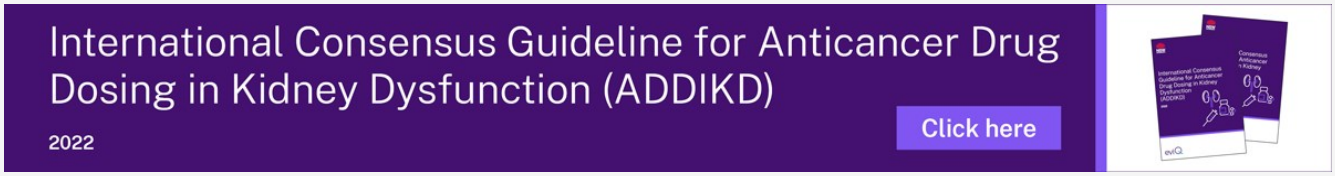
Acute lymphoblastic leukaemia Ph+ hyper CVAD Part B and daSATinib

ID: 3531 v.3 **Under review** Essential Medicine List

Patients with leukaemia should be considered for inclusion into clinical trials. Link to ALLG website and ANZCTR 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:

- Acute lymphoblastic leukaemia Ph+ hyper CVAD and daSATinib Part A and B/maintenance overview
- Acute lymphoblastic leukaemia Ph+ hyper CVAD part A and daSATinib
- Acute lymphoblastic leukaemia Ph+ maintenance therapy (daSATinib prednisolone vinCRISTine)
- CNS prophylaxis for acute lymphoblastic leukaemia hyper CVAD protocol

Treatment schedule - Overview

Cycle 2 and 4

Drug	Dose	Route	Day
daSATinib	70 mg ONCE a day	PO	1 to 21
Methylprednisolone sodium succinate	50 mg TWICE a day	IV infusion	1 to 3
Methotrexate	200 mg/m^2	IV infusion	1
Methotrexate	800 mg/m^2 over 22 hours	IV infusion	1
Calcium folinate (Leucovorin)	15 mg/m^2 every 6 hours *	IV infusion	2
Cytarabine (Ara-C)	3,000 mg/m^2 TWICE a day **	IV infusion	2 and 3
Methotrexate ***	12 mg	Intrathecal	2
Filgrastim	10 micrograms/kg	Subcut	4 and continue daily until neutrophil recovery
Cytarabine (Ara-C) ***	100 mg	Intrathecal	8

Cycle 6 and 8

Drug	Dose	Route	Day
daSATinib	70 mg ONCE a day	PO	1 to 21

Drug	Dose	Route	Day
Methylprednisolone sodium succinate	50 mg TWICE a day	IV infusion	1 to 3
Methotrexate	200 mg/m^2	IV infusion	1
Methotrexate	800 mg/m^2 over 22 hours	IV infusion	1
Calcium folinate (Leucovorin)	15 mg/m^2 every 6 hours *	IV infusion	2
Cytarabine (Ara-C)	3,000 mg/m^2 TWICE a day **	IV infusion	2 and 3
Filgrastim	10 micrograms/kg	Subcut	4 and continue daily until neutrophil recovery

* Every 6 hours until methotrexate level less than 0.1 micromol/L. Start 36 hours after commencement of methotrexate infusion

** For patients over 60 years, the cytarabine dose was reduced to 1000 mg/m^2 in the Kantarjian et al. studies[1, 2] (refer to 'dose modifications' section).

*** The total number of intrathecal (IT) treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol (i.e. IT therapy on cycles 1 and 3). The IT dose of methotrexate when given via an Ommaya reservoir is 6 mg.[1] Link to intrathecal CNS prophylaxis schedule .

Frequency: 21 days
Commence next cycle (i.e. Part A) after 21 days or when WCC is greater than 3 x10^9 and platelets are greater than 60 x10^9, whichever is earlier.

Cycles: 4
This hyper CVAD protocol consists of 4 cycles of Part B (Cycles 2, 4, 6, 8) alternating with 4 cycles of Part A (Cycles 1, 3, 5, 7) for a total of 8 cycles, followed by maintenance therapy for 2 years. Dasatinib is then continued indefinitely as a sole agent.

Notes:

- Methylprednisolone has been included in this protocol as in the Kantarjian et al. studies[1, 2] for consistency with the ALL Ph- Hyper CVAD protocol.
- Rituximab - in patients with CD20+ disease, a total of 8 doses of rituximab 375 mg/m^2 should be given on days 1 and 11 of hyper CVAD A and days 1 and 8 of hyper CVAD B for the first four cycles of treatment.[3]

Drug status: **Filgrastim** and **dasatinib:** PBS authority

All other drugs in this protocol are on the PBS general schedule

Dasatinib is available as **20 mg, 50 mg, 70 mg** and 1**00 mg** tablets

Cost: ~ $4,320 per cycle

Treatment schedule - Detail

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

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

Cycle 2 and 4

Day 1		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.
Methylprednisolone sodium	50 mg (IV infusion)	TWICE a day (every 12 hours) in 100 mL sodium

Day 1		
succinate		chloride 0.9% over at least 30 minutes
Methotrexate	200 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 2 hours
Methotrexate	800 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 22 hours

Day 2		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.
Methylprednisolone sodium succinate	50 mg (IV infusion)	TWICE a day (every 12 hours) in 100 mL sodium chloride 0.9% over at least 30 minutes
Calcium folinate (Leucovorin)	15 mg/m^2 (IV infusion)	start 36 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level less than 0.1 micromol/L
Cytarabine (Ara-C)	3,000 mg/m^2 (IV infusion)	in 500 mL to 1000 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours). For patients over 60 years, the cytarabine dose was reduced to 1000 mg/m2 in the Kantarjian et al. studies (refer to 'dose modifications' section).
Methotrexate	12 mg (Intrathecal)	adhere to local institution intrathecal policy. Total number of intrathecal treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol - see CNS prophylaxis schedule below* (dose is 6 mg if given via an Ommaya reservoir)

Day 3		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.
Methylprednisolone sodium succinate	50 mg (IV infusion)	TWICE a day (every 12 hours) in 100 mL sodium chloride 0.9% over at least 30 minutes
Cytarabine (Ara-C)	3,000 mg/m^2 (IV infusion)	in 500 mL to 1000 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours). For patients over 60 years, the cytarabine dose was reduced to 1000 mg/m2 in the Kantarjian et al. studies (refer to 'dose modifications' section).

Day 4		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.
Filgrastim	10 micrograms/kg (Subcut)	inject subcutaneously once daily starting day 4 and continue until neutrophil recovery.

Day 5 to 7		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.

Day 8		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.
Cytarabine (Ara-C)	100 mg (Intrathecal)	adhere to local institution intrathecal policy. Total number of intrathecal treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol - see CNS

Day 8		
		prophylaxis schedule below*

Day 9 to 21		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.

Cycle 6 and 8

Day 1		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.
Methylprednisolone sodium succinate	50 mg (IV infusion)	TWICE a day (every 12 hours) in 100 mL sodium chloride 0.9% over at least 30 minutes
Methotrexate	200 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 2 hours
Methotrexate	800 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 22 hours

Day 2		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.
Methylprednisolone sodium succinate	50 mg (IV infusion)	TWICE a day (every 12 hours) in 100 mL sodium chloride 0.9% over at least 30 minutes
Calcium folinate (Leucovorin)	15 mg/m^2 (IV infusion)	start 36 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level less than 0.1 micromol/L
Cytarabine (Ara-C)	3,000 mg/m^2 (IV infusion)	in 500 mL to 1000 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours). For patients over 60 years, the cytarabine dose was reduced to 1000 mg/m2 in the Kantarjian et al. studies (refer to 'dose modifications' section).

Day 3		
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Cytarabine (Ara-C)	3,000 mg/m^2 (IV infusion)	in 500 mL to 1000 mL sodium chloride 0.9% over 3 hours TWICE a day (every 12 hours). For patients over 60 years, the cytarabine dose was reduced to 1000 mg/m2 in the Kantarjian et al. studies (refer to 'dose modifications' section).

Day 4		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.
Filgrastim	10 micrograms/kg (Subcut)	inject subcutaneously once daily starting day 4 and continue until neutrophil recovery.

Day 5 to 21		
daSATinib	70 mg (PO)	ONCE a day with or without food, continuously throughout cycles 2 to 8.

* The total number of intrathecal (IT) treatments is dependent on patient risk category. The 'Unknown Risk' category is included as default in this protocol (i.e. IT therapy on cycles 1 and 3). The IT dose of methotrexate when given via an Ommaya reservoir is 6 mg

.[1] Link to intrathecal CNS prophylaxis schedule .

Frequency: 21 days
Commence next cycle (i.e. Part A) after 21 days or when WCC is greater than 3 $x10^9$ and platelets are greater than 60 $x10^9$, whichever is earlier.

Cycles: 4
This hyper CVAD protocol consists of 4 cycles of Part B (Cycles 2, 4, 6, 8) alternating with 4 cycles of Part A (Cycles 1, 3, 5, 7) for a total of 8 cycles, followed by maintenance therapy for 2 years. Dasatinib is then continued indefinitely as a sole agent.

Indications and patient population

Indications:

- Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL)

Caution:

- Not generally for treatment of Philadelphia chromosome negative acute lymphoblastic leukaemia, refer to:
  - Hyper CVAD Part A and B/POMP

Clinical information

Venous access	Central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
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. As a steroid has been included as part of this protocol, additional antiemetic steroids are not 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
Prolongation of QT interval	This treatment may prolong the QT interval and increase the risk of cardiac arrhythmia. Use with caution in patients with a congenital long QT syndrome, patients treated with a high cumulative dose of anthracycline therapy, patients taking medications that may prolong the QT interval and those with electrolyte disturbances. Risk factors (e.g. electrolyte abnormalities) should be corrected, where possible, prior to commencement of treatment and the concurrent use of drugs that may prolong the QT interval should be avoided. Baseline and periodic monitoring of electrocardiogram (ECG) and electrolytes (potassium, magnesium, calcium) should be considered in patients at high risk of QT prolongation. Read more about drugs that may prolong QTc interval at crediblemeds.org (registration required).

Cardiac toxicity	Tyrosine kinase inhibitors have been associated with cardiac complications of varying degrees and severity. Patients, especially those with pre-existing cardiovascular disease, should have a baseline cardiac assessment including an electrocardiogram (ECG) and biochemistry and be closely monitored; consider an echocardiogram (ECHO) as clinically indicated. Cardiac assessment should then be repeated as clinically indicated or when starting new medication which affects the QT interval. Read more about cardiac toxicity associated with anti-cancer drugs
Administration details	Long-term suppression of gastric secretions may decrease the absorption of some tyrosine kinase inhibitors (TKIs). Patients should avoid taking H2-receptor antagonists or proton-pump inhibitors while undergoing therapy with this TKI. Antacids may be used instead, but should be avoided within 2 hours of the TKI dose.
Pre-hydration	Pre-hydration with sodium bicarbonate 8.4% infusion. Urinary pH must be greater than 7 prior to commencing methotrexate infusion. Consider prescribing sodium bicarbonate oral capsules for administration prior to methotrexate infusion. Sodium bicarbonate 8.4% should continue until the methotrexate level is equal to or less than 0.1 micromol/L. Read more about high dose methotrexate-induced toxicity.
Ocular toxicities	Administer corticosteroid eye drops to minimise corneal toxicity from high dose cytarabine. Commence on the day of first dose of cytarabine and continue for at least 72 hours after completion of final cytarabine dose. Read more about ocular toxicities associated with high dose cytarabine
Cytarabine induced neurotoxicity	This may occur in patients treated with high dose cytarabine. Assess cerebellar function prior to each cytarabine dose. Read more about neurotoxicity associated with high dose cytarabine and access the cytarabine cerebellar neurotoxicity assessment chart
Cytarabine syndrome	Treatment with cytarabine may cause a "cytarabine syndrome" characterised by flu-like symptoms, skin rash and occasionally chest pain.
Fluid retention/oedema	Dasatinib may cause severe fluid retention, including pleural and pericardial effusions, severe ascites, severe pulmonary oedema, and generalised oedema. This may be dose-related. Risk increases in patients greater than 65 years, patients with hypertension or prior cardiac history and those treated with twice daily dosing. (Note: once daily dosing is the recommended dosing schedule for all phases). Monitor regularly for signs and symptoms of fluid retention. Chest x-ray is recommended for symptoms suggestive of pleural effusion (eg. cough, dyspnoea).
Pulmonary complications	Clinicians should evaluate patients for signs and symptoms of underlying cardiopulmonary disease before starting treatment and during treatment. Pleural effusions are dose dependent events and dose interruption, reduction or steroids should be considered. They are more common with dasatinib than with imatinib and may be bilateral or unilateral. Up to 35 % of patients treated with dasatinib on phase I/II studies developed pleural effusions, most often exudative. Pulmonary arterial hypertension (PAH) is an uncommon but serious complication. Echocardiogram is recommended in symptomatic patients (i.e. dyspnoea, cough, fatigue) and those with pleural effusions. Dasatinib should be withheld during evaluation if symptoms are severe, and permanently discontinued if PAH is confirmed i.e. not rechallenged. Pneumonitis and interstitial lung disease has also been reported.
Diarrhoea	Consider prescribing prophylactic anti-diarrhoeal (e.g. loperamide) to prevent treatment induced diarrhoea. If severe diarrhoea occurs, discontinue dasatinib until condition improves or resolves. Read more about treatment induced diarrhoea

High dose methotrexate	Monitoring of methotrexate levels is essential as delayed methotrexate excretion is potentially an emergency situation. Methotrexate levels to be monitored every 24 hours until level is less than 0.1 micromol/L. Methotrexate is renally eliminated. Kidney function must be evaluated prior to treatment. Methotrexate exits slowly from third space compartments (e.g. pleural effusions or ascites), resulting in a prolonged terminal plasma half-life and unexpected toxicity. In patients with significant third space accumulations, it is advisable to evacuate the fluid before treatment and to monitor plasma methotrexate levels. Glucarpidase is recommended in patients with high dose methotrexate (HDMTX)-induced acute kidney injury and delayed methotrexate clearance. It can rapidly lower methotrexate levels and early administration within 48 to 60 hours from the start of the HDMTX infusion is critical, as life-threatening toxicities may not be preventable beyond this time point.[4] Read more about high dose methotrexate-induced toxicity.
Methotrexate interactions	Avoid administering the following drugs in combination with high dose methotrexate: ciprofloxacin, NSAIDs, probenecid, proton pump inhibitors (PPIs) (e.g. esomeprazole, omeprazole, pantoprazole), sulphonamides (e.g. sulfamethoxazole (in Bactrim®, Septrin®)), penicillins (e.g. piperacillin (in Tazocin®)) and trimethoprim. Severe mucositis may occur if administered together.
Efficacy of therapy	Measure efficacy of therapy using a standardised RT-PCR assay for BCR-ABL transcripts. Assess after the first cycle, at 2 to 4 month intervals while on hyper CVAD, and at 4 to 6 month intervals thereafter. Alternate therapies should be considered for patients who do not achieve a major molecular remission (defined as BCR-ABL less than 0.1% in the marrow) by 3 months and for those who lose their initial response on serial monitoring.
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. Myelosuppression may be exacerbated if trimethoprim/sulfamethoxazole is used in combination with methotrexate. Read about prophylaxis of pneumocystis jirovecii (carinii) in cancer patients
Antifungal prophylaxis	Antifungal prophylaxis is recommended. e.g. posaconazole 300 mg PO twice daily for one day then 300 mg PO daily. 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, eGFR, LFTs, LDH, calcium, magnesium and phosphate at baseline and prior to each cycle. TSH and BSL at baseline and regularly throughout treatment as clinically indicated. Methotrexate levels to be monitored every 24 hours until level is less than 0.1 micromol/L.
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. Pregnancy must be avoided while a female patient is on tyrosine kinase inhibitor (TKI) therapy. There are very few reports of pregnancy outcomes in partners of men receiving second or third-generation TKIs. Although the majority of infants fathered by men taking dasatinib were reported to be without congenital disabilities at birth, the general advice is for couples to avoid pregnancy (Carlier et al., 2017; Cortes et al., 2015). The safety of these drugs has not been proven, and therefore, pregnancy should be avoided. Effective contraception methods and adequate contraception timeframes 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. Link to Carlier et al. and Cortes et al. references.

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
- All dasatinib dose modifications are taken directly from the dasatinib product information and should be considered at the discretion of the treating Haematologist

Haematological toxicity	
ANC less than 0.5 x 10^9/L and/or platelets less than 10 x 10^9/L	1. Stop dasatinib until ANC ≥ 1.0 x 10^9/L and platelets ≥ 50 x 10^9/L 2. Resume at the original starting dose of dasatinib 3. If platelets < 25 x 10^9/L and/or recurrence of ANC < 0.5 x 10^9/L for > 7 days, a dose reduction may be necessary at the discretion of the haematologist.

Note: *The effects of dasatinib on platelet activation may also contribute to bleeding in addition to the thrombocytopenia*

Age older than 60 years
For patients aged older than 60 years, reduce cytarabine dose to 1000 mg/m^2 [1, 2]

Methotrexate level > 20 micromol/L after completion of infusion
If methotrexate level is greater than 20 micromol/L at 0 hours post completion of methotrexate therapy, reduce cytarabine dose to 1000 mg/m^2 [1, 2]

Renal impairment	
Creatinine clearance (mL/min)	
10 to 50	Reduce methotrexate by 50% and reduce cytarabine dose to 1000 mg/m^2
less than 10	Methotrexate contraindicated

NOTE: an increased risk of neurotoxicty has been associated with high dose cytarabine when creatinine clearance is less than 60 mL/min.

Hepatic impairment	
Hepatic dysfunction	
Mild to moderate	No dose modifications necessary
Severe	Reduce methotrexate by 25%

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

Patients with mild, moderate or severe hepatic impairment may receive the recommended starting dose of dasatinib. However, dasatinib is metabolised extensively in the liver and caution is recommended.

Mucositis, stomatitis and diarrhoea	
Grade 3 or Grade 4	Diarrhoea and ulcerative stomatitis require interruption of therapy otherwise, haemorrhagic enteritis and death from intestinal perforation may occur; reduce methotrexate by 25%

Non-Haematological toxicity	
Severe	Interrupt until resolved, then resume as appropriate at a reduced dose depending on the severity and recurrence of the event.

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*

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

Dasatinib		
	Interaction	**Clinical management**
H2 blockers (e.g. famotidine, ranitidine etc.) and Proton Pump Inhibitors (e.g.omeprazole, pantoprazole, rabeprazole etc.) and Antacids	Reduced efficacy of dasatinib due to decreased absorption when gastric acid secretion suppressed (dasatinib requires acidic environment for absorption)	Avoid combination; acid neutralising antacids, e.g. Gastrogel®, Mylanta® (which have a shorter duration of action), may be used if separated from dasatinib administration by at least 2 hours
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of dasatinib possible due to reduced clearance	Avoid combination or monitor for dasatinib toxicity and reduce the dose appropriately
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of dasatinib possible due to increased clearance	Avoid combination or monitor for decreased clinical response to dasatinib
Drugs metabolised by CYP3A4 (e.g. atorvastatin, benzodiazepines, calcineurin inhibitors, clarithromycin, dihydroergotamine, simvastatin, etc.)	Increased effect/toxicity of these drugs possible due to inhibition of CYP3A4 by dasatinib resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity. (e.g. simvastatin exposure can be increased by 20%; heightening the risk of QT prolongation)
Drugs that may prolong the QTc interval (e.g. azole antifungals, tricyclic antidepressants, antiarrhythmics etc.)	Additive effect with dasatinib; may lead to torsades de pointes and cardiac arrest	Avoid combination or minimise additional risk factors (e.g. correct electrolyte imbalances) and monitor ECG for signs of cardiac arrhythmia
Paracetamol	Risk of liver toxicity due to inhibition of metabolism of paracetamol by dasatinib	Avoid combination or monitor liver function closely

Methotrexate		
	Interaction	**Clinical management**
Ciprofloxacin **NSAIDS** **Probenecid** **Proton pump inhibitors (e.g. esomeprazole, omeprazole, pantoprazole)**	Increased toxicity of methotrexate possible due to reduced clearance	Avoid combination or monitor for methotrexate toxicity Important note: with high-dose methotrexate therapy, many of these drug combinations are *contraindicated*
Sulphonamides and penicillins (e.g. sulfamethoxazole (in Bactrim®, Septrin®), piperacillin (in Tazocin®) etc.)	Increased toxicity of methotrexate possible due to displacement from serum protein binding	Avoid combination or monitor for methotrexate toxicity
Trimethoprim	Increased toxicity of methotrexate possible due to additive antifolate activity	Avoid combination or monitor for methotrexate toxicity
Mercaptopurine	Increased toxicity of mercaptopurine possible due to reduced clearance	Avoid combination or monitor for mercaptopurine toxicity
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Hepatotoxic drugs (e.g. azathioprine, leflunomide, retinoids, sulfasalazine)	Additive hepatotoxicity	Avoid combination or monitor liver function closely
Folic acid (e.g. as in multivitamins) **Asparaginase (administered immediately prior or concurrently)**	Reduced efficacy of methotrexate possible due antagonism of its action	Avoid combination or monitor for decreased clinical response to methotrexate Note: asparaginase administered shortly after methotrexate can enhance its efficacy and reduce its toxicity

Methylprednisolone		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of methylprednisolone possible due to reduced clearance	Avoid combination or monitor for methylprednisolone toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of methylprednisolone possible due to increased clearance	Avoid combination or monitor for decreased clinical response to methylprednisolone

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 Cycles 2 and 4

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.

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).

Access CVAD.

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

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

Note: Commence corticosteroid eye drops and continue for 72 hours after the last dose of cytarabine.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Methylprednisolone

- administer via IV infusion over at least 30 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- there are reports of cardiac arrhythmias, circulatory collapse and/or cardiac arrest following rapid administration of large IV doses (greater than 500 mg over less than 10 minutes)

Administer second dose of methylprednisolone 12 hours after first dose.

Chemotherapy - Time out

Methotrexate

Prehydration:

- administer 100 mL sodium bicarbonate 8.4% in 1000 mL glucose **OR** sodium chloride 0.9% over 4 hours
- continue hydration with sodium bicarbonate 8.4% as prescribed
- when urine pH is greater than 7 commence methotrexate

If the urine pH drops below 7 during the methotrexate infusion:

- administer stat dose of 100 mL sodium bicarbonate 8.4% over 15 minutes
- continue to test all urine for pH, if the pH continues to drop below 7 seek medical review as further doses of sodium bicarbonate may be required.

Note: A large volume of intravenous fluid is given with this protocol if weight increases by more than 1 kg from baseline or fluid

balance becomes positive by one litre or any other signs of fluid overload is present review by medical officer (diuretics may be required).

First dose of methotrexate

- administer via IV infusion over 2 hours
- the starting time of the methotrexate infusion **must** be documented as the calcium folinate (leucovorin) rescue is to commence exactly 36 hours after the commencement of the methotrexate and continue until the methotrexate level is less than 0.1 micromol/L

Second dose of methotrexate (to commence immediately after the first dose):

- administer via IV infusion over 22 hours
- flush with ~50 mL of sodium chloride 0.9%
- **Stop the methotrexate infusion after 22 hours even if the infusion is not completed**

Post methotrexate:

- continue hydration with sodium bicarbonate 8.4% until methotrexate level is less than 0.1 micromol/L
- continue to monitor all urine pH and fluid input and output
- monitor methotrexate concentration every 24 hours until the level is less than 0.1 micromol/L

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

Day 2

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

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

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Methylprednisolone

- administer via IV infusion over at least 30 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- there are reports of cardiac arrhythmias, circulatory collapse and/or cardiac arrest following rapid administration of large IV doses (greater than 500 mg over less than 10 minutes)

Administer second dose of methylprednisolone 12 hours after first dose.

Calcium Folinate (Leucovorin)

Commence 36 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L.

- administer via IV bolus via the side port of the IV line over 1 to 2 minutes
- flush with ~ 50 mL of sodium chloride 0.9%

Chemotherapy - Time out

Cytarabine

Prior to administration:

Ensure corticosteroid eye drops have been administered before starting cytarabine.

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

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

Administer cytarabine:

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

Administer second dose of cytarabine 12 hours after first dose.

Intrathecal methotrexate

Note:

- intrathecal methotrexate may not be administered with every cycle
- the number of IT treatments is dependent on patient risk category

⚠ 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 3

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.

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

be required).

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

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

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Methylprednisolone

- administer via IV infusion over at least 30 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- there are reports of cardiac arrhythmias, circulatory collapse and/or cardiac arrest following rapid administration of large IV doses (greater than 500 mg over less than 10 minutes)

Administer second dose of methylprednisolone 12 hours after first dose.

Chemotherapy - Time out

Cytarabine

Prior to administration:

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

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

Administer cytarabine:

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

Administer second dose of cytarabine 12 hours after first dose.

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

Days 4 to 7

Safe handling and waste management (reproductive risk only)

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.

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

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

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Filgrastim

- administer filgrastim by subcutaneous injection on day 4 and continue until neutrophil recovery

Continue safe handling precautions (reproductive risk only) for 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.

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Chemotherapy - Time out

Intrathecal cytarabine

- intrathecal cytarabine may not be administered with every cycle
- the number of IT treatments is dependant on patient risk category

Cytarabine intrathecal

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

Access the clinical procedure for the safe administration of intrathecal cytarabine.

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)

Days 9 to 21

This is an oral treatment

Safe handling and waste management (reproductive risk only)

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.

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

- continue daily weigh

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).

Discharge information

Dasatinib tablets

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

Antiemetics

- Antiemetics as prescribed.

Corticosteroid eye drops

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

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

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

Patient information

- Ensure patient receives patient information sheet.

Administration Cycles 6 and 8

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.

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).

Access CVAD.

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

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

Note: Commence corticosteroid eye drops and continue for 72 hours after the last dose of cytarabine.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Methylprednisolone

- administer via IV infusion over at least 30 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- there are reports of cardiac arrhythmias, circulatory collapse and/or cardiac arrest following rapid administration of large IV doses (greater than 500 mg over less than 10 minutes)

Administer second dose of methylprednisolone 12 hours after first dose.

Chemotherapy - Time out

Methotrexate

Prehydration:

- administer 100 mL sodium bicarbonate 8.4% in 1000 mL glucose **OR** sodium chloride 0.9% over 4 hours
- continue hydration with sodium bicarbonate 8.4% as prescribed
- when urine pH is greater than 7 commence methotrexate

If the urine pH drops below 7 during the methotrexate infusion:

- administer stat dose of 100 mL sodium bicarbonate 8.4% over 15 minutes
- continue to test all urine for pH, if the pH continues to drop below 7 seek medical review as further doses of sodium bicarbonate may be required.

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

First dose of methotrexate

- administer via IV infusion over 2 hours
- the starting time of the methotrexate infusion **must** be documented as the calcium folinate (leucovorin) rescue is to commence exactly 36 hours after the commencement of the methotrexate and continue until the methotrexate level is less than 0.1 micromol/L

Second dose of methotrexate (to commence immediately after the first dose):

- administer via IV infusion over 22 hours
- flush with ~50 mL of sodium chloride 0.9%
- **Stop the methotrexate infusion after 22 hours even if the infusion is not completed**

Post methotrexate:

- continue hydration with sodium bicarbonate 8.4% until methotrexate level is less than 0.1 micromol/L
- continue to monitor all urine pH and fluid input and output
- monitor methotrexate concentration every 24 hours until the level is less than 0.1 micromol/L

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

Day 2

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

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

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Methylprednisolone

- administer via IV infusion over at least 30 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- there are reports of cardiac arrhythmias, circulatory collapse and/or cardiac arrest following rapid administration of large IV doses (greater than 500 mg over less than 10 minutes)

Administer second dose of methylprednisolone 12 hours after first dose.

Calcium Folinate (Leucovorin)

Commence 36 hours after commencement of methotrexate infusion and repeat every 6 hours until methotrexate level is less than 0.1 micromol/L.

- administer via IV bolus via the side port of the IV line over 1 to 2 minutes
- flush with ~ 50 mL of sodium chloride 0.9%

Chemotherapy - Time out

Cytarabine

Prior to administration:

Ensure corticosteroid eye drops have been administered before starting cytarabine.

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

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

Administer cytarabine:

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

Administer second dose of cytarabine 12 hours after first dose.

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

Day 3

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.

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

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

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

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Methylprednisolone

- administer via IV infusion over at least 30 minutes
- flush with ~ 50 mL of sodium chloride 0.9%
- there are reports of cardiac arrhythmias, circulatory collapse and/or cardiac arrest following rapid administration of large IV doses (greater than 500 mg over less than 10 minutes)

Administer second dose of methylprednisolone 12 hours after first dose.

Chemotherapy - Time out

Cytarabine

Prior to administration:

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

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

Administer cytarabine:

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

Administer second dose of cytarabine 12 hours after first dose.

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

Day 4

Safe handling and waste management (reproductive risk only)

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.

- daily weight
- monitor pH on all urine output
- strict fluid balance input and output

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

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Filgrastim

- administer filgrastim by subcutaneous injection on day 4 and continue until neutrophil recovery

Deaccess CVAD.

Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).

Days 5 to 21

This is an oral treatment

Safe handling and waste management (reproductive risk only)

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.

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

- continue daily weigh

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).

Discharge information

Dasatinib tablets

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

Antiemetics

- Antiemetics as prescribed.

Corticosteroid eye drops

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

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

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

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

Immediate (onset hours to days)	
Bone pain	Bone pain, usually in the lower back or pelvis, associated with G-CSF.
Cytarabine (Ara-C) syndrome	Flu-like symptoms including fever, myalgia and malaise can occur 6 to 12 hours after cytarabine administration. Symptoms generally resolve within 24 hours of completing therapy.
Headache	Mild headache is common with this treatment.
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
Neurotoxicity	High dose cytarabine has been associated with acute cerebellar syndrome and diffuse cerebral dysfunction. Read more about neurotoxicity associated with high dose cytarabine
Ocular toxicities	Reversible corneal toxicity (keratitis), haemorrhagic conjunctivitis, vision loss and other ocular side effects can occur with high dose cytarabine. Corticosteroid eye drops must be administered concurrently with treatment. Read more about ocular toxicities associated with cytarabine
Taste and smell alteration	Read more about taste and smell changes

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. 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.
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Cardiotoxicity	Cardiotoxicity may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, hypertension, cardiac ischaemia and congestive heart failure (CHF). The risk of cardiotoxicity is increased by a number of factors, particularly a history of heart disease and electrolyte imbalances. Read more about cardiotoxicity associated with anti-cancer drugs
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.
Haemorrhage	
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.
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
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
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

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
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)
Depression	
Periorbital oedema	Accumulation of fluid in the tissue surrounding the eye sockets (orbits).

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

Evidence

Dasatinib has significant clinical activity in patients with Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant to imatinib. Ravandi et al.[5] examined the efficacy and safety of combining hyper CVAD chemotherapy with dasatinib for 35 newly diagnosed patients with a median age of 53 (21-79). Dasatinib 50 mg twice a day or 100 mg once a day was given orally for the first 14 days of each 8 cycles of alternating hyper CVAD Part A and B. Patients who achieved complete remission (CR) were given maintenance of daily dasatinib and monthly vincristine and prednisone for 2 years, followed by dasatinib indefinitely. 94% of patients achieved CR, and a median disease-free survival (DFS) and median overall survival (OS) had not been reached at a median follow-up of 14 months, with an estimated 2-year survival of 64%.[5]

Efficacy

A follow-up study confirmed long-term efficacy of the hyper CVAD chemotherapy in combination with dasatinib. 72 patients, median age 55 (21-80) with Ph+ ALL, either untreated or 1 or 2 prior cycles of therapy, were enrolled between 2006 and 2012. This study established dose equivalence between dasatinib 50 mg orally twice daily and dasatinib 100 mg daily and also further amended the protocol to give dasatinib 100 mg daily in the first 14 days of the first cycle, followed by 70 mg daily continuously from the second cycle. Maintenance with dasatinib, vincristine and prednisone was given monthly to patients who achieved CR for 2 years, followed by dasatinib indefinitely. Allogeneic stem cell transplant (SCT) was given in first complete remission (CR1) to eligible patients.[6]

69 patients (96%) achieved CR, of which 57 (83%) achieved cytogenetic (CG) CR after 1 cycle and 64 (93%) a major molecular response (MMR) at a median of 4 weeks (range, 2 – 38 weeks). At a median of 3 weeks (range, 2–37), minimal residual disease by flow cytometry was negative in 65 (94 %) patients. At a median follow-up of 67 months (range, 33–97), 33 patients (46%) were alive, and 30 (43%) in CR. 12 patients received an allogeneic SCT, and 39 patients died. The median DFS and OS was 31 months (range, 0.3 to 97) and 47 months (range, 0.2 to 97), respectively. Seven relapsed patients had ABL mutations, including 4 with T315I.[6]

Figure 1: A) Disease-free survival, B) Overall survival and C) Event-free survival[6]

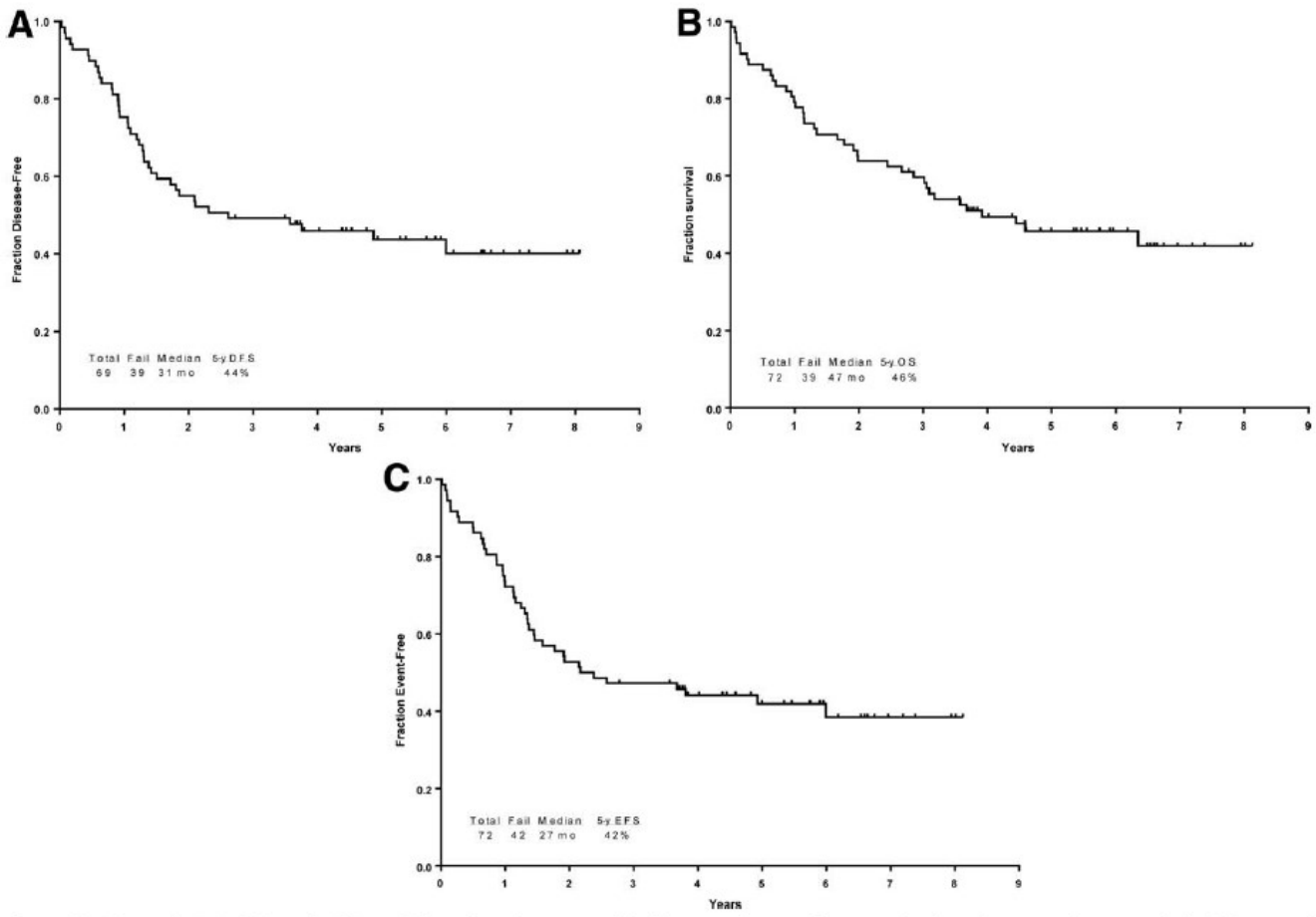


Figure 1. (A) DFS, (B) OS, and (C) EFS for all patients. DFS indicates disease-free survival; EFS, event-free survival; OS, overall survival.

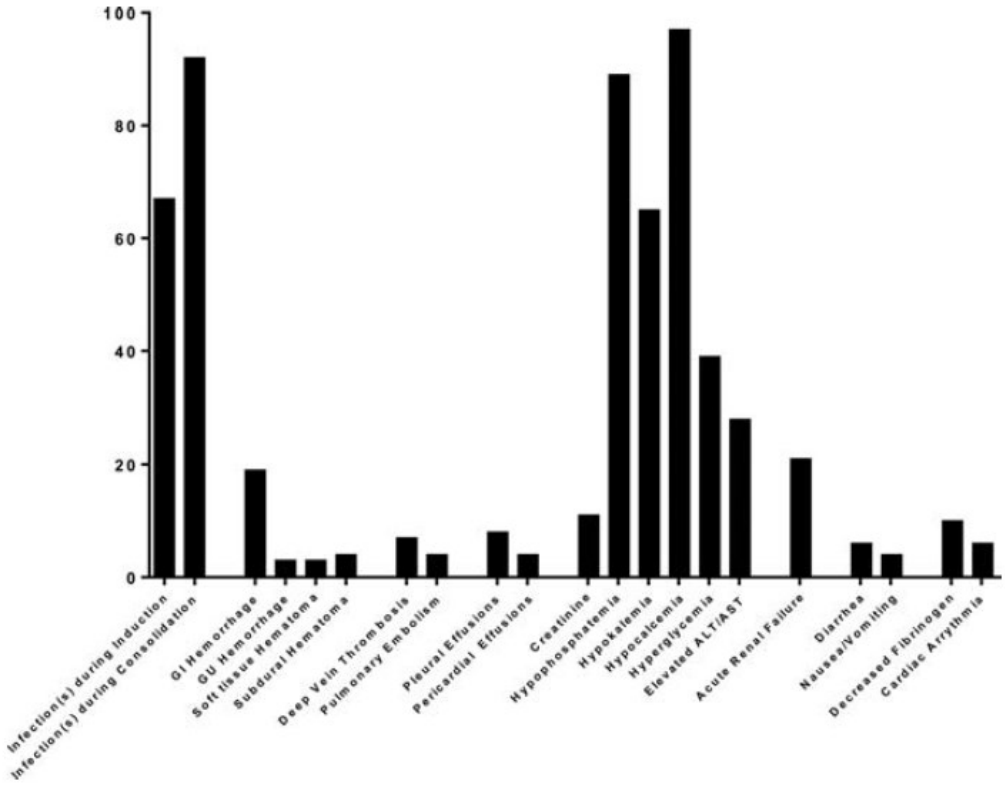
Furthermore, a multicentre trial found the addition of dasatinib in combination with chemotherapy followed by an allogeneic haematopoietic cell transplant (HCT) in patients with Ph+ ALL was feasible. Hyper CVAD + dasatinib treatment was administered, and of the 83 (88%) patients who achieved CR1, 41 patients received an allogeneic HCT where a donor was available, followed by daily dasatinib 100 mg starting from day 100. 33 patients actually received dasatinib post-HCT, and 30 (91%) of them required at least one dose reduction. Others received maintenance therapy with vincristine and prednisone for 2 years and dasatinib indefinitely. At median follow-up of 36 months (range, 9 - 63) for the overall cohort, overall survival (OS) was 69%, event-free survival (EFS) 55%, and relapse-free survival (RFS) 62%. The 12-month RFS was 71% and OS 87% after transplant.[7]

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Ravandi et al. 2010[5]	**Yes**	Yes	-
Phase II trials	Ravandi et al. 2015[6]	**Yes**	Yes	-
Phase II trials	Ravandi et al. 2016[7]	**Yes**	Yes	Hyper CVAD + dasatinib followed by allogeneic HCT
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	Acute lymphoblastic leukaemia Version 1, 2021	**Yes**	Yes	-
BCCA	N/A	**N/A**	N/A	-
CCO	N/A	**N/A**	N/A	-

Toxicity

Dasatinib was discontinued in 12 patients due to pleural effusions (n=6), pulmonary artery hypertension (n=2), gastrointestinal bleeding (n=2), skin cancer (n=1) and subdural bleeding (n=1).[6]

Figure 2: Dasatinib-related grade 3 and 4 adverse events included bleeding, pleural/pericardial effusions, and elevated transaminases.



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7 Ravandi, F., M. Othus, S. M. O'Brien, et al. 2016. "US Intergroup Study of Chemotherapy Plus Dasatinib and Allogeneic Stem

Cell Transplant in Philadelphia Chromosome Positive ALL." Blood Adv 1(3):250-259.

History

Version 3

Date	Summary of changes
04/05/2023	Methotrexate target level updated. Version number changed to v.3
25/07/2023	• Updated wording of rituximab note in "Treatment schedule" for clarity • Frequency and cycle notes updated for clarity • Updated fertility information • Minor formatting updates

Version 2

Date	Summary of changes
22/09/2020	Biosimilar drug added to clinical information. Version number changed to v.2
23/10/2020	Protocol reviewed electronically by Haematology Reference Committee, no changes. Review in 2 years.
06/08/2021	Note added to treatment schedule for addition of rituximab in CD20+ disease.
21/01/2022	Blood tests updated in clinical information. Pulmonary toxicity added to side effects.
08/02/2022	PJP prophylaxis clinical information block updated.

Version 1

Date	Summary of changes
21/09/2018	New protocol proposed at Haematology Reference Committee meeting. Developed out of session (discussed electronically via email).
15/05/2019	Approved and published on eviQ v.1. Review in 1 year.
05/08/2019	Drug status of dasatinib changed to reflect PBS update.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.

First approved: 26 April 2019
Last reviewed: 23 October 2020
Review due: 31 December 2022

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/3531
31 Jul 2023

Patient information - Acute lymphoblastic leukaemia (ALL) - hyper CVAD part B and dasatinib

Patient's name:

Your treatment

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

Hyper CVAD Part B and dasatinib

This treatment cycle alternates with Hyper CVAD Part A and dasatinib, and usually continues for a total of 8 cycles of chemotherapy. When you receive you next treatment cycle depends on how long it takes for your blood counts to recover.

Day	Treatment	How it is given	How long it takes
	Dasatinib *(duh-sat-in-nib)*	Take orally ONCE a day with or without food and a large glass of water continuously with cycle 2 to 8. After cycle 8 you will go on to have maintenance treatment. Tablet(s) should be swallowed whole. If you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.	
1	**Methylprednisolone** *(methil-predd-niz-oh-lone)*	By a drip into a vein	About 30 minutes TWICE a day
	Methotrexate *(meth-o-TREX-ate)*	By a drip into a vein	For 24 hours
2	**Methylprednisolone**	By a drip into a vein	About 30 minutes TWICE a day
	Calcium folinate (Leucovorin) (loo-koe-VOR-in)	By a drip into a vein	About 5 minutes repeated every 6 hours
	Cytarabine *(sye-TARE-a-been)*	By a drip into a vein	About 3 hours TWICE a day
	Methotrexate (intrathecal)	By injection into your spine (this may not be with every cycle - check with your doctor)	About 4 hours
3	**Methylprednisolone**	By a drip into a vein	About 30 minutes TWICE a day
	Cytarabine	By a drip into a vein	About 3 hours TWICE a day
4	**Granulocyte Colony Stimulating Factor** *(G-CSF)*	By injection under the skin	About 5 minutes
8	**Cytarabine**	By injection into your spine (this may not be with every cycle - check with your doctor)	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
• 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).

Other information about your treatment

Changes to your dose or treatment delays

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

Blood tests and monitoring

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

Central venous access devices (CVADs)

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

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 will be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover.
- **Eye drops:** you will be given eye drops to help prevent sore eyes. You will start using the eye drops before you have your first dose of cytarabine and continue to use the eye drops until 72 hours after your last dose of cytarabine.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

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

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

Immediate (onset hours to days)	
Bone pain after G-CSF injection	• You may have discomfort or a dull ache in your pelvis, back, arms or legs. • To reduce the pain, take paracetamol before each injection. • **Tell your doctor or nurse as soon as possible if your pain is not controlled.**
Flu-like symptoms from cytarabine	• You may get a fever, skin rash, aches and pains or increased sweating. • These symptoms are caused by the drug cytarabine. • Symptoms usually happen 6 to 12 hours after your dose, and may last until 24 hours after your treatment has finished. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Talk to your doctor or nurse about what you can take for any pain or fever. • Tell your doctor or nurse if these symptoms do not get better after 24 hours.
Headache	• Talk to your doctor or nurse about what you can take if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
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.**

Nervous system changes from cytarabine	• High doses of cytarabine can affect the nervous system.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms during or soon after your treatment:**
	  ◦ **dizziness, drowsiness or double vision**
	  ◦ **agitation**
	  ◦ **difficulty walking in a straight line**
	  ◦ **difficulty writing with a pen or pencil**
	  ◦ **jerky movements**
	  ◦ **slow, slurred speech.**

Eye problems from cytarabine	• You may get:
	  ◦ eye pain or irritation
	  ◦ blurred vision
	  ◦ watery or gritty eyes
	  ◦ sensitivity to light.
	• You will be given eye drops to help prevent and control these symptoms. It is important to use these eye drops as directed.
	• Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you have lost your eyelashes.
	• Tell your doctor or nurse if you get any of the symptoms listed above.

Taste and smell changes	• You may find that food loses its taste or tastes different. • 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.**

Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.

Heart problems	• You may get:
	  ◦ chest pain or tightness
	  ◦ shortness of breath
	  ◦ swelling of your ankles
	  ◦ an abnormal heartbeat.
	• Heart problems can occur months to years after treatment.
	• Tell your doctor if you have a history of heart problems or high blood pressure.
	• Before or during treatment, you may be asked to have a test to see how well your heart is working.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

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.**

Bleeding (haemorrhage)	• Tell your doctor or nurse if you have a wound that does not heal. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **unusual bleeding or bruising** ◦ **bright red or black, tarry bowel motions (stools, poo)** ◦ **stomach pain** ◦ **slurred speech** ◦ **shortness of breath** ◦ **a fast heartbeat.**
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.**
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.**
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.

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.**

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 loss (alopecia)	• 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
Chemo brain (chemotherapy-related cognitive impairment)	• You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. • These symptoms usually improve once treatment is completed. • Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). • Tell your doctor or nurse if you get any of the symptoms listed above.
Depression	• You may find that you: ◦ have a low mood ◦ are tired ◦ don't have much energy ◦ lose interest in everyday activities ◦ have trouble concentrating or making decisions. • Keep a diary of how you are feeling once your treatment has started. • Let your friends and family know how you are feeling. • Tell your doctor or nurse if you get any of the signs or symptoms listed above.
Swelling around the eyes	• You may get: ◦ swelling or heaviness around your eyes ◦ irritated eyes ◦ eye discharge ◦ changes to your vision. • **Tell your doctor or nurse if you get any of these symptoms.**

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.
- Some pain medications, e.g. paracetamol, can interact with your treatment. Check with your doctor or pharmacist before taking any medications for a headache or mild pain.
- 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.

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)

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 – aci.health.nsw.gov.au/resources/blood-and-marrow-transplant
- 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
- 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

Additional notes:

First approved: 26 April 2019
Last reviewed: 23 October 2020
Review due: 31 December 2022

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/pi/3531
31 Jul 2023