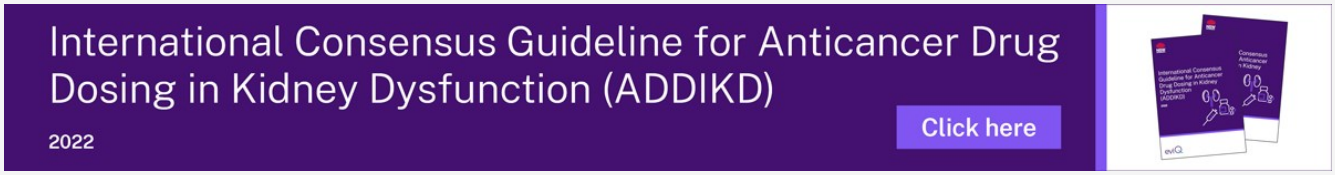
# Non-Hodgkin lymphoma R-DHAP (rituximab dexamethasone cytarabine ciSplatin)

**ID: 1584** v.6 **Endorsed**

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.




## Treatment schedule - Overview

### Cycle 1 to 3

| Drug | Dose | Route | Day |
|---|---|---|---|
| Dexamethasone | 40 mg ONCE a day | IV/PO | 1 to 4 |
| Rituximab | 375 mg/m$^2$ | IV infusion | 1 |
| ciSplatin | 100 mg/m$^2$ | IV infusion over 24 hours | 1 |
| Cytarabine (Ara-C) | 2,000 mg/m$^2$ TWICE a day (12 hours apart) | IV infusion | 2 |

**Frequency:** 21 days

**Cycles:** 3 then plan for peripheral blood stem cell harvest and autologous stem cell transplant (ASCT) as indicated.

**Notes:**

- Velasquez et al.[1] modified the cytarabine dose for patients aged older than 70 years to 1 g/m$^2$.

**Drug status:** All drugs in this protocol are on the PBS general schedule

Dexamethasone is available as **0.5 mg** and **4 mg** tablets

**Cost:** ~ $1,430 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 3

| Day 1 | | |
|---|---|---|
| Paracetamol | 1,000 mg (PO) | 60 minutes before treatment |
| Loratadine | 10 mg (PO) | 60 minutes before treatment |
| Dexamethasone | 40 mg (IV/PO) | ONCE a day orally in the morning with food OR by IV infusion on days 1 to 4.* |
| Rituximab | 375 mg/m$^2$ (IV infusion) | in 500 mL sodium chloride 0.9% as per graded administration rate |
| Netupitant | 300 mg (PO) | 60 minutes before chemotherapy (fixed dose preparation with palonosetron) |
| Palonosetron | 0.5 mg (PO) | 60 minutes before chemotherapy (fixed dose preparation with netupitant) |
| ciSplatin | 100 mg/m$^2$ (IV infusion) | in 1000 mL sodium chloride 0.9% over 24 hours |
| **Day 2** | | |
| Dexamethasone | 40 mg (IV/PO) | ONCE a day orally in the morning with food OR by IV infusion on days 1 to 4.* |
| Cytarabine (Ara-C) | 2,000 mg/m$^2$ (IV infusion) | in 500 mL sodium chloride 0.9% over 3 hours TWICE a day (12 hours apart) |
| **Day 3 and 4** | | |
| Dexamethasone | 40 mg (IV/PO) | ONCE a day orally in the morning with food OR by IV infusion on days 1 to 4.* |

* Dose for day 1 should be given 30 to 60 minutes before rituximab infusion.

**Note:**

- Velasquez et al.[1] modified the cytarabine dose for patients aged older than 70 years to 1 g/m$^2$.

**Frequency:** 21 days

**Cycles:** 3 then plan for peripheral blood stem cell harvest and autologous stem cell transplant (ASCT) as indicated.

## Indications and patient population

- Relapsed CD20 positive B-cell non-Hodgkin lymphoma
- Newly diagnosed mantle cell non-Hodgkin lymphoma prior to autologous stem cell transplant

## Clinical information

| | |
|---|---|
| **Venous access** | Central venous access device (CVAD) is required to administer this treatment.<br>Read more about central venous access device line selection |
| **Hypersensitivity/infusion related reaction** | High risk with rituximab.<br>Read more about Hypersensitivity reaction |
| **Premedication** | The product information states that premedication is required for this treatment.<br>**Note**: a corticosteroid is included as part of this treatment and therefore additional corticosteroid may not be required as premedication.<br>Please refer to the treatment schedule for the suggested premedication regimen. This may be substituted to reflect institutional policy. |

| | |
|---|---|
| **Emetogenicity HIGH** | Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy.<br>As a steroid has been included as part of this protocol, additional antiemetic steroids are not required.<br>Ensure that patients also have sufficient antiemetics for breakthrough emesis:<br>Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR<br>Prochlorperazine 10 mg PO every 6 hours when necessary.<br>Read more about preventing anti-cancer therapy induced nausea and vomiting |
| **Rituximab rapid infusion** | This regimen is not in line with the product monograph, however published literature indicates that it can be completed safely.<br>Read more about the rapid infusion of rituximab |
| **Progressive multifocal leukoencephalopathy** | 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.<br>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. |
| **Cytarabine-induced neurotoxicity** | This may occur in patients treated with high-dose cytarabine. Assess cerebellar function prior to each cytarabine dose.<br>Note: an increased risk of cytarabine-induced neurotoxicity has been associated with kidney dysfunction.<br>Read more about neurotoxicity associated with high-dose cytarabine and access the cytarabine cerebellar neurotoxicity assessment chart |
| **Ocular toxicities** | Administer corticosteroid eye drops to minimise corneal toxicity from high dose cytarabine. Commence on the day of first dose of cytarabine and continue for at least 72 hours after completion of final cytarabine dose.<br>Read more about ocular toxicities associated with high dose cytarabine |
| **Cytarabine syndrome** | Treatment with cytarabine may cause a "cytarabine syndrome" characterised by flu-like symptoms, skin rash and occasionally chest pain. |
| **Ototoxicity** | Ototoxicity may occur with platinum-based therapy; patients should be monitored for signs and symptoms. Platinum compounds should be used with caution in patients with pre-existing conditions or risk factors.<br>Ototoxicity may become more severe in patients being treated with other drugs with nephrotoxic potential e.g. aminoglycosides.<br>An audiometry test should be performed if symptoms develop.<br>Read more about ototoxicity - tinnitus and hearing loss |
| **Hydration** | Hydration helps to prevent cisplatin-induced nephrotoxicity.<br>The default regimen is appropriate for patients with normal electrolytes, kidney function, fluid status etc. and should be adjusted according to individual requirements.<br>Read more about cisplatin hydration regimens |
| **Peripheral neuropathy** | Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment.<br>Read more about peripheral neuropathy<br>Link to chemotherapy-induced peripheral neuropathy screening tool |
| **Corticosteroids** | 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.<br>Read more about acute short term effects from corticosteroids |

| | |
|---|---|
| **Central nervous system (CNS) prophylaxis** | Consider CNS relapse assessment in patients with high grade lymphoma.<br>Read more about CNS prophylaxis in diffuse large cell lymphoma |
| **Tumour lysis risk** | Patients are at high risk of developing tumour lysis syndrome, prophylaxis is recommended.<br>Read more about the prevention and management of tumour lysis syndrome. |
| **Pneumocystis jirovecii pneumonia (PJP) prophylaxis** | Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients |
| **Antiviral prophylaxis** | Read more about antiviral prophylaxis drugs and doses |
| **Antifungal prophylaxis** | Read more about antifungal prophylaxis drugs and doses. |
| **Growth factor support** | G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk.<br>Access the PBS website |
| **Biosimilar drug** | Read more about biosimilar drugs on the Biosimilar Awareness Initiative page |
| **Blood tests** | FBC, EUC, eGFR, LFTs, LDH, calcium, magnesium, phosphate and BSL at baseline, and prior to each treatment and/or as clinically indicated. |
| **Hepatitis B screening and prophylaxis** | Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy.<br>Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy |
| **Vaccinations** | Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.<br>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook.<br>Read more about COVID-19 vaccines and cancer. |
| **Fertility, pregnancy and lactation** | 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.<br>Read more about the effect of cancer treatment on fertility |

## 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 reductions for haematological toxicity not usually recommended. Discuss with Haematologist. Consider adding G-CSF |

| **Renal impairment** | |
|---|---|
| No specific dose modifications recommended for cytarabine in renal impairment, but please note an increased risk of neurotoxicity has been associated with high dose cytarabine with creatinine clearance less than 60 mL/min. | |
| **Creatinine clearance (mL/min)** | |
| greater than or equal to 70 | No dose modifications necessary |
| 50 to less than 70 | Reduce cisplatin by 25% |
| 30 to less than 50 | Reduce cisplatin by 50% |
| less than 30 | Withhold treatment |

*Refer to Nephrotoxicity associated with cisplatin for more information*

| **Hepatic impairment** |
|---|
| Elevations in liver function tests occur with both standard and high dose cytarabine. Significant liver function abnormalities may require discontinuation or a dose reduction. |

| **Peripheral neuropathy** | |
|---|---|
| Grade 2, Grade 3 or Grade 4 | Omit cisplatin |

## 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*

| Cisplatin | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)** | Additive nephrotoxicity | Avoid combination or monitor kidney function closely |
| **Ototoxic drugs (e.g. aminoglycosides, frusemide, NSAIDs)** | Additive ototoxicity | Avoid combination or perform regular audiometric testing |
| **Neurotoxic drugs (e.g. vincristine, paclitaxel)** | Additive neurotoxicity | Monitor closely for neuropathy if combination used |
| **Paclitaxel** | Administration schedule may influence the development of myelosuppression | Minimise toxicity by administering paclitaxel first in regimens using the combination |
| **Carbamazepine, phenytoin, valproate** | Decreased antiepileptic plasma levels | Monitor antiepileptic serum levels and seizure frequency for efficacy; adjust dosage as appropriate or select alternative antiepileptic (e.g. clonazepam, diazepam, lorazepam) |

| Cytarabine | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Cytidine deaminase (CDA) inhibitors (e.g. cedazuridine)** | Potential increased effect/toxicity of cytarabine due to reduced clearance | Avoid combination or monitor for increased cytarabine effect/toxicity |

| Dexamethasone | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **CYP3A4 interactions** | Dexamethasone is a substrate of CYP3A4 and a weak to moderate inducer of CYP3A4. The clinical relevance of CYP3A4 induction by dexamethasone is unknown as the mechanism has yet to be established | The effects of the concomitant use of dexamethasone with other CYP3A4 inducers, inhibitors or substrates is variable. If used concomitantly, monitor patients closely for adverse drug reactions |
| **Warfarin** | Concurrent use may result in increased risk of bleeding or diminished effects of warfarin | Monitor prothrombin time / INR (especially during initiation or discontinuation) and for signs of drug toxicity during concomitant use; adjust warfarin dose as required |
| **Oral hypoglycaemics** | Corticosteroids may cause hyperglycaemia and worsen diabetes control | Monitor blood glucose levels and adjust oral hypoglycaemic dose as required |

| 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 |

| NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Dexamethasone** | Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4 | Reduce dose of **antiemetic dexamethasone** by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of **antiemetic dexamethasone** has already been taken into account.<br><br>If **dexamethasone is part of the chemotherapy protocol**, dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover. |
| **Warfarin** | Reduced anticoagulant efficacy of warfarin due to increased clearance (aprepitant induces CYP2C9). *Note interaction only applicable to aprepitant/ fosaprepitant | INR should be monitored in the 2 week period, particularly at 7 to 10 days following the administration of aprepitant/ fosaprepitant |
| **Combined oral contraceptive** | Reduced contraceptive efficacy due to increased clearance. *Note interaction only applicable to aprepitant/ fosaprepitant | Alternative non-hormonal methods should be used during and for 1 month after stopping aprepitant/ fosaprepitant |
| **CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)** | Reduced efficacy of NK-1 antagonist possible due to increased clearance | Avoid combination or monitor for decreased antiemetic effect. Consider using an alternative antiemetic regimen |
| **CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)** | Increased toxicity of NK-1 antagonist possible due to reduced clearance | Avoid combination or monitor for increased adverse effects of NK-1 antagonist (e.g. headache, hiccups, constipation) |
| **Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)** | Increased effects/toxicity of these drugs possible due to inhibition of CYP3A4 by NK-1 antagonist | Avoid combination or monitor for increased toxicity especially with orally administered drugs |

| 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.<br><br>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.<br><br>Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors.<br><br>Dabigatran: avoid combination with strong P-gp inducers and inhibitors.<br><br>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.<br>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.<br>If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia).<br>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.<br>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*

*product information monographs via the TGA website for further information.*

## Day 1

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.

- baseline weight
- strict fluid balance
- dipstick urinalysis prior to treatment

**Note**: A large volume of intravenous fluid may be given with this protocol. If weight increases by more than 1 kg from baseline or fluid balance becomes positive by one litre or any other signs of fluid overload are present, review by medical officer (diuretics may be required).

Commence corticosteroid eye drops 24 hours before starting cytarabine. Continue for 72 hours after completion of the last dose of cytarabine.

Prime IV line(s).

Access TIVAD or CVAD.

### Treatment - Time out

#### Dexamethasone

- administer orally ONCE a day in the morning with food **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%
- patients may receive dexamethasone on day 3 and 4 orally as an outpatient or administered via IV infusion if still an inpatient

**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: dexamethasone (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:

- perform baseline observations and repeat observations prior to each rate increase
- **commence** rituximab infusion at 100 mg/hr
- 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

### Cisplatin

**Commence prehydration for cisplatin:**

- administer 10 mmol magnesium sulphate ($MgSO_4$) in 1000 mL sodium chloride 0.9% over 60 minutes
- ensure patient has passed urine prior to cisplatin administration as per institutional policy.

**Administer cisplatin (irritant):**

- via IV infusion over 24 hours
- flush with 100 mL of sodium chloride 0.9%.

**Post hydration:**

- 1000 mL sodium chloride 0.9% over 60 minutes.

*20/11/23 Mannitol information removed to align with updated ID 184 Prevention and management of cisplatin induced nephrotoxicity.*

**Continue safe handling precautions until 7 days after completion of drug(s)**

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## Day 2

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

- daily weight
- strict fluid balance

Continue corticosteroid eye drops until 72 hours after completion of the last dose of cytarabine.

Hydration if prescribed

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

### Dexamethasone

- administer orally ONCE a day in the morning with food **OR**
- via IV infusion over 15 minutes

- flush with ~ 50mL sodium chloride 0.9%
- patients may receive dexamethasone on day 3 and 4 orally as an outpatient or administered via IV infusion if still an inpatient

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

### Chemotherapy - Time out

#### Cytarabine

**Prior to administration:**

Ensure corticosteroid eye drops have been administered before starting cytarabine. Please see ocular toxicities associated with high dose cytarabine for more information.

Verify that cytarabine neurological assessment has been performed prior to administration of cytarabine:

- if the patient scores 0 then administer cytarabine as charted
- if the patient scores 1 or above, do not administer the cytarabine and immediately notify medical officer.

**Administer cytarabine:**

- via IV infusion over 3 hours
- flush with ~50 mL of sodium chloride 0.9%.

**Administer second dose of cytarabine 12 hours after first dose.**

**Continue safe handling precautions until 7 days after completion of drug(s)**

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## Days 3 and 4

General patient assessment prior to each day of treatment.

- daily weight

Continue corticosteroid eye drops until 72 hours after completion of the last dose of cytarabine.

#### Dexamethasone

- administer orally ONCE a day in the morning with food **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%
- patients may receive dexamethasone on day 3 and 4 orally as an outpatient or administered via IV infusion if still an inpatient

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

Deaccess TIVAD or CVAD.

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## Discharge information

**Dexamethasone tablets**

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

**Antiemetics**

- Antiemetics as prescribed.

**Corticosteroid eye drops**

- Continue corticosteroid eye drops for at least 72 hours after completion of final cytarabine dose.

**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) | |
|---|---|
| **Cytarabine (Ara-C) syndrome** | Flu-like symptoms including fever, myalgia and malaise can occur 6 to 12 hours after cytarabine administration. Symptoms generally resolve within 24 hours of completing therapy. |
| **Headache** | |
| **Hypersensitivity reaction** | Anaphylaxis and infusion related reactions can occur with this treatment.<br>Read more about hypersensitivity reaction |
| **Nausea and vomiting** | Read more about prevention of treatment induced nausea and vomiting |
| **Neurotoxicity** | High dose cytarabine has been associated with acute cerebellar syndrome and diffuse cerebral dysfunction.<br>Read more about neurotoxicity associated with high dose cytarabine |
| **Ocular toxicities** | Reversible corneal toxicity (keratitis), haemorrhagic conjunctivitis, vision loss and other ocular side effects can occur with high dose cytarabine. Corticosteroid eye drops must be administered concurrently with treatment.<br>Read more about ocular toxicities associated with cytarabine |
| **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.<br>Read more about immediate management of neutropenic fever |
| **Thrombocytopenia** | A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding.<br><br>Read more about thrombocytopenia |
| **Diarrhoea** | Read more about treatment induced diarrhoea |
| **Fatigue** | Read more about fatigue |
| **Hypomagnesaemia, hypokalaemia, hypocalcaemia** | Abnormally low levels of magnesium, potassium and calcium in the blood. |
| **Nephrotoxicity** | Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature. |
| **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).<br>Read more about oral mucositis |
| **Ototoxicity** | Tinnitus and hearing loss may occur due to damage in the inner ear. Tinnitus is usually reversible, while hearing loss is generally irreversible. Hearing loss is dose-related, cumulative and may be worse in those with pre-existing hearing problems.<br>Read more about ototoxicity - tinnitus and hearing loss |
| **Palmar-plantar erythrodysaesthesia (PPE) - hand-foot syndrome (HFS)** | Bilateral erythema, tenderness, pain, swelling, tingling, numbness, pruritus, dry rash, or moist desquamation and ulceration of the palms and soles. It is also known as hand-foot syndrome (HFS). Symptoms appear to be dose dependent and palms are affected more than soles.<br>Read more about hand-foot syndrome associated with chemotherapy |
| **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.<br>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. |
| **Skin rash** | Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction.<br>Read more about skin rash |

| Late (onset weeks to months) | |
|---|---|
| **Anaemia** | Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood.<br>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.<br>Read more about alopecia and scalp cooling |
| **Cognitive changes (chemo fog)** | Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'.<br>Read more about cognitive changes (chemo fog) |
| **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.<br>Read more about progressive multifocal leukoencephalopathy (PML) |

## Evidence

In 1988 Velasquez et al showed that DHAP (cisplatin, high dose cytarabine and dexamethasone) was shown to be an effective salvage regimen for recurrent non Hodgkin lymphoma (NHL). Of the 90 patients reported in this study, 58 had diffuse large B cell histology (DLBCL). Seventeen of these patients achieved CR and fourteen achieved PR.[1]

DHAP was employed as the salvage chemotherapy regimen in the PARMA trial published in NEJM in 1995. This randomised trial examined the role of autologous bone marrow transplantation (ABMT) compared to conventional salvage chemotherapy in relapsed, but chemotherapy sensitive NHL.[2]

Randomisation occurred after two cycles of DHAP – patients showing no response were excluded – to either 4 additional courses of DHAP or ABMT. Bone marrow was harvested after cycle 1 in all patients except those with clearly progressive disease, or in those who had marrow harvested previously.[2]

Involved field radiation therapy up to 26 Gy was allowed, as per defined indications, in both groups, and was administered *prior* to high dose chemotherapy (BEAC – carmustine, etoposide, cytarabine and cyclophosphamide) in the ABMT group.[2]

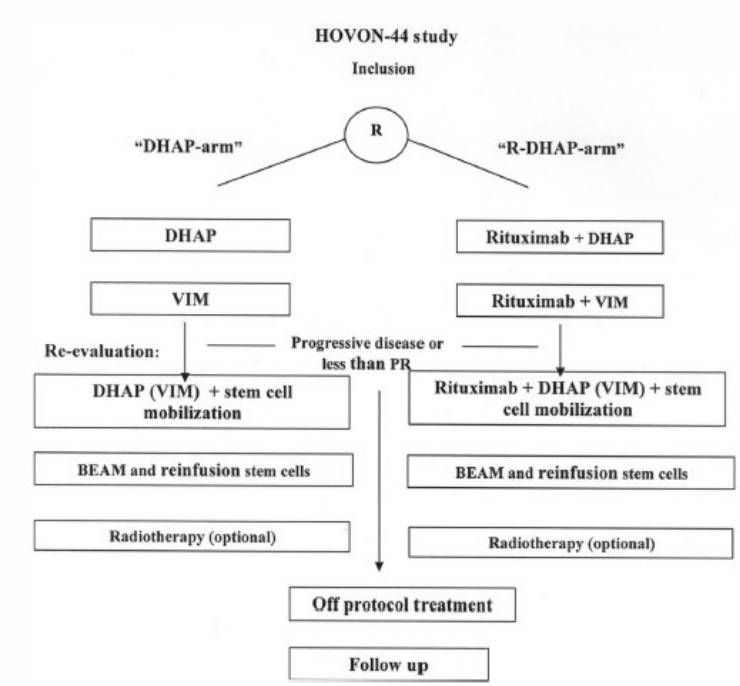
A total of 215 patients were enrolled, with a median age of 43 and median follow up of 63 months. There were 163 with 'intermediate grade' histology (DLBCL in 37), and 52 with 'high grade' histology. Note this is a comparatively favourable group of patients, with only 36 out of 105 having a raised LDH. Nevertheless, there was a highly significant advantage in favour of ABMT in EFS as well as OS[2]– see below in '*Efficacy*' section.

Vose in a review in 1998[3] commented that DHAP followed by high dose chemotherapy and autologous haemopoietic stem cell transplant was then the standard of care for relapsed or refractory DLBCL

### DHAP + Rituximab (R-DHAP)

With the widespread use of rituximab in frontline as well as in salvage treatment for various types of CD-20 positive NHL, it is logical to examine the role of incorporating rituximab with DHAP. In this regard, one of the first abstracts on R-DHAP was from Guibert et al in 2006. This report described 24 patients with newly diagnosed mantle cell lymphoma treated with 4 to 6 courses of R-DHAP followed by autologous stem cell transplantation (ASCT) for patients under 65 (group 1); those over 65 were treated with R-DHAP alone (group 2). In group 1, 16 out of 17 attained CR or CRu; fourteen were scheduled to have ASCT. Blood stem cells were harvested after 3 to 4 courses, with 3 failures. Ten patients in total proceeded to ASCT using BEAM (carmustine, etoposide, cytarabine and melphalan), after a total of 4 to 6 courses of R-DHAP. On intention-to-treat, 3-year OS and EFS were 75% and 76% respectively. In group 2, six of seven patients entered CR or CRu after 4 courses of R-DHAP; five received an additional two courses.[4]

Addition of rituximab to DHAP type chemotherapy in re-induction of relapsed, or progressive aggressive CD20+ NHL was reported in the HOVON-44 trial in 2008. Chemotherapy consisted of DHAP alternating with VIM (etoposide, ifosfamide, methotrexate), with the sequence DHAP – VIM – DHAP. Patients proceeded to blood stem cell mobilisation on the back of the third chemotherapy cycle (DHAP number 2). If required, a fourth cycle, VIM, can be given. The experimental arm consisted of the same, plus rituximab. Patients in CR or PR after two cycles of chemotherapy are candidates for ASCT (BEAM). Radiation therapy following ASCT is allowed. The following is the schema for the trial:[5]




*© Blood 2008*

## Efficacy

The PARMA trial provided excellent data on the role of DHAP in treatment of relapsed NHL, with or without high dose chemotherapy followed by ABMT. At the end of the first two cycles of DHAP, 109 patients (41% in CR, and 59% in PR) were randomised to either BEAC followed by ABMT, or continuing with up to 4 more cycles of DHAP.[2]

The following points are worth noting:

- the group was by and large a favourable group, with the aim at that time to test the toxicities of ABMT
- source of stem cells was unstimulated (no G-CSF) bone marrow
- involved field radiation therapy was built into the protocol for both arms of the study, according to predefined criteria (bulky disease = 5cm or extranodal T3 or T4 lesions as defined by EORTC)
- the study was conducted well before the rituximab era.[2]

Comparing the ABMT arm vs chemotherapy:

- response rate (CR+PR) 84% vs 44% at completion of all treatment
- EFS 46% vs 12% (p=0.001)
- OS at 5 years 32% vs 13% (p=0.038)[2]

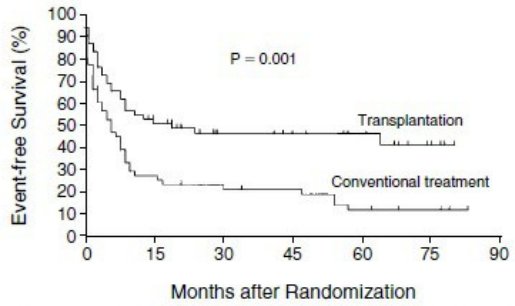



Figure 1. Kaplan–Meier Curves for Event-free Survival of Patients in the Transplantation and Conventional-Treatment Groups. The data are based on an intention-to-treat analysis. Tick marks represent censored data.

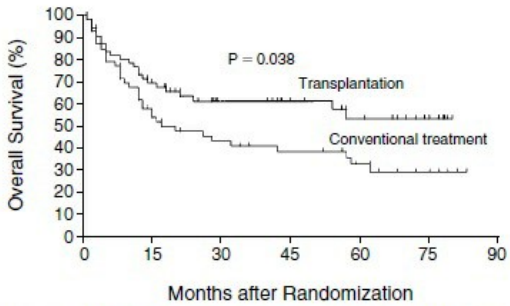



Figure 2. Kaplan–Meier Curves for Overall Survival of Patients in the Transplantation and Conventional-Treatment Groups. The data are based on an intention-to-treat analysis. Tick marks represent censored data.

*© New England Journal of Medicine 1995*

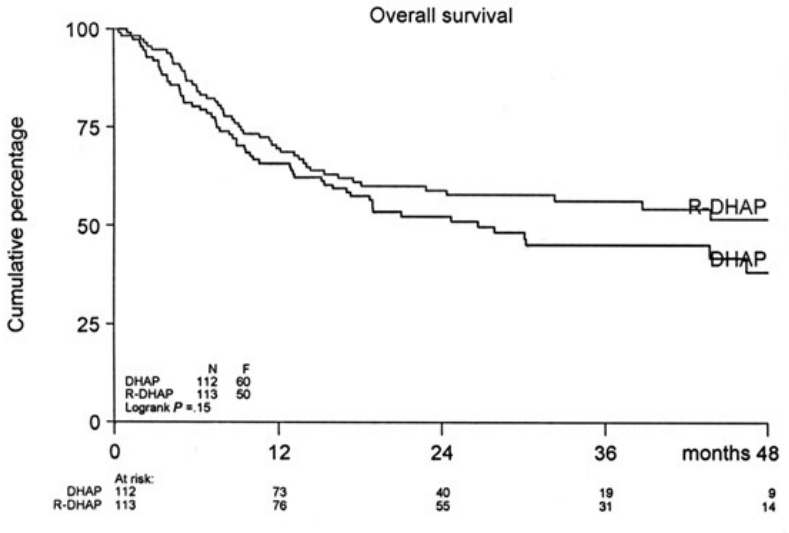
Time to first relapse is correlated with response after the first two cycles of DHAP, as well as 8-year survival rates in the PARMA trial.[6] Age adjusted IPI at relapse is correlated with OS in the DHAP group but it has no effect in the BEAC group. In addition, ABMT was not superior in patients with an age adjusted IPI of 0.[7]

In the HOVON-44 trial comparing DHAP to R-DHAP, 14 out of 239 patients enrolled, were excluded from analysis. A total of 225 patients were analysed on ITT basis – 112 in DHAP arm, and 113 in R-DHAP arm. The majority of the patients had DLBCL and had

received CHOP-like first line treatment. Only 4 patients in each arm had prior exposure to rituximab. The two groups were well balanced in prognostic factors and demographics.[5]

Response rate following chemotherapy favoured the R-DHAP arm: 75% vs 54%. Patients showing response were eligible to proceed to ASCT. Inadequate blood PBSC harvest was observed in 1 patient in the DHAP arm, and 3 in the R-DHAP arm. Six patients in DHAP and 7 in the R-DHAP arm respectively progressed prior to ASCT and went off protocol. Radiation therapy after ASCT was given to 3 patients in the DHAP arm and 9 patients in the R-DHAP arm. The overall response rates were: DHAP – CR 35%, PR 15%; R-DHAP – CR 46% and PR 27%.[5]

Median follow up was 31 months. At 24 months, FFS was 24% in DHAP arm, and 50% in the R-DHAP arm (p<0.001). PFS at 24 months were: 31% vs 52% (p<0.002). OS at 24 months were: 52% vs 59% (p=0.15).[5]

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Thus, in this essentially rituximab-naïve group of patients, addition of rituximab to DHAP-like salvage regimen prior to ASCT led to significant improvement in EFS and PFS, without significant increase in toxicities or delay in haemopoietic recovery following ASCT (data not shown). However, the benefit for OS cannot be demonstrated with confidence.[5] This may be due to successful third line salvage treatment. Note (1) there were only 3 doses in total of rituximab in the R-DHAP arm, and (2) patients relapsing or progressing after rituximab-containing front line therapy are not adequately examined in this study (see CORAL study, below).

R-DHAP vs R-ICE (ifosfamide, carboplatin, etoposide) was examined in the *CORAL study*, a phase III multicentre randomised trial in relapsed or primary refractory DLBCL.[8, 9] Of a total of 396 patients (median age 55 years), 62% had received prior rituximab. Overall efficacy measurements were similar between R-DHAP and R-ICE, with different toxicity profiles. Overall, 3-year EFS was inferior in patients with prior rituximab treatment (21% vs 47%). Of interest, patients with initial CR >12 months after diagnosis had similar EFS whether they had received rituximab (D below). This suggests patients with early relapses after rituximab-containing front-line therapy constitute a prognostically adverse group (C below).[9] Data for rituximab maintenance was not sufficiently mature for analysis at time of publication.

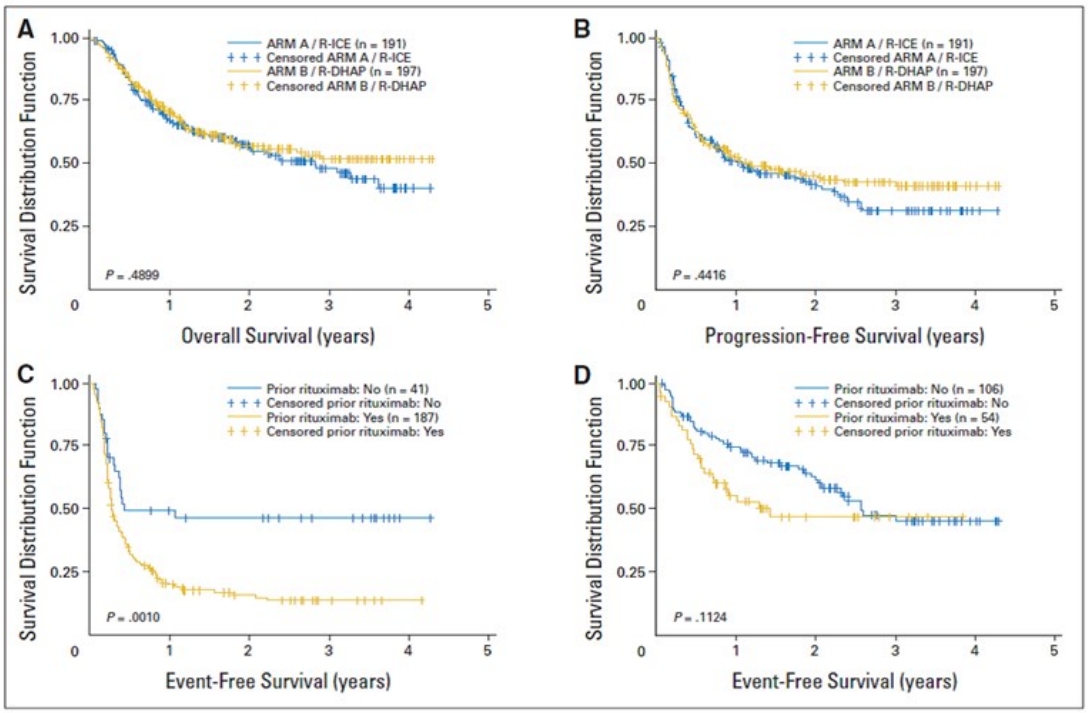



**Fig 3.** (A) Overall survival according to the first random assignment (intent to treat). (B) Progression-free survival according to treatment arm. (C) Event-free survival (EFS) according to prior rituximab treatment and relapse less than 12 months after diagnosis. (D) EFS according to prior rituximab treatment and relapse more than 12 months after diagnosis. R-ICE, rituximab, ifosfamide, carboplatin, etoposide; R-DHAP, rituximab, dexamethasone, high-dose cytarabine, cisplatin.

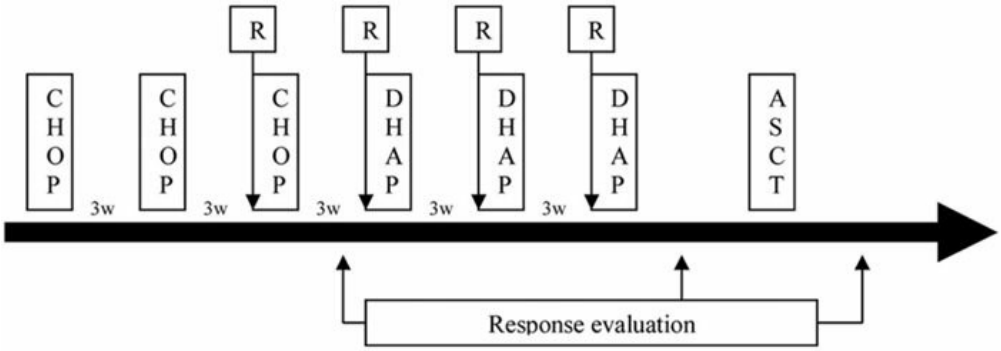
*© Journal of Clinical Oncology 2010*

A GELA phase 2 study examining R-DHAP, alternating with R-CHOP 21, followed by ASCT in mantle cell lymphoma patients younger than 66 years was reported in 2013. Patients had at least stage-3 disease. Sixty patients were enrolled, with a median age of 57 years. This study examines the role of adding high dose cytarabine and 4 doses of rituximab to this particular chemotherapy backbone in mantle cell lymphoma, which has been investigated previously by GELA.[10] The following table shows the demographics:

| | **Present study (N = 60)** |
|---|---|
| Median age, y (range) | 57.5 (40-66) |
| Sex ratio | 49 male/11 female |
| Stage 3/4, no. (%) | 60/60 (100) |
| B symptoms, no. (%) | 15/60 (25) |
| PS > 1, no. (%) | 4/60 (7) |
| LDH > N, no. (%) | 23/60 (38) |
| $\beta_2$-microglobulin > N, no. (%) | 18/38 (47) |
| Median albumin, g/L (range) | 41 (26-60) |
| Bone marrow involvement, no. (%) | 51/60 (85) |
| Leukemic phase, no. (%) | 29/60 (48) |
| Gastrointestinal involvement, no. (%) | 15/29 (52) |
| **MIPI, no. (%)** | |
| Low | 33/60 (55) |
| Intermediate | 19/60 (32) |
| High | 8/60 (13) |

*© Blood 2013*

The following is the treatment schedule






Peripheral blood stem cells were harvested after the third cycle of R-DHAP. ASCT conditioning included TBI of 10 Gy over 3 days in twice daily fractions, high dose cytarabine and high dose melphalan. Primary end point was EFS. Of 53 patients still on study at the end of induction, 49 proceeded to ASCT. BEAM was used in 7 patients because of unavailability of TBI, or induction toxicity. At end of induction, 57% of patients were in CR and 30% in PR. There was a notable proportion who converted from PR after R-CHOP to CR after R-DHAP. For patients who received the entire planned treatment, including ASCT, CR was 96% and PR 4%. On ITT analysis for the entire cohort, CR was 78%, and ORR 82%.[10]

Median follow-up from diagnosis was 67 months. Median EFS was 83.9 months with 5-year EFS estimate of 64%. Relapse or progression occurred in 16 patients. Median PFS was 84 months, and median OS was not reached. OS rate at 5 years was 75%.[10]

### Toxicity

In the PARMA trial there were 6 (out of 55 patients) early toxic deaths in the BEAC arm. Of these, 22 had received radiation therapy. There were no early toxic deaths in 54 patients in the DHAP arm. Out of these, 12 had received radiation therapy. As expected, the BEAC arm also had much higher adverse events such as infections and mucositis, one case of septic shock, and one had grade 4 cardiac toxicity.[2]

A high incidence of second malignancies was observed in the GELA (R-DHAP) study. With the limited follow-up, 11 of 60 patients were diagnosed with a second malignancy, mostly renal cancer. No cases of MDS or acute leukaemia were observed.[10]

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10 Delarue, R., C. Haioun, V. Ribrag, et al. 2013. "CHOP and DHAP plus rituximab followed by autologous stem cell transplantation in mantle cell lymphoma: a phase 2 study from the Groupe d'Etude des Lymphomes de l'Adulte." Blood 121(1):48-53.

## History

### Version 6

| Date | Summary of changes |
|---|---|
| **28/04/2023** | Protocol electronically reviewed by Haematology Reference Committee. Subcutaneous rituximab information removed from the following sections – treatment schedule, clinical information, administration, patient information.<br><br>Increased to version 6. Review in 4 years. |

### Version 5

| Date | Summary of changes |
|---|---|
| **09/03/2020** | Biosimilar rituximab added to clinical information. Version number changed to V.5 |
| **06/07/2020** | Note added for modified cytarabine dose for patients aged older than 70 years to 1g/$m^2$.<br>Reviewed by Haematology Reference Committee, nil significant changes, review in 4 years. |
| **01/10/2021** | Drug status updated: rituximab SC is TGA registered but no longer PBS listed. |
| **20/01/2022** | Interactions updated. |

### Version 4

| Date | Summary of changes |
|---|---|
| **12/03/2018** | **Added:**<br>• Link to subcutaneous rituximab document underneath the treatment schedule.<br>• Clinical information block on subcutaneous rituximab<br>• Link to the subcutaneous rituximab document into administration section<br>• Injection-site reaction side effect<br>• Note about subcutaneous rituximab to the patient information<br>• Version number changed to V.4. |
| **25/05/2018** | Reviewed by Haematology Reference Committee with no significant changes, review in 2 years |
| **13/09/2019** | Reviewed by Haematology Reference Committee, no changes made. Review in 5 years. |
| **10/10/2019** | Clinical information updated with PBS expanded indications for GCSF. |

### Version 3

| Date | Summary of changes |
|---|---|
| **11/10/2013** | Presented at Haematology reference committee meeting (new Protocol). |
| **11/11/2013** | Published on eviQ. |
| **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** | Reviewed at reference committee meeting, no changes. Review in 2 years. Updated cost of drugs for treatment. |
| **20/06/2016** | Drug status updated as per PBS: Removed 'NB: Rituximab is not on the PBS for mantle cell lymphoma'. |

| Date | Summary of changes |
|---|---|
| **31/05/2017** | Transferred to new eviQ website. Version number change to V.3.<br><br>Antiemetic change: Netupitant/palonosetron combination has replaced aprepitant and a $5HT_3$ receptor antagonist in combination with dexamethasone for all highly emetogenic regimens. |



**First approved:** 11 October 2013
**Last reviewed:** 28 April 2023
**Review due:** 30 June 2027

***The currency of this information is guaranteed only up until the date of printing, for any updates please check:***
*https://www.eviq.org.au/p/1584*
*23 Nov 2023*

# Patient information - Non-Hodgkin lymphoma (NHL) - R-DHAP (rituximab, dexamethasone, cytarabine, cisplatin)

**Patient's name:**

## Your treatment

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

| R-DHAP (rituximab, dexamethasone, cytarabine, cisplatin) | | | |
|---|---|---|---|
| This treatment cycle is repeated every 21 days. 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 4 | **Dexamethasone** (*dex a METH a sone*) | By a drip into a vein **OR** take orally ONCE a day in the morning with food on days 1 to 4 only.<br><br>If you forget to take your tablets or vomit your tablets, contact your treating team. | About 15 minutes if given by a drip |
| 1 | **Rituximab** (*ri-TUX-i-mab*) | By a drip into a vein | **1st cycle:** About 4 to 6 hours<br><br>**Cycles thereafter:** About 3 to 4 hours |
| | **Cisplatin** (*siss-PLAT-in*) | By a drip into a vein | About 24 hours |
| 2 | **Cytarabine** (*sye-TARE-a-been*) | By a drip into a vein | About 3 hours TWICE a day |

## 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.

| **IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:** | **Emergency contact details**<br><br>Ask your doctor or nurse from your treating team who to contact if you have a problem |
|---|---|
| • a temperature of 38ºC or higher<br>• chills, sweats, shivers or shakes<br>• shortness of breath<br>• uncontrolled vomiting or diarrhoea<br>• pain, tingling or discomfort in your chest or arms<br>• you become unwell. | Daytime:<br>Night/weekend:<br>Other instructions: |

**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.

### Central venous access devices (CVADs)

This treatment involves 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.

### 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.

### 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.
- **Eye drops:** you will be given eye drops to help prevent sore eyes. You will start using the eye drops before you have your first dose of cytarabine and continue to use the eye drops until 72 hours after your last dose of cytarabine.
- **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 may 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. Your doctor will decide if you need this medication. 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) |
|---|

| | |
|---|---|
| **Flu-like symptoms from cytarabine** | • You may get a fever, skin rash, aches and pains or increased sweating.<br>• These symptoms are caused by the drug cytarabine.<br>• Symptoms usually happen 6 to 12 hours after your dose, and may last until 24 hours after your treatment has finished.<br>• To reduce any pain or fever, take paracetamol, if needed.<br>• Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to.<br>• Tell your doctor or nurse if these symptoms do not get better after 24 hours. |
| **Headache** | • You can take paracetamol if you have a headache.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.** |
| **Allergic reaction** | • Allergic reactions are uncommon but can be life threatening.<br>• **If you feel unwell during the infusion or shortly after it, or:**<br>◦ **get a fever, shivers or shakes**<br>◦ **feel dizzy, faint, confused or anxious**<br>◦ **start wheezing or have difficulty breathing**<br>◦ **have a rash, itch or redness of the face**<br><br>**<u>While you are in hospital:</u> Tell your doctor or nurse immediately.**<br>**<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.** |
| **Nausea and vomiting** | • You may feel sick (nausea) or be sick (vomit).<br>• Take your anti-sickness medication as directed even if you don't feel sick.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat small meals more frequently.<br>• Try food that does not require much preparation.<br>• Try bland foods like dry biscuits or toast.<br>• Gentle exercise may help with nausea.<br>• Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment.<br>• **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.** |
| **Nervous system changes from cytarabine** | • High doses of cytarabine can affect the nervous system.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms during or soon after your treatment:**<br>◦ **dizziness, drowsiness or double vision**<br>◦ **agitation**<br>◦ **difficulty walking in a straight line**<br>◦ **difficulty writing with a pen or pencil**<br>◦ **jerky movements**<br>◦ **slow, slurred speech.** |
| **Eye problems from cytarabine** | • You may get:<br>◦ eye pain or irritation<br>◦ blurred vision<br>◦ watery or gritty eyes<br>◦ sensitivity to light.<br>• You will be given eye drops to help prevent and control these symptoms. It is important to use these eye drops as directed.<br>• Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you have lost your eyelashes.<br>• Tell your doctor or nurse if you get any of the symptoms listed above. |

| | |
|---|---|
| **Taste and smell changes** | • You may find that food loses its taste or tastes different.<br>• These changes are likely to go away with time.<br>• Do your mouth care regularly.<br>• Chew on sugar-free gum or eat sugar-free mints.<br>• Add flavour to your food with sauces and herbs.<br>• Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment. |

| Early (onset days to weeks) | |
|---|---|
| **Infection risk (neutropenia)** | • 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.<br>• Wash your hands often.<br>• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.<br>• Do your mouth care regularly.<br>• Inspect your central line site (if you have one) daily for any redness, pus or swelling.<br>• Limit contact with people who are sick.<br>• Learn how to recognise the signs of infection.<br>• Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:**<br>◦ **a temperature of 38°C or higher**<br>◦ **chills, shivers, sweats or shakes**<br>◦ **a sore throat or cough**<br>◦ **uncontrolled diarrhoea**<br>◦ **shortness of breath**<br>◦ **a fast heartbeat**<br>◦ **become unwell even without a temperature.** |
| **Low platelets (thrombocytopenia)** | • 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.<br>• Try not to bruise or cut yourself.<br>• Avoid contact sport or vigorous exercise.<br>• Clear your nose by blowing gently.<br>• Avoid constipation.<br>• Brush your teeth with a soft toothbrush.<br>• Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to.<br>• Tell your doctor or nurse if you have any bruising or bleeding.<br>• **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.** |
| **Diarrhoea** | • You may get bowel motions (stools, poo) that are more frequent or more liquid.<br>• You may also get bloating, cramping or pain.<br>• Take your antidiarrhoeal medication as directed by your doctor.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat and drink small amounts more often.<br>• Avoid spicy foods, dairy products, high fibre foods, and coffee.<br>• Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment.<br>• **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.** |

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| **Tiredness and lack of energy (fatigue)** | • You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy.<br>• Do not drive or operate machinery if you are feeling tired.<br>• Nap for short periods (only 1 hour at a time)<br>• Prioritise your tasks to ensure the best use of your energy.<br>• Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted).<br>• Try some gentle exercise daily.<br>• Allow your friends and family to help.<br>• **Tell your doctor or nurse if you get any of the symptoms listed above.** |
| **Low blood magnesium, potassium and calcium levels (hypomagnesaemia, hypokalaemia, hypocalcaemia)** | • This may be found from your routine blood tests and treated by your doctor.<br>• If it is severe you may get:<br>◦ muscle cramps or twitches<br>◦ numbness or tingling in your fingers, toes or around your mouth<br>◦ constipation<br>◦ an irregular heartbeat<br>◦ sleepy, drowsy or confused<br>• **Tell your doctor or nurse as soon as possible if you get any of the signs or symptoms listed above.** |
| **Kidney damage** | • This treatment can cause changes to how your kidneys work.<br>• You will have blood tests to make sure your kidneys are working properly.<br>• You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this.<br>• **Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.** |
| **Mouth pain and soreness (mucositis)** | • You may have:<br>◦ bleeding gums<br>◦ mouth ulcers<br>◦ a white coating on your tongue<br>◦ pain in the mouth or throat<br>◦ difficulty eating or swallowing.<br>• Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks.<br>• Try bland and soft foods.<br>• Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so.<br>• Rinse your mouth after you eat and brush your teeth, using either:<br>◦ 1/4 teaspoon of salt in 1 cup of warm water, or<br>◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water<br>• Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment.<br>• **Tell your doctor or nurse if you get any of the symptoms listed above.** |
| **Hearing changes (ototoxicity)** | • You may get ringing in your ears or loss of hearing.<br>• You may have your hearing tested before and during your treatment.<br>• **Tell your doctor or nurse as soon as possible if you notice any changes to your hearing.** |

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| **Hand-foot syndrome (palmar-plantar erythrodysaesthesia)** | • The palms of your hands and soles of your feet may become:<br>  ◦ red and hot<br>  ◦ swollen<br>  ◦ painful and tender<br>  ◦ blistered.<br>• The skin in the area may also peel.<br>• Moisturise your hands and feet daily with sorbolene or aqueous cream.<br>• Keep your hands and feet clean and dry.<br>• Avoid hot water, instead use lukewarm water to bathe.<br>• Avoid direct sunlight.<br>• Avoid unnecessary walking, jogging or exercise.<br>• Wear cotton socks and avoid tight-fitting shoes.<br>• **Tell your doctor or nurse as soon as possible if you notice any skin changes on your hands or feet.** |
| **Nerve damage (peripheral neuropathy)** | • You may notice a change in the sensations in your hands and feet, including:<br>  ◦ tingling or pins and needles<br>  ◦ numbness or loss of feeling<br>  ◦ pain.<br>• You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects.<br>• Test water temperature with your elbow when bathing to avoid burns.<br>• Use rubber gloves, pot holders and oven mitts in the kitchen.<br>• Wear rubber shoes or boots when working in the garden or garage.<br>• Keep rooms well lit and uncluttered.<br>• Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment.<br>• Tell your doctor or nurse if you get any of the symptoms listed above. |
| **Side effects from steroid medication** | • Steroid medication may cause:<br>  ◦ mood swings and behaviour changes<br>  ◦ an increased appetite<br>  ◦ weight gain<br>  ◦ swelling in your hands and feet<br>  ◦ stomach upsets<br>  ◦ trouble sleeping<br>  ◦ fragile skin and bruising<br>  ◦ an increase in your blood sugar level<br>  ◦ weak and brittle bones (osteoporosis)<br>• Take your steroid medication with food to reduce stomach upset<br>• If you have diabetes, your blood sugar levels may be tested more often.<br>• Tell your doctor or nurse if you get any of the symptoms listed above. |
| **Skin rash** | • You may get a red, bumpy rash and dry, itchy skin.<br>• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.<br>• Do not scratch your skin.<br>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.<br>• **Talk to your doctor or nurse about other ways to manage your skin rash.** |

| Late (onset weeks to months) | |
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| **Low red blood cells (anaemia)** | • You may feel dizzy, light-headed, tired and appear more pale than usual.<br>• Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion.<br>• **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)** | • Your hair may start to fall out from your head and body.<br>• Hair loss usually starts 2 to 3 weeks after your first treatment.<br>• You may become completely bald and your scalp might feel tender.<br>• Use a gentle shampoo and a soft brush.<br>• Take care with hair products like hairspray, hair dye, bleaches and perms.<br>• Protect your scalp from the cold with a hat, scarf or wig.<br>• Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher.<br>• Moisturise your scalp to prevent itching.<br>• Ask your doctor or nurse about the Look Good Feel Better program |
| **Chemo brain (chemotherapy-related cognitive impairment)** | • You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory.<br>• These symptoms usually improve once treatment is completed.<br>• Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain).<br>• Tell your doctor or nurse if you get any of the symptoms listed above. |
| **Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]** | • This treatment can affect your central nervous system. This can be very serious.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms:**<br>◦ **trouble with your speech or vision**<br>◦ **confusion or memory loss**<br>◦ **changes in your personality**<br>◦ **weakness in your arms and legs**<br>◦ **poor balance or coordination**<br>◦ **fits (seizures).** |

## 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.
- 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 more 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
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – https://aci.health.nsw.gov.au/networks/bmtct
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

### General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- Carer Help - carerhelp.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

### Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information - patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

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