R-GemOx

INDICATION

Relapsed or Refractory Lymphoma, for patients unsuitable for R-GDP regimen.

Omit rituximab if CD20- negative

TREATMENT INTENT

Disease modification

PRE-ASSESSMENT

1. Ensure histology is confirmed prior to administration of chemotherapy and document in notes.
2. Record stage and IPI of disease - CT scan (neck, chest, abdomen and pelvis), and/or PET-CT, presence or absence of B symptoms, clinical extent of disease, consider bone marrow aspirate and trephine.
3. Blood tests – FBC, U&Es, LDH, ESR, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, β2, microglobulin, hepatitis B core antibody and hepatitis B surface Ag, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent, group and save.
4. Urine pregnancy test - before cycle 1 of each new chemotherapy course for women of child-bearing age unless they are post-menopausal, have been sterilised or undergone a hysterectomy.
5. ECG +/- Echo if clinically indicated.
6. Record performance status (WHO/ECOG).
7. Record height and weight.
8. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment.
9. Fertility - it is very important the patient understands the potential risk of infertility. All patients should be offered fertility advice by referring to the Oxford Fertility Unit.
10. Hydration – in patients with bulky disease pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. For patients at high risk of tumour lysis, refer to the tumour lysis protocol.
11. Consider dental assessment / Advise dental check is carried out by patient’s own dental practitioner before treatment starts.
12. Treatment should be agreed in the relevant MDT.
DRUG REGIMEN

Day 1  Pre med  Paracetamol 1g PO, Chlorphenamine 10 mg IV, and Hydrocortisone 100mg IV 30 minutes before rituximab.

**RITUXIMAB**  375 mg/m² IV infusion in 500 mL sodium chloride 0.9%.
(Refer to rituximab care plan for titration of infusion rate. If first dose well tolerated, consider rapid infusion rituximab for dose 2 onwards).

**GEMCITABINE**  1000 mg/m² IV infusion in 250mL sodium chloride 0.9% over 30 minutes

**OXALIPLATIN**  100 mg/m² IV infusion in 250mL glucose 5% over 2 hours

CYCLE FREQUENCY

Cycle repeats every 14 days for up to 6 cycles.

RESTAGING

Give 3-4 courses and restage with CT.
If partial or complete remission, continue to 6 courses of R-GemOx.

DOSE MODIFICATIONS

Haematological Toxicity
Each cycle should normally only be given if platelets > 100 x 10⁹/L and neutrophils > 1 x 10⁹/L. If neutrophil count <1 x 10⁹/L or platelets <100 x 10⁹/L, delay treatment by one week.
Gemcitabine may be reduced to 750mg/m² at consultant’s discretion to maintain dose intensity.

Neuropathic Toxicity
Peripheral sensory neuropathy usually occurs after a cumulative dose of 800mg/m² but can also occur at an earlier stage. It can occur during or after treatment with oxaliplatin. It is usually reversible but may take 3 – 5 months to recovery.

| Grade 2 sensory or motor neuropathy resolved before beginning of the next cycle | Reduce oxaliplatin dose to 75mg/m² |
| Grade 3 or above sensory or motor neuropathy or Grade 2 but not resolved before beginning of the next cycle | Omit oxaliplatin until symptoms improve then restart at 75mg/m² |
| Acute Pharyngolaryngeal Dysesthesia | Extend oxaliplatin infusion to over 6 hours trying to put this in a separate table and can’t |
Renal/Hepatic Impairment

**Gemcitabine**

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
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<tbody>
<tr>
<td>CrCl &lt;30mL/min: Consider dose reduction – clinical decision</td>
<td>Bilirubin &gt; 27 umol/L, give 800mg/m²</td>
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**Oxaliplatin**

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
</tr>
</thead>
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<tr>
<td>CrCl &lt;20mL/min: Consider dose reduction – clinical decision</td>
<td>No dose adjustment required.</td>
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**CONTRAINDICATIONS**

- Hypersensitivity to the active substance or to any of the excipients.
- Peripheral sensitive neuropathy with functional impairment prior to first course.
- Severely impaired renal function (CrCl < 30 mL/min).
- Previous exposure to oxaliplatin within last 12 months.

**SPECIAL WARNINGS / PRECAUTIONS**

**Extravasation:** Oxaliplatin is an exfoliant. Follow oxaliplatin-specific pathway in the TVCN Extravasation Guideline for treatment.

**Acute Neurosensory Manifestations** start within hours of administration and often occur on exposure to cold. They commonly present as transient paresthesia of hands & feet, dysesthesia and hypoesthesia (up to 95% patients). Symptoms usually resolve within minutes to days. No treatment is usually required. Advise patient to avoid exposure to cold air or drinks.

**Acute Pharyngolaryngeal Dysesthesia** occurs in 1%–2% of patients and is characterised by subjective sensations of dysphagia or dyspnoea/feeling of suffocation, without any objective evidence of respiratory distress (no cyanosis or hypoxia) or of laryngospasm or bronchospasm (no stridor or wheezing). The symptoms are rapidly reversible even in the absence of treatment. Subsequent infusion should be given over 6 hours to reduce the incidence. Gemcitabine and Oxaliplatin can be scheduled on Day 2 of each cycle if time is limited for Day Case.

**Hypersensitivity reactions** may occur during oxaliplatin infusion. It can be distinguished from acute pharyngolaryngeal dysesthesia with the presence of bronchospasm, laryngospasm, decreased O₂ saturation and pruritus. Stop oxaliplatin infusion and seek medical help immediately. Treat with chlorphenamine 10mg IV and hydrocortisone 100mg. Oxygen, adrenaline, bronchodilators and fluid should be given as appropriate. Cross-sensitivity with other platinum products has been reported.

**INVESTIGATIONS**

FBC, U&Es and LFTs.
CONCURRENT MEDICATION

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<th>Details</th>
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<tr>
<td>Allopurinol</td>
<td>300 mg daily for 7 days starting 24-48 hours prior to chemotherapy (first course / cycle only)</td>
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<tr>
<td>Ranitidine (or PPI - discuss with consultant)</td>
<td>150mg twice daily for the duration of treatment</td>
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<tr>
<td>Aciclovir</td>
<td>200 mg three times a day for duration of treatment and for 3 months after completion</td>
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<tr>
<td>G-CSF</td>
<td>Starting from Day 5 for 7 days if required.</td>
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EMETIC RISK

High

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
(Consult with pharmacist and refer to SPC for full details)

Very commonly reported with regimen: neutropenia, thrombocytopenia, anaemia, infection and nausea.

- **Rituximab**: severe cytokine release syndrome characterised by severe dyspnoea, often accompanied by bronchospasm, hypoxia, fever, chills, rigors, urticaria, and angioedema, hepatitis B reactivation – see pathway for treatment and management of HBV positive patient.
- **Gemcitabine**: alopecia, peripheral oedema.
- **Oxaliplatin**: deranged liver enzymes, alopecia, peripheral neuropathy, hypersensitivity.

EXTRAVASTAION RISK

- Gemcitabine: neutral
- Oxaliplatin: exfoliant
- Rituximab: neutral

TREATMENT-RELATED MORTALITY

<5%
REFERENCES


Review

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