PANITUMUMAB in Metastatic Colorectal Cancer

Indication: First line treatment of RAS wild-type metastatic colorectal cancer

NCDF criteria to be met:
- Metastatic colorectal cancer
- 1st line indication
- Patients with wild-type RAS
- Given in combination with the FOLFOX4 or FOLFOX6 or OxMdG chemotherapy regimens
  No previous treatment with Panitumumab or Cetuximab

NOTE: Panitumumab is not approved for use as 1st line treatment with other oxaliplatin-based regimens, irinotecan-based combinations, or upfront single agent fluoropyrimidine chemotherapy

NOTE: Not to be used with capecitabine and oxaliplatin combinations

NOTE: No treatment breaks of more than 4 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or in the case of intercurrent co-morbidities)

NOTE: If excessive toxicity with oxaliplatin, panitumumab can be continued with a fluoropyrimidine alone until disease progression only.

Cancer drug fund application and approval is required before starting treatment.

Regimen details:

Panitumumab 6mg/kg IV D1

Panitumumab is given in combination with FOLFOX - see separate protocol for details of doses, monitoring and ongoing treatment.

Administration:

Panitumumab in 100ml sodium chloride 0.9% infused over 60 minutes* via a 0.2 micron in-line filter, prior to FOLFOX chemotherapy.

If the initial 60 minute panitumumab infusion is well tolerated, subsequent doses may be given over 30 minutes.

Panitumumab is concentration dependent; maximum final concentration 10mg/ml - pharmacy to check final fluid volume.

*Doses >1000mg must be infused over 90 minutes.

Availability of resuscitation equipment must be ensured as a standard precaution. Patients should be observed for infusion-related symptoms (fever, chills, flushing, rash, urticaria and pruritis), the infusion should be slowed down or interrupted and the necessary supportive medication should be administered.

For severe infusion-related symptoms (bronchospasm, dyspnoea, angioedema and anaphylaxis) discontinue the infusion immediately and follow the local anaphylaxis policy – discuss with consultant before continuing with further treatment.

Extravasation: Non vesicant
Frequency: Day 1, every 2 weeks until disease progression or unacceptable toxicity, given in combination with FOLFOX chemotherapy. Treatment break of more than 4 weeks beyond the cycle length is not allowed.

Anti-emetics: Low emetogenicity
Follow local anti-emetic policy

Supportive medication: Hydrocortisone, chlorphenamine and paracetamol can be given for chills / fever / rigor during the infusion if required.

Treatment of dermatologic reactions may include a moisturiser, sunscreen (SPF >15 UVA/UVB), topical steroids and/or oral antibiotics – discuss with the consultant. Advise patients to wear sunscreen, a hat and limit sun exposure.

Regular investigations:
- FBC Prior to D1 of each cycle
- LFTs Prior to D1 of each cycle
- U&Es Prior to D1 of each cycle
- Electrolytes (Mg, Ca, K) Prior to D1 of each cycle, and for 8 weeks after treatment

Note: see FOLFOX protocol for additional investigations required

Toxicities: Cutaneous reactions (rash, dermatitis acneiform, erythema, dry skin, pruritis, PPE), diarrhoea, nausea, electrolyte disturbances (hypomagnesemia, hypocalcaemia, hypokalaemia), paronychia, ocular disorders, interstitial lung disease, infusion-related reactions, vomiting, constipation, abdominal pain, fatigue, pyrexia, mucositis, anorexia.

See separate protocol for toxicities associated with FOLFOX.

DOSE MODIFICATIONS:

Haematological toxicity

Panitumumab is given with FOLFOX chemotherapy – refer to separate protocol
If FOLFOX chemotherapy is delayed, panitumumab should be deferred.

Non-haematological Toxicities

Renal impairment No clinical studies have been conducted in patients with renal impairment

Hepatic impairment No clinical studies have been conducted in patients with hepatic impairment
### Dose modifications for other toxicities

**Dermatologic reactions and soft tissue toxicity**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Panitumumab dose</th>
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<tbody>
<tr>
<td>1 or 2 (tolerable)</td>
<td>Continue 100%</td>
</tr>
<tr>
<td>2 (intolerable)</td>
<td>1st occurrence: Withhold for 2 to 4 weeks, initiate supportive therapies. If recovered to ≤ Grade 2 – resume treatment at 100% dose. Discontinue panitumumab if no improvement.</td>
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<tr>
<td>OR 3</td>
<td>2nd occurrence: Withhold for 2 to 4 weeks, initiate supportive therapies. If recovered to ≤ Grade 2 – resume treatment at 80% dose. Discontinue panitumumab if no improvement.</td>
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<tr>
<td>3rd occurrence: Withhold for 2 to 4 weeks, initiate supportive therapies. If recovered to ≤ Grade 2 – resume treatment at 60% dose. Discontinue panitumumab if no improvement.</td>
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<td>4th occurrence: Discontinue permanently</td>
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**Comments:**

**Interstitial lung disease (ILD)** ILD, which may be acute in onset, has been observed in 1.3% of patients, and some cases have been fatal. If patients experience worsening of respiratory symptoms such as dyspnoea, cough and fever, panitumumab should be interrupted and the patient should be promptly investigated. If ILD is confirmed, panitumumab should be discontinued and the patient treated appropriately.

**Sodium content** Contains 3.45mg sodium per ml of concentrate – to be taken into consideration by patients on a sodium-controlled diet.

**Drug interactions** Drug interaction studies have not been performed with panitumumab. Risk of interactions with other concomitant medication cannot be excluded.

**References**

