failure or serious cardiac arrhythmias. Most patients who develop cardiac dysfunction respond to appropriate medical therapy and in some cases (where the benefit outweighs the risk) may continue trastuzumab under close medical supervision.
- 2. Trastuzumab infusion-associated symptoms,** usually chills and fever, occur in 40% of patients during the first trastuzumab infusion (infrequent with subsequent infusions). Other signs and symptoms may include nausea, vomiting, pain (sometimes at tumour sites), rigors, headache, dizziness, dyspnea, hypotension, rash and asthenia. Symptoms may be treated with acetaminophen, diphenhydramine and meperidine with or without an infusion rate reduction.
Rarely, serious infusion-related reactions have been reported (3 per 1000 patients) sometimes leading to death (4 per 10,000). Reactions include dyspnea, hypotension, wheezing, bronchospasm, tachycardia, reduced oxygen saturation and respiratory distress, and, uncommonly, allergic-like reactions. Patients experiencing dyspnea at rest due to pulmonary metastases and other pulmonary/cardiac conditions may be at increased risk of a fatal infusion reaction and should be treated with extreme caution, if at all. For serious reactions, discontinue the trastuzumab infusion and provide supportive therapy such as oxygen, beta-agonists and corticosteroids.
- 3. Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- 4. Extravasation:** Vinorelbine causes pain and tissue necrosis if extravasated. It is recommended to flush thoroughly with 75-125 mL NS after infusing vinorelbine. Hydrocortisone 100mg IV prior to vinorelbine may be of benefit. Refer to BCCA Extravasation Guidelines.

5. **A possible interaction between trastuzumab and 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. An INR prior to starting the trastuzumab is recommended, then weekly for the first 3 months and then monthly if stable. Inform patient to watch for any bleeding. Modification of the warfarin dose may be needed. (JAMA 1999;282:2299-301)

Call Dr. Karen Gelmon or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 01 Oct 2001

Date revised: 1 June 2011 (Infusion section revised)

References:

1. Burstein HJ, Kuter I, Campos SM et al. Clinical activity of trastuzumab and vinorelbine in women with HER2-overexpressing metastatic breast cancer. J Clin Oncol 2001;19:2722-30.
2. Perez A, Rodeheffer R. Clinical Cardiac Tolerability of Trastuzumab. J Clin Oncol 2004;22:322-329