### FLOT for Perioperative treatment of Gastric Cancer

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0-2</td>
<td>Dexamethasone</td>
<td>8mg BD</td>
<td>Oral</td>
<td>For 3 days start at one day prior to treatment</td>
</tr>
<tr>
<td></td>
<td>Sodium Chloride 0.9%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Fast Running for Line Flush</td>
</tr>
<tr>
<td></td>
<td>Ondansetron</td>
<td>8mg</td>
<td>Oral /Slow bolus/15 min infusion</td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td><strong>Docetaxel</strong></td>
<td>50mg/m²</td>
<td>IV Infusion</td>
<td>250ml Sodium Chloride 0.9% over 1 hour</td>
</tr>
<tr>
<td></td>
<td>Glucose 5%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Line Flush</td>
</tr>
<tr>
<td></td>
<td>Calcium Leucovorin (folinic acid)</td>
<td>300mg or 200mg/m²* (See Note)</td>
<td>IV Infusion</td>
<td>250ml Glucose 5% over 2 hours concurrent with oxaliplatin</td>
</tr>
<tr>
<td></td>
<td>Oxaliplatin</td>
<td>85 mg/m²</td>
<td>IV Infusion</td>
<td>250ml Glucose 5% over 2 hours concurrent with folinic acid</td>
</tr>
<tr>
<td></td>
<td>Glucose 5%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Line Flush</td>
</tr>
<tr>
<td></td>
<td><strong>5 Fluorouracil</strong></td>
<td>2600 mg/m²</td>
<td>via infusor device</td>
<td>0.9% Sodium Chloride over 24 hours</td>
</tr>
<tr>
<td>Day 2</td>
<td>Attend ward/clinic for removal of 5-FU infusor device</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.

### CYCLE LENGTH AND NUMBER OF DAYS

Every 14 days - usually 4 cycles before and after surgery.

### APPROVED INDICATIONS
- For perioperative treatment of gastric cancers

### ELIGIBILITY CRITERIA
- ECOG performance status 0-1, Karnofsky performance status >70%, adequate hepatic, renal, marrow and cardiac function

### EXCLUSION CRITERIA

Patients with baseline renal function less than 30ml/min

### PREMEDICATION

As above

### RECOMMENDED TAKE HOME MEDICATION

Ondansetron 8mg twice daily for 2 days  
Dexamethasone 4mg twice daily for 3 days starting 24 hours prior to chemotherapy. Note if patient has forgotten to take oral steroids, give 20mg IV dexamethasone pre-treatment.  
Metoclopramide 10mg three times daily as required  
*Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details*

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FLOT is expected to carry a risk of febrile neutropenia > 20% so patients must be given GCSF primary prophylaxis. See local Area Team GCSF policy. Daily GCSF is recommended for the majority of patients using the locally agreed schedule below. Pegylated filgrastim is an option for patients unable to self-administer.
FLOT for Perioperative treatment of Gastric Cancer

Day | Drug | Weight | Dose | Route | Diluent & Rate |
--- | --- | --- | --- | --- | --- |
3 | Biosimilar Filgrastim | <78kg* | 300 microg (30 MU) | S/C | ONCE daily for SEVEN days starting TWO days after chemo |
    | | ≥78kg* | 480 microg (48 MU) | | |
2 | Lipegfilgrastim (Lonquex®) or Pegfilgrastim (Neulasta®) | All | 6mg | S/C | Single dose given 24 hours after chemo |

INVESTIGATIONS / MONITORING REQUIRED

*Pre-treatment: Assessment of renal function, FBC, Cardiac history
*Prior to each cycle: FBC, U&E’s, LFT’s & tumour markers as appropriate
FBC on the day of treatment
Where CEA is elevated this should be measured before each cycle.

ASSESSMENT OF RESPONSE

Adjuvant: There will be no visible disease to monitor for adjuvant treatment.

REVIEW BY CLINICIAN

To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW

On cycles where not seen by clinician.

ADMINISTRATION NOTES

- Before docetaxel is given, make sure the patient has taken oral dexamethasone premedication. Docetaxel has been known to produce hypersensitivity reactions; steroid co-medication will also reduce the risk of fluid retention and skin reactions.
- Facilities to treat anaphylaxis MUST be present when the chemotherapy is given.
- Do not need to stop treatment for minor hypersensitivity e.g. reactions, flushing, localised rash.
- Must be stopped for major reactions, e.g. hypotension, bronchospasm and generalised rash.

- **Oxaliplatin is incompatible with saline.** Must use 5% dextrose as diluent /line flush
- Bronchospasm can occur. * If severe laryngeal spasm occurs consider increasing Oxaliplatin infusion to 6 hours
- Patient requires semi-permanent IV access for this treatment, e.g. PICC line/ Hickman catheter
- Diarrhoea is common, and may require intervention with fluids and electrolytes if severe. If diarrhoea is a problem, give loperamide 2 to 4 mg four times daily as required or codeine phosphate 30mg four times daily and stop 5FU infusion if diarrhoea moderate/severe.
- Two forms of Folinic Acid are available. The doses given above refer to 'standard' racemic calcium folinate only. If the pure active enantiomer, calcium levofolinate (Isovorin®) is used the dose will generally be half that of the 'standard' folinate.
Laryng-o-pharyngeal Dysesthesia

As with all platinum based chemotherapy, patients may experience allergic reaction during administration. The following table is intended to help differentiate between Platinum Hypersensitivity and Laryngo-pharyngeal Dysesthesia.

<table>
<thead>
<tr>
<th>Clinical Symptoms</th>
<th>Laryngo-pharyngeal Dysesthesia</th>
<th>Platinum Hypersensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnoea</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>O₂ saturation</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
<td>Present (loss of sensation)</td>
<td>Absent</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Cold induced</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Normal or Increased</td>
<td>Normal or Decreased</td>
</tr>
</tbody>
</table>

**Treatment**

**Platinum Hypersensitivity**

Patients who have previously experienced Grade I or II Platinum Hypersensitivity should be pre-medicated as below:

45 minutes prior to Oxaliplatin
- Dexamethasone 20 mg IV in 50 mL NS over 15 minutes (or Hydrocortisone 100mg)

30 minutes prior to Oxaliplatin
- Chlorphenamine 10 mg IV and Ranitidine 50 mg IV in 50 mL NS over 20 minutes

**EXTRAVASATION** See NCA / local Policy

**TOXICITIES**

- Anaphylaxis and hypersensitivity reactions
- Fluid retention syndrome
- Pain on administration
- Joint pains
- Deranged LFT’s
- Peripheral neurotoxicity very common with Oxaliplatin. (dose limiting toxicity)
- Myelosuppression
- Cold induced parathesia
- Nausea and Vomiting
- Allergic reaction
- Diarrhoea
- Stomatitis
- Palmar/Plantar Erythrodysthesia
- Darkening/discoloration of veins
- Cardiotoxicity - Occasionally patients may experience coronary artery spasm
- Laryngopharyngeal dysesthesia
DPD Deficiency and Severe Toxicity Risk

Dihydropyrimidine dehydrogenase (DPD) plays an important role in the metabolism of fluoropyrimidine drugs 5-fluorouracil (5FU) and capecitabine. Patients with DPD deficiency may be predisposed to experience increased or severe toxicity when receiving 5-FU or capecitabine, and in some cases these events can be fatal.

For all patients having capecitabine or fluorouracil, the risk of severe side effects from capecitabine or 5FU if patients have a deficiency of DPD must be mentioned and patient given a copy of the DPD toxicity information leaflet from cancer research UK.


DOSE MODIFICATION / TREATMENT DELAYS

Haematological toxicity:
- Delay 1 week if ANC < 1.5 and/or Platelets < 100
- No dose reduction for CTC grade I/II ANC

Non-Haematological toxicity:
- No dose reduction should apply to oxaliplatin in case of PPE
- In case of Grade III/IV stomatitis or diarrhoea despite a 20% reduction of 5FU, Oxaliplatin should be reduced by 20%

Neurotoxicity:
- Cold related paraesthesia of hands/feet or dysesthesia/laryngeal spasm syndrome lasts a few hours and should not routinely require treatment or dose reduction.
- If severe laryngeal spasm occurs, consider increasing Oxaliplatin infusion to 6 hours
- If symptoms persist for 14 days and/or there is pain, functional loss, omit Oxaliplatin and continue with 5FU/FA until fully recovered, then restart Oxaliplatin at 20% dose reduction

TREATMENT LOCATION
Can be given at Cancer Centre or Cancer Unit

REFERENCES: