

Non-Hodgkin lymphoma R-CHOP14 (rituximab CYCLOPHOSPHamide DOXOrubicin vinCRISTine prednisolone)

ID: 71 v.8 Endorsed Essential Medicine List

Patients with lymphoma should be considered for inclusion into clinical trials. Link to [ALLG website](#), [ANZCTR website](#) and [Lymphoma Australia website](#).

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the [eviQ Estimated Glomerular Filtration Rate \(eGFR\) calculator](#).

International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADIKD)

2022

[Click here](#)



Related pages:

- [Non-Hodgkin lymphoma R-CHOP21 \(rituximab CYCLOPHOSPHamide DOXOrubicin vinCRISTine prednisolone\)](#)

Treatment schedule - Overview

Cycle 1 to 6

Drug	Dose	Route	Day
Prednisolone	100 mg ONCE a day	PO	1 to 5
Rituximab	375 mg/m ²	IV infusion	1
DOXOrubicin	50 mg/m ²	IV	1
vinCRISTine	1.4 mg/m ² (Cap dose at 2 mg)	IV infusion	1
CYCLOPHOSPHamide	750 mg/m ²	IV infusion	1
Pegfilgrastim	6 mg	Subcut	4

Frequency: 14 days

Cycles: 6 +/- 2 cycles of rituximab only.

Notes:

- Rituximab product information states that rituximab should be administered before chemotherapy. In clinical trials, this was done to distinguish and treat adverse events associated with rituximab. However, rituximab is frequently given concurrently with chemotherapy, and at least in the case of R-CHOP, there appears to be various studies supporting the administration of rituximab before, concurrently and after CHOP.
- Consideration should be given to administering the first dose of rituximab on the day prior to CHOP in patients who have very bulky disease and are at risk of reaction/tumour lysis.
- A **prephase treatment** of prednisolone 100 mg PO daily for seven days prior to cycle 1 was administered in the RICOVER-60 trial¹ to improve the performance status of their patients (aged 61 to 80 years) and reduce the side effects of the first cycle of chemotherapy. It is the consensus opinion of the Haematology Reference Committee to consider the use of prephase prednisolone 100 mg PO daily for 5 to 7 days prior to cycle 1.

Drug status: Pegfilgrastim: (PBS authority)

All other drugs in this protocol are on the [PBS general schedule](#)

Prednisolone is available as **25 mg, 5 mg and 1 mg** tablets

Cost: ~ \$690 per cycle

Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. [Select here for recommended doses of alternative antiemetics.](#)*

Cycle 1 to 6

Day 1		
Paracetamol	1,000 mg (PO)	60 minutes before treatment
Loratadine	10 mg (PO)	60 minutes before treatment
Prednisolone	100 mg (PO)	ONCE a day on days 1 to 5.* Take in the morning with food.
Rituximab	375 mg/m ² (IV infusion)	in 500 mL sodium chloride 0.9% as per graded administration rate
Palonosetron	0.25 mg (IV bolus)	30 minutes before chemotherapy
DOXOrubicin	50 mg/m ² (IV)	over 5 to 15 minutes
vinCRISTine	1.4 mg/m ² (IV infusion) (Cap dose at 2 mg)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes via minibag
CYCLOPHOSPHamide	750 mg/m ² (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Day 2 and 3		
Prednisolone	100 mg (PO)	ONCE a day on days 1 to 5.* Take in the morning with food.
Day 4		
Prednisolone	100 mg (PO)	ONCE a day on days 1 to 5.* Take in the morning with food.
Pegfilgrastim	6 mg (Subcut)	inject subcutaneously on day 4
Day 5		
Prednisolone	100 mg (PO)	ONCE a day on days 1 to 5.* Take in the morning with food.

* Dose for day 1 should be taken 60 minutes before rituximab infusion.

Frequency: 14 days

Cycles: 6 +/- 2 cycles of rituximab only.

Indications and patient population

- CD20 positive B-cell lymphomas

Clinical information

Safety alert vincristine administration	For safe administration of vincristine refer to the safety alert issued by the Australian Commission on Safety and Quality in Health Care
Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with rituximab. Read more about Hypersensitivity reaction
Premedication	The product information states that premedication is required for this treatment. Note: a corticosteroid is included as part of this treatment and therefore additional corticosteroid may not be required as premedication. Please refer to the treatment schedule for the suggested premedication regimen. This may be substituted to reflect institutional policy.
Emetogenicity MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. As a steroid has been included as part of this protocol, additional antiemetic steroids are not required. For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist may be available on the PBS in combination with a 5HT ₃ antagonist and steroid. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cumulative lifetime dose of anthracyclines	Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone). Criteria for reducing the total anthracycline cumulative lifetime dose include: <ul style="list-style-type: none"> • patient is elderly • prior mediastinal radiation • hypertensive cardiomegaly • concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine). Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation. Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) > 50%) and low risk patients require LVEF monitoring when greater than 70% of the anthracycline threshold is reached or if the patient displays symptoms of cardiac impairment. Post-treatment cardiac monitoring is recommended for patients who have received high levels of total cumulative doses of anthracyclines at the clinician's discretion. Read more about cardiac toxicity associated with anthracyclines
Rituximab rapid infusion	This regimen is not in line with the product monograph, however published literature indicates that it can be completed safely. Read more about the rapid infusion of rituximab

Progressive multifocal leukoencephalopathy	<p>Use of monoclonal antibodies may be associated with an increased risk of progressive multifocal leukoencephalopathy (PML), a rare but potentially fatal opportunistic viral infection of the brain. Patients must be monitored for any new or worsening neurological symptoms.</p> <p>Read more about progressive multifocal leukoencephalopathy and the Therapeutic Goods Administration Medicines Safety update on progressive multifocal leukoencephalopathy from the Australian Government, Department of Health.</p>
Peripheral neuropathy	<p>Assess prior to each treatment. Based on clinical findings, temporary omission, dose reduction or cessation of the vinca alkaloid may be indicated; review by medical officer before commencing treatment.</p> <p>Read more about peripheral neuropathy</p> <p>Link to chemotherapy-induced peripheral neuropathy screening tool</p>
Constipation	<p>Prescribe prophylactic laxatives to prevent constipation related to the use of vinca alkaloids.</p>
Corticosteroids	<p>Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate.</p> <p>Read more about acute short term effects from corticosteroids</p>
Central nervous system (CNS) prophylaxis	<p>Consider CNS relapse assessment in patients with high grade lymphoma.</p> <p>Read more about CNS prophylaxis in diffuse large cell lymphoma</p>
Tumour lysis risk	<p>Patients are at high risk of developing tumour lysis syndrome, prophylaxis is recommended.</p> <p>Read more about the prevention and management of tumour lysis syndrome.</p>
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	<p>PJP prophylaxis is recommended e.g. trimethoprim/sulfamethoxazole 160/800 mg PO one tablet twice daily, twice weekly (e.g. on Mondays and Thursdays) OR one tablet three times weekly (e.g. on Mondays, Wednesdays and Fridays).</p> <p>Read more about prophylaxis of pneumocystis jirovecii (carinii) in cancer patients</p>
Antiviral prophylaxis	<p>Read more about antiviral prophylaxis drugs and doses</p>
Antifungal prophylaxis	<p>Read more about antifungal prophylaxis drugs and doses.</p>
Growth factor support	<p>G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk.</p> <p>Access the PBS website</p>
Biosimilar drug	<p>Read more about biosimilar drugs on the Biosimilar Awareness Initiative page</p>
Blood tests	<p>FBC, EUC, eGFR, LFTs, LDH and BSL baseline then as clinically indicated.</p>
Hepatitis B screening and prophylaxis	<p>Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy.</p> <p>Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy</p>
Vaccinations	<p>Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.</p> <p>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook.</p> <p>Read more about COVID-19 vaccines and cancer.</p>
Fertility, pregnancy and lactation	<p>Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients.</p> <p>Read more about the effect of cancer treatment on fertility</p>

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences. Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus. The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on [Common Terminology Criteria for Adverse Events \(CTCAE\)](#) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer.

The dose recommendations in kidney dysfunction (i.e. renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.

[International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction \(ADDIKD\)](#).

Note: All dose reductions are calculated as a percentage of the starting dose

Haematological toxicity

Dose modification is not generally indicated. Discuss with Haematologist. Consider lengthening time between cycles to 21 days if there is prolonged myelosuppression.

Renal impairment

Creatinine clearance (mL/min)

10 to 50	No reduction
less than 10	Reduce cyclophosphamide by 25%

Hepatic impairment

Bilirubin (micromol/L)

20 to 50	Reduce doxorubicin by 50%
51 to 85	Reduce doxorubicin by 75%
greater than 85	Omit doxorubicin

Note: Consider reducing vincristine dose for hepatic impairment.

Peripheral neuropathy

Grade 2 or greater	Consider omitting vincristine
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Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. [References & Disclaimer](#)

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- [MIMS - interactions tab](#) (includes link to a CYP-450 table) (login required)
- [Australian Medicines Handbook \(AMH\) – interactions tab](#) (login required)
- [Micromedex Drug Interactions](#) (login required)

- [Cancer Drug Interactions](#)
- [Cytochrome P450 Drug Interactions](#)

Cyclophosphamide		
	Interaction	Clinical management
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Increased toxicity of cyclophosphamide possible due to increased conversion to active (and inactive) metabolites	Avoid combination or monitor for cyclophosphamide toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Reduced efficacy of cyclophosphamide possible due to decreased conversion to active (and inactive) metabolites	Avoid combination or monitor for decreased clinical response to cyclophosphamide
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Amiodarone	Possible additive pulmonary toxicity with high-dose cyclophosphamide (i.e. doses used prior to stem cell transplant; 60 mg/kg daily or 120 to 270 mg/kg over a few days)	Avoid combination or monitor closely for pulmonary toxicity
Allopurinol, hydrochlorothiazide, indapamide	Delayed effect. Increased risk of bone marrow depression; probably due to reduced clearance of active metabolites of cyclophosphamide	Avoid combination, consider alternative antihypertensive therapy or monitor for myelosuppression
Ciclosporin	Reduced efficacy of ciclosporin due to reduced serum concentration	Monitor ciclosporin levels; adjust dosage as appropriate; monitor response to ciclosporin
Suxamethonium	Prolonged apnoea due to marked and persistent inhibition of cholinesterase by cyclophosphamide	Alert the anaesthetist if a patient has been treated with cyclophosphamide within ten days of planned general anaesthesia

Doxorubicin		
	Interaction	Clinical management
Cardiotoxic drugs (eg. bevacizumab, calcium channel blockers, propranolol, trastuzumab etc.)	Increased risk of doxorubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity
Cyclophosphamide	Sensitises the heart to the cardiotoxic effects of doxorubicin; also, doxorubicin may exacerbate cyclophosphamide induced cystitis	Monitor closely for cardiotoxicity and ensure adequate prophylaxis for haemorrhagic cystitis when combination is used
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs etc.)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Glucosamine	Reduced efficacy of doxorubicin (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II <i>in vitro</i>)	The clinical effect of glucosamine taken orally is unknown. Avoid combination or monitor for decreased clinical response to doxorubicin
CYP2D6 inhibitors (e.g. SSRIs (esp. paroxetine), perhexiline, cinacalcet, doxepin, flecainide, quinine, terbinafine, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of doxorubicin possible due to increased clearance	Monitor for decreased clinical response to doxorubicin

Prednisolone		
	Interaction	Clinical management
Antidiabetic agents (e.g. insulin, glibenclamide, glicazide, metformin, pioglitazone, etc)	The efficacy of antidiabetic agents may be decreased	Use with caution and monitor blood glucose
Azole antifungals (e.g. fluconazole, itraconazole, ketoconazole, posaconazole)	Increased toxicity of prednisolone possible due to reduced clearance	Avoid combination or monitor for prednisolone toxicity
Oestrogens (e.g. oral contraceptives)	Increased toxicity of prednisolone possible due to reduced clearance	Avoid combination or monitor for prednisolone toxicity. Dose reduction of prednisolone may be required
Ritonavir	Increased toxicity of prednisolone possible due to reduced clearance	Avoid combination or monitor for prednisolone toxicity

Rituximab		
	Interaction	Clinical management
Antihypertensives	Additive hypotensive effect	Consider withholding antihypertensive medications 12 hours prior to the rituximab infusion
Immunosuppressants (eg. abatacept and baricitinib etc.)	Increased risk of infection	Concurrent use not recommended. If an immunosuppressant must be used, monitor closely for signs of infection

Vincristine		
	Interaction	Clinical management
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of vincristine possible due to reduced clearance	Monitor for vincristine toxicity (esp. neurotoxicity, paralytic ileus)
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of vincristine possible due to increased clearance	Monitor for decreased clinical response to vincristine
Mitomycin	Acute shortness of breath and severe bronchospasm has occurred following use of vincristine in patients who had received mitomycin simultaneously or within 2 weeks	Use combination with caution
Ototoxic drugs (e.g. cisplatin, aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity	Avoid combination or perform regular audiometric testing

General		
	Interaction	Clinical management
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual

Day 1

Approximate treatment time: 8 hours (initial); 4 to 6 hours (subsequent)

[Safe handling and waste management](#)

[Safe administration](#)

[General patient assessment](#) prior to each day of treatment.

[Peripheral neuropathy assessment tool](#)

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before commencing treatment.

- weigh patient each visit
- dipstick urinalysis each visit

Prime IV line(s).

Insert IV cannula or access [TIVAD](#) or [CVAD](#).

Hydration if prescribed

⌚ Treatment - Time out

Prednisolone

- administer orally ONCE a day on **days 1 to 5**
- to be taken in the morning with or immediately after food

Note: if a dose is forgotten or vomited, contact treating team.

Rituximab

Prior to administration:

- check baseline observations
- check for previous adverse events during previous infusions
- verify premedication has been taken. If not, administer 30 to 60 minutes prior to rituximab administration:
 - paracetamol 1000 mg orally AND
 - loratadine 10 mg orally (or similar antihistamine)
 - a steroid may also be included as a premed according to local guidelines: prednisolone 100 mg orally (part of this protocol) or hydrocortisone 100 mg IV

Initial infusion:

- commence rituximab infusion at 50 mg/hr for 30 minutes
- repeat observations prior to each rate increase
- increase rate by 50 mg/hr every 30 minutes, up to a maximum of 400 mg/hr if observations are stable
- flush with ~ 50 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have completely resolved, recommence the infusion at half the rate prior to the reaction
- for severe reactions stop infusion and manage as per emergency

Transient hypotension may occur. Consider withholding antihypertensive medication for 12 hours before and during infusion.

Subsequent infusions:

If an adverse event was experienced with initial infusion recommence infusion at the same rate as initial infusion

If no adverse event experienced with initial infusion:

- commence rituximab infusion at 100 mg/hr

- repeat observations prior to each rate increase
- increase rate by 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr if observations are stable
- flush with ~ 50 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at half the rate prior to the reaction
- for severe reactions stop infusion and manage as per emergency

Read more about rapid infusion rituximab

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

🕒 Chemotherapy - Time out

Doxorubicin

Administer doxorubicin (vesicant):

- over 5 to 15 minutes
 - via a minibag **OR**
 - by IV bolus via a side port of a freely flowing IV infusion
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%
- potential for flare reaction during administration of doxorubicin (facial flushing and red streaking along the vein) stop infusion and exclude extravasation before continuing at a slower rate of infusion.

Although rare, cardiac arrhythmias may occur during or immediately after doxorubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.

Vincristine

Administer vincristine (vesicant)

- via a minibag over 5 to 10 minutes
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%.

Cyclophosphamide

Administer cyclophosphamide:

- via IV infusion over 30 to 60 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- rapid infusion can cause dizziness, rhinitis, nausea and perioral numbness. If symptoms develop, slow infusion rate.

Remove IV cannula and/or deaccess [TIVAD](#) or [CVAD](#).

Continue [safe handling](#) precautions until 7 days after completion of drug(s)

Day 4

[General patient assessment](#) prior to each day of treatment.

Prednisolone

- administer orally ONCE a day on **days 1 to 5**
- to be taken in the morning with or immediately after food

Note: if a dose is forgotten or vomited, contact treating team.

Pegfilgrastim

- administer subcutaneously on day 4; or ensure arrangements have been made for administration

Discharge information

Prednisolone tablets

- Prednisolone tablets with written instructions on how to take them.

Antiemetics

- Antiemetics as prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antifungals, antivirals.

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)

Bone pain	Bone pain, usually in the lower back or pelvis, associated with G-CSF.
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Flare reaction	Anthracycline flare reaction is caused by a localised allergic reaction. It is characterised by erythematous vein streaking, urticaria and pruritus which may occur during drug administration and is often associated with too rapid an infusion. Extravasation must be ruled out if flare occurs.
Flu-like symptoms	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
Taste and smell alteration	Read more about taste and smell changes

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Constipation	
Fatigue	Read more about fatigue
Haemorrhagic cystitis	An inflammatory process, characterised by diffuse bladder mucosal inflammation resulting in haemorrhage. Patients are at risk following blood and marrow transplant (BMT) or treatment with cyclophosphamide, ifosfamide and/or radiation therapy. Read more about haemorrhagic cystitis
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Progressive multifocal leukoencephalopathy (PML)	A rare opportunistic viral infection of the brain, usually leading to death or severe disability, can occur with monoclonal antibodies (e.g. rituximab, obinutuzumab, ofatumumab, brentuximab vedotin) and other targeted therapies (e.g. ibrutinib, ruxolitinib, idelalisib). Onset may occur up to months after the final dose. Read more about progressive multifocal leukoencephalopathy (PML)
Delayed (onset months to years)	
Cardiotoxicity	Anthracyclines are the most frequently implicated anti-cancer drugs associated with cardiotoxicity, which typically manifests as a reduction in left ventricular ejection fraction (LVEF), cardiomyopathy, or symptomatic CHF. Anthracycline induced cardiotoxicity has been categorised into acute, early-onset chronic progressive and late-onset chronic progressive and is usually not reversible. The risk of clinical cardiotoxicity increases with a number of risk factors including higher total cumulative doses. Read more about cardiac toxicity associated with anthracyclines
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

The role of rituximab

Rituximab is a key component to the treatment of diffuse large B-cell lymphoma (DLBCL), with numerous trials showing a clear improvement in survival when rituximab is added to standard chemotherapy.

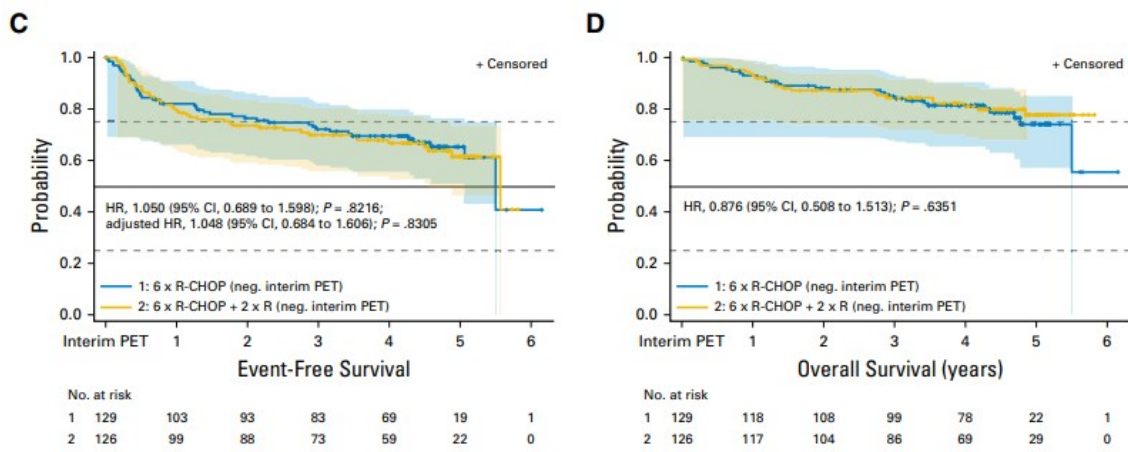
Trial Name	Study Group Characteristics	Treatment	Outcome
LNH 98.5 ²	<ul style="list-style-type: none"> DLBCL 60-80 years of age n = 399 	<ul style="list-style-type: none"> CHOP21 x 8 or R-CHOP21 x 8 	10 year-event-free survival (EFS) 35.1% vs 19.8%, P<0.0001, median overall survival (OS) 8.4 years vs 3.5 years, P<0.0001.
RICOVER-60 ³	<ul style="list-style-type: none"> DLBCL 61-80 years of age n = 1222 	<ul style="list-style-type: none"> CHOP14 x 6 or 8 or R-CHOP14 x 6 or 8 	Six cycles of CHOP14 had the worst outcome. Progression-free survival (PFS) improved after 6 cycles of R-CHOP14 (relative risk (RR) 0.50, P<0.0001), and 8 cycles of R-CHOP14 (RR 0.59, P=0.0001). OS improved only with 6 cycles of R-CHOP14 (RR 0.63, P=0.0031). Of the four regimens assessed in this study, 6 cycles of R-CHOP14 was the preferred treatment for elderly patients.
ECOG 4494/CALGB 9793 ⁴	<ul style="list-style-type: none"> DLBCL > 60 years of age n = 632 	<ul style="list-style-type: none"> CHOP21 (x 6 or 8) +/- Maintenance rituximab (MR) or R-CHOP21 (x 6 or 8) +/- MR 	Two-year failure-free survival (FFS) rates from the second random assignment were 77%, 79%, 74%, and 45% for R-CHOP, R-CHOP+MR, CHOP+MR, and CHOP, respectively. Rituximab administered as induction or maintenance with CHOP significantly prolonged FFS; however, after R-CHOP, no benefit was provided by maintenance rituximab.
MinT ⁵	<ul style="list-style-type: none"> DLBCL 18-60 years of age n = 842 	<ul style="list-style-type: none"> CHOP21 x 6 or R-CHOP21 x 6 	Compared with chemotherapy alone, rituximab plus chemotherapy improved the complete response (CR) rate (68% vs 86%, respectively; P<0.0001), increased the 3-year EFS rate (59% vs 79%, respectively; P<0.0001), and improved the 3-year OS rate (84% vs 93%, respectively; P=0.0001).

The number of cycles

No randomised trial has specifically addressed the issue of the number of R-CHOP21 cycles, but a prospective, randomised trial has directly addressed this question with CHOP14. The RICOVER-60 trial compared six and eight cycles of CHOP14, each with and without rituximab. It included 1222 patients between the ages of 61 to 80 years with aggressive non-Hodgkin lymphoma (80% DLBCL).¹ There was no difference in the 3 year OS in the six versus eight cycles of R-CHOP14 (78 vs 73% respectively). A randomised trial of 1080 patients with DLBCL treated with 8 cycles of R-CHOP21 or 6 cycles of R-CHOP14 + 2 further doses of rituximab showed that at 46 months of follow up there was no significant difference in OS or PFS.⁵ Another randomised trial of 600 older adults with DLBCL compared 8 cycles of R-CHOP14 with 8 cycles of R-CHOP21 showed similar response rate (RR), EFS and OS in both groups.⁶

Number of rituximab doses

The PETAL study demonstrated that two additional rituximab doses failed to improve outcomes in CD 20 positive lymphoma's who achieved a negative interim PET scan (cycle 2).⁷



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R-CHOP21 versus R-CHOP14

Three large phase III studies have demonstrated that R-CHOP14 is not more effective than R-CHOP21 in both DLBCL and indolent B-cell lymphoma.^{5, 6, 8} R-CHOP14 (mandatory G-CSF prophylaxis) appears to have a lower frequency of neutropenia and infection compared with R-CHOP21 (discretionary G-CSF prophylaxis).^{5, 9}

No role for maintenance rituximab in DLBCL

While there is a benefit with maintenance rituximab after R-CHOP in follicular lymphoma (FL), this has not been proven in DLBCL. The role of maintenance rituximab (MR) was assessed in randomised trial of 632 older adults. The trial compared R-CHOP to CHOP. The 415 patients who achieved a CR were randomised to either maintenance rituximab or observation. MR did not improve failure-free survival rates.³

Older adults

In elderly patients, unfit for standard treatment with R-CHOP consideration should be given to dose reduced [R-mini-CHOP](#).

Follicular or Indolent lymphoma

The role of rituximab

Rituximab is a key component to the treatment of FL with numerous trials showing a clear improvement in survival when rituximab is added to standard chemotherapy. These trials have shown improved RR, time to progression, PFS and OS.^{8, 10, 11, 12, 13} A meta-analysis of seven randomised trials including 1943 patients with previously untreated or previously treated indolent non-Hodgkin lymphoma showed that the addition of rituximab to chemotherapy resulted in a higher overall response rate (ORR) (relative risk of obtaining a tumour response 1.21; 95% CI 1.16-1.27), improved disease control (hazard ratio (HR) of developing a disease-associated event 0.62; 95% CI 0.55-0.71) and better OS (HR for mortality 0.65; 95% CI 0.54-0.78).^{14, 15}

R-CHOP21 versus R-CHOP14

The phase III JCOG 0203 trial⁹ randomised 300 patients aged 20-69 years old, with untreated stages III to IV indolent B-cell lymphoma, to receive 6 cycles of R-CHOP21 or R-CHOP14. G-CSF was given to all patients with R-CHOP14 and to those with R-CHOP21. Maintenance rituximab was not allowed. The primary endpoint was PFS, with secondary endpoints of OS and toxicity. At 6 years, there was no significant difference in PFS or OS between arms (R-CHOP21 vs R-CHOP14 PFS: 41% vs 43% respectively, $P=0.30$; OS: 87% v 88% respectively, $P=0.65$). Although grade 4 neutropenia and grade 3 infections were more frequent in the R-CHOP21 group, R-CHOP was feasible in both arms.

The role of maintenance rituximab

The role of maintenance rituximab in FL has been clearly demonstrated in a number of trials. Refer to [Non-Hodgkin Lymphoma Rituximab Maintenance](#).

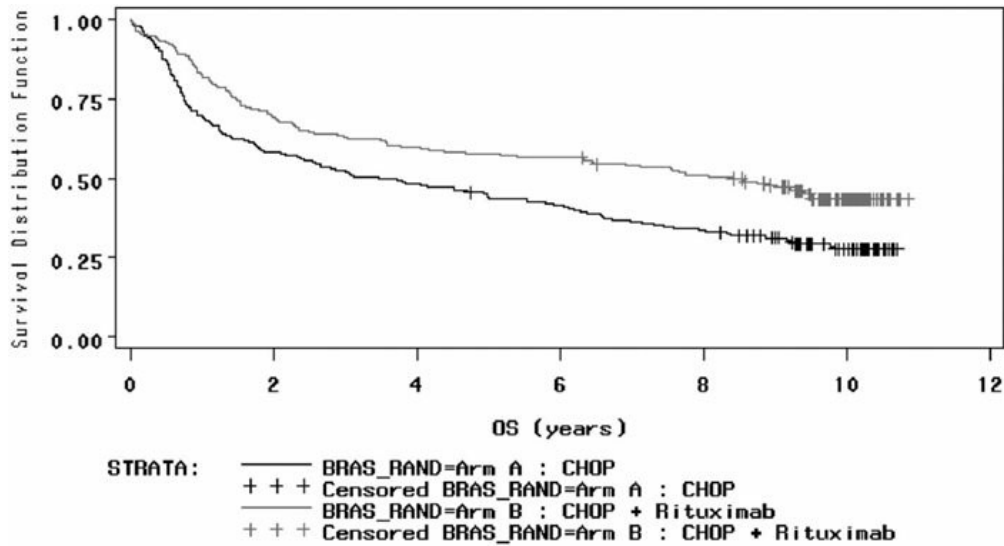
Efficacy

R-CHOP versus CHOP

Diffuse Large B-Cell Lymphoma:

Overall survival (OS) was investigated in elderly DLBCL patients (60-80 years old) treated with CHOP and R-CHOP in the LNH 98.5 trial.¹⁶ Median OS was 3.5 years (95% CI: 2.2-5.5) in the CHOP arm and 8.4 years (95% CI: 5.4-not reached) in the R-CHOP arm

(P<0.0001).



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In the MInT trial⁴ of young DLBCL patients (18-60 years old), compared with CHOP-like chemotherapy alone, rituximab plus CHOP-like therapy increased the 3-year event-free survival rate (59% vs 79%, respectively; P<0.0001), and improved the 3-year OS rate (84% vs 93%, respectively; P=0.0001).

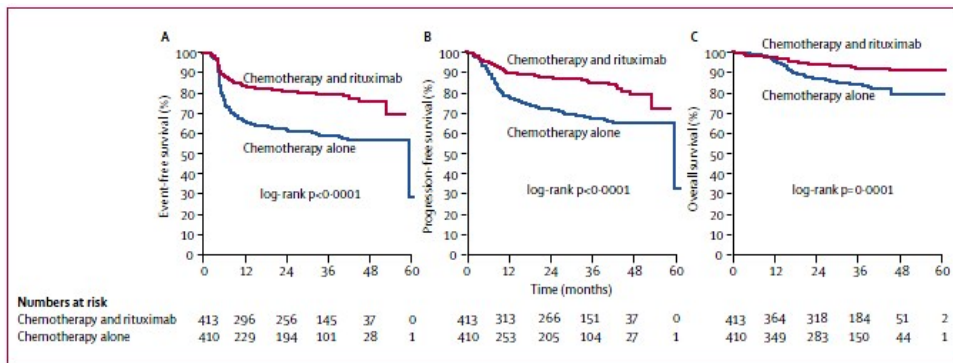


Figure 2: (A) Event-free survival, (B) progression-free survival, and (C) overall survival of 823 patients assigned to CHOP-like chemotherapy alone (n=410) or to CHOP-like chemotherapy and rituximab (n=413)

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Follicular Lymphoma:

The GLSG study of R-CHOP21 versus CHOP21 in untreated, advanced-stage FL⁸ demonstrated superior OS with R-CHOP at 3 years follow up (6 vs 17 deaths, respectively, P=0.016).

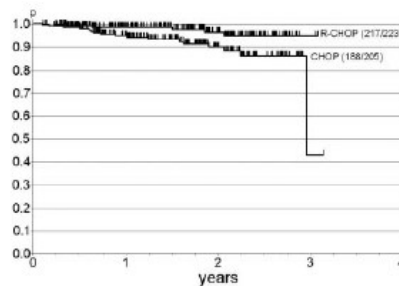


Figure 3. OS after start of therapy for CHOP and R-CHOP. Median OS has not been reached in either group. After 3 years, 6 patients in the R-CHOP arm have died compared with 17 patients in the CHOP arm (P = .016).

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R-CHOP14 versus R-CHOP21

Diffuse Large B-Cell Lymphoma:

The UK Clinical Research Network trial of R-CHOP14 versus R-CHOP21 in untreated bulky stage IA to stage IV DLBCL⁵ found no significant difference between groups in 2-year OS (82.7% vs 80.8; HR 0.90; P=0.3763) or PFS (75.4% vs 74.8%; HR 0.94;

P=0.5907).

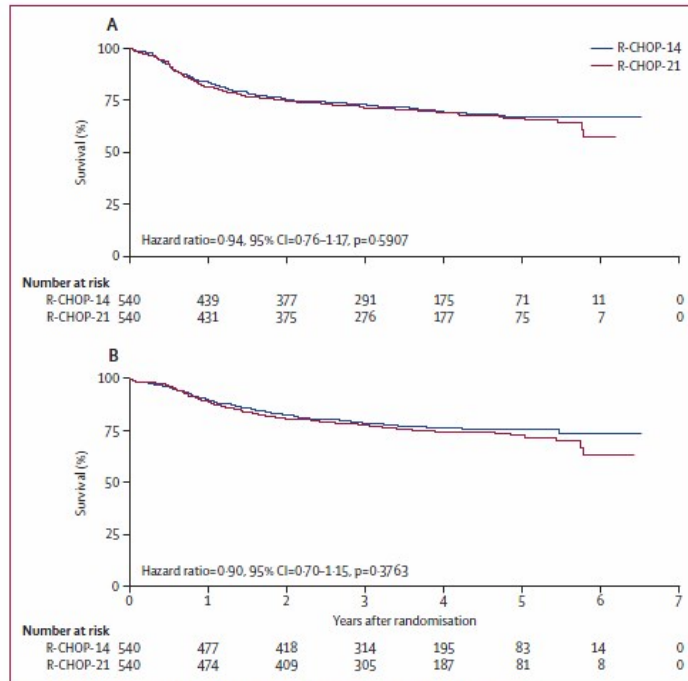


Figure 2: Progression-free survival (A) and overall survival (B) according to treatment
 R-CHOP-14=cycles of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone every 14 days.
 R-CHOP-21=cycles of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone every 21 days.

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Follicular Lymphoma:

The JCOG 0203 Trial⁹ of R-CHOP21 versus R-CHOP14 in untreated stages III to IV indolent B-cell lymphoma demonstrated no significant difference in PFS (41% vs 43% respectively, P=0.30) or OS (87% vs 88% respectively, P=0.65) at 6 years.

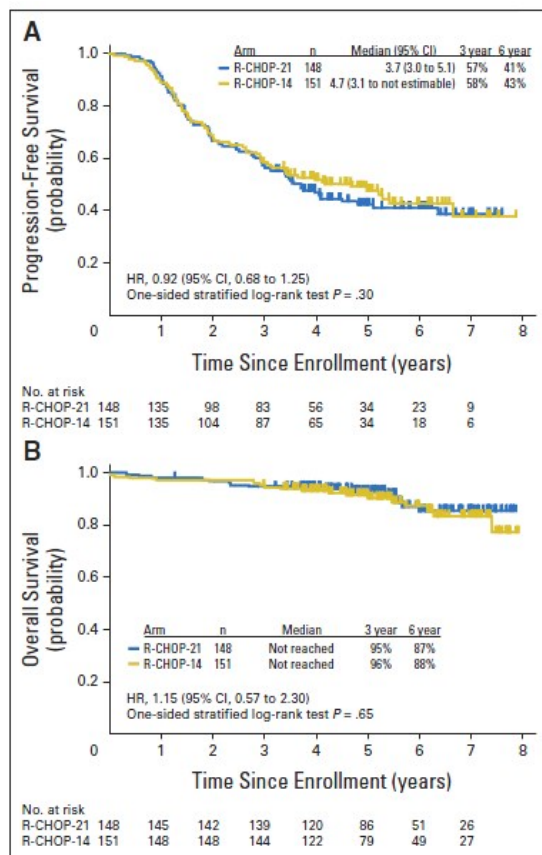


Fig 2. (A) Progression-free survival and (B) overall survival by treatment for patients with previously untreated, advanced-stage indolent B-cell non-Hodgkin's lymphoma. The median follow-up time was 5.2 years. HR, hazard ratio; R-CHOP-14, rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) administered every 2 weeks with granulocyte colony-stimulating factor; R-CHOP-21, R-CHOP administered every 3 weeks.

Toxicity

R-CHOP versus CHOP

In the RICOVER-60 trial,¹ there was a greater number of patients who experienced more toxicities in the 8-cycle treatment arms when compared to the 6-cycle treatment arms. There were 92 treatment-related deaths - 50 in the 8 cycle treatment arms and 42 in the 6 cycle regimens. 62 second malignancies were reported after a median follow up of 34.5 months. Toxicities are summarised in the table below.

	6xCHOP-14 (n=307)	8xCHOP-14 (n=305)	6xR-CHOP-14 (n=306)	8xR-CHOP-14 (n=304)	p
Leucocytopenia*	93/193 (48)	93/195 (48)	103/197 (52)	108/218 (50)	0.8017
Thrombocytopenia	18/187 (10)	34/198 (17)	23/192 (12)	33/212 (16)	0.1242
Anaemia	46/284 (16)	66/287 (23)	45/283 (16)	77/283 (27)	0.0013
Arrhythmia	13/280 (5)	8/281 (3)	11/281 (4)	18/287 (6)	0.2437
Cardiac function	5/277 (2)	5/281 (2)	7/279 (3)	8/284 (3)	0.7917
Neuropathy	20/279 (7)	30/284 (11)	20/284 (7)	24/290 (8)	0.3946
Mucositis	8/281 (3)	18/283 (6)	15/282 (5)	25/288 (9)	0.0278
Infection	83/284 (29)	88/286 (31)	79/287 (28)	101/291 (35)	0.2784
Red-blood-cell transfusions	116/286 (41)	148/291 (51)	134/288 (47)	150/291 (52)	0.0312
Platelet transfusions	7/285 (2)	13/290 (4)	9/286 (3)	11/289 (4)	0.5840
Antibiotics—interventional	131/288 (45)	161/291 (55)	151/285 (53)	180/289 (62)	0.0008

Data are numbers of patients with toxicity or therapeutic intervention/number of patients with information and percentage of patients. p values are over all treatment regimens. *Common Toxicity Criteria grade 4 only.

Table 4: Grade 3 and 4 Common Toxicity Criteria toxicities and therapeutic interventions

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R-CHOP14 versus R-CHOP21

In the UK Clinical Research Network trial of R-CHOP14 versus R-CHOP21 in DLBCL, rates of grade 3 or 4 neutropenia and febrile neutropenia were higher in the R-CHOP21 group (with no mandatory G-CSF), whereas grade 3 or 4 thrombocytopenia was higher with R-CHOP14.⁵

	R-CHOP-21 (n=534)	R-CHOP-14 (n=534)	p value*
All toxicity	380 (71%)	290 (54%)	..
Neutropenia	318 (60%)	167 (31%)	<0.0001
Febrile neutropenia	58 (11%)	28 (5%)	0.0007
Thrombocytopenia	28 (5%)	50 (9%)	0.010
Infection	125 (23%)	96 (18%)	..
Mucositis	10 (2%)	14 (3%)	..
Cardiac toxicity	2 (<1%)	11 (2%)	..
Nausea	20 (4%)	22 (4%)	..
Vomiting	17 (3%)	19 (4%)	..
Neurological toxicity	38 (7%)	53 (10%)	..

Data are number (%), unless otherwise indicated. R-CHOP-21=cycles of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone every 21 days. R-CHOP-14=cycles of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone every 14 days. *Only p values judged to be significant in multiple testing are provided.

Table 4: Grade 3 or 4 adverse events

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History

Version 8

Date	Summary of changes
05/06/2023	Subcutaneous rituximab information removed from the following sections – treatment schedule, clinical information, administration, patient information. Increased to version 8.
07/09/2023	Updated with the following changes:

- Antifungal prophylaxis added to Clinical information for consistency across protocols. Block contains link to ID 1604 Antifungal prophylaxis in immunocompromised adults.
- Central venous access devices (CVADs) (optional) information added to "Other information about your treatment" category of Patient information sheet.

Version 7

Date	Summary of changes
09/03/2020	Biosimilar rituximab added to clinical information. Version number changed to V.7.
16/06/2020	Evidence section updated.
22/12/2020	Related pages updated - ID 1385 Non-Hodgkin lymphoma rituximab maintenance replaced with ID 3909 Non-Hodgkin lymphoma rituximab maintenance subcutaneous
25/01/2022	Reviewed by Haematology Reference Committee, next review due in 4 years. <ul style="list-style-type: none"> • Drug status updated: rituximab SC is TGA registered but no longer PBS listed. • Note added to dose modifications. • Pulmonary toxicity added to side effects.

Version 6

Date	Summary of changes
13/09/2019	Reviewed by Haematology Reference Committee, next review due in 2 years. <ul style="list-style-type: none"> • Updated dose modifications • Rationalised and updated evidence section • Version number changed to V.6.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.

Version 5

Date	Summary of changes
08/09/2009	Reviewed and transferred to eviQ.
16/03/2011	New format to allow for export of protocol information. Protocol version number changed to V.2. Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link. Rituximab and antihypertensives interaction reworded to 'consider withholding.....'.
19/08/2011	Full protocol review at Haematology Reference Committee meeting: <ul style="list-style-type: none"> - indication updated to '<i>treatment of CD20 positive B-cell lymphomas</i>'; grading removed as used more widely in low grade setting - statement included in Notes section regarding prephase treatment - PCP prophylaxis recommendations included - vincristine dose modifications to amended to '<i>consider omitting vincristine with grade 2 neuropathy</i>' - addition of information on PML associated with rituximab (preclinical information and side effect) - evidence section updated and rewritten. CHOP14 and CHOP 21 now have the same evidence sections
07/12/2011	Updated PHC view.
04/07/2012	Palonosetron added as default 5HT3 antagonist antiemetic in treatment schedule.
11/10/2013	Protocol reviewed at Haematology Reference Committee meeting: <ul style="list-style-type: none"> - pegfilgrastim administration day changed from day 2 to 4 as per recent evidence. - the number of cycles changed from 6-8 to "6 cycles followed by 2 cycles of rituximab alone" as per RICOVER60 trial. - removed "the decision to proceed to 8 cycles will be at the discretion of the clinician and will be based upon consideration of disease response and regimen-related toxicity" from notes section as it is no longer applicable. - evidence section updated and rewritten. RCHOP14 and RCHOP21 have the same evidence sections.

Date	Summary of changes
	- PHC view removed.
18/08/2014	Added link to ALLG, ANZCTR and Lymphoma Australia website with statement 'Patients with NHL should be considered for inclusion into clinical trials'.
11/09/2015	Protocol reviewed at Haematology Reference Committee meeting: - notes: point about the order of rituximab administration added; vincristine prephase removed - evidence section updated
20/07/2016	New evidence added. Review in 2 years.
31/05/2017	Transferred to new eviQ website. Version number change to V.4. Other changes include: <ul style="list-style-type: none"> diluent volume of vincristine changed from '50 to 100 mL' to '50 mL' as per Australian Injectable Handbook Sixth Edition.
12/03/2018	Added: <ul style="list-style-type: none"> Link to subcutaneous rituximab document underneath the treatment schedule. Clinical information block on subcutaneous rituximab Link to the subcutaneous rituximab document into administration section Injection-site reaction side effect Note about subcutaneous rituximab to the patient information Version number changed to V.5.

The information contained in this protocol is based on the highest level of available evidence and consensus of the eviQ reference committee regarding their views of currently accepted approaches to treatment. Any clinician (medical oncologist, haematologist, radiation oncologist, medical physicist, radiation therapist, pharmacist or nurse) seeking to apply or consult this protocol is expected to use independent clinical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use is subject to eviQ's disclaimer available at www.eviq.org.au

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<https://www.eviq.org.au/p/71>
23 Nov 2023

Patient information - Non-Hodgkin lymphoma (NHL) - R-CHOP14 (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone)

Patient's name:


Your treatment

The treatment schedule below explains how the drugs for this treatment are given.

R-CHOP14 (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone)			
This treatment cycle is repeated every 14 days. You will usually have 6 cycles of R-CHOP, followed by 2 cycles of rituximab alone. Your doctor will advise you of the number of treatments you will have.			
Day	Treatment	How it is given	How long it takes
1 to 5	Prednisolone (<i>pred-NIS-oh-lone</i>)	Take orally ONCE a day in the morning with food on days 1 to 5 only. If you forget to take your tablets or vomit your tablets, contact your treating team	
1	Rituximab (<i>ri-TUX-i-mab</i>)	By a drip into a vein	1st cycle: About 4 to 6 hours Cycles thereafter: About 3 to 4 hours
	Doxorubicin (<i>dox-oh-roo-bi-sin</i>)	By a drip into a vein	About 5 to 15 minutes
	Vincristine (<i>vin-KRIS-teen</i>)	By a drip into a vein	About 5 to 10 minutes
	Cyclophosphamide (<i>SYE-kloe-FOS-fa-mide</i>)	By a drip into a vein	About 1 hour
4	Granulocyte Colony Stimulating Factor (G-CSF)	By injection under the skin	About 5 minutes

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you become unwell.

	<p>IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:</p>	<p>Emergency contact details</p> <p>Ask your doctor or nurse from your treating team who to contact if you have a problem</p>
<ul style="list-style-type: none"> • a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms 	<p>Daytime:.....</p> <p>Night/weekend:.....</p> <p>Other instructions:.....</p> <p>.....</p>	

- you become unwell.

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

Blood tests and monitoring

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

Treatment with cyclophosphamide

You should drink at least 8 to 10 glasses of fluid (unless you are fluid restricted) for 2 days after treatment with cyclophosphamide. You should also empty your bladder often.

Medications for blood pressure

Rituximab may lower your blood pressure. Tell your doctor if you are taking any blood pressure medications. Your doctor may advise you to temporarily stop your blood pressure medications before your rituximab infusions.

Central venous access devices (CVADs)

This treatment may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the [eviQ patient information sheets](#) on CVADs.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Laxatives:** you may be given some medication to prevent or treat constipation. Your doctor or nurse will tell you how and when to take the laxatives.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you will be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Follow this link to read more information on [how to give this injection](#).
- **Rituximab premedication:** before your treatment with rituximab you will need to take some tablets called a premedication to help prevent you from having a reaction to the rituximab.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side

effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Bone pain after G-CSF injection	<ul style="list-style-type: none"> You may have discomfort or a dull ache in your pelvis, back, arms or legs. To reduce the pain, take paracetamol before each injection. Tell your doctor or nurse as soon as possible if your pain is not controlled.
Pain or swelling at injection site (extravasation)	<ul style="list-style-type: none"> This treatment can cause serious injury if it leaks from the area where it is going into the vein. This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. If not treated correctly, you may get blistering and ulceration. Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.
Redness and itching along vein	<ul style="list-style-type: none"> You may get redness and itching along the vein where your chemotherapy is being infused. This will usually go away within 30 minutes of stopping the injection. Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above. Your nurse will check to make sure the drug has not leaked out of the vein.
Flu-like symptoms	<ul style="list-style-type: none"> You may get: <ul style="list-style-type: none"> a fever chills or sweats muscle and joint pain a cough headaches. Tell your doctor or nurse if you get any of the symptoms listed above. Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have a temperature of 38°C or higher.
Allergic reaction	<ul style="list-style-type: none"> Allergic reactions are uncommon but can be life threatening. If you feel unwell during the infusion or shortly after it, or: <ul style="list-style-type: none"> get a fever, shivers or shakes feel dizzy, faint, confused or anxious start wheezing or have difficulty breathing have a rash, itch or redness of the face <p><u>While you are in hospital:</u> Tell your doctor or nurse immediately.</p> <p><u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.</p>
Nausea and vomiting	<ul style="list-style-type: none"> You may feel sick (nausea) or be sick (vomit). Take your anti-sickness medication as directed even if you don't feel sick. Drink plenty of fluids (unless you are fluid restricted). Eat small meals more frequently. Try food that does not require much preparation. Try bland foods like dry biscuits or toast. Gentle exercise may help with nausea. Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.

Urine turning orange or red	<ul style="list-style-type: none"> • Your urine will turn an orange or red colour. • This is not harmful and should only last for up to 48 hours after treatment.
Taste and smell changes	<ul style="list-style-type: none"> • You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

Early (onset days to weeks)

Infection risk (neutropenia)	<ul style="list-style-type: none"> • This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms: <ul style="list-style-type: none"> ◦ a temperature of 38°C or higher ◦ chills, shivers, sweats or shakes ◦ a sore throat or cough ◦ uncontrolled diarrhoea ◦ shortness of breath ◦ a fast heartbeat ◦ become unwell even without a temperature.
Low platelets (thrombocytopenia)	<ul style="list-style-type: none"> • This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.
Constipation	<ul style="list-style-type: none"> • You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: <ul style="list-style-type: none"> ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • Tell your doctor or nurse if you have not opened your bowels for more than 3 days.

<p>Tiredness and lack of energy (fatigue)</p>	<ul style="list-style-type: none"> • You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • Tell your doctor or nurse if you get any of the symptoms listed above.
<p>Bladder irritation (haemorrhagic cystitis)</p>	<ul style="list-style-type: none"> • You may get: <ul style="list-style-type: none"> ◦ blood in your urine, sometimes with blood clots ◦ pain or burning when you urinate ◦ the urge to urinate more than normal ◦ stomach or pelvic pain or discomfort. • When you go home, make sure you drink plenty of fluids (unless you are fluid restricted). • Empty your bladder often. • Tell your doctor or nurse as soon as possible if you notice any blood in your urine.
<p>Mouth pain and soreness (mucositis)</p>	<ul style="list-style-type: none"> • You may have: <ul style="list-style-type: none"> ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: <ul style="list-style-type: none"> ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.
<p>Nerve damage (peripheral neuropathy)</p>	<ul style="list-style-type: none"> • You may notice a change in the sensations in your hands and feet, including: <ul style="list-style-type: none"> ◦ tingling or pins and needles ◦ numbness or loss of feeling ◦ pain. • You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects. • Test water temperature with your elbow when bathing to avoid burns. • Use rubber gloves, pot holders and oven mitts in the kitchen. • Wear rubber shoes or boots when working in the garden or garage. • Keep rooms well lit and uncluttered. • Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.

Side effects from steroid medication	<ul style="list-style-type: none"> • Steroid medication may cause: <ul style="list-style-type: none"> ◦ mood swings and behaviour changes ◦ an increased appetite ◦ weight gain ◦ swelling in your hands and feet ◦ stomach upsets ◦ trouble sleeping ◦ fragile skin and bruising ◦ an increase in your blood sugar level ◦ weak and brittle bones (osteoporosis) • Take your steroid medication with food to reduce stomach upset • If you have diabetes, your blood sugar levels may be tested more often. • Tell your doctor or nurse if you get any of the symptoms listed above.
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Late (onset weeks to months)

Low red blood cells (anaemia)	<ul style="list-style-type: none"> • You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.
Hair loss (alopecia)	<ul style="list-style-type: none"> • Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program
Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]	<ul style="list-style-type: none"> • This treatment can affect your central nervous system. This can be very serious. • Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms: <ul style="list-style-type: none"> ◦ trouble with your speech or vision ◦ confusion or memory loss ◦ changes in your personality ◦ weakness in your arms and legs ◦ poor balance or coordination ◦ fits (seizures).

Delayed (onset months to years)

Heart problems	<ul style="list-style-type: none">• You may get:<ul style="list-style-type: none">◦ chest pain or tightness◦ shortness of breath◦ swelling of your ankles◦ an abnormal heartbeat.• Heart problems can occur months to years after treatment.• Tell your doctor if you have a history of heart problems or high blood pressure.• Before or during treatment, you may be asked to have a test to see how well your heart is working.• Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.
Lung problems	<ul style="list-style-type: none">• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment.• You may get:<ul style="list-style-type: none">◦ shortness of breath◦ fever◦ dry cough◦ wheezing◦ fast heartbeat◦ chest pain.• Your doctor will monitor how well your lungs are working during your treatment.• Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.

General advice for people having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - [Chemotherapy safety at home](#).

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

Diet and food safety

- While you are receiving this treatment, it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For further information on foods to avoid and food hygiene please ask for a copy of the [Listeria and food brochure](#).

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our [Patient and carers](#) section.

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org

This document is a guide only and cannot cover every possible situation. The health professionals caring for you should always consider your individual situation when making decisions about your care. Contact your cancer clinic staff or doctor if you have any questions or concerns about your treatment, or you are having problems coping with side effects. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use of this document is subject to eviQ's disclaimer available at www.eviq.org.au

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