

BCCA Protocol Summary for Palliative Third Line Treatment of Metastatic Colorectal Cancer Using Panitumumab

Protocol Code:

UGIAVPANI

Tumour Group:

Gastrointestinal

Contact Physician:

GI Systemic Therapy

ELIGIBILITY:

Patients with:

- metastatic colorectal adenocarcinoma previously treated with fluorouracil, irinotecan and oxaliplatin,
- wild type KRAS primary or metastatic tumours,* and
- ECOG performance status less than or equal to 2
- Adequate marrow reserve (ANC greater than or equal to $1.5 \times 10^9/L$, platelets greater than $100 \times 10^9/L$)
- Adequate renal (creatinine less than or equal to 1.5x ULN) and liver function (has not been studied in patients with hepatic impairment)

A BCCA “Compassionate Access Program” request with appropriate clinical information for each patient must be approved prior to treatment. **Note:** Approvals will only be given for one of UGIAVPANI or UGIAVCETIR – not both.

[*www.bccancer.bc.ca/HPI/labservices/PathologyRequestForms](http://www.bccancer.bc.ca/HPI/labservices/PathologyRequestForms)

EXCLUSIONS:

Patients with:

- mutant KRAS tumours
- Symptomatic brain metastases, interstitial pneumonitis or pulmonary fibrosis

TESTS:

Baseline: CBC and differential, electrolytes, magnesium, calcium, serum creatinine, bilirubin, AST/Alkaline Phosphatase

Prior to each cycle: electrolytes, magnesium, calcium

Post-treatment: monthly electrolytes, magnesium, calcium for 2 months after last panitumumab treatment

PREMEDICATIONS:

- Antiemetic protocol for low emetogenicity (see SCNAUSEA). Antiemetics are not usually required.

TREATMENT:

A cycle equals -

Drug	Dose	BCCA Administration Guideline
Panitumumab	6 mg/kg	IV in 100 mL NS over 1 hour using a 0.22 micron in-line filter*

* in 150 mL over 1 hour 30 min if dose greater than 1000 mg

- repeat every 2 weeks until either toxicity or disease progression.

DOSE MODIFICATIONS:

1. Dermatologic toxicities:

As a class, EGFR Inhibitors are characterized by cutaneous adverse effects, most commonly a papulopustular reaction involving the skin of the face and upper torso. This can leave the skin vulnerable to bacterial overgrowth and serious infection which may require aggressive interventions.

A well characterized clinical course has been identified. Within week 1 of treatment patients experience sensory disturbance with erythema and edema. During weeks 1-3 (median time of 14 days after start of therapy) the papulopustular eruption manifests, followed by crusting at week 4. Despite effective treatment for rash, erythema and dry skin may persist in the areas previously affected during weeks 4-6. Most patients exhibit some degree of partial improvement during therapy and the rash generally resolves completely and without scarring following cessation of therapy (median time of 84 days after the last dose.)

Grade	Toxicity	Panitumumab dose
1	Macular or papular eruption or erythema with no associated symptoms	Maintain dose level Consider clindamycin 2% and hydrocortisone 1% in a lotion to be applied topically BID as needed.
2	Macular or papular eruption or erythema with pruritus or other symptoms that are tolerable or interfere with daily life	Maintain dose level Consider clindamycin 2% and hydrocortisone 1% in a lotion to be applied topically BID as needed + Minocycline 100 mg PO BID for 1-2 weeks or longer as needed.
3	Severe, generalised erythroderma or macular, papular or vesicular eruption	Withhold infusion for 2 to 4 weeks: <ul style="list-style-type: none"> ▪ When improvement to Grade 2 or less, continue at 50% of original dose (3mg/kg); If toxicities do not worsen, escalate by 25% increments of original dose (4.5 mg/kg, then 6 mg/kg) until recommended starting dose is reached ▪ If no improvement, discontinue panitumumab Continue treatment with clindamycin 2% and hydrocortisone 1% in a lotion to be applied topically BID as needed + Minocycline 100 mg PO BID for 1-2 weeks or longer as needed.
4	Generalized exfoliative, ulcerative or blistering skin toxicity	Discontinue treatment.

There is evidence that prophylactic therapy with topical products and antibiotics can be beneficial, however this is not the standard of care at this time due to the unknown impact on treatment efficacy.

It is recommended that patients wear sunscreen and a hat and limit sun exposure as sunlight can exacerbate any skin reactions.

Activities and skin care products that dry the skin should be avoided such as long, hot showers, alcohol-based or perfumed skin care products. Greasy ointments should be avoided. Frequent moisturizing with alcohol-free emollient creams is recommended.

This rash is distinct from acne vulgaris and topical acne treatments should not be applied.

Other less frequent manifestations are: dry skin, pruritus, fissures, palmar-plantar rash, hyperkeratosis, telangiectasia, hyperpigmentation, and blisters.

2. Hypomagnesemia

Serious cases may be symptomless and have been reported greater than 6 weeks after initiation of treatment. Symptoms include severe weakness and fatigue. Concern is cardiac arrhythmias which may be associated with hypokalemia. Magnesium levels should be monitored closely and regular infusions of Magnesium Sulfate as well as oral supplementation may be required. Monitoring of potassium and calcium may also be required.

Grade	Serum Magnesium	Management
1	0.5 mmol/L to less than LLN	Continue Panitumumab. Consider daily oral magnesium replacement
2	0.4 to 0.49 mmol/L	Continue Panitumumab and initiate daily oral magnesium replacement and magnesium sulfate 4G IV every 2 weeks
3	0.3 to 0.39 mmol/L	if symptomatic - hold Panitumumab until improved to Grade 2. If asymptomatic – increase supplementation to magnesium sulfate 4G IV weekly
4	Less than 0.3 mmol/L	Hold Panitumumab until asymptomatic and improved to Grade 2 – increase supplementation to magnesium sulfate 4G IV twice weekly.

Oral preparations of magnesium may be poorly tolerated resulting in poor compliance due to potential for diarrhea. Diarrhea is dose dependent. Combination product with calcium may reduce incidence of diarrhea.

Magnesium Preparation	Elemental Magnesium content	Dosage
Magnesium complex	Each 250 mg tablet contains 250 mg	1 tablet twice daily
Magnesium glucoheptonate	Each 15ml of 100 mg/mL solution contains 76.8 mg	15 – 30 mL up to 4 times daily
Magnesium oxide	Each 420 mg tablet contains 252 mg	1 tablet twice daily
Calcium:Magnesium	Each 333/167 tablet contains 167 mg	1 tablet 3 times daily

PRECAUTIONS:

- 1. Hypersensitivity Reactions:** severe infusion reactions, including anaphylactic reactions, bronchospasm and hypotension have occurred with the administration of Panitumumab in approximately 1% of patients, very rarely with a fatal outcome. Late onset hypersensitivity reactions have also occurred and it is recommended that patients be warned of this possibility.
- 2. Interstitial Lung Disease:** has been observed with EGFR inhibitors. Panitumumab should be withheld in the event of onset or worsening of respiratory symptoms. If pneumonitis or lung infiltrates are confirmed, treatment should be discontinued.
- 3. Severe Diarrhea and Dehydration:** Panitumumab should be withheld until resolution. Acute renal failure has been observed in patients with severe diarrhea and dehydration receiving Panitumumab.

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: July 1, 2009

Date revised: 1 June 2011 (Infusions section revised)

References:

1. Van Cutsem E, Peeters M, Siena S, et al: Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. *J Clin Oncol* 2007;25:1658-64.
2. Fakih, Marwan: Management of anti-EGFR targeting monoclonal antibody-induced hypomagnesemia. *Oncology* 2008; 22:74-76.
3. Melosky, B, Burkes, R, Rayson, D, Alcindor, T, Shear, N and Lacouture M: Management of skin rash during EGFR-targeted monoclonal antibody treatment for gastrointestinal malignancies: Canadian recommendations. *Curr Onc.* 2009; 16:14-24.