Rituximab + Cladribine

Indication

Relapsed Hairy Cell Leukaemia

Table 1 – Treatment regimen details

Cycle 1 (3 week length)

DRUG	DOSE	DILUENT	ROUTE	FREQUENCY/DURATION
Rituximab*	375mg/m2	500mL Sodium Chloride 0.9%	IV	Days 1,8,
Cladribine (Litak®)	0.14mg/Kg (note dose may vary for other brands		SC	Day 1-5

Cycle 2 onwards (2 week length)

DRUG	DOSE	DILUENT	ROUTE	FREQUENCY/DURATION
Rituximab*	375mg/m2	500mL Sodium Chloride 0.9%	IV	Days 1

Repeat every 14 days for up to 6 doses of Rituximab in total

Administration

*Refer to local Trust Rituximab Infusion Policy

Pre-medication

Paracetamol 1000mg PO 1hr prior to each dose of Rituximab
Chlorphenamine 10mg IV 30min prior to each dose of Rituximab
Hydrocortisone 100mg IV 30min prior to each dose of Rituximab

Emetogenicity

Cycle 1 – Low Risk (Category C) - Metoclopramide tds prn only
Cycle 2+ - Minimum Risk (Category D)

Additional supportive medication

Cotrimoxazole 480mg od (starting day 14 of cycle 1)[†] until lymphocytes > 1.0
Aciclovir 400mg bd until lymphocytes > 1.0
Allopurinol 300mg od for 7 days (cycle 1 only)

[†]Co-administration of Cladribine & Co-trimoxazole can result in skin rash occurring

Extravasation

Table 2 – Extravasation Risk Category for each intravenous drug in the regimen

Rituximab	Neutral: Group 1
Cladribine	Neutral: Group 1

Investigations – pre first cycle

Table 3 - Standard Investigations prior to first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Hepatitis Screen Prior to Rituximab	28 days

If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Discuss potential for infertility - offer semen cryopreservation to male patients.

If the lymphocyte count is > 20 x 109/L the patient is at greater risk of cytokine-release Syndrome: see Rituximab

infusion protocol

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)

Standard limits for administration to go ahead

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

Table 4 – Standard test result limits for each administration to go ahead

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 60 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

Dose modifications

Dose modification for haematological toxicity and infection

- Pancytopenia with first cycle is due to marrow infiltration – there are no dose modifications for this
- Delay subsequent cycles until neutrophils ≥ 1.0
- Patient must be monitored closely and infection must be treated promptly
- Give blood product support as necessary
- If there is neutropenic sepsis despite use of GCSF consider using 60% dose - *discuss with consultant*

Dose modification for renal impairment

- There is limited information and it is a clinical decision whether to modify treatment.
- If Cr.Cl<30-60ml/min consider using 60% dose e.g reduce course from 5 to 3 days. If Cr.Cl <30ml/min cladribine may be contraindicated - *discuss with consultant*

Dose modification for liver dysfunction

- Limited information – clinical decision

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

- **Serious side effects**

Infusion related reactions with Rituximab (including cytokine-release syndrome, tumour-lysis syndrome)
Infections
Cardiovascular events
Hepatitis B reactivation
Progressive multifocal leukoencephalopathy (PML)

- **Frequently occurring side effects**

Neutropenia
Leucopenia
Thrombocytopenia
Sepsis
Anaeima
Angeioedema

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

Additional comments

After treatment with Cladribine, blood and platelet transfusions must be irradiated indefinitely.

References

1. [British Society for Haematology 14 October 2020]