Acute myeloid leukaemia consolidation IDAC (cytarabine) SUPERSEDED



ID: 1663 v.3 Superseded Essential Medicine List

This protocol has been superseded due to the availability of superior alternatives. The preferred regimen is ID 4285 Acute myeloid leukaemia consolidation cytarabine (age under 60 years) or ID 4354 Acute myeloid leukaemia consolidation cytarabine (age 60 years and over).

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 <u>may</u> 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 <u>eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.</u>

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

Click here



2022

Related pages:

Acute myeloid leukaemia consolidation HiDAC (cytarabine) 1,2,3 SUPERSEDED

Treatment schedule - Overview

Cycle 1 to 3

Drug	Dose	Route	Day
Cytarabine (Ara-C)	1,000 mg/m ² TWICE a day	IV infusion	1, 3, 5

Frequency: 28 days, or after bone marrow recovery

Cycles: 3 or 4.

Notes:

The definition of 'high dose cytarabine' (HiDAC) varies throughout the literature, ranging from 1 to 3 g/m²; this protocol has been named 'intermediate dose cytarabine' (IDAC) per the Sperr et al. study.¹

Drug status: Cytarabine is available on the PBS general schedule

Cost: ~ \$1,400 per cycle

Treatment schedule - Detail

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

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

Cycle 1 to 3

Day 1, 3, 5		
Cytarabine (Ara-C)	1,000 mg/m ² (IV infusion)	in 500 mL sodium chloride 0.9% over 3 hours TWICE a day. Each dose to be 12 hours apart (6 doses in total).

Frequency: 28 days, or after bone marrow recovery

Cycles: 3 or 4

Indications and patient population

• Acute myeloid leukaemia (AML) in remission, in patients older than 60 years of age

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment.	
	Read more about central venous access device line selection	
Antiemetics for multi-day protocols	Antiemetic therapy should be administered throughout the duration of the chemotherapy protocol and to cover delayed nausea. The acute and delayed emetic risk of multi-day chemotherapy protocols will overlap depending on the individual drugs and their sequence of administration. More or less antiemetic cover may be required.	
	Ensure that patients also have sufficient antiemetics for breakthrough emesis:	
	Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR	
	Prochlorperazine 10 mg PO every 6 hours when necessary.	
	Read more about preventing anti-cancer therapy induced nausea and vomiting	
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 syndrome	Treatment with cytarabine may cause a "cytarabine syndrome" characterised by flu-like symptoms, skin rash and occasionally chest pain.	
Cytarabine-induced neurotoxicity	This may occur in patients treated with high-dose cytarabine. Assess cerebellar function prior to each cytarabine dose.	
	Note: an increased risk of cytarabine-induced neurotoxicity has been associated with kidney dysfunction.	
	Read more about neurotoxicity associated with high-dose cytarabine and access the cytarabine cerebellar neurotoxicity assessment chart	
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome.	
	Read more about prevention and management of tumour lysis syndrome.	
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients	
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses	
Antifungal prophylaxis	Read more about antifungal prophylaxis drugs and doses.	

Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website	
Blood tests	FBC, EUC, eGFR and LFTs at baseline and throughout treatment as clinically indicated.	
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy	
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.	
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility	

Dose modifications

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

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

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

Haematological toxicity

Dose reductions for haematological toxicity not usually recommended. Discuss with Haematologist. Consider adding G-CSF from Day 6

Renal impairment

No specific dose modifications recommended for cytarabine in renal impairment, but please note an increased risk of neurotoxicity has been associated with high dose cytarabine with creatinine clearance less than 60 mL/min

Hepatic impairment

Hepatic impairment

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

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

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

Administration

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

Days 1, 3 and 5

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

- · baseline weight
- · dipstick urinalysis prior to treatment

Hydration if prescribed.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

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

Ochemotherapy - 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.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Discharge information

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 day	rs)
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.
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.		
Anorexia	Loss of appetite accompanied by decreased food intake.		
	Read more about anorexia		
Diarrhoea	Read more about treatment induced diarrhoea		
Fatigue	Read more about fatigue		
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		
Palmar-plantar erythrodysaesthesia (PPE) - hand-foot syndrome (HFS)	Bilateral erythema, tenderness, pain, swelling, tingling, numbness, pruritus, dry rash, or moist desquamation and ulceration of the palms and soles. It is also known as hand-foot syndrome (HFS). Symptoms appear to be dose dependent and palms are affected more than soles. Read more about hand-foot syndrome associated with chemotherapy		
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)	
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.	

Evidence

This protocol has been superseded due to the availability of superior alternatives. The preferred regimen is ID 4285 Acute myeloid leukaemia consolidation cytarabine (age under 60 years) or ID 4354 Acute myeloid leukaemia consolidation cytarabine (age 60 years and over).

A search of the literature found limited evidence to support the use of IDAC in the consolidation treatment of AML. The expert reference panel supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by the Sperr et al. study.¹

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Sperr et al 2004 ¹	Yes	Yes	1 g/m²/day bd, days 1,3,5
Observational studies	N/A	N/A	N/A	-
Guidelines	Date published/revised	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
NCCN	3.2021	Yes	Yes	-
BCCA	N/A	N/A	N/A	-

High-dose cytarabine is not recommended for patients over 60 years of age due to the high rate of neurologic toxicity.² The AML NCCN guidelines suggest the use of cytarabine at a dose of 1-2 g/m² as a consolidation option for the elderly patients with AML.³ The ideal number of consolidation cycles with this cytarabine dose has not been studied. In patients who are candidates for allogenic stem cell transplant, it is recommended that patients proceed to transplant once morphologic remission is attained.

Sperr et al. studied 47 patients who were consolidated with cytarabine 1 g/m² every 12 hours on days 1, 3 and 5 (total 6 doses) for four cycles of consolidation. 25 of 47 patients (53%) completed the scheduled 4 cycles whereas, 32% discontinued due to severe infection and 33% relapsed during consolidation. The probability of remaining free of leukaemia was 22% at 5 years. The median overall survival (OS) of patients receiving IDAC was 31.8 months. Importantly, patients with an adverse AML karyotype had a median OS of only 5 months.¹

This was a non-randomised trial but was well conducted with the dropout and loss to follow-up rate being low. The majority (70%) of patients completed 3-4 consolidation cycles indicating that the therapy was well tolerated. Supportive care strategies are well described and can be applied in our setting. Outcomes and toxicities are well described.

There are several cytarabine based consolidation protocols which have been studied in elderly AML patients and are worth comparing to IDAC. Most have little in common with one another and it is not possible to compare the outcomes objectively. The trials used various combinations of chemotherapeutic agents with cytarabine, various doses, and methods of administration (bolus, infusion and oral).

Table 1: List of cytarabine-based AML consolidation protocols for patients aged over 60 years.

Source	Study and Year Published	Consolidation option	Consolidation option 2	Overall Survival (OS)	Progression- free survival (PFS)	Comments
Prospective phase II	Sperr et al. 2004 ¹	ARA-C 1 g/m 2 bd (D1, 3 and 5) x 4 cycles	No comparison arm	Median OS 10.6 months	Median DFS 15.5 months	N=47 Age >60
Prospective randomised controlled trial	Huang et al. 2014 ⁴	DNR 45 mg/m ² day 1-3 ARA-C 100 mg/m ² D1- 7 x 2 cycles followed by ARA-C 1.5 g/m ² daily (D1-4) x 4 cycles N= 141	DNR 30 mg/m ² D1-3 ARA-C 75 mg/m ² D1-7 x 2 cycles followed by ARA-C 1 g/m ² daily (D1-3) x 4 cycles (n=156)	5 year median OS 24 vs 39 months (p<0.001)	Median PFS 23 vs 35 months (p<0.001)	Age >65
Prospective randomised controlled trial	Gardin et al. 2007 ⁵	"Ambulatory": DNR 45 mg/m ² D1 (or IDA 9 mg/m ² D1) with SC ARA-C 60 mg/m ² bd D1-5 (n=81)	"Intensive": DNR 45 mg/m ² D1- 4 or IDA 9 mg/m ² D1-4 with infusion ARA-C 200 mg/m ² D1- 7 (n=68)	2-year OS 56% vs. 37% in favour of ambulatory consolidation	2-year DFS 28% vs 17% in favour of ambulatory consolidation	Ambulatory consolidation in outpatient setting compared with intensive consolidation Age ≥65
Prospective randomised controlled trial	Jehn et al. 2006 ⁶	IV: IDA 8 mg/m ² D1, 3, 5, etop 100 mg/m ² D1- 3, ARA-C infusion 100 mg/m ² D1-5 (n=166)	Oral: IDA 20 mg/m ² D1, 3, 5 etop 100 mg/m ² bd D1-3 ARA-C 50 mg/m ² SC BD D1-5 (n=165)	Median OS 15.7 months (oral) vs. 17.8 months (IV) (p=0.19)	Median DFS 9 months (oral) vs. 10.4 months (IV) (p=0.15)	Infusional versus non- infusional consolidation Age 61-80
Prospective randomised controlled trial	Mayer et al. 1994 ²	ARA-C infusion 100 mg/m ² D1-5	ARA-C infusion 400 mg/m ² D1-5	Median DFS was 12 months (equal between groups)	OS at 4 years was 9% (equal between groups)	Age >60
Retrospective phase II	Prebet et al. 2009 ⁷	ARA-C SC + oral MTX and 6MP	IV bolus ARA-C doses higher than 500 mg/m² for "at least 2 days" (n=48)	No difference in survival between	LFS 26 months (IV ARA-C) vs. 14 months (SC ARA-C)	Core binding factor (CBF) AML only Age >60

NB: ARA-C: Cytarabine, DNR: Daunorubicin, IDA: Idarubicin, Etop: Etoposide, MTX: Methotrexate, 6MP: 6 Mercaptopurine, DFS: Disease-free survival, LFS: leukaemia-free survival, D:day, vs:versus, SC:subcutaneous, IV:intravenous.

On the basis of these trials several general conclusions can be made regarding consolidation chemotherapy in elderly patients with AML:

- 1. In elderly AML patients with adverse risk cytogenetics there did not appear to be a benefit with using higher doses of cytarabine than 1 g/m^2 .
- 2. Patients who were palliated and did not receive any consolidation had a worse OS than those who had consolidation.⁵
- 3. Similarly, patients who received low dose subcutaneous cytarabine or hydroxyurea has a poorer OS and progression-free survival (PFS) than those who received intravenous cytarabine doses over 500 mg/m² for at least 2 days.⁷
- 4. Treatment with azacitidine results in worse OS than with age appropriate intensive chemotherapy based on treatment.8
- 5. In the core binding factor AML population there was no difference in the outcome of the patients treated with one cycle of intermediate dose cytarabine compared to those who received more than one cycle although this was based on a small population of patients and the authors explained that the study was underpowered to detect a significant difference.⁷
- 6. There was no difference between the disease-free survival (DFS) and OS in patients over 60 who were randomised to HiDAC compared to 100 mg/m^2 or 400 mg/m^2 infusional cytarabine consolidation.²

7. Infusional cytarabine has not been compared to bolus cytarabine in a randomised format in adults over the age of 60.

Efficacy

The use of IDAC consolidation in elderly patients with AML results in acceptable long term outcomes. There are no trials directly comparing this regimen with the others tabulated above. In the study by Sperr et al. overall disease-free surviva (DFS) was 22% at 5 years and median DFS was 15 months. Patients with poor risk cytogenetics had a median DFS of only 6 months and median OS of 6 months. Patients who attained a complete remission (CR) and received consolidation had a median DFS of 31 months. The authors state that elderly patients with *de novo* AML who receive IDAC consolidation while in remission post induction had long-term outcomes similar to that of younger patients with AML.¹

Overall survival, influence of age and karyotype on OS and continuos complete remission in patients receiving post-remission cytarabine consolidation.¹

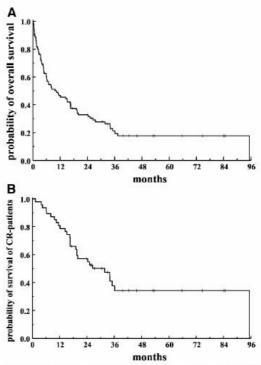


Fig. 2 Overall survival. A, overall survival in all patients treated with induction chemotherapy. B, overall survival in responding patients who received postremission therapy.

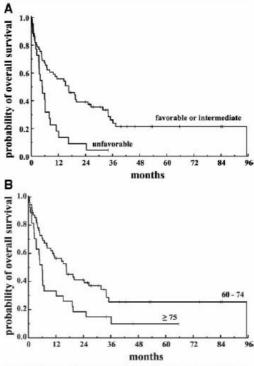


Fig. 3 Influence of karyotype and age on overall survival. A, influence of the karyotype. B, comparison of overall survival between elderly patients \geq 75 and those <75 years of age.

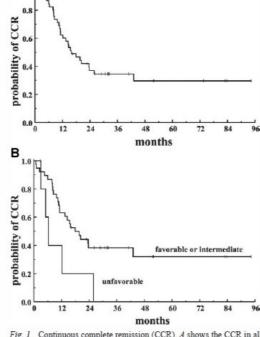


Fig. 1 Continuous complete remission (CCR). A shows the CCR in all patients. In B, CCR rates in patients with different cytogenetic risk groups (favorable + intermediate versus unfavorable) are shown. The CCR rate was different in these two groups of patients (P < 0.05). CCR rates were determined by the product limit method of Kaplan and Meier.

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Toxicity

Quality of life (QOL) data was not presented, however authors detailed the haematologic and non-haematologic toxicity of the protocol. Overall, IDAC was well tolerated and the toxicity was acceptable. There were no neurologic toxicities and no deaths due to sepsis. This is compared to the 30% of the 60 year olds who experienced neurotoxicity with high-dose cytarabine (HiDAC). Neurologic recovery was seen in 40% of these patients only. Median duration of neutropenia was short (9 days) and neutropenic sepsis occurred in 49% with IDAC; rash was seen in 17% and grade 3 hepatotoxicity in 0.7% of patients. G-CSF was not used routinely unless patients had severe sepsis. Prophylaxis with trimethoprim/sulfamethoxazole and ciprofloxacin was recommended.¹

Toxicity profile based on data from Sperr et al.¹

Causes	Number of events (total patients=47 and total IDAC cycles=145)
Febrile neutropenia	55% of all cycles
	Specifically: 49% cycle 1, 60% cycle 2, 44% cycle 3 and 72% cycle 4
Prolonged aplasia	4
Treatment related death	2
Non treatment related death	2
Median duration of neutropenia	9 days
Use of G-CSF	41% IDAC cycles
Grade 3 or 4 neurotoxicity	0%
Drug fever	32% IDAC cycles
Hepatotoxicity	less than 1%
Nephrotoxicity	0%

References

- Sperr, W. R., M. Piribauer, F. Wimazal, et al. 2004. "A novel effective and safe consolidation for patients over 60 years with acute myeloid leukemia: intermediate dose cytarabine (2 x 1 g/m2 on days 1, 3, and 5)." Clin Cancer Res 10(12 Pt 1):3965-3971.
- 2 Mayer, R. J., R. B. Davis, C. A. Schiffer, et al. 1994. "Intensive postremission chemotherapy in adults with acute myeloid leukemia. Cancer and Leukemia Group B." N.Engl.J.Med. 331(14):896-903.
- 3 NCCN- Clinical Practice Guidelines in Oncology Acute Myeloid Leukaemia V.3. 2021
- 4 Huang, B. T., W. H. Zhao, Q. C. Zeng, et al. 2014. "Standard intensive chemotherapy is less effective and far more toxic than attenuated induction and post-induction regimen in elderly patients with acute myeloid leukemia." Med Oncol 31(5):962.
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- 7 Prebet, T., N. Boissel, S. Reutenauer, et al. 2009. "Acute myeloid leukemia with translocation (8;21) or inversion (16) in elderly patients treated with conventional chemotherapy: a collaborative study of the French CBF-AML intergroup." J Clin Oncol 27(28):4747-4753.
- 8 Bories, P., S. Bertoli, E. Berard, et al. 2014. "Intensive chemotherapy, azacitidine or supportive care in older acute myeloid leukemia patients: An analysis from a regional healthcare network." Am J Hematol.

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History

Version 3

Date	Summary of changes	
24/02/2023	Protocol reviewed by Haematology Reference Committee.	
25/09/2023	Protocol superseded due to the availability of alternatives. Review in 1 years. Version changed to V.3	

Version 2

Date	Summary of changes	
16/12/2014	Approved and published on eviQ	
02/02/2016	Reviewed, no changes	
31/05/2017	Transferred to new eviQ website. Version number change to V.2.	
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.	
11/08/2021	Protocol reviewed at the Haematology reference committee. Changes as per below: Title changed from IDAC-1 to IDAC Removed related pages link to HiDAC 1,3,5 and replaced with HiDAC 1,2,3 References updated For review in 2 years	

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

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https://www.eviq.org.au/p/1663

12 Oct 2023





Patient's name:

Your treatment

The treatment schedule below explains how the drug for this treatment is given.

Consolidation IDAC (cytarabine)

This treatment cycle is repeated every 28 days or after your bone marrow has recovered. You will usually have 3 to 4 cycles. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1, 3, 5	Cytarabine (sye-TARE-a-been)	By a drip into a vein	About 3 hours TWICE a day

When to get help

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

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	Emergency contact details 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 may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the eviQ patient information sheets on CVADs.

Other medications given during this treatment

- Anti-sickness (anti-nausea) medication: you may be given some anti-sickness medication. Make sure you take this
 medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- Eye drops: you will be given eye drops to help prevent sore eyes. You will start using the eye drops before you have your first dose of cytarabine and continue to use the eye drops until 72 hours after your last dose of cytarabine.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF**: you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication. Follow this link to read more information on how to give this injection.

Superseded treatments

This treatment is superseded meaning that better treatments have taken its place. Uncommonly superseded treatments are still used. Your doctor will explain why this treatment has been selected for you.

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) · You may get a fever, skin rash, aches and pains or increased sweating. Flu-like symptoms from • These symptoms are caused by the drug cytarabine. cytarabine • Symptoms usually happen 6 to 12 hours after your dose, and may last until 24 hours after your treatment has finished. • To reduce any pain or fever, take paracetamol, if needed. · Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. Tell your doctor or nurse if these symptoms do not get better after 24 hours. • You may feel sick (nausea) or be sick (vomit). Nausea and vomiting • 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. • High doses of cytarabine can affect the nervous system. Nervous system changes • Tell your doctor or nurse immediately, or go to the nearest hospital Emergency from cytarabine Department if you get any of the following symptoms during or soon after your treatment: o dizziness, drowsiness or double vision agitation o difficulty walking in a straight line o difficulty writing with a pen or pencil jerky movements slow, slurred speech. · You may get: Eye problems from eye pain or irritation cytarabine blurred vision watery or gritty eyes o 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. • You may find that food loses its taste or tastes different. Taste and smell changes • 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:
 - o a temperature of 38°C or higher
 - o chills, shivers, sweats or shakes
 - o 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
 - o cramping or pain
 - o 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.

Appetite loss (anorexia)

- · You may not feel like eating.
- Try to avoid drinking fluids at meal times.
- Try to eat small meals or snacks regularly throughout the day.
- Try to eat food that is high in protein and calories.
- If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.

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.

Mouth pain and soreness (mucositis)

- · You may have:
 - bleeding gums
 - o mouth ulcers
 - a white coating on your tongue
 - pain in the mouth or throat
 - o 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:
 - o 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.

Hand-foot syndrome (palmar-plantar erythrodysaesthesia)

- The palms of your hands and soles of your feet may become:
 - o red and hot
 - swollen
 - painful and tender
 - o blistered.
- The skin in the area may also peel.
- Moisturise your hands and feet daily with sorbolene or aqueous cream.
- Keep your hands and feet clean and dry.
- Avoid hot water, instead use lukewarm water to bathe.
- Avoid direct sunlight.
- Avoid unnecessary walking, jogging or exercise.
- Wear cotton socks and avoid tight-fitting shoes.
- Tell your doctor or nurse as soon as possible if you notice any skin changes on your hands or feet.

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 mont	hs)
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 chemotherap (chemo brain). Tell your doctor or nurse if you get any of the symptoms listed above.
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 colou the whites of your eyes look yellow, or if you have stomach pain.

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

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

rotavirus vaccine.

Other medical and dental treatment

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

Diet and food safety

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

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

Quitting smoking

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

Staying active

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

For more information about cancer treatment, side effects and side effect management see our Patient and carers section.

Where to get more information

Telephone support

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

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation arrow.org.au
- Australasian Menopause Society menopause.org.au
- Chris O'Brien Lifehouse Total Body Irradiation mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/

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

General cancer information and support

- Australian Rare Cancer (ARC) Portal arcportal.org.au/
- Beyondblue beyondblue.org.au
- Cancer Australia canceraustralia.gov.au
- Cancer Council Australia cancer.org.au
- Cancer Voices Australia cancervoicesaustralia.org
- CanTeen canteen.org.au
- Carers Australia carersaustralia.com.au
- Carer Help carerhelp.com.au
- eviQ Cancer Treatments Online eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- LGBTQI+ People and Cancer cancercouncil.com.au/cancer-information/lgbtgi
- Look Good Feel Better Igfb.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:

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

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