Cladribine

INDICATION

Hairy cell leukaemia.
Histiocytosis (Langerhans or non-Langerhans)
Low-grade non-Hodgkin Lymphoma (NHL)

Cladribine may be used in combination with rituximab for relapsed or refractory hairy cell leukaemia or relapsed NHL.

TREATMENT INTENT

Disease Modification.

PRE-ASSESSMENT

1. Ensure histology is confirmed prior to administration of chemotherapy and document in notes.
2. 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.
3. Blood tests - FBC, ESR, DAT, U&Es, LDH, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, β₂ microglobulin, hepatitis B core antibody and hepatitis B surface Ag, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent.
4. For histiocytosis patients refer to OUH investigations and pathway documents on NSSG website.
5. 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'.
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. ECG +/- Echo - if clinically indicated.
8. Record performance status (WHO/ECOG).
9. Record height and weight.
10. 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 prior to treatment.
11. Fertility - it is very important the patient understands the potential risk of reduced fertility. All patients should be offered fertility advice by referring to the Oxford Fertility Unit.
12. Hydration - in patients with bulky disease pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. For patients at high risk of tumour lysis, refer to tumour lysis protocol.
13. Consider dental assessment / Advise dental check is carried out by patient's own dental practitioner before treatment starts.
14. Treatment should be agreed in the relevant MDT.
DRUG REGIMEN

Days 1 to 5  CLADRIBINE (LITAK®) 0.14 mg/kg SC bolus daily
OR
Days 1 to 7  CLADRIBINE (LEUSTAT®) 0.09 mg/kg/day in 500mL sodium chloride 0.9% by continuous intravenous infusion.

For Hairy cell leukaemia add Rituximab.
For relapsed / refractory CD20 positive NHL consider Rituximab

Day 1  Premedication
Paracetamol 1g PO, Chlorphenamine 10 mg IV, Hydrocortisone 100 mg IV.
Give 30 minutes before rituximab.

RITUXIMAB 375 mg/m² IV infusion in 500 mL sodium chloride 0.9%

CYCLE FREQUENCY

For Hairy cell leukaemia:
CLADRIBINE: normally once only.
RITUXIMAB: weekly for 4 weeks.

For CD20 positive NHL:
CLADRIBINE: consider 2-6 cycles, frequency every 28 days.
RITUXIMAB: on day 1 of each cycle of cladribine.

For Histiocytosis:
CLADRIBINE: 2 cycles at full dose (as above) every 28 days, then restaged (with CT NCAP/MRI). Consider giving up to 6 cycles.

RE-STAGING

After count recovery and at least 4 months after cladribine therapy, bone marrow and ultrasound or CT.

DOSE MODIFICATIONS

LITAK®
Renal and hepatic impairment
There are no data on the use of LITAK in patients with renal or hepatic impairment. LITAK is contraindicated in patients with moderate to severe renal impairment (creatinine clearance ≤50 ml/min) or with moderate to severe hepatic impairment (Child-Pugh score >6).

LEUSTAT®
Acute renal insufficiency has developed in some patients receiving high doses of LEUSTAT. In addition, there are inadequate data on dosing of patients with renal or hepatic insufficiency. Until more information is available, caution is advised when administering the drug to patients with known or suspected renal or hepatic insufficiency. As with other potent chemotherapeutic agents,
monitoring of renal and hepatic function should be performed as clinically indicated, especially in patients with underlying kidney or liver dysfunction. Physicians should consider delaying or discontinuing therapy if renal toxicity occurs.

### INVESTIGATIONS
FBC, renal and liver profiles.

### CONCURRENT MEDICATION

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage/Details</th>
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<tr>
<td>Co-trimoxazole</td>
<td>Start at completion of Cladribine treatment to minimize confusion about cladribine-induced or co-trimoxazole-induced rash. 480 mg daily Mondays, Wednesdays and Fridays and continue for 3 months after treatment. Consider reducing to 480 mg twice weekly during neutropenic periods.</td>
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<tr>
<td>Allopurinol</td>
<td>300 mg daily for 7 days starting 24-48 hours prior to chemotherapy (first cycle only)</td>
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<td>Aciclovir</td>
<td>200 mg TDS during treatment and for 3 months after completion.</td>
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<td>G-CSF</td>
<td>Incidence of Grade III/IV neutropenia without G-CSF: 74% Consider prophylactic GSCF from Day 8 for high risk patients as per local policy</td>
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<tr>
<td>Fluconazole</td>
<td>50 mg daily for 4 weeks or until neutrophil count recovery</td>
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### EMETIC RISK
Minimal.

### EXTRAVASATION RISK
Cladribine: neutral

### ADVERSE EFFECTS
Very common: neutropenia, anaemia, thrombocytopenia, infection, fever, skin rashes, lethargy, anorexia, fever, nausea, vomiting, headache.
Risk of secondary malignancy.

### TREATMENT RELATED MORTALITY
1-5%

### 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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</thead>
<tbody>
<tr>
<td>NSSG Lymphoma Group</td>
<td>Annual protocol review</td>
<td>May 2017</td>
<td>3.7</td>
<td></td>
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<tr>
<td>NSSG Lymphoma Group</td>
<td>Annual protocol review</td>
<td>May 2019</td>
<td>3.8</td>
<td>May 2021</td>
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<tr>
<td>Stephen Booth and Sara Castro</td>
<td>Clarification of Rituximab schedule and addition of Rituximab to first line HCL treatment</td>
<td>Oct 2020</td>
<td>3.9</td>
<td>Oct 2021</td>
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