CLADRIBINE

Hairy cell leukaemia

May be used in combination with rituximab for relapsed or refractory hairy cell leukaemia, for patients who have already received cladribine or pentostatin

Drug/Dosage: **Cladribine** 0.14mg/kg/day bolus subcutaneous injection once daily on Day 1 to Day 5 (5 doses total)

Administration: **Subcutaneous route:** Cladribine 2mg/ml solution (Litak® from Lipomed, available via AAH) is the only licensed product for subcutaneous use.
Each subcutaneous dose should be injected as a single injection into abdominal tissue at approximately 24 hour intervals. Up to 7ml may be injected into one site and there is no need to split the daily dose into 2 or 3 injections.
Allow the injection to warm to room temperature, then inject the dose slowly (over approx. 1 minute) and massage the injection site smoothly to distribute the volume.

The IV brand, Leustat®, is still available, and is an option if there are supply problems with the Litak® brand. The dosing for the IV route is as follows:

Cladribine IV (Leustat®) 0.14mg/kg/day IV infusion in 500ml Sodium Chloride 0.9% over 2 hours once daily on Day 1 to Day 5

Other drugs: Allopurinol 300mg po daily for 2 weeks
Ideally, delay starting any co-trimoxazole and aciclovir until immediately after the cladribine course is completed, as patients often develop a rash on cladribine and this minimises confusion as to the cause.
PCP prophylaxis - prescribe according to unit practice/protocol (generally until 6 months after completion of treatment, or according to CD_4 counts)
Consider aciclovir prophylaxis (400mg bd), especially if history of VZV or HSV reactivation
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Rituximab 375mg/m^2 IV once weekly x 8 weeks, starting either concurrently with cladribine, or immediately after the cladribine course is completed
(for details on rituximab administration, follow the Rituximab for follicular lymphoma protocol)

Frequency: a single 5 day course
Response usually seen within 10 – 12 weeks after treatment

Main Toxicities: myelosuppression - neutropenia in 70% patients, usually resolving by Day 15, thrombocytopenia also common; fever; rash; ovarian failure; infertility

Anti-emetics: mildly emetogenic

Extravasation: non-vesicant

Reason for Update: included info on use with rituximab; review of IV dose, in line with BCSH guidelines	Approved by Chair of Network TSSG: Dr A Laurie
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Prepared by: S Taylor	Checked by: C Tucker

Regular Investigations:	FBC	Day 1, then weekly for 2 – 4 weeks depending on value of counts, then fortnightly until blood counts have recovered sufficiently for less frequent monitoring
	U&Es	Day 1
	LFTs	Day 1
	BM aspirate/biopsy	after peripheral counts have recovered (usually after 4 – 6 months)

Comments: All patients must receive irradiated blood products for all future transfusions - inform patient and blood bank.

Complete response is defined as the absence of hairy cells from the peripheral blood and bone marrow along with resolution of organomegaly and cytopenias.
In CR, immunohistochemistry reveals no clustering (≥3 cells) of CD20-positive or DBA.44-positive cells.

Dose Modifications

Haematological Toxicity: No pre-treatment dose reductions or delays should be made for anaemia, neutropenia or thrombocytopenia.

Renal and Hepatic Impairment: The Litak SPC states that cladribine is contra-indicated in patients with moderate or severe renal impairment (CrCl ≤ 50ml/min) and in patients with moderate or severe hepatic impairment.
The Leustat SPC advises to use caution when using cladribine in patients with renal or hepatic impairment.

There are no studies in patients with renal or hepatic impairment. Consequently, there is no formal advice on any required dose adjustments. There is also little information available on the metabolism or route of excretion of cladribine, but approximately 18% is eliminated unchanged by the kidney. The fate of the remainder is unknown.
The potential risks and benefits of cladribine should therefore be carefully considered before treatment is commenced in any patient with renal impairment (CrCl ≤ 50ml/min) or hepatic impairment, and it should only be used with caution and close monitoring.

Patient Information: Macmillan leaflet for Cladribine

References:

Hoffman, MA et al; JCO (1997); 15: 1138 – 1142 (Leustat)
Saven et al; Blood (1998); 92: 1918 – 1926 (Leustat)
Robak et al; Eur J Haem 1999; 62: 49 – 56 (Leustat 2 hour infusion)
Von Rohr, A et al; Annals of Oncology (2002); 13: 1641 – 1649 (Litak)
Else, M et al; Leukaemia & Lymphoma 2011; 52 (Suppl 2): 75 – 78 (R-cladribine)