Alemtuzumab (Campath)

INDICATION

T-CELL PROLYMPHOCYTIC LEUKAEMIA (T-PLL) [ICD-10 code: C.91]

Alemtuzumab (Campath) is not licensed* in the United Kingdom but is available through the Clinigen Alemtuzumab Patient Access Scheme on an individual patient basis.

*Ensure compliance with treating Trust's governance framework

TREATMENT INTENT

Disease modification (but curative if combined with allogeneic transplant).

PRE-ASSESSMENT

1. Record stage of disease - CT scan (neck, chest, abdomen and pelvis), presence or absence of B symptoms, clinical extent of disease, bone marrow aspirate and trephine.
2. Blood tests - CMV serology, CMV PCR, hepatitis B core antibody and hepatitis B surface Ag, hepatitis C antibody, EBV, VZV, HIV 1+2 after consent, TP53 mutation analysis, FBC, biochemistry, glucose
3. ECG +/-Echo if clinically indicated.
4. Record performance status.
5. Record patient's height and weight.
6. 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.
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. Hydration - in patients with bulk disease pre-hydrate with 1 litre sodium chloride 0.9% over 4 - 6 hours. Patients at high risk of tumour lysis refer to tumour lysis protocol. Assess and document tumour lysis risk as part of pre-assessment. Refer to the Tumour Lysis Syndrome in Adults protocol (H.8).
9. **Contact local Blood Transfusion lab and inform of the need for indefinite irradiated blood products following the administration of Alemtuzumab.** Ensure irradiation card is attached to the patient's notes. See 'Guidelines for the use of blood components in adult haematology' [Link]
10. Treatment should be agreed in the relevant MDT.

DRUG REGIMEN

Pre-medication:
Chlorphenamine 10mg IV and Paracetamol 1g PO, and Hydrocortisone 100 mg IV 30 minutes before the first dose and with each dose escalation, thereafter as clinically indicated.

Week 1: IV Alemtuzumab is given at the dosage level outlined below as an infusion.

Wednesday	**ALEMTUZUMAB**	3 mg IV*
Thursday	**ALEMTUZUMAB**	10 mg IV*
Friday	**ALEMTUZUMAB**	30 mg IV*

Weeks 2-12:

Mondays	**ALEMTUZUMAB**	30 mg IV*
Wednesdays	**ALEMTUZUMAB**	30 mg IV*
Fridays	**ALEMTUZUMAB**	30 mg IV*

***Dilute in 100mL sodium chloride 0.9% and infuse over 2 hours**

If acute moderate to severe adverse reactions due to cytokine release (hypotension, rigors, fever, shortness of breath, chills, rashes and bronchospasm) occur at either the 3 mg or 10 mg dose levels, then those doses should be repeated until they are well tolerated before further dose escalation is attempted.

DURATION OF TREATMENT

Minimum 4 weeks, maximum 18 weeks of treatment.

Consensus guidelines: If disease is progressing, discontinue treatment. If disease is stabilised or responding, continue for 6 additional weeks. If there is no further clinical response (i.e. a plateau) over a period of 4 weeks, discontinue treatment. If complete response in blood & nodes, check bone marrow every 4 - 6 weeks, then continue Alemtuzumab until complete marrow clearance or no further response. Unless contraindicated, treatment should be carried out to a maximum 16 weeks.

CMV REACTIVATION

If CMV PCR blood testing indicates CMV reactivation, see guidelines on management of CMV reactivation.

DOSE MODIFICATIONS - discuss with consultant

Alemtuzumab
If treatment is delayed for more than 7 days, it should be reinstituted with the dose escalation from 3 mg.

Anaemia
- For anaemic patients, Alemtuzumab may be given with transfusion or erythropoietin support
- Transfusion support should be with irradiated blood products

Thrombocytopenia
- If platelets <25 x 10^9/L but no haemorrhage, administer full dose
- Transfusion support should be given as required (e.g. platelet count <10 x 10^9/L)
- In the event of haemorrhage, stop Alemtuzumab & reinitiate when bleeding has stopped

Neutropenia
- Clinical judgement should be used for institution of G-CSF when ANC drops to <0.5 x 10^9/L. However, at a level of >0.5 x 10^9/L, cytopenias are likely to resolve spontaneously and support may not be needed
- Temporarily discontinue Alemtuzumab if ANC <0.25 x 10^9/L
- Temporarily interrupt therapy in the event of febrile neutropenia
- Reduction in Alemtuzumab dose is not recommended

Infusion related toxicity
If there are no adverse events with the first dose of Alemtuzumab, the dose may be increased the next day. If any infusion related reactions do occur, administer the same dose the next day. Only escalate the dosage once the patient has become tolerant.

Renal or hepatic impairment
No data - discuss with consultant.

INVESTIGATIONS

FBC, U&Es, LFTs weekly, weekly CMV PCR, glucose.

EMETIC RISK

Minimal

CONCURRENT MEDICATION

Allopurinol	300mg daily for 7 days [Cycle 1 only]. Refer for full details to "Tumour Lysis Syndrome in Adults" protocol (H.8) [Link]
Aciclovir	200 mg three times a day for duration of treatment and for 3 months after completion
Co-trimoxazole	480 mg daily on Monday / Wednesday / Friday for duration of treatment and for 3 months afterwards (consider reducing the dose to 480 mg twice weekly during neutropenic periods)
PPI (as per local formulary)	daily for duration of treatment
Fluconazole	50 mg daily for duration of treatment

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Rigors develop during the first few injections. Infusion-related fever more common during the first week and commonly begins 5 - 6 hours after the infusion starts. Hypotension, dyspnoea, rashes, headache and diarrhoea. Thrombocytopenia most common during weeks 2-4 and neutropenia common between weeks 4 - 8.

MANAGEMENT OF ADVERSE EVENTS

- Hydrocortisone 50-100 mg IV may be given pre-treatment in the event of continued infusion related toxicity.
- If rigors develop, halt infusion and administer IV Chlorphenamine.
- In patients experiencing rash, an additional 4 mg Chlorphenamine PO every 4 - 6 hours as needed is indicated. In patients experiencing severe rash, pre-medication with H2 receptor antagonist (e.g. famotidine) is recommended.
- Treating physicians are advised to use antibiotics and G-CSF support according to their clinical judgment for febrile neutropenia.
- If hypotension develops, hydration with normal saline is indicated, unless contraindicated based on underlying cardiac status.
- If dyspnoea develops, infusion should be stopped and treatment with inhaled beta2 agonists should be administered if needed - severe dyspnoea may require the temporary use of steroids.

TREATMENT RELATED MORTALITY:

Approximately 2-10%

REFERENCES

1. Claire E. Dearden, Amit Khot, Monica Else, Mike Hamblin, Effie Grand, Ashok Roy, Saman Hewamana, Estella Matutes, Daniel Catovsky. Alemtuzumab therapy in T-cell prolymphocytic leukemia: comparing efficacy in a series treated intravenously and a study piloting the subcutaneous route. Blood (2011) 118 (22): 5799–5802.
2. Keating MJ, Cazin B, Coutre S, Birhiray R, Kovacsovics T, Langer W, et al. Campath-1H treatment of T-cell prolymphocytic leukemia in patients for whom at least one prior chemotherapy regimen has failed. J Clin Oncol. 2002;20(1):205–13.
3. MabCampath product information, Schering Healthcare, July 2001.
4. UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)
5. UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009)

Review

Name	Revision	Date	Version	Review date
Cheuk-kie Jackie Cheung (Haematology Pharmacist) Graham Collins (Consultant Haematologist) Anna Schuh (Consultant Haematologist)	New document (Re-drafted from previous alemtuzumab –dex protocol)	May 2018	1.0	
NSSG Lymphoma Group	Annual protocol review	May 2019	1.2	May 2021
NSSG Lymphoma Group	Annual protocol review	June 2022	1.3	June 2024

Nursing Care Plan: Alemtuzumab (Campath)

Indication: Disease modification (but curative if combined with allogeneic transplant) in patients with T-PLL
Frequency: 3 times a week on Monday, Wednesday and Friday, maximum 16 weeks.
Alopecia: No
Emetic risk: Low
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

ALEMTUZUMAB is a lymphocyte depleting monoclonal antibody, which targets the CD52 antigen on mature lymphocytes
Administered as an IV infusion over 2 hours
Classification of extravasation: neutral
Side effects: hypotension, fever, rigors, urticarial, nausea, bronchospasm. This infusion related reactions are more common during the first dose. Doses are increased over the first week and if a delay of more than 7 days occurs in treatment, escalation from starting rate is necessary. Bone marrow depression occurs with continued use.

Regime Specific Considerations

- If acute moderate to severe adverse reactions occur at either the 3 mg or 10 mg escalation dose levels, then those doses should be repeated daily until they are well tolerated before further dose escalation is attempted.

- Premed pre first dose and before each dose escalation. In the first week a second dose of paracetamol should be given 4 hours after administration. Hydrocortisone 50-100 mg IV may be given pre-treatment in the event of continued infusion related toxicity.

- Withdraw the necessary amount of alemtuzumab into a syringe. **Filter with a 5 micron filter needle as you inject into 100ml bottle of sodium chloride 0.9%.** One ampoule contains 30mg alemtuzumab. The dose very rarely exceeds one ampoule; please contact the pharmacist if you think that more than one ampoule is required, to confirm the dose.

- Weekly bloods: FBC, U&Es, LFTs, CMV PCR, glucose.