Alemtuzumab

Indication

High risk or very high risk Chronic Lymphocytic Leukaemia (CLL):

- 1st line therapy in CLL with 17p deletion
- 2nd line therapy in CLL with 17p deletion previously treated with chemotherapy (but not alemtuzumab)
- refractory or relapsed CLL with or without 17p deletion

Note alemtuzumab may also be used for 1st and 2nd line treatment of T-cell prolymphocytic leukaemia where only the IV route must be used- see separate protocol.

ICD-10 codes

Codes with a prefix C91.10, C91.12

Regimen details

Week 1 - Initial Dose Escalation

Day	Drug	Dose	Route
1	Alemtuzumab	3mg	SC or IV infusion
3	Alemtuzumab	10mg	SC or IV infusion
5	Alemtuzumab	30mg	SC or IV infusion

Week 2 onwards

Day	Drug	Dose	Route
1	Alemtuzumab	30mg	SC or IV infusion
3	Alemtuzumab	30mg	SC or IV infusion
5	Alemtuzumab	30mg	SC or IV infusion

If, at any point, therapy is withheld for more than 7 days, alemtuzumab should be restarted with gradual dose escalation from 3mg, as week 1.

Alemtuzumab may be combined with high dose steroid for patients with 17p deletion and/or bulky disease:
Methylprednisolone 1 gram/m^2 orally daily for 5 consecutive days repeated every 28 days for 4 cycles

Cycle frequency

Weekly (as above)

Number of cycles

Maximum of 12 cycles (12 weeks)

Administration

Alemtuzumab is administered by subcutaneous injection into the thigh. Injection site reactions with the subcutaneous route may require switching to the IV route. Such reactions are less common when given with high dose steroids, and usually resolve within 2 weeks of starting treatment.

Alemtuzumab may be administered intravenously in 100mL sodium chloride 0.9% over 2 hours. In the event of mild infusion-related reactions, the infusion should be temporarily stopped. Severe reactions should be treated with IV corticosteroids, or pethidine for severe rigors, and re-challenge with the same dose on the next day. If recurrent problems with infusion-related reactions, consider extending the infusion time.

Patients must be observed for 2 hours after the first three doses for delayed reactions. Observations (temperature, BP, respiratory rate and saturations) should be recorded every 30 minutes.

Pre-medication

30-60 minutes prior to alemtuzumab:

- Paracetamol 1 gram PO
- Chlorphenamine 4mg PO or 10mg IV
- Dexamethasone 4-8mg IV or PO during dose escalation. (Note: if patient is also receiving methylprednisolone, omit dexamethasone on that day and give the methylprednisolone 30-60 minutes prior to alemtuzumab).

Emetogenicity

This regimen has low emetic potential - no anti-emetics routinely required

Additional supportive medication

Allopurinol 300mg PO OD (100mg OD if CrCl < 20mL/min) for the first 1-2 weeks for patients with bulky disease or high white cell count (high risk of tumour lysis syndrome)
Proton pump inhibitor for patients receiving high dose steroids.
PCP prophylaxis, antiviral prophylaxis and antifungal prophylaxis as per local policy. Continue during therapy and for 6 months after completion of treatment (or until $CD4^+$ cell count >200 cells/µL)
GCSF and/or ciprofloxacin as per local policy if neutrophils <0.5 x 10^9/L.

Extravasation

Alemtuzumab is a non-vesicant.

Investigations – pre first cycle

Investigation	Validity period
FBC	7 days
U+Es (including creatinine)	7 days
LFTs	7 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Twice weekly
U+Es (including creatinine)	Twice weekly
LFTs	Twice weekly
Cytomegalovirus (CMV) levels	Weekly and for 2 months post treatment

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Platelets	> 25 x 10^9/L
Neutrophils	> 0.5 x 10^9/L

Dose modifications

- **Haematological toxicity**

If normal baseline blood counts:

Haematological toxicity		Dose modification
Platelet count < 25 x 10^9/L and/or neutrophils < 0.25 x 10^9/L	1st occurrence	Discontinue alemtuzumab. Restart at 30mg when platelet count > 50 x 10^9/L and neutrophils > 0.5 x 10^9/L*
	2nd occurrence	Discontinue alemtuzumab. Restart at 10mg when platelet count > 50 x 10^9/L and neutrophils > 0.5 x 10^9/L*
	3rd occurrence	Discontinue alemtuzumab

*If the duration of interruption in alemtuzumab therapy is ≥7 days, then restart at 3mg and increase dose according to week 1 initial dose escalation, to 10mg and then 30mg as tolerated.

If baseline platelet count ≤ 25 x 10^9/l and/or baseline neutrophil count ≤ 0.25 x 10^9/L:

Haematological toxicity		Dose modification
≥50% decrease from baseline in patients starting therapy with a baseline platelet count ≤ 25 x 10^9/L and/or a baseline neutrophils ≤ 0.25 x 10^9/L	1st occurrence	Discontinue alemtuzumab. Restart at 30mg when FBC returns to baseline values*
	2nd occurrence	Discontinue alemtuzumab. Restart at 10mg when FBC returns to baseline values*
	3rd occurrence	Discontinue alemtuzumab

*If the duration of interruption in alemtuzumab therapy is ≥7 days, then restart at 3mg and increase dose according to week 1 initial dose escalation, to 10mg and then 30mg as tolerated.

Haematological toxicity	Dose modification
Autoimmune haemolytic anaemia	Discontinue alemtuzumab. No data exist on the resumption of alemtuzumab in patients with autoimmune cytopenias or marrow aplasia.
Autoimmune thrombocytopenia	
Pure red cell aplasia	
Bone marrow aplasia	

- **Renal impairment**

No studies in renal impairment but unlikely to require a dose modification.

- **Hepatic impairment**

No studies in hepatic impairment but unlikely to require a dose modification.

- **Other toxicities**

Toxicity	Definition	Dose adjustment
Cytomegalovirus (CMV) viraemia	≥ 2 positive CMV PCR tests 1 week apart	Withhold alemtuzumab until resolution.
Local inflammatory reaction at injection site	Injection site reaction ≥ grade 3	Withhold alemtuzumab until resolution to ≤ grade 1.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Pancytopenia
Potentially life-threatening bacterial, viral, fungal and protozoan infections
Myocardial infarction, cardiac arrest

- **Frequently occurring side effects**

Myelosuppression
Injection site reaction (SC)
Infusion related reactions (IV)
Diarrhoea
Abdominal pain
Insomnia

- **Other side effects**

Anxiety

Significant drug interactions – for full details consult product literature/ reference texts

No formal drug interaction studies are available.

Additional comments

All patients who receive alemtuzumab are at risk of transfusion-associated graft versus host disease and must receive **IRRADIATED BLOOD PRODUCTS** lifelong.

Patients should not receive live viral vaccines for at least 12 months after treatment.

Patients of reproductive age should use effective contraception methods during treatment and for a minimum of 6 months following alemtuzumab therapy.

Alemtuzumab (Campath) is no longer licensed in the United Kingdom but is made available free of charge through the Alemtuzumab Access Programme. All stock must be obtained on an individual patient basis via the Clinigen Alemtuzumab Patient Access Scheme or via the appropriate clinical trial. Prospective patients should be identified at least two weeks in advance and the "Alemtuzumab Access Programme Patient Access and Monitoring Form" completed and submitted according to local hospital policy; for further information on the access programme, contact Clinigen at customer.services@clinigengroup.com

References

- Full Prescribing Information CAMPATH® (Alemtuzumab) Injection for intravenous use, accessed 13 October 2014 via http://www.campath.com/pdfs/2014-09-Campath_US_PI.pdf
- Oscier D, Dearden C, Eren E, et al. Guidelines on the diagnosis, investigation and management of chronic lymphocytic leukaemia. BJH 159 (5): 541-64 (2012)
- Pettit A, Jackson R, Carruthers S, et al. Alemtuzumab in combination with Methylprednisolone is a highly effective induction regimen for patients with chronic lymphocytic leukaemia and deletion of TP53: Final results of the National Cancer Research Institute CLL206 Trial. JCO 30 (14): 1647-55 (2012)
- Keating et al. Management Guidelines for Use of Alemtuzumab in B-cell Chronic Lymphocytic Leukaemia. Clin Lymphoma. Mar 2004

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