Rituximab (B-ALL)

Please note this protocol has been produced in a new format that is currently being piloted. Any feedback on this new format should be sent to SSGMeetings@uhbw.nhs.uk

Index

Indication

Addition of rituximab to first line standard chemotherapy for Philadelphia negative de novo CD20+ precursor B-ALL, if the patient is fit enough to be treated on either UKALL 2011, UKALL-14 or similar intensive protocols.

(NHSE CCP 1748)

Response Rates

Phase III open label GRAALL-2005R trial

- 2-year EFS: rituximab 65% (95% CI, 56 to 75) v control 52% (95% CI, 43 to 63).
- 3-year complete remission duration: rituximab 67% versus control 40% (p=0.002)

Regimen details

Cycle	Drug	Dose	Route
Induction Phase I: D3, 10, 17 and 24	Rituximab	375mg/m^2	IV infusion
Induction Phase II: D2 and D16	Rituximab	375mg/m^2	IV infusion
Intensification: D3	Rituximab	375mg/m^2	IV infusion
Consolidation 1: D1	Rituximab	375mg/m^2	IV infusion
Consolidation 2: D1	Rituximab	375mg/m^2	IV infusion
Consolidation 3 (delayed intensification): D2	Rituximab	375mg/m^2	IV infusion
Maintenance: 6 doses to be given every 2 months over the first 12-month period ie. give in months 1, 3, 5, 7, 9 and 11.	Rituximab	375mg/m^2	IV infusion

Cycle frequency
As above

Number of cycles
Up to a maximum of 16 doses administered following the above schedule during induction phase I and II, intensification, consolidation 1, 2 and 3 and in the first 12 months of maintenance.

Pre-medication
Rituximab premedication:

- Paracetamol 1g PO 60 minutes prior to rituximab
- Chlorphenamine 10mg IV bolus (or 4mg PO) 15 minutes prior to rituximab
- Hydrocortisone 100mg IV bolus or dexamethasone 8mg IV bolus 15 minutes prior to rituximab*

*If the patient is due dexamethasone as part of chemotherapy on the day of a rituximab infusion, (as may be the case in induction phase I and maintenance), they should take this prior to rituximab being given, without the need for an additional dose of steroids immediately prior to rituximab administration

Supportive medication
Nil

Emetogenicity
This regimen has low emetic potential.

Administration
Intravenous rituximab is administered in 500mL sodium chloride 0.9%. The first infusion should be initiated at 50mg/hour and if tolerated the rate can be increased by 50mg/hour every 30 minutes to a maximum of 400mg/hour. Subsequent rituximab infusions should be initiated at 100 mg/hour and if tolerated increased by 100mg/hour increments every 30 minutes to a maximum of 400 mg/hour

Extravasation
Rituximab is neutral (Group 1)

Mandatory investigations – pre first cycle

Investigation	Validity period
FBC	7 days*
U&E (including creatinine)	7 days
LFT	7 days
Virology (Hep B/C, HIV)	3 months or as per local policy

*During induction phase I treatment it is accepted/expected that the patients' counts may be initially low and so treatment with rituximab would continue to be administered, regardless of FBC results.

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	7 days
U&E (including creatinine)	7 days
LFT	7 days

Standard limits for administration to go ahead

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

Investigation	Limit
Neutrophils	≥ 1.5 x 10^9 /L*
Platelet count	≥ 75 x 10^9 /L*

*During induction phase I induction treatment it is accepted/expected that the patients' counts may be initially low and so treatment with rituximab would continue to be administered, regardless of FBC results.

Dose modifications

Haematological toxicity

If counts low, discuss with consultant as to whether to proceed with planned treatment.

Renal impairment

No dose modification is required for mild, moderate or severe renal impairment.

Hepatic impairment

No dose modification required.

Side Effects

Specific drug related side effects:

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
Infections	Oedema	Progressive Multifocal Leukoencephalopathy
Myelosuppression	Dizziness	
Infusion related reactions	Myalgia/arthralgia	Cardiac disorders
Nausea	Fatigue	Tumour lysis syndrome
Rash, pruritis	Hypotension (infusion related and usually transient)	Cytokine release syndrome
Angioedema		Peripheral neuropathy
Headache		Anaphylaxis

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

Nil significant, although data is limited.

References

- NCRI Adult Acute Lymphoblastic Leukaemia - Interim Guidelines 2023. N Morley and C Rowntree.
- NHS England. Clinical Commissioning Policy (URN:1748): Addition of Rituximab to standard chemotherapy for newly diagnosed CD20 positive B-cell precursor Acute Lymphoblastic Leukaemia accessed via: 1748-Addition-of-rituximab-to-first-line-standard-chemotherapy-for-CD20-positive-B-cell-precursor-acute-lympho.pdf (england.nhs.uk)
- Maury, S et al. Rituximab In B-Lineage Adult Acute Lymphoblastic Leukemia. N Engl J Med 2016; 375 (11): 1044-1053.

Version	Issue date	Review date	Revision	Written/Checked/Authorised
1	Aug 2024	Aug 2027	New protocol	Written: Dr E Booth (Leukaemia Clinical Fellow, UHBW NHS Trust), Dr K Hodby (Consultant Haematologist, UHBW NHS Trust) Checked: Kate Gregory (Lead Pharmacist for SACT Protocols, SWAG Cancer Alliance) Authorised: Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)