GEMTUZUMAB OZOGAMICIN (MYLOTARG®)

INDICATION

Induction and consolidation chemotherapy for patients with Acute Myeloid Leukaemia (AML) and Acute Promyelocytic Leukaemia (APL).

Unlicensed

- Available on a named-patient basis only.
- Individual funding must be obtained.

TREATMENT INTENT

Curative

PRE-ASSESSMENT

1. Blood tests - FBC, coagulation screen, U&Es, LDH, urate, calcium, magnesium, creatinine, eGFR, LFTs, glucose, Hepatitis B core antibody and Hepatitis BsAg, Hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent, group and save
2. Ensure bone marrow findings are confirmed and documented in the notes prior to administration of chemotherapy.
3. Urine pregnancy test - before cycle 1 of each new chemotherapy course in women aged 12 – 55 years of age unless they have been sterilised or undergone a hysterectomy
4. ECG +/- Echo - if clinically indicated
5. Record performance status (WHO/ECOG)
6. Record height and weight
7. 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
8. Fertility - it is very important the patient understands the potential risk of infertility, all patients should be offered fertility advice (see Fertility Guidelines)
9. Hydration - refer to Tumour Lysis protocol
10. Consider dental assessment / advise dental check is carried out by patient's own dental practitioner before treatment starts
11. Treatment should be agreed in the relevant MDT
12. Gemtuzumab must not be started if WCC ≥ 30 x 10⁹/L because of the risks of tumour lysis and hypersensitivity reactions. Hydroxycarbamide (40-60 mg/kg/day) can be used to reduce WCC before commencing Gemtuzumab.
13. Patients are only eligible to receive Gemtuzumab if ALT/AST ≤ 2 x ULN and bilirubin ≤ 2 x ULN, due to the risk of veno-occlusive disease, and have not experienced side effects to any previous exposure to Gemtuzumab.
14. Patients should not be given any azole antifungals until 5 days after Gemtuzumab administration
DRUG REGIMEN / CYCLE FREQUENCY

<table>
<thead>
<tr>
<th>Day</th>
<th>Chemotherapy</th>
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<tbody>
<tr>
<td>1</td>
<td>Pre-medication one hour before Gemtuzumab administration:</td>
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<tr>
<td></td>
<td>CHLORPHENAMINE 10mg IV stat</td>
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<td></td>
<td>PARACETAMOL 1000mg PO stat</td>
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<tr>
<td></td>
<td>GEMTUZUMAB OZOGAMICIN 3mg/m² (max 5mg) in 100ml 0.9% Sodium Chloride IVI over 2 hours.</td>
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</tbody>
</table>

- Visually inspect infusion bag for particulate matter and discoloration before administration.
- Protect from light during administration.
- Diluted Gemtuzumab must be given through a peripheral or central vein using an IV line equipped with an in-line filter of the low protein-binding, e.g. ‘Intrapur® Lipid’ (Braun product number 4099702), 0.22 micron PES, 0.20 micron cellulose acetate, 0.8 to 1.2 micron cellulose acetate/cellulose nitrate (mixed ester), or 1.2 micron acrylic copolymer.
- Do not co-administer other drugs through the same infusion line.
- Monitor vital signs during infusion and for 4 hours following infusion.

CONTRAINDICATIONS
Known hypersensitivity to Gemtuzumab Ozogamicin or any of its components.

DOSE MODIFICATIONS
Discuss with consultant.
Gemtuzumab should not be routinely used if hepatic or renal impairment is present.

Renal / Hepatic Impairment

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Hepatic impairment</th>
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<tbody>
<tr>
<td>Clinical decision</td>
<td>Not studied. Use with caution – may increase the risk of veno-occlusive disease.</td>
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</table>

INVESTIGATIONS
FBC, U&E, LFT
CONCURRENT MEDICATION

<table>
<thead>
<tr>
<th>TUMOUR LYSIS PROPHYLAXIS</th>
<th>Local tumour lysis guidelines should be observed for 14 days.</th>
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<tbody>
<tr>
<td>ACICLOVIR</td>
<td>200mg PO three times a day</td>
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<tr>
<td>PPI</td>
<td>Daily if clinically indicated</td>
</tr>
<tr>
<td>ANTIFungal PROPHYLAXIS</td>
<td>Refer to local antifungal policy. Patients should not be given azole antifungals until 5 days after Gemtuzumab administration</td>
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</tbody>
</table>

INTERACTIONS
No formal drug-interaction studies performed
Azole antifungals should also be avoided until 5 days after Gemtuzumab administration

ANTI-EMETICS
Low emesis risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Myelosuppression
Severe and prolonged myelosuppression can occur.

Infusion Reactions
Monitor vital signs during infusion and for four hours following infusion. Gemtuzumab can produce a post-infusion symptom complex of fever and chills, and less commonly hypotension and dyspnea may occur within 24 hours of administration. Grade 3 or 4 non-haematologic infusion-related adverse events included chills, fever, hypotension, hypertension, hyperglycaemia, hypoxia, and dyspnoea.

Pulmonary Events
Dyspnoea, pulmonary infiltrates, pleural effusions, non-cardiogenic pulmonary oedema, pulmonary insufficiency and hypoxia, and acute respiratory distress syndrome may occur. Patients with symptomatic intrinsic lung disease may also be at greater risk of severe pulmonary reactions.

Hepatotoxicity
Monitor patients carefully for symptoms of hepatotoxicity, particularly VOD.

Other Reported Adverse Reactions
Fever, chills, nausea, vomiting, headache, dyspnoea, hypotension, hypertension, hyperglycaemia, infection, bleeding, mucositis, rash, cutaneous herpes simplex, early mortality, abdominal pain, asthenia, back pain, pain, sepsis, tachycardia, anorexia, constipation, diarrhoea, abnormal LFTs, stomatitis, hypokalemia, raised LDH, peripheral oedema, anxiety, depression, dizziness, insomnia, cough, epistaxis, pharyngitis, pneumonia, local reaction.

MORTALITY
There is no reliable mortality data for Gemtuzumab.
REFERENCES

1. NCRI (2016) Adults with Acute Myeloid Leukaemia or High-Risk Myelodysplastic Syndrome (AML19), Version 5.0.

REVIEW

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
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<tbody>
<tr>
<td>Julia Wong, Cheuk-kie Jackie Cheung Prof Paresh Vyas</td>
<td>Major changes</td>
<td>March 2017</td>
<td>4.0</td>
<td>March 2019</td>
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