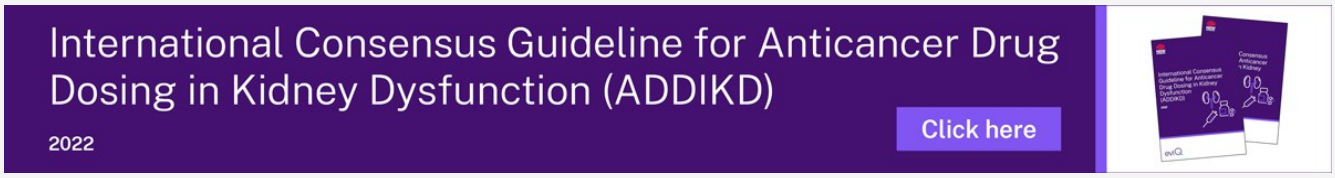
NK T-Cell lymphoma DDGP (dexamethasone ciSplatin gemcitabine pegaspargase)

ID: 3803 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.



Related pages:

- Management of asparaginase therapy

Treatment schedule - Overview

Cycle 1 to 6

Drug	Dose	Route	Day
Dexamethasone	15 mg/m^2 ONCE a day	IV/PO	1 to 5
Pegaspargase	2,500 Units/m^2 *	IM **	1
Gemcitabine	800 mg/m^2	IV infusion	1 and 8
ciSplatin	20 mg/m^2	IV infusion	1 to 4
Pegfilgrastim ***	6 mg	Subcut	9

* Pegaspargase dose 2500 units/m^2 based on studies by Li et al.[1] and Zhang et al.[2]
** Intramuscular (IM) injection is the preferred route of administration due to the lower incidence of hepatotoxicity, coagulopathy, and gastrointestinal and kidney disorders, compared to the intravenous route.[3, 4] Pegaspargase can be administered intravenously over 1 - 2 hours.
*** Pegfilgrastim or equivalent G-CSF can be used. If bone pain develops consider switching to a daily G-CSF alternative for next cycle.

Frequency: 21 days

Cycles: 3 or 4 for early stage; 6 cycles for advanced stage or relapsed/refractory disease (unless disease progression or unacceptable toxicity).

Notes:
For newly diagnosed early stage disease, radiation therapy was administered following completion of DDGP treatment.[5, 6, 7]

Drug status: **Cisplatin, gemcitabine, dexamethasone** are on the PBS general schedule

Filgrastim: (PBS authority)

Pegaspargase: Not TGA approved or PBS reimbursed for this indication

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

Treatment schedule - Detail

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

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

Cycle 1 to 6

Day 1		
Dexamethasone	15 mg/m^2 (IV/PO)	ONCE a day orally in the morning with food OR by IV infusion on days 1 to 5.
Granisetron	2 mg (PO)	60 minutes before chemotherapy
Pegaspargase	2,500 Units/m^2 (IM)	inject intramuscularly. Rotate site of administration.*
Gemcitabine	800 mg/m^2 (IV infusion)	in 100 mL to 500 mL sodium chloride 0.9% over 30 minutes
ciSplatin	20 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 60 minutes

Day 2 to 4		
Dexamethasone	15 mg/m^2 (IV/PO)	ONCE a day orally in the morning with food OR by IV infusion on days 1 to 5.
Granisetron	2 mg (PO)	60 minutes before chemotherapy
ciSplatin	20 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 60 minutes

Day 5		
Dexamethasone	15 mg/m^2 (IV/PO)	ONCE a day orally in the morning with food OR by IV infusion on days 1 to 5.

Day 8		
Gemcitabine	800 mg/m^2 (IV infusion)	in 100 mL to 500 mL sodium chloride 0.9% over 30 minutes

Day 9		
Pegfilgrastim	6 mg (Subcut)	inject subcutaneously on day 9 at least 24 hours after chemotherapy**

*Intramuscular (IM) injection is the preferred route of administration due to the lower incidence of hepatotoxicity, coagulopathy, and gastrointestinal and kidney disorders, compared to the intravenous route.[3, 4] Pegaspargase can be administered intravenously over 1 - 2 hours. Pegaspargase dose 2500 units/m^2 based on studies by Li et al.[1] and Zhang et al.[2]

**Pegfilgrastim or equivalent G-CSF (filgrastim or lipegfilgrastim) can be used. If bone pain develops consider switching to a daily G-CSF alternative for next cycle.

Frequency: 21 days

Cycles: 3 or 4 for early stage; 6 cycles for advanced stage or relapsed/refractory disease (unless disease progression or unacceptable toxicity).

Indications and patient population

Indications:

- Newly diagnosed early- or advanced-stage, or relapsed/refractory extranodal NK/T-cell lymphoma

Contraindications

Pegaspargase should not be used in patients who have:

- previous anaphylaxis or severe hypersensitivity to asparaginase formulations
- severe hepatic impairment
- existing or a history of pancreatitis
- previous haemorrhagic or severe thrombotic events

Cautions/exclusions:

- CNS involvement
- Pegaspargase should be used with caution in patients over 40 years of age and those with a body mass index (BMI) greater than 30 due to an increased risk of side effects.

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with pegaspargase. Hypersensitivity reactions may occur, e.g. life-threatening anaphylaxis, particularly in patients with known hypersensitivity to the other forms of asparaginase. Adequate medical treatment and provisions should be available for immediate use in the event of an anaphylactic reaction. Patients that develop hypersensitivity to the E. coli derived formulation may be able to switch to Erwinia asparaginase. Read more about Management of asparaginase therapy Read more about Hypersensitivity reaction
Antiemetics for multi-day protocols	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. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Pulmonary toxicity	Dyspnoea developing within hours of the infusion has been reported in about 10% of patients treated with gemcitabine. Read more about pulmonary toxicity associated with anti-cancer drugs.
Hydration	Hydration helps to prevent cisplatin-induced nephrotoxicity. The default regimen is appropriate for patients with normal electrolytes, kidney function, fluid status etc. and should be adjusted according to individual requirements. Read more about cisplatin hydration regimens

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. Ototoxicity may become more severe in patients being treated with other drugs with nephrotoxic potential e.g. aminoglycosides. An audiometry test should be performed if symptoms develop. Read more about ototoxicity - tinnitus and hearing loss
Pegaspargase	Pegaspargase is associated with numerous toxicities including hypersensitivity, hepatotoxicity, coagulation abnormalities, pancreatitis, hyperlipidaemia, hyperglycaemia and CNS effects. Therefore routine monitoring and assessment of several parameters are required throughout treatment. For comprehensive information on formulations, dosing, interactions, adverse reactions and specific monitoring parameters for asparaginase, see Management of asparaginase therapy document.
Pancreatitis	Pancreatitis (both haemorrhagic or necrotising) has been reported in patients receiving pegaspargase with fatal outcomes. If pancreatitis is suspected pegaspargase should be discontinued and not restarted if confirmed. Serum amylase and/or lipase measurements should be performed frequently to identify early signs of pancreatic inflammation. If treatment is discontinued due to pancreatitis, appropriate investigations (e.g. ultrasound) should be performed at least four months following termination of therapy.
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. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Thrombotic events	Serious thrombotic events may occur in patients receiving pegaspargase and should be discontinued if they occur. Increased prothrombin time (PT), increased activated partial thromboplastin time (APTT), and hypofibrinogenaemia may occur in patients receiving pegaspargase. A baseline coagulation profile (including antithrombin III) should be established and periodically monitored during and after treatment. Patients should be on thromboprophylaxis with enoxaparin to prevent thrombotic events unless contraindicated. Read more about Management of asparaginase therapy
Hepatotoxicity	Caution is required when pegaspargase is given in combination with other hepatotoxic substances. If pegaspargase is given in combination with hepatotoxic substances, the patient should be closely monitored for liver impairment, especially if there is pre-existing hepatic impairment.
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. Read more about acute short term effects from corticosteroids
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	PJP prophylaxis is recommended e.g. trimethoprim/sulfamethoxazole 160/800 mg PO one tablet twice daily, twice weekly (e.g. on Mondays and Thursdays) OR one tablet three times weekly (e.g. on Mondays, Wednesdays and Fridays). Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Antifungal prophylaxis	Antifungal prophylaxis is recommended. Read more about antifungal prophylaxis drugs and doses.
Biosimilar drug	Read more about biosimilar drugs on the Biosimilar Awareness Initiative page

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. Access the PBS website
Blood tests	FBC, EUC, BSL, LDH, uric acid, albumin, triglycerides and total cholesterol levels at baseline and prior to each cycle. LFTs, bilirubin, lipase, amylase, APTT, PT, INR, fibrinogen, antithrombin III levels at baseline and at least once or twice a week 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 .

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	
ANC x 10^9/L (pre-treatment blood test)	
less than 1.0	Delay treatment for 1 week* If after 1 week:

Haematological toxicity	
	• ANC < 1.0 but ≥ 0.5, consider proceeding with treatment • ANC < 0.5, delay treatment until ANC ≥ 0.5
Platelets x 10^9/L (pre-treatment blood test)	
Less than 75	Delay treatment for 1 week.* If after 1 week: • platelets < 75 but ≥ 50, consider proceeding treatment with platelet transfusions as necessary • platelets <50, delay treatment until platelets ≥ 50
Day 8: Platelets x 10^9/L (pre-treatment blood test)	
Less than 75 and greater or equal to 50	Reduce gemcitabine by 25% from this cycle's day 1 dose
Less than 50	Omit gemcitabine and pegaspargase

*If counts presume to be low due to marrow involvement, treat after 1 week delay (i.e. at 4 weeks or day 28) despite counts

Non-haematological toxicity	
Grade 2†	No dose reduction required
Grade 3††	Reduce gemcitabine and cisplatin by 25%
Grade 4	Delay treatment until recovery and consider resuming at a reduced dose at the clinician's discretion.

† Except grade 2 pneumonitis thought to be secondary to gemcitabine, discontinue gemcitabine permanently.

†† In the event of grade 3 tinnitus, reduce cisplatin dose only

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	Consider reducing cisplatin by 25%
less than 30	Omit cisplatin and consider gemcitabine dose reduction.

Hepatic impairment	
Hepatic dysfunction	
Moderate	Consider gemcitabine dose reduction if bilirubin>27 micromol/L
Severe	Pegaspargase contraindicated if bilirubin > 3 x ULN or transaminases > 10 x ULN

Cease treatment if any one of the following develops:
• Pulmonary toxicity • Severe hypersensitivity reaction or anaphylaxis • Thrombotic microangiopathy (TMA)/haemolytic uraemic syndrome (HUS) • Grade 4 non-haematologic toxicities • Elevations of serum creatinine levels greater than 200 mmol/L

Pegaspargase-related reactions	
Grade 1 local allergic reactions not requiring intervention	Continue pegaspargase
Grade 2 or greater systemic reactions	Consider discontinuation of pegaspargase and substitute with erwinia asparaginase if available
Grade 3 or 4 allergic reaction/hypersensitivity (such as	Discontinue pegaspargase, if discontinued due to allergy/hypersensitivity only, consider changing to erwinia asparaginase.

Pegaspargase-related reactions	
anaphylaxis), pancreatitis or thrombotic events	
Pegaspargase should not be withheld for asymptomatic coagulation laboratory abnormalities. Cryoprecipitate and anti-thrombin III infusions may be required.	

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)

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

Gemcitabine		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Warfarin	Increased anticoagulant effect/increased bleeding risk due to decreased hepatic metabolism of warfarin and decreased synthesis of clotting factors	Monitor INR regularly and adjust warfarin dosage as appropriate
Cytidine deaminase (CDA) inhibitors (e.g. cedazuridine)	Increased effect/toxicity of gemcitabine possible due to reduced clearance	Avoid combination or monitor for increased gemcitabine effect/toxicity

Pegaspargase		
There are no documented interactions for pegaspargase. However, a range of clinical effects can occur due to the mechanism of action of pegaspargase.		
Clinical effect	**Action**	**Clinical management**
Effect on use with other chemotherapy agents	Pegaspargase may affect the action of other cytotoxic drugs requiring cell division for their effect (i.e. methotrexate, cytarabine). This effect can be either synergistic or antagonistic, depending on the timing of administration of the agents.	Adherence to the treatment schedule is recommended to minimise these potential interactions.
	Immediately preceding or concomitant treatment with vincristine can increase the toxicity of pegaspargase and increases the risk of anaphylactic reactions.	Administer vincristine 12 hours prior to pegaspargase to minimise toxicity.
Effects on protein-bound drugs	Due to its effects on protein synthesis and hepatic function, pegaspargase can potentially interfere with metabolism and clearance of other drugs including chemotherapy drugs known to interact with CYP enzymes.	Monitor for hepatotoxicity if used concomitantly.
Coagulation effects	Use of pegaspargase can lead to fluctuating levels of coagulation factors. This may increase the risk of bleeding and/or thrombosis.	Caution is needed when anticoagulants are given concomitantly.
	Alterations in coagulation parameters can be more pronounced when glucocorticoids (e.g. prednisolone) and pegaspargase are given concomitantly.	Monitor levels of coagulation parameters such as fibrinogen and ATIII
Oral contraceptive effects	Pegaspargase hepatotoxicity may impair the hepatic clearance of oral contraceptives.	Concomitant use of pegaspargase and oral contraceptives is not recommended. A method other than oral contraception should be used in women of childbearing potential
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

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

Administration

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

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.

Prime IV line(s) with sodium chloride 0.9%.

Insert IV cannula or access TIVAD or CVAD.

- baseline weight

Dexamethasone

- administer orally ONCE a day in the morning with food **OR**
- via IV infusion over 15 minutes on **days 1 to 5**
- flush with ~ 50mL sodium chloride 0.9%

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Pegaspargase

- administer via intramuscular (IM) injection (alternatively may be administered intravenously over 1 to 2 hours)
- when administered IM, the volume at the injection site should be less than or equal to 2 mL; if volume to administer is larger than 2 mL, use multiple injection sites and ensure site rotation

Note: monitor patient during and for one hour after drug administration, as anaphylaxis may occur. Ensure immediate access to emergency / adverse-reaction kit is available.

Gemcitabine

Administer gemcitabine (irritant):

- via IV infusion over 30 minutes
  - if pain develops along the vein, verify the drug has not extravasated
  - further dilution (using a second saline line), warmth or temporarily slowing the infusion may help
- flush with ~ 100 mL of sodium chloride 0.9%
- prolonged infusion times have been shown to increase toxicity.

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 60 minutes
- flush with 100 mL of sodium chloride 0.9%.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Days 2 to 4

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.

Prime IV line(s) with sodium chloride 0.9%.

Insert IV cannula or access TIVAD or CVAD.

Dexamethasone

- administer orally ONCE a day in the morning with food **OR**
- via IV infusion over 15 minutes on **days 1 to 5**
- flush with ~ 50mL sodium chloride 0.9%

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

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 60 minutes
- flush with 100 mL of sodium chloride 0.9%.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Day 8

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Prime IV line(s) with sodium chloride 0.9%.

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Gemcitabine

Administer gemcitabine (irritant):

- via IV infusion over 30 minutes
  - if pain develops along the vein, verify the drug has not extravasated
  - further dilution (using a second saline line), warmth or temporarily slowing the infusion may help
- flush with ~ 100 mL of sodium chloride 0.9%
- prolonged infusion times have been shown to increase toxicity.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Day 9

Pegfilgrastim

- administer subcutaneously at least 24 hours post chemotherapy.

Discharge information

Dexamethasone tablets

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

Antiemetics

- Antiemetics as prescribed.

Antidiarrhoeals

- Antidiarrhoeals as prescribed.

Growth factor support

- Arrangements for administration if prescribed.

Patient information

- Ensure patient receives patient information sheet.

Prophylaxis medications

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

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)	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Flu-like symptoms	
Injection-site reactions	Inflammation of or damage to the tissue surrounding the area where a drug was injected.
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Taste and smell alteration	Read more about taste and smell changes
Early (onset days to weeks)	

Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Hyperbilirubinaemia	An abnormal increase in the amount of bilirubin circulating in the blood which may result in jaundice.
Hyperglycaemia	High blood sugar, an excess of glucose in the blood stream.
Hyperlipidaemia and hypercholesterolaemia	Abnormally elevated levels of lipids and cholesterol in the blood.
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). 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. Read more about ototoxicity - tinnitus and hearing loss
Pancreatitis	Inflammation of the pancreas with impairment of function is associated with asparaginase formulations.
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
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
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. Read more about skin rash
Thromboembolism	Serious thromboembolic events can occur in patients receiving pegaspargase. The majority of thromboses occur in the CNS. Patients should be carefully assessed for risk factors with baseline and regular monitoring of coagulation profile (including PT, APTT, fibrinogen, antithrombin III) during and after treatment. Antithrombotic prophylaxis is recommended. Read more about Management of asparaginase therapy

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia - partial	Hair thinning and/or patchy hair loss. 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

Evidence

Treatment results for extranodal natural killer/T-cell lymphoma (ENKTL) have historically been poor. With CHOP and CHOP-like chemotherapy, median survival is only 2-7.8 months with 5-year overall survival (OS) of ~30%.[2] The poor outcome is partly due to NK-cell expression of high levels of multi-drug resistant (MDR) P-glycoprotein, so that anthracycline-containing regimens are ineffective. Standard of care for advanced stage ENKTL has been SMILE (dexamethasone, methotrexate, ifosfamide, asparaginase and etoposide), based on a phase II study of 38 patients[8] and a phase II multicentre study in a non-trial setting of 87 patients.[9] These studies have shown an overall response rate (ORR) of 79-81% and complete response (CR) of 50-56% after 2-3 cycles. 5-year OS was 50%, and 4-year disease-free survival (DFS) was 64%. SMILE has significant toxicity, with grade III/IV neutropenia in 72.7% and a treatment-related mortality (TRM) of 7%.

The DDGP protocol was developed due to toxicity issues related to SMILE, as well as the high rates of hypersensitivity reactions to L-asparaginase. The expert reference panel supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by the randomised controlled, open-label, multicentre study published in 2016 by Li et al. comparing DDGP and SMILE in 42 advanced stage, newly diagnosed patients.[1] An abstract of the follow-up to this study was presented at ASH 2019.[10] A total of 80 patients with newly diagnosed advanced stage ENKTL with an ECOG of 0-2 and aged between 14 and 70 years old were recruited between 2011 and 2019. Patients were randomised 1:1 to SMILE or DDGP, and given up to 6 cycles unless disease progression, unacceptable toxicity or patient choice.

Zhang et al. published a retrospective study of 80 patients in 2016, with 60% of patients being newly diagnosed, 11% in first relapse, and 29% in a primary refractory disease.[2] Of the newly diagnosed, 42% were stage I-II and the remainder were stage III-IV. More recently, DDGP has also been trialled in early-stage disease. A randomised, controlled, open-label, multicentre study compared DDGP combined with radiation therapy (RT) vs RT alone in newly diagnosed stage I-II NKTL.[5] Published in 2021, the study reported on 65 patients, with 35 patients receiving RT alone, and 30 treated with DDGP and RT. Another prospective cohort study from 2011 to 2016 examined effects of DDGP followed by RT (DDGP+RT) versus VIPD followed by RT (VIPD+RT) in 40 newly diagnosed stage I-II ENKTL patients.[6]

A real-world retrospective analysis of 376 patients on asparaginase-based vs non-asparaginase-based chemotherapy combined with RT in the treatment of early-stage ENKTCL demonstrated a significantly improved 5-year OS (84.5% vs 73.2%) and distant metastasis-free survival (84.4% vs 74.5%) with the asparaginase-based regimen in intermediate- to high-risk patients.[7] Out of the asparaginase-based group, 13 patients had DDGP overall, and 8 were in the intermediate- to high-risk group. Other asparaginase-based regimens included were GELOX, P-GEMOX and GDP-L.

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Li et al. 2016[1]	**Yes**	Yes	Newly diagnosed, advanced stage.
	Wang et al. 2019[10] (Abstract)	**Yes**	Yes	Newly diagnosed, advanced stage.

	Zhang et al. 2021[5]	**Yes**	Yes	Newly diagnosed, early stage
Observational studies	Zhang et al. 2016[2]	**Yes**	Yes	Newly diagnosed, relapsed and primary refractory. 25% stage I-II.
	Wang et al. 2021[11]	**Yes**	Yes	Relapsed/refractory
	Zhang et al. 2022[6]	**Yes**	Yes	Newly diagnosed, early stage
	Zheng et al. 2021[7]	**Yes**	N/A	Newly diagnosed, early stage

Guidelines	Date published/revised	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
NCCN	V 1.2022	**Yes**	N/A	Consider clinical trial, DDGP, modified SMILE or P-GEMOX for induction in advanced disease
BCCA	N/A	**N/A**	N/A	N/A
CCO	Jan 2022	**Yes**	Yes	N/A

Efficacy

For advanced stage, newly diagnosed ENKTL, Li et al. reported an overall response rate (ORR) of 95% vs 67% for SMILE; and a complete response (CR) of 71% vs 29% for SMILE. 1-year (overall survival) OS was 90% vs 57% for DDGP vs SMILE and progression-free survival (PFS) 86% for DDGP vs 38% for SMILE. 2-year OS was 74% vs 45% for DDGP and SMILE, respectively. The response rates for SMILE were significantly lower than those reported in previous clinical trials.[1] In the follow-up study, the ORR was significantly higher in DDGP vs SMILE (90% vs 60%), but there was no significant difference in CR (67.5% for DDGP vs 47.5% for SMILE). The 3-year PFS was 56.6% for DDGP and 41.8% for SMILE; 5-year OS 74.3% for DDGP and 51.7% for SMILE.[10]

Figure 1.Overall survival (A) and progression-free survival (B) curves[1]

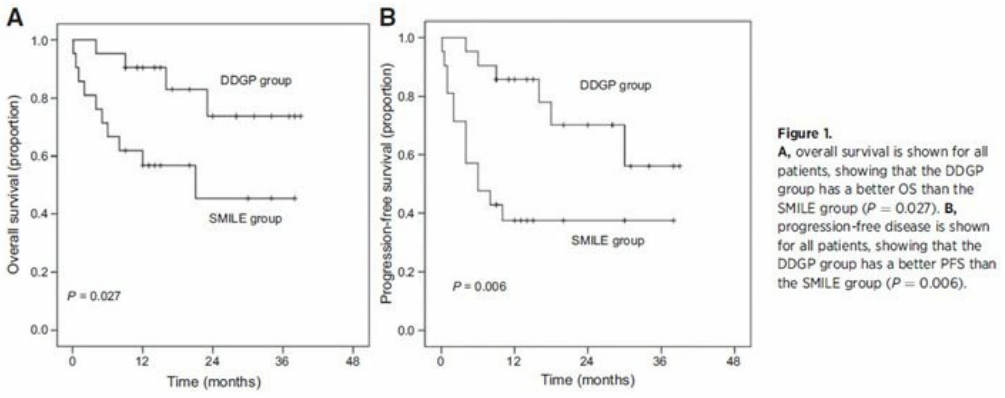


Figure 1.
A, overall survival is shown for all patients, showing that the DDGP group has a better OS than the SMILE group ($P = 0.027$). **B,** progression-free disease is shown for all patients, showing that the DDGP group has a better PFS than the SMILE group ($P = 0.006$).

The 2016 retrospective study by Zhang et al. reported an ORR of 91.3% and CR of 60%. The 1-year OS and PFS were 88.6% and 86.1%, and 2-year OS and PFS were 87% and 81%.[2] Another retrospective study of 54 patients with relapsed/refractory disease treated with either DDGP or SMILE in 2021 demonstrated that the 31 patients who received DDGP had a higher CR rate (61.3% vs 30.4%) and 5-year PFS (45.4% vs 27.6%) and 5-year OS (50.1% vs 32.5%) compared to the SMILE group.[11] There was no significant difference in the ORR (83.9% vs 60.9%) between the two groups.

The 2021 study by Zhang et al. comparing DDGP+RT versus RT alone reported the combined modality group having superior CR (73.3% vs 48.6%) and ORR (83.3% vs 60%). 5-year PFS (82.9% vs 56.5%) and OS (85.7% vs 60.4%) were also significantly better in the combined modality group.[5] Another prospective cohort study comparing DDGP+RT and VIPD+RT reported better CR rate (85% vs 50%) and OR rate (95% vs 65%) in the DDGP+RT arm .[6] Whilst 5-year PFS was better in the DDGP+RT group (83.3% vs 44.4%), there was no significant difference in the 5-year OS between the two groups (83.0% vs 72.1%).

Toxicity

Li et al. reported significantly fewer adverse events in the DDGP arm; particularly lower rates of leukopenia, neutropenia, hypersensitivity reactions and gastrointestinal side effects.[1] DDGP had higher rates of anaemia and coagulation abnormalities. Grade 3 or 4 leukopenia occurred in 13 patients (54%) with DDGP, compared to 19 (90%) with SMILE. Grade 3 or 4 anaemia occurred in 11 (52%) and thrombocytopenia in 13 (62%). There were no documented cases of allergic reactions with DDGP, but they occurred in 7 patients (33%) in the SMILE group. There were no reported deaths.

Adverse effects between DDGP and SMILE groups[1]

Table 5. Adverse effects between DDGP and SMILE groups

Toxicity	Grade of adverse reaction						P
	DDGP ($n = 21$)			SMILE ($n = 21$)			
Grade	0	1–2	3–4	0	1–2	3–4	
Hematologic							
Leukopenia	0	8	13	0	2	19	0.030
Neutropenia	0	6	15	0	3	18	0.259
Anemia	0	10	11	5	10	6	0.039
Thrombocytopenia	4	4	13	3	7	11	0.569
Non-hematologic							
Hypofibrinogenemia	9	12	0	13	8	0	0.217
Prolonged APTT	9	12	0	14	7	0	0.121
Hyperbilirubinemia	15	5	1	18	1	2	0.195
ALT elevation	6	15	0	9	9	3	0.078
AST elevation	10	11	0	12	7	2	0.215
Creatinine	21	0	0	17	3	1	0.110
BUN	20	1	0	17	3	1	0.326
Nausea	0	16	5	0	16	5	1.000
Vomiting	0	16	5	0	16	5	1.000
Diarrhea	21	0	0	18	0	3	0.072
Mucositis	21	0	0	18	1	2	0.199
Baldness	9	9	3	5	12	4	0.424
Allergy	21	0	0	14	5	2	0.015
Heart failure	21	0	0	19	0	2	0.147
Arrhythmia	21	0	0	20	1	0	0.311

NOTE: *P*, Mann–Whitney test.
Abbreviations: ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen.

In the expanded cohort, grade 3 or 4 haematologic toxicity occurred in 25 patients (62.5%) compared to 34 (85%) in the SMILE group.[10] Grade 3 or 4 neutropenia occurred in 26 patients (65%). Non-haematologic toxicity including elevated transaminases, mucositis or allergic reactions did not occur with DDGP in this study. A ~10% treatment-related mortality was reported for DDGP, compared to 17.5% with SMILE, both significantly higher compared to previous studies. These were mainly due to infection and haemorrhage in the SMILE group.

Wang et al. reported no episodes of allergic reaction or pancreatitis. 49% had prolonged APTT and 41% hypofibrinogenaemia.[11] Grade 3 - 4 neutropenia occurred in 65% of patients, grade 4 thrombocytopenia in 35% and grade 4 anaemia in 5%. There were no treatment-related deaths. If there was a grade 4 toxicity, doses were reduced not more than 20% for subsequent cycles.

For early stage disease, reported adverse events of the DDGP+RT were as follows: grade 3 or 4 myelosuppression in 20-25%, grade 3 or 4 liver dysfunction in 3.3%, grade 3 or 4 gastrointestinal reactions in 16.7%, grade 3 or 4 alopecia in 16.7%.[5] There were no grade 3 or 4 coagulation abnormalities. It is noted that the RT only group was biased towards having more patient with a lower ECOG. Another study examining combined modality treatment noted the DDGP+RT group were more prone to grade I-II clotting dysfunction compared to the VIPD+RT group.[6]

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History

Version 3

Date	Summary of changes
11/11/2022	Reviewed by Haematology Reference Committee. Updates include: • Treatment schedule - notes about radiation therapy and pegaspargase dosing added, number of cycles updated • Indications - early-stage disease added • Clinical information - blood tests amended • Evidence - studies supporting early-stage disease added • Patient information - number of cycles For review in 4 years.

Version 2

Date	Summary of changes
22/09/2020	Biosimilar drug added to clinical information. Version number changed to v.2
22/10/2021	Electronically reviewed by Haematology Reference Committee; nil changes. Review in 2 years.
22/01/2022	Interactions updated.

Version 1

Date	Summary of changes
27/03/2020	New protocol presented at the Haematology Reference Committee meeting. Discussion continued over email and protocol approved for publication. For review in 1 year.

First approved: 27 March 2020
Last reviewed: 11 November 2022
Review due: 31 December 2026

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/3803
26 Nov 2023

Patient information - Natural killer/T-Cell lymphoma - DDGP (dexamethasone, cisplatin, gemcitabine, pegaspargase)

Patient's name:

Your treatment

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

DDGP (dexamethasone, cisplatin, gemcitabine, pegaspargase)

This treatment cycle is repeated every 21 days. You may have up to 6 cycles. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	**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 5 only. If you forget to take your tablets or vomit your tablets, contact your treating team.	About 15 minutes if given by a drip
	Pegaspargase (*peg-AS-par-jase*)	by injection into a large muscle	About 5 to 10 minutes
	Gemcitabine (*jem-sie-ta-been*)	By a drip into a vein	About 30 minutes
	Cisplatin (*siss-PLAT-in*)	By a drip into a vein	About 1 hour
2 to 4	**Dexamethasone**	By a drip into a vein **OR** take orally ONCE a day in the morning with food on days 1 to 5 only. If you forget to take your tablets or vomit your tablets, contact your treating team.	About 15 minutes if given by a drip
	Cisplatin	By a drip into a vein	About 30 minutes
5	**Dexamethasone**	By a drip into a vein **OR** take orally ONCE a day in the morning with food on days 1 to 5 only. If you forget to take your tablets or vomit your tablets, contact your treating team.	About 15 minutes if given by a drip
8	**Gemcitabine**	By a drip into a vein	About 30 minutes
9	**Granulocyte Colony Stimulating Factor** (*G-CSF*)	By injection under the skin	About 5 minutes

When to get help

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

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
• a temperature of 38ºC 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).

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

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **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.

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)	

Allergic reaction	• Allergic reactions are uncommon but can be life threatening.
	• **If you feel unwell during the infusion or shortly after it, or:**
	  ◦ **get a fever, shivers or shakes**
	  ◦ **feel dizzy, faint, confused or anxious**
	  ◦ **start wheezing or have difficulty breathing**
	  ◦ **have a rash, itch or redness of the face**
	
	<u>While you are in hospital:</u> Tell your doctor or nurse immediately.
	<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.

Flu-like symptoms	• You may get:
	  ◦ a fever
	  ◦ chills or sweats
	  ◦ muscle and joint pain
	  ◦ a cough
	  ◦ headaches.
	• The drug gemcitabine can cause a fever or flu-like illness within the first day or two of having the treatment.
	• You can take paracetamol to help settle these symptoms.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if the symptoms do not settle or you become unwell.**

Injection-site reaction	• At the injection site you may get pain, redness, swelling or bruising. • These symptoms are usually not serious. • **Tell your doctor or nurse immediately if you notice any redness or pain during or after treatment.**
Nausea and vomiting	• 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.**
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.
Early (onset days to weeks)	

Infection risk (neutropenia)	• 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:** ◦ **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)	• 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.**
Stomach pain	• You may get: ◦ dull aches ◦ cramping or pain ◦ bloating or flatulence (gas). • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have stomach pain that you are unable to control.**
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **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.**

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. • 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.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**
Liver problems	• You may get: ◦ yellowing of your skin or eyes ◦ itchy skin ◦ pain or tenderness in your stomach ◦ nausea and vomiting ◦ loss of appetite • You will have regular blood tests to check how well your liver is working. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**
High blood bilirubin levels (hyperbilirubinaemia)	• You may get: ◦ yellowing of your skin or eyes ◦ itchy skin ◦ pain or tenderness in your stomach ◦ nausea and vomiting ◦ loss of appetite. • You will have regular blood tests to check how well your liver is working. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**
High blood sugar level (hyperglycaemia)	• You may feel thirsty and need to urinate more often than normal. • You may get repeated infections, especially thrush. • If you are a diabetic you will need to have your blood sugar levels checked more often. You may also need to have your diabetes medication increased. • **Tell your doctor or nurse if you get any of the signs or symptoms listed above.**
High blood cholesterol levels	• This treatment may increase your blood cholesterol levels. This is not a side effect you will notice. • Your cholesterol levels will be checked during your treatment.

Low blood magnesium, potassium and calcium levels (hypomagnesaemia, hypokalaemia, hypocalcaemia)	• This may be found from your routine blood tests and treated by your doctor. • If it is severe you may get: ◦ muscle cramps or twitches ◦ numbness or tingling in your fingers, toes or around your mouth ◦ constipation ◦ an irregular heartbeat ◦ sleepy, drowsy or confused • **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. • You will have blood tests to make sure your kidneys are working properly. • 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. • **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: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Hearing changes (ototoxicity)	• You may get ringing in your ears or loss of hearing. • You may have your hearing tested before and during your treatment. • **Tell your doctor or nurse as soon as possible if you notice any changes to your hearing.**
Inflamed pancreas (pancreatitis)	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get:** ◦ **abdominal (stomach) pain** ◦ **a swollen stomach** ◦ **nausea or vomiting** ◦ **fever or chills** ◦ **a fast heartbeat.**

Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including:
	  ◦ tingling or pins and needles
	  ◦ numbness or loss of feeling
	  ◦ pain.
	• You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects.
	• Test water temperature with your elbow when bathing to avoid burns.
	• Use rubber gloves, pot holders and oven mitts in the kitchen.
	• Wear rubber shoes or boots when working in the garden or garage.
	• Keep rooms well lit and uncluttered.
	• Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment.
	• Tell your doctor or nurse if you get any of the symptoms listed above.

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.**

Side effects from steroid medication	• Steroid medication may cause:
	  ◦ 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.

Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

Blood clots (thromboembolism)	• Blood clots can occur with this 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:** ◦ **redness, heat or pain in your leg(s)** ◦ **numbness or weakness in your face, arm or leg** ◦ **chest pain** ◦ **sudden shortness of breath** ◦ **dizziness** ◦ **trouble speaking** ◦ **blurred vision** ◦ **severe headache** ◦ **unexplained falls or loss of balance.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• 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 thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)

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
- 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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https://www.eviq.org.au/pi/3803
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