CHLORAMBUCIL +/- RITUXIMAB for low grade lymphomas

R-Chlorambucil is routinely funded for first, second or third line use in patients with low grade lymphoma
R-Chlorambucil is NICE-approved (2012) as an option for previously untreated patients with symptomatic Stage III or IV follicular lymphoma

All patients should be screened for hepatitis B virus before starting treatment with rituximab

Drugs/Dosage:

Chlorambucil 10mg/m^2/day PO once daily for 7 days, on Days 1 – 7
+/-
Rituximab 375mg/m^2 IV Day 1
(dose 'banded' according to dosing table below)

Rituximab Premedication (to be administered before **all** rituximab infusions):
Paracetamol 1000mg po 60 minutes before rituximab
Chlorphenamine 10mg IV 15 minutes before rituximab
Dexamethasone 8mg IV 15 minutes before rituximab

Other Drugs: Allopurinol 300mg po daily, ideally starting 24 hours before treatment - review after 4 weeks

Frequency: 4 weekly cycle for 6 – 8 cycles, then consider maintenance rituximab, if funding in place for the patient's indication

Administration: Chlorambucil available as 2mg tablets, which need to be stored in the fridge.
The daily dose may be divided to reduce the incidence of nausea.

Rituximab should be diluted in 500ml 0.9% sodium chloride & administered according to following instructions:

First infusion#: start at 50mg/hr, according to infusion table below; escalate in 50mg/hr increments every 30 minutes to a maximum of 400mg/hr.
Monitor patient's vital signs signs (blood pressure, pulse, temperature and O_2 saturation) at baseline and then every 30 minutes (before each increase in infusion rate) until end of infusion.

	Infusion Rate (mg/hour)							
	50	100	150	200	250	300	350	400
Rituximab 'banded' dose	**Infusion Rate (ml/hour) for rituximab in 500ml volume only**							
450mg	55	111	166	222	277	333	388	444
500mg	50	100	150	200	250	300	350	400
600mg	42	83	125	167	208	250	292	333
700mg	36	71	107	143	178	214	250	286
800mg	31	62	94	125	156	187	219	250
900mg	28	56	83	111	139	167	194	222
1000mg	25	50	75	100	125	150	175	200
1100mg	23	45	68	90	114	136	159	182

Subsequent Infusions: *** Patients who tolerated their first infusion at the standard recommended rate only ***
Give 20% of dose (i.e. 100ml) over 30 minutes, then the remaining 80% (i.e. 400ml) over 1 hour, to give a total infusion time of 90 minutes.

Reason for Update: ritux split dosing info added	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 3	Date: 22.8.16
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Prepared by: S Taylor	Checked by: C Tucker

Monitor patient's vital signs at baseline, then every 30 minutes until end of infusion.

*** Patients who did not tolerate their first infusion at the standard rate ***
Administer and monitor as per first infusion, or at a slower rate if required.

#If WBC ≥ 25 x 10^9/l, there is an increased risk of severe cytokine release syndrome with rituximab administration. Options include omitting the rituximab for this cycle, or splitting rituximab dosing over two days, as follows:

Day 1: **rituximab 50mg/m^2** in 50ml sodium chloride 0.9% IV infusion at 50mg/hr fixed rate throughout.

Day 2: **rituximab 325mg/m^2** in 250-500ml sodium chloride 0.9% IV infusion, start at 50mg/hr, escalate in 50mg/hr increments every 30 mins to max 400mg/hr.

Full resuscitation equipment must be available, with immediate access to clinical staff trained in resuscitation for the first hour of the first rituximab infusion.

If reactions occur at any time, stop the infusion. If symptoms improve, restart at half the previous infusion rate, and escalate as tolerated.

Main Toxicities: severe cytokine release syndrome – usually occurs within 1–2 hours of the first rituximab infusion (see Comments) and consists of fever, headache, rigors, flushing, nausea, rash, URTI symptoms;
transient hypotension and bronchospasm are usually infusion rate related, manage as above;
tumour lysis syndrome (ensure pre-medicated with allopurinol and good hydration);
myelosuppression; mucositis; ovarian failure; infertility

Anti - emetics: mildly emetogenic

Extravasation: rituximab is a non-vesicant

Regular Investigations:		
	FBC	Day 1
	LFTs	Day 1
	U&Es	Day 1
	LDH	every other cycle

Dose Modifications

Haematological Toxicity:

Cycle 1:
For any low initial counts thought to be disease-related, proceed with full dose treatment.

Subsequent Cycles:
Treatment should be deferred if neutrophil count is < 1.0 x 10^9/L and/or if platelet count is < 100 x 10^9/L, unless secondary to bone marrow infiltration.
Consider reducing the number of days of chlorambucil treatment per cycle if significant thrombocytopenia or neutropenia occurs, that is thought to be due to the treatment rather than the disease.

Renal Impairment: Patients with impaired renal function may be more prone to myelosuppression with chlorambucil.

Hepatic Impairment: Dose reduction of chlorambucil is only recommended with gross hepatic dysfunction, with dose adjustment according to response.

Patient Information: Macmillan leaflets for Rituximab and Chlorambucil

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