

GMALL 2002 pre-phase (patients under 55 years)

ID: 1915 v.3 Endorsed

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

This protocol is based on limited evidence; refer to the evidence section of this protocol for more information.

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 (ADDIKD)

2022

[Click here](#)



Related pages:

- [GMALL 2002 overview \(patients under 55 years\)](#)
- [GMALL 2002 overview \(patients over 55 years\)](#)

Treatment schedule - Overview

Drug	Dose	Route	Day
Prednisolone	60 mg/m ² ONCE a day	PO	1 to 5
CYCLOPHOSPHamide	200 mg/m ²	IV infusion	1 to 5
Methotrexate	15 mg	Intrathecal	1

Duration: 5 days

Cycles: 1. After a break on day 6, patients will proceed to treatment with Block A1.

Stage I/II disease	Total of 4 cycles (A1-B1-C1-A2) followed by two additional doses of rituximab every 21 days after completion of A2. ²
Stage III/IV disease or mediastinal and extra-nodal involvement	Total of 6 cycles (A1-B1-C1-A2-B2-C2) followed by two additional doses of rituximab every 21 days after completion of C2. ²

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

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

Cost: ~ \$140 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.](#)

Day 1		
Prednisolone	60 mg/m ² (PO)	ONCE a day on days 1 to 5. Take in the morning with food.
CYCLOPHOSPHamide	200 mg/m ² (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes
Methotrexate	15 mg (Intrathecal)	adhere to local institution intrathecal policy

Day 2 to 5		
Prednisolone	60 mg/m ² (PO)	ONCE a day on days 1 to 5. Take in the morning with food.
CYCLOPHOSPHamide	200 mg/m ² (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes

Duration: 5 days

Cycles: 1. After a break on day 6, patients will proceed to treatment with Block A1.

Stage I/II disease	Total of 4 cycles (A1-B1-C1-A2) followed by two additional doses of rituximab every 21 days after completion of A2. ²
Stage III/IV disease or mediastinal and extra-nodal involvement	Total of 6 cycles (A1-B1-C1-A2-B2-C2) followed by two additional doses of rituximab every 21 days after completion of C2. ²

Indications and patient population

- Burkitt lymphoma and/or mature B-cell acute lymphoblastic leukaemia in patients 18 to 55 years of age

Clinical information

Venous access	Central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Antiemetics for multi-day protocols	<p>Antiemetic therapy should be administered throughout the duration of the chemotherapy protocol and to cover delayed nausea. The acute and delayed emetic risk of multi-day chemotherapy protocols will overlap depending on the individual drugs and their sequence of administration. More or less antiemetic cover may be required.</p> <p>For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist is available on the PBS in combination with a 5HT₃ receptor antagonist and dexamethasone.</p> <p>As a steroid has been included as part of this protocol, additional antiemetic steroids are not required.</p> <p>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.</p> <p>Read more about preventing anti-cancer therapy induced nausea and vomiting</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>

Tumour lysis risk	Patients are at high risk of developing tumour lysis syndrome, prophylaxis is recommended. Read more about the prevention and management of tumour lysis syndrome .
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Read more about prophylaxis of pneumocystis jirovecii (carinii) in cancer patients
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Blood tests	FBC, EUC, eGFR, LFTs, LDH and BSL baseline then 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. 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. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook . 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. 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.

Haematological toxicity

Dose reduction may be required at the discretion of the Haematologist

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

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

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	<p>Interaction with both CYP3A4 and P-gp inhibitors /inducers.</p> <p>DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).</p>	<p>Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers.</p> <p>Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors.</p> <p>Dabigatran: avoid combination with strong P-gp inducers and inhibitors.</p> <p>If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.</p>
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-HT ₃ receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	<p>Avoid combination.</p> <p>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</p>
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	<p>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.</p> <p>For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook</p>

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

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.

Prime IV line(s).

Access [TIVAD](#) or [CVAD](#).

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

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

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.


Chemotherapy - Time out

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.

Intrathecal methotrexate

 Intrathecal methotrexate is to be administered today. The intrathecal procedure is to be done separately to the IV administration of all other cytotoxic drugs

Read more about the [procedure for intrathecal methotrexate administration](#).

Post intrathecal care:

Local policies and guidelines regarding bed rest post dural puncture should be adhered to. At a minimum:

- the patient should have at least 1 set of observations including:
 - vital signs and GCS
 - any abnormal neurological signs such as nausea, vomiting, chills, fever, confusion, headache or other changes in neurological status
- educate the patient to recognise and immediately report any adverse reactions including blurred vision, dizziness, pain and or headache
- observe the lumbar puncture site for any leakage or bleeding post procedure
- document the procedure including outcomes in the patients notes

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

Day 2 to 5

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
- daily dipstick urinalysis
- strict fluid balance

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

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.

Chemotherapy - Time out

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.

Deaccess [TIVAD](#) or [CVAD](#).

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

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)	
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
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

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
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.
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
Fatigue	Read more about fatigue

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

Delayed (onset months to years)	
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

Evidence

This GMALL B-ALL/NHL 2002 protocol was developed for treatment of mature B-ALL and Burkitt lymphoma and evolved from 3 preceding protocols: B-NHL83, B-NHL86 and B-NHL90.¹ The GMALL study group developed these protocols based on concepts employed successfully in the treatment of paediatric mature B-ALL. All used short, alternating cycles of intensive chemotherapy (in an ABABAB pattern) that included high doses of methotrexate and cyclophosphamide. The B-NHL90 protocol incorporated an increase in methotrexate doses to 3 g/m² but this did not result in improvement in outcomes when compared with B-NHL86.¹

GMALL B-ALL/NHL 2002 differs from the preceding protocols in the addition of 8 doses of rituximab and of cycle C, incorporating high dose cytarabine and methotrexate for patients ≤55 years (changing the schedule to ABCABC).^{1,2} The methotrexate dose is reduced back to 1.5 g/m². In patients over 55 years, no high dose cytarabine is given and the methotrexate dose is 500 mg/m² (schedule ABABAB).² In all patients with stage I/II disease and CR after 2 cycles, treatment is abbreviated to 4 cycles.² In addition to the chemo-immunotherapy, the GMALL group recommend radiation therapy to the CNS (24Gy; for CNS involvement) and to large mediastinal tumours (36Gy; >7.5 cm mass).²

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Oriol et al. 2008 ³	Yes	Yes	
Prospective study	Intermesoli et al. 2013 ⁴	Yes	Yes	
	Hoelzer et al. 2014 ²	Yes	Yes	
Observational studies	N/A	N/A	N/A	

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Guidelines	Date published/revised	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
NCCN	N/A	N/A	N/A	
BCCA	N/A	N/A	N/A	
CCO	N/A	N/A	N/A	

Efficacy

The outcomes of 363 patients with Burkitt Lymphoma and Burkitt's Leukaemia (mature B cell or L3-ALL) treated with the GMALL B-ALL/NHL 2002 protocol were reported in 2014.² The complete remission (CR) rate was 88% with 5 year progression free survival (PFS) 75% and overall survival (OS) 80%. There were significant differences in CR, PFS and OS between the ≤55 years and >55 years groups (see table).

Table 2. Overall results in Burkitt lymphoma/leukemia patients according to age: 15 to 55 years and older than 55 years

	Total	Age group, y		P
		15 to ≤55	>55	
No. of patients	363	265	98	
Response				
CR	319 (88)	237 (89)	82 (84)	.0002
PR	13 (4)	9 (3)	4 (4)	
Failure/progression	16 (4)	15 (6)	1 (1)	
Death	15 (4)	4 (2)	11 (11)	
Outcome of CR patients				
Relapse	37 (12)	20 (8)	17 (21)	
Death in CR	2 (1)	2 (1)	0	
PFS	0.75 ± 0.03	0.82 ± 0.03	0.60 ± 0.05	<.0001
OS	0.80 ± 0.02	0.86 ± 0.02	0.62 ± 0.02	<.0001

Values are n (%) or mean ± standard deviation.

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Multivariate analysis revealed the following factors predicted overall survival in this group of patients: age (≤55 vs >55 years), bone marrow involvement, LDH, and gender.²

The GMALL B-ALL/NHL 2002 protocol has been trialled by other groups. The Northern Italy Leukemia Group (NILG) treated 105 patients with Burkitt lymphoma and leukaemia (mature B-ALL, 48%) with GMALL B-ALL/NHL 2002.⁴ Twenty-five percent of their cohort were over 55 years old, 14% were HIV positive and 37% had an ECOG >1.⁴ The CR rate was 79%, 3 year OS 67% and disease free survival (DFS) 75%. Outcomes were better in the younger group (≤60 years), with OS 75% and DFS 82%. On multivariate analysis, the two significant indicators of prognosis were age (≤60 vs >60 years) and performance status (0-1 vs >1).⁴

Oriol et al also reported CR rates of 84 to 88% in 36 patients with Burkitt's lymphoma/leukaemia treated with the GMALL regimen. Nineteen (56%) of the patients were HIV positive and there were no significant differences in response rates or 2 year survival in the HIV positive, compared with negative, patients.³

Toxicity

The GMALL group listed the major grade 3 and 4 toxicities of the GMALL B-ALL/NHL 2002 protocol as haematological, especially grade 3-4 neutropenia during cycle A1, and infections (occurring in 38% of patients in cycle A1). Liver toxicity was most common during the first cycle and grade 3/4 mucositis was common during the first 2 cycles.² Therapy related deaths occurred in 2% of the ≤55 years patients but 11% of the >55 group, with >90% of deaths caused by infection.²

The NILG reported treatment related mortality in 14 (of 105) patients during induction (79% due to infection) and 5 patients during consolidation therapy. Severe neutropenia (<0.5x10⁹/L) was present for a median of 7 days (0-25) in ≤55 year olds and 8 days (0-23) in the older patients. Thrombocytopenia (<20x10⁹/L) was present for a median of 3(0-45) and 5(0-32) days respectively.⁴ The

rate of infection was 48%. Chemotherapy-induced mucositis and severe infections were more common in HIV positive patients compared with HIV negative.³

References

1

Gokbuget, N., D. Hoelzer, R. Arnold, et al. 2000. "Treatment of Adult ALL according to protocols of the German Multicenter Study Group for Adult ALL (GMALL)." Hematol Oncol Clin North Am 14(6):1307-1325, ix.

2

Hoelzer, D., J. Walewski, H. Dohner, et al. 2014. "Improved outcome of adult Burkitt lymphoma/leukemia with rituximab and chemotherapy: report of a large prospective multicenter trial." Blood 124(26):3870-3879.

3

Oriol, A., J. M. Ribera, J. Bergua, et al. 2008. "High-dose chemotherapy and immunotherapy in adult Burkitt lymphoma: comparison of results in human immunodeficiency virus-infected and noninfected patients." Cancer 113(1):117-125.

4

Intermesoli, T., A. Rambaldi, G. Rossi, et al. 2013. "High cure rates in Burkitt lymphoma and leukemia: a Northern Italy Leukemia Group study of the German short intensive rituximab-chemotherapy program." Haematologica 98(11):1718-1725.

History

Version 3

Date	Summary of changes
08/11/2016	Approved and published on eviQ
31/05/2017	Transferred to new eviQ website. Version number change to V.2.
21/09/2018	Reviewed by Haematology Reference Committee with no significant changes, review in 1 year. Version number changed to V.3.
13/09/2019	Reviewed by Haematology Reference Committee, no changes made. Review in 5 years.
24/01/2022	Pulmonary toxicity added to side effects.
11/11/2022	Reviewed electronically by the Haematology Reference Committee. Minor formatting changes. Review in 2 years.

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](http://www.eviq.org.au)

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<https://www.eviq.org.au/p/1915>
26 Nov 2023

Patient information - GMALL 2002 pre-phase (patients under 55 years)

Patient's name:


Your treatment

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

GMALL 2002 pre-phase (patients under 55 years)			
This treatment cycle is given ONCE only.			
Day	Treatment	How it is given	How long it takes
1 to 5	Prednisolone (pred-NIS-oh-lone)	Take orally ONCE a day in the morning with food on days 1 to 5. If you forget to take your tablets or vomit your tablets, contact your treating team.	
	Cyclophosphamide (SYE-kloe-FOS-fa-mide)	By a drip into a vein	About 1 hour
1	Methotrexate (intrathecal) (meth-o-TREX-ate)	By injection into your spine	About 4 hours

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 Ask your doctor or nurse from your treating team who to contact if you have a problem
<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• you become unwell.	Daytime:..... Night/weekend:..... 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).

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

You will need to have a blood test before you start treatment and regularly throughout your treatment. 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.

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.

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.
- **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.

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)	
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.
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.
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.

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.
Bladder irritation (haemorrhagic cystitis)	<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.
Tiredness and lack of energy (fatigue)	<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.
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

Delayed (onset months to years)

Lung problems

- Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment.
- You may get:
 - 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
- 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

