NELARABINE

INDICATION

Licensed / CDF indication:

Refractory T-cell acute lymphoblastic leukaemia or T-cell lymphoblastic non-Hodgkin's lymphoma, with intention to proceed to bone marrow transplantation.

Licensed / unfunded indication:

Refractory T-cell acute lymphoblastic leukaemia or T-cell lymphoblastic non-Hodgkin's lymphoma, whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens.

TREATMENT INTENT

Curative

PRE-ASSESSMENT

1. Blood tests - FBC, coagulation screen, U&Es, LDH, ESR, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, $\beta_2$microglobulin, hepatitis B core antibody, hepatitis BsAg, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent
2. **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.
3. Ensure histology and diagnosis are confirmed prior to administration of chemotherapy and document in notes
4. Record stage of disease
5. Urine pregnancy test - before cycle 1 of each new chemotherapy course in women aged 12 – 55 years of age unless they have been sterilised or undergone a hysterectomy
6. Record performance status (WHO/ECOG)
7. Record height and weight (also needed to calculate CrCl)
8. 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
9. Fertility - it is very important the patient understands the potential risk of infertility, all patients should be offered fertility advice (see Fertility Guidelines)
10. Hydration - refer to Tumour Lysis protocol

DRUG REGIMEN

Days 1, 3 and 5 **NELARABINE** 1500mg/m^2 intravenous infusion over 2 hours.

CYCLE FREQUENCY

Cycle repeated every 21 days. Usually only 1 – 2 cycles will be given.

DOSE MODIFICATIONS

Haematological Toxicity

Discuss with consultant.

Neurological Toxicity

Nelarabine must be discontinued at the first sign of neurological events of National Cancer Institute Common Terminology Criteria Adverse Event (NCI CTCAE) grade 2 or greater.

Renal / Hepatic Impairment

Renal impairment	Hepatic impairment
Not studied. Nelarabine and its active metabolite are partially renally excreted. Monitor closely for toxicity if CrCl <50mL/min.	Not studied. Use with caution.

INVESTIGATIONS

- FBC, Coagulation screen.
- U&E, LFT.
- Calculated creatinine clearance.
- Recent bone marrow aspirate/trephine.
- CT scan if appropriate.

CONCURRENT MEDICATION

Allopurinol	300mg PO once daily for 14 days. (Cycle 1 only)
Aciclovir	200mg PO three times a day
PPI	Daily if clinically indicated
Antifungal Prophylaxis	Refer to local antifungal policy.
Co-trimoxazole	480mg OD on Monday, Wednesday and Friday if neutrophils > 1 x 10^9/L and platelets > 100 x 10^9/L.

ANTI-EMETICS

Low risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

NEUROLOGICAL ADVERSE REACTIONS

Severe neurological reactions have been reported with the use of nelarabine. These reactions have included altered mental states including severe somnolence, central nervous system effects including convulsions, and peripheral neuropathy ranging from numbness and paresthesias to motor weakness and paralysis. There have also been reports of reactions associated with demyelination, and ascending peripheral neuropathies similar in appearance to Guillain-Barré Syndrome.

Patients treated previously or concurrently with intrathecal chemotherapy or previously with craniospinal irradiations are potentially at increased risk for neurological adverse events and therefore concomitant intrathecal therapy and/or craniospinal irradiation is not recommended.

Full recovery from these reactions has not always occurred with cessation of nelarabine. Therefore, close monitoring for neurological reactions is strongly recommended, and nelarabine must be discontinued at the first sign of neurological reactions of NCI CTCAE Grade 2 or greater.

Other very commonly reported adverse effects
Infection, leukopenia, thrombocytopenia, anaemia, neutropenia (including febrile neutropenia), dyspnoea, cough, diarrhoea, constipation, peripheral oedema, fatigue

MORTALITY

5-10%

REFERENCES

1. Novartis (2015) Nelarabine Summary of Product Characteristics. http://www.medicines.org.uk. Accessed online 09March2017.
2. DeAngelo DJ et al (2007) Nelarabine induces complete remissions in adults with relapsed or

refractory T-lineage acute lymphoblastic leukemia or lymphoblastic lymphoma: Cancer and Leukemia Group B study 19801. Blood 109(12):5136-42.

REVIEW

Name	Revision	Date	Version	Review date
Cheuk-kie Jackie Cheung, Haematology Pharmacist	Re- drafted protocol	March 2017	2.0	March 2019