Brentuximab vedotin

INDICATION

1. Relapsed / refractory CD30-positive Hodgkin lymphoma (NICE TA524 - BLUETEQ required)
   - following autologous stem cell transplant (ASCT)
   - following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option
   - re-use after ASCT as bridge to allogenic stem cell transplant or donor lymphocyte infusion after a previous partial/ complete response to brentuximab vedotin
2. Relapsed / refractory systemic anaplastic large cell lymphoma (NICE TA478- BLUETEQ required)
3. Relapsed / refractory CD30+ cutaneous T cell lymphoma after at least 1 line of systemic therapy (Cancer Drug Fund- BLUETEQ required)
   CD30-positive Hodgkin’s lymphoma at increased risk of relapse or progression following ASCT (Licensed but not funded by NHS England)
5. First line salvage option for CD30- positive Hodgkin lymphoma, to replace salvage chemotherapy, in order to reduce toxicity of treatment and number of admissions needed for intensive treatment. **COVID Bluteq approval is required**

TREATMENT INTENT

Disease modification or curative when used as a bridge to transplant.

PRE-ASSESSMENT

1. Ensure histology is confirmed prior to administration of chemotherapy and document in notes.
2. Record stage of disease - PET-CT (preferably with contrast) scan, presence or absence of B symptoms, clinical extent of disease.
3. Blood tests - FBC, U&Es, LDH, ESR, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, hepatitis B core antibody and hepatitis B surface Ag, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent.
4. Send a "group and save" sample to transfusion and inform patient and transfusion laboratory that they will require irradiated blood products for all future transfusions. Ensure irradiation card is attached to the patient’s notes and copy given to the patient. See ‘Guidelines for the use of blood components in adult haematology’.
5. If raised glucose or previously diagnosed diabetes: ensure blood glucose monitored frequently during treatment and oral hypoglycaemic agents / subcutaneous insulin administered as appropriate.
6. If symptoms of peripheral neuropathy pre-treatment, perform nerve conduction studies. If clinical or electrophysiological evidence of neuropathy, discuss with consultant as to whether treatment should commence.
7. 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 have undergone a hysterectomy.
8. ECG +/- Echo - if clinically indicated.
10. Record height and weight.
11. 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.

12. 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).

13. Hydration - in patients with bulky disease pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. Patients at high risk of tumour lysis, refer to the tumour lysis protocol.

14. Consider dental assessment / Advise dental check is carried out by patient's own dental practitioner before treatment starts.

15. Treatment should be agreed in the relevant MDT.

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**DRUG REGIMEN**

**Day 1**  **BRENTUXIMAB VEDOTIN** 1.8 mg/kg in 150 mL sodium chloride 0.9% (final concentration 0.4-1.2 mg/mL) IV infusion over 30 minutes (maximum dose: 180 mg)

NB: The routine use of steroids as pre-medication is NOT indicated. In patients who sustain mild infusional reactions, pre-medication with paracetamol 1 g PO and chlorphenamine 10 mg IV 30 min before infusion for subsequent infusions should be tried.

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**CYCLE FREQUENCY**

Repeat every 3 weeks up to 16 cycles. Patients should be re-staged after every 3-4 cycles (or earlier if clinically indicated) usually with PET-CT scan.

Discontinue if:
- patient has no response after 4 courses
- patient has progressive disease

If brentuximab vedotin is re-used after ASCT as bridge to allogenic stem cell transplant or donor lymphocyte infusion, patient may receive up to a maximum of 16 cycles in combination with previous cycles of brentuximab vedotin.

This treatment alone is not considered curative. Patients responding to treatment should be considered for a possible curative treatment as consolidation, e.g. allogeneic or autologous stem cell transplantation.

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**RESTAGING**

After every 3-4 cycles (or earlier if clinically indicated) usually with PET-CT (preferably with contrast).
DOSE MODIFICATIONS

Haematological dysfunction

<table>
<thead>
<tr>
<th>Severity of neutropenia</th>
<th>Modification</th>
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</thead>
<tbody>
<tr>
<td>Grade 1 or 2 ( &gt; 1x10⁹/L)</td>
<td>Continue with same dose</td>
</tr>
<tr>
<td>Grade 3 or 4 ( ≤ 1x10⁹/L)</td>
<td>Withhold until neutropenia grade 2 or less then resume at previous dose and schedule; consider adding in GCSF to subsequent cycles</td>
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</tbody>
</table>

Renal impairment

The recommended starting dose in patients with severe renal impairment is 1.2 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Patients with renal impairment should be closely monitored for adverse events.

Hepatic impairment

The recommended starting dose in patients with mild hepatic impairment is 0.9 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Patients with hepatic impairment should be closely monitored for adverse events.

Neuropathy

New / worsening grade 2/3 neuropathy: withhold dose until improved to grade 1 or baseline, then re-start at 1.2 mg/kg. Grade 4: discontinue.

INVESTIGATIONS

FBC, U&Es, Creatinine, LFTs, glucose, Mg²⁺, Ca²⁺ and PO₄ at clinic attendance.

CONCURRENT MEDICATION

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Ranitidine (or PPI if specifically indicated - discuss with consultant)</td>
<td>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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EMETIC RISK

Low risk.

EXTRAVASATION RISK

Brentuximab vedotin: neutral
ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

1. Myelosuppression including neutropenia. Advice should be given to all patients that neutropenia is likely and advice given as to local institution policy
2. Infusional reactions: Can be given subsequently with suitable pre-medications. NB routine premedication is not advised
3. Peripheral neuropathy – this occurs in up to 30% of patients but usually does resolve to an extent in most patients once the treatment is stopped.
4. Hyperglycaemia
5. Rash / Stevens-Johnson syndrome (rare)
6. Should be assumed to be teratogenic although no data is available
7. Diarrhoea
8. Nausea
9. Pyrexia
10. Fatigue

TREATMENT RELATED MORTALITY

<1%

REFERENCES


Review

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
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<tbody>
<tr>
<td>NSSG Lymphoma Group</td>
<td>Annual protocol review</td>
<td>May 2017</td>
<td>1.8</td>
<td></td>
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<tr>
<td>Cheuk-kie Jackie Cheung</td>
<td>Annual protocol review.</td>
<td>May 2019</td>
<td>1.9</td>
<td>May 2021</td>
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<tr>
<td>(Haematology Pharmacist)</td>
<td>Indication, cycle number, hepatic dose modification updated.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NSSG Lymphoma Group</td>
<td>Update with a new indication during COVID-19 pandemic</td>
<td>June 2020</td>
<td>2.0</td>
<td>May 2021</td>
</tr>
<tr>
<td>Faouzi Djebbari (Haematology Pharmacist)</td>
<td>Nursing care plan added</td>
<td>Sept 20</td>
<td>2.1</td>
<td>May 2021</td>
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**Nursing Care Plan: Brentuximab Vedotin**

**Indication:** Relapsed / refractory Hodgkin Lymphoma or Anaplastic Large Cell Lymphoma) or used as a bridge to allogeneic transplant post autologous transplant.

**Frequency:** once every 3 weeks for up to 16 cycles or until disease progression. (With PET CT scans every 3-4 cycles).

**Emetic risk:** low.

**Alopecia:** rare.

Send a group and save sample to blood transfusion and inform patient and laboratory that they will require irradiated blood products for all future transfusions. Give patient an irradiated blood product booklet and card.

**BRENTUXIMAB:** Monoclonal antibody for CD30.

Administered as IV infusion on day 1 over 30 minutes.

**Classification of extravasation:** neutral.

**Side effects:** dosing reactions (no premed given as standard, paracetamol and chlorphenamine given as premed if reactions occur), rash, diarrhoea, nausea, fever, fatigue, neutropenia, peripheral neuropathy occurs in 30% of patients (usually resolves in most patients once treatment stops).

**Regime specific considerations:**

- Ensure patient is well before taking drug off hold – high cost drug.

- Advise patients to maintain fluid intake of 2-3 litres a day for next few days.

- Advice should be given to all patients that neutropenia is likely.