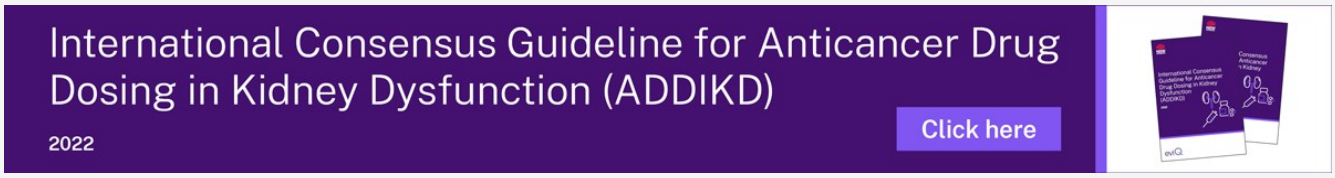
Acute myeloid leukaemia gilteritinib

ID: 3907 v.1 **Endorsed**

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

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.



Treatment schedule - Overview

Drug	Dose	Route
Gilteritinib	120 mg ONCE a day *	PO

*Response may be delayed; therefore, continuation of treatment at the prescribed dose for up to 6 months should be considered to allow time for a clinical response. In the absence of a response (patient did not achieve a composite complete remission (CRc)) after 4 weeks of treatment, the dose can be increased to 200 mg once daily, if tolerated or clinically warranted.

Continuous until disease progression or unacceptable toxicity

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Drug status: **Gilteritinib:** (PBS authority)

Gilteritinib is available as **40 mg** tablets

Treatment schedule - Detail

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

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

Continuous treatment		
Gilteritinib	120 mg (PO)	ONCE a day at the same time with or without food. Swallow tablets whole with a glass of water.

Note: Response may be delayed; therefore, continuation of treatment at the prescribed dose for up to 6 months should be considered to allow time for a clinical response. In the absence of a response (patient did not achieve a composite complete remission (CRc)) after 4 weeks of treatment, the dose can be increased to 200 mg once daily, if tolerated or clinically warranted.

Continuous until disease progression or unacceptable toxicity

Indications and patient population

- Relapsed or refractory acute myeloid leukaemia (AML) in patients with a FMS-like tyrosine kinase 3 (FLT3) mutation.

Clinical information

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
Hypersensitivity	Serious hypersensitivity reactions, including anaphylaxis, have been reported with gilteritinib. Read more about Hypersensitivity reaction
Emetogenicity minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Prolongation of QT interval	Gilteritinib has been associated with prolonged QT interval, increasing the risk of cardiac arrhythmia. Patients with QTc > 500 msec should not be commenced on gilteritinib, and treatment should be interrupted. QT prolongation can be observed in the first 3 months of treatment. Therefore, an electrocardiogram (ECG) should be performed prior to commencement of treatment and on day 8 and 15 of cycle 1, and prior to the start of the next 3 subsequent months of treatment. In addition, an ECG should be performed in case of dose increase, following the same schedule. Hypokalaemia or hypomagnesaemia may increase the QT prolongation risk. Risk factors (e.g. electrolyte abnormalities) should be corrected, where possible, prior to commencement of gilteritinib and the concurrent use of drugs that may prolong the QT interval should be avoided. Note that azole antifungals may contribute to QTc prolongation. If QT prolongation occurs, treatment interruption, dose modification or treatment discontinuation may be required. Consider review by a cardiologist. Read more about drugs that may prolong QTc interval at crediblemeds.org (registration required).
Differentiation syndrome	Gilteritinib has been associated with differentiation syndrome occurring as early as one day and up to 82 days after treatment initiation. This is life-threatening or potentially fatal if not treated. Signs and symptoms of differentiation syndrome include fever, dyspnoea, pleural effusion, pericardial effusion, pulmonary oedema, hypotension, rapid weight gain, peripheral oedema, rash, and kidney dysfunction. If differentiation syndrome is suspected, corticosteroid therapy should be initiated along with haemodynamic monitoring until symptom resolution.
Reversible posterior leukoencephalopathy syndrome (RPLS)	Reversible posterior leukoencephalopathy syndrome (RPLS) has been reported in patients receiving this treatment and may be fatal. Discontinue drug in patients developing RPLS. Read more about reversible posterior leukoencephalopathy syndrome (RPLS)
Pancreatitis	Pancreatitis has been reported in patients receiving gilteritinib. Patients who develop signs and symptoms suggestive of pancreatitis should be evaluated and monitored. Treatment with gilteritinib should be interrupted and can be resumed at a reduced dose when the signs and symptoms of pancreatitis have resolved.
Hepatotoxicity	Serious cases of hepatic toxicity have occurred in patients treated with gilteritinib. Liver enzymes and bilirubin level should be monitored.
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
PJP prophylaxis	PJP prophylaxis at the discretion of the treating clinician. Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients

Antifungal and antiviral prophylaxis	Antifungal and antiviral prophylaxis should be determined according to individual institutional policy. Note that azole antifungals may contribute to QTc prolongation. Read more about antiviral and antifungal prophylaxis
Blood tests	FBC, EUC, eGFR, CMP, LFTs, TFTs, coagulation studies, D-dimer and creatine phosphokinase at baseline, day 15 and then monthly for the duration of treatment or as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. 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).

Criteria	Gilteritinib dosing
Differentiation syndrome	• If differentiation syndrome is suspected, administer systemic corticosteroids and initiate haemodynamic monitoring until symptom resolution and for a minimum of 3 days • Interrupt gilteritinib if severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids • Resume gilteritinib at the same dose when signs and symptoms improve to Grade 2[a] or lower.
Reversible posterior leukoencephalopathy syndrome	• Discontinue gilteritinib

(RPLS)	
QTc interval >500 msec	• Interrupt treatment and resume at a reduced dose (80 mg or 120 mg[b]) when QTc interval returns to within 30 msec of baseline or ≤480 msec
QTc interval increased by >30 msec on ECG on day 8 of cycle 1	• Confirm with ECG on day 9 • If confirmed, consider dose reduction to 80 mg or 120 mg[b] • Azole antifungals may contribute to QTc prolongation.
Symptoms of pancreatitis	• Interrupt treatment until pancreatitis is resolved and resume at a reduced dose (80 mg or 120 mg[b])
Other Grade 3[a] or higher toxicity considered related to treatment.	• Gilteritinib should be interrupted until toxicity resolves or improves to Grade 1[a] • Treatment with gilteritinib can be resumed at a reduced dose (80 mg or 120 mg[b]) • Consider a liver biopsy if the patient has deranged LFTs post-HSCT to differentiate between drug-related hepatotoxicity and hepatic GVHD.
Planned haematopoietic stem cell transplantation (HSCT)	• Interrupt treatment with gilteritinib one week prior to administration of the conditioning regimen for HSCT • Treatment can be resumed 30 days after HSCT if engraftment was successful, the patient did not have grade ≥2 acute graft versus host disease and was in CRc[c].

a. Grade 1 is mild, Grade 2 is moderate, Grade 3 is serious, Grade 4 is life-threatening.
b. The daily dose can be reduced from 120 mg to 80 mg or from 200 mg to 120 mg.
c. Composite complete remission (CRc) is defined as the remission rate of all CR , CRp [achieved CR except for incomplete platelet recovery (<100 x 10^9/L)] and CRi (achieved all criteria for CR except for incomplete haematological recovery with residual neutropenia <1 x 10^9/L with or without complete platelet recovery).

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*

Gilteritinib		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of gilteritinib possible due to reduced clearance	Monitor for gilteritinib toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of gilteritinib possible due to increased clearance	Avoid combination or monitor for decreased clinical response to gilteritinib.
Drugs that target $5HT_{2B}$ receptor or sigma non-specific receptor (e.g. escitalopram, sertraline etc.)	Concomitant use of gilteritinib may reduce the effects of drugs that target $5HT_{2B}$ receptor or the sigma non-specific receptor.	Avoid combination unless the use is considered essential for care of the patient.

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

Administration

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

product information monographs via the TGA website for further information.

Administration

This is a continuous oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

Pre treatment medication

Administer antiemetics if required

Treatment - Time out

Gilteritinib

- administer orally ONCE daily, at approximately the same time each day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food

Note: if a dose is missed or not taken at the usual time, the dose should be taken as possible on the same day, and patients should return to the normal schedule the following day. If vomiting occurs after dosing, patients should not take another dose but should return to the normal schedule the following day.

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

Discharge information

Gilteritinib tablets

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

Antiemetics

- Antiemetics as prescribed.

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)	
Headache	
Hypersensitivity reaction	Anaphylaxis and treatment related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
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
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
Dizziness	Feeling faint or lightheaded, weak or unsteady. Advise patients to stand up slowly from sitting down or lying down positions and increase fluid intake if dehydrated.
Dyspnoea	
Fatigue	Read more about fatigue
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Hypotension	Low blood pressure can occur with this treatment.

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
QT prolongation	This treatment can cause QTc interval prolongation. QTc prolongation can lead to ventricular arrhythmias that may be fatal.

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

The evidence supporting this protocol is provided by the phase III multicentre international randomised ADMIRAL trial, involving 371 patients.[1] The ADMIRAL trial compared gilteritinib with salvage chemotherapy in patients with relapsed or refractory acute myeloid leukaemia (AML) with mutations in the FMS-like tyrosine kinase 3 (FLT3) gene. This trial included patients with both FLT3 internal tandem duplication (ITD) and FLT 3 tyrosine kinase domain (TKD) mutations. Between October 2015 and September 2018, 247 patients were randomised to receive gilteritinib at 120 mg per day in 28-day cycles, and 124 patients were randomised to receive salvage chemotherapy. Salvage chemotherapy regimens included mitoxantrone, etoposide and cytarabine (MEC); fludarabine, cytarabine, granulocyte colony-stimulating factor and idarubicin (FLAG-IDA); low-dose cytarabine and azacitidine.

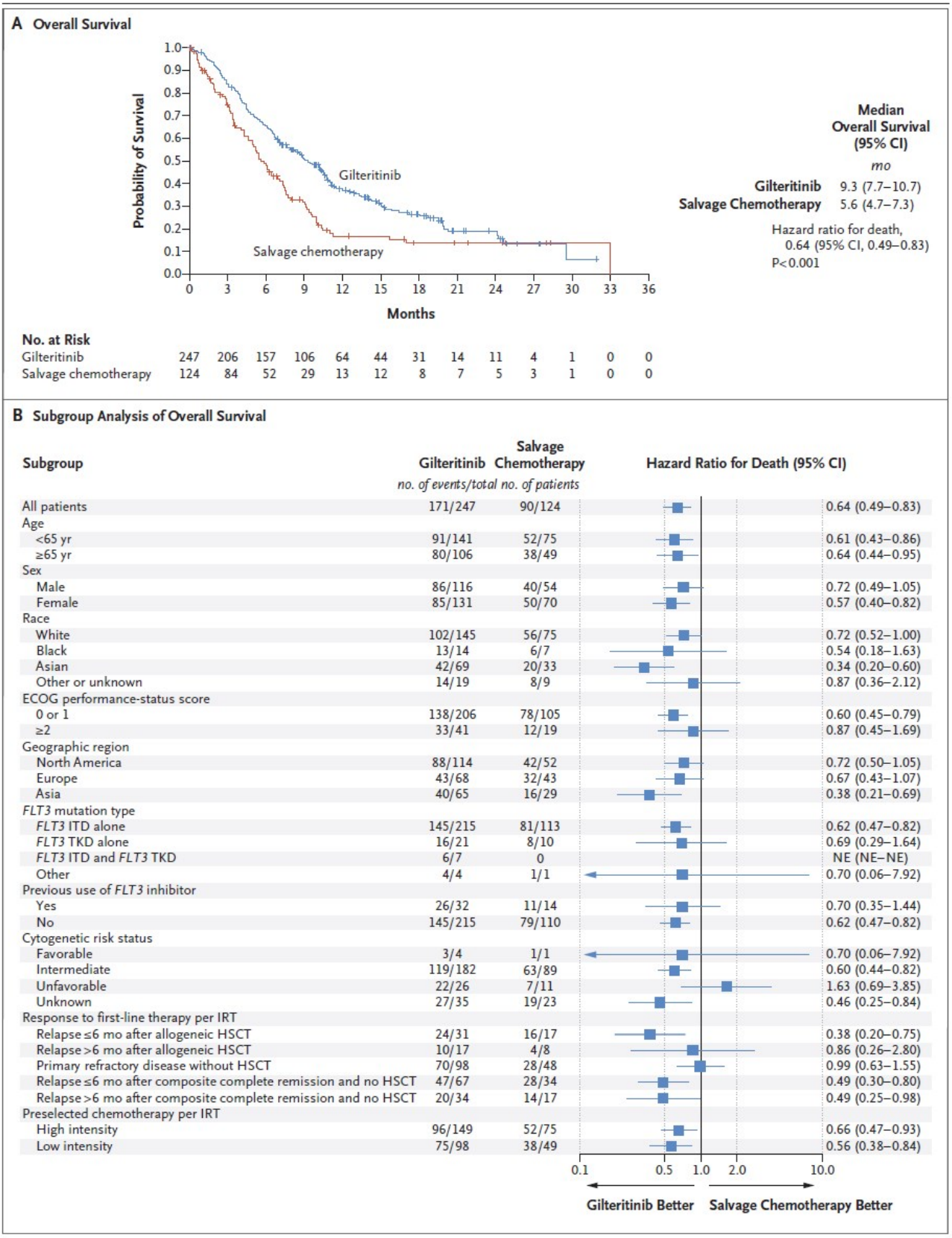
The two primary endpoints were overall survival (OS) and the percentage of patients who had complete remission (CR) with full or partial haematological recovery. Secondary endpoints included event-free survival (freedom from treatment failure) and the percentage of patients who achieved CR.

Gilteritinib resulted in significantly longer survival and higher percentages of patients with remission than salvage chemotherapy among patients with relapsed or refractory FLT-3 mutated AML.

Efficacy

After a median follow up of 17.8 months, the median OS was 9.3 months in the gilteritinib group vs. 5.6 months in the chemotherapy group (HR=0.64; CI 95% 0.49 to 0.83; p<0.0001). A consistent pattern of longer survival with gilteritinib than with chemotherapy was noted across multiple subgroups including the high-intensity and low-intensity chemotherapy cohorts and the high FLT3 ITD allelic ratio subgroup.[1]

Figure A and B: Overall survival among patients with FLT3-mutated relapsed or refractory AML treated with gilteritinib or salvage chemotherapy (intention-to-treat population)[1]



The percentage of patients who achieved CR with full or partial haematological recovery was 34% in the gilteritinib group and 15.3% in the chemotherapy group. The median event-free survival was 2.8 months in the gilteritinib group and 0.7 months in the chemotherapy group and did not differ significantly between the treatment groups.[1]

Toxicity

Common adverse events of grade 3 or higher in the gilteritinib group were febrile neutropenia (45.9%), anaemia (40.7%) and thrombocytopenia (22.8%). Drug-related adverse events leading to the discontinuation of gilteritinib occurred in 27 patients (11%); the most common events were elevated aspartate aminotransferase level, elevated alanine aminotransferase level and pneumonia. Prolonged corrected QT intervals that were calculated with Fridericia's formula that were considered to be possibly related to gilteritinib therapy occurred in 12 patients (4.9%).[1]

There were 251 deaths in the safety population of 355 patients, including 170 deaths among 246 patients (69.1%) in the gilteritinib group and 81 deaths among 109 patients (74.3%) in the chemotherapy group. Common fatal adverse events in both groups were disease progression and infection.[1]

Incidence of adverse events (ADMIRAL trial)[1]

Table 3. Incidence of Adverse Events during Treatment That Occurred in at Least 20% of the Patients in Either Treatment Group (Safety Analysis Population).*

Event	Gilteritinib (N=246)			Salvage Chemotherapy (N=109)		
	Adverse Event of Any Grade	Grade ≥3 Adverse Event	Serious Adverse Event	Adverse Event of Any Grade	Grade ≥3 Adverse Event	Serious Adverse Event
	number of patients (percent)					
Febrile neutropenia	115 (46.7)	113 (45.9)	76 (30.9)	40 (36.7)	40 (36.7)	9 (8.3)
Anemia	116 (47.2)	100 (40.7)	8 (3.3)	38 (34.9)	33 (30.3)	0
Pyrexia	105 (42.7)	8 (3.3)	32 (13.0)	32 (29.4)	4 (3.7)	1 (0.9)
Alanine aminotransferase increased	103 (41.9)	34 (13.8)	13 (5.3)	10 (9.2)	5 (4.6)	0
Diarrhea	81 (32.9)	9 (3.7)	10 (4.1)	32 (29.4)	3 (2.8)	0
Aspartate aminotransferase increased	99 (40.2)	36 (14.6)	10 (4.1)	13 (11.9)	2 (1.8)	0
Hypokalemia	71 (28.9)	32 (13.0)	0	34 (31.2)	12 (11.0)	1 (0.9)
Constipation	76 (30.9)	2 (0.8)	0	16 (14.7)	0	0
Fatigue	70 (28.5)	6 (2.4)	4 (1.6)	14 (12.8)	2 (1.8)	1 (0.9)
Platelet count decreased	56 (22.8)	54 (22.0)	5 (2.0)	28 (25.7)	27 (24.8)	0
Cough	72 (29.3)	1 (0.4)	2 (0.8)	11 (10.1)	0	0
Thrombocytopenia	63 (25.6)	56 (22.8)	4 (1.6)	18 (16.5)	18 (16.5)	1 (0.9)
Headache	64 (26.0)	3 (1.2)	5 (2.0)	16 (14.7)	0	0
Peripheral edema	59 (24.0)	1 (0.4)	0	13 (11.9)	0	0
Vomiting	53 (21.5)	1 (0.4)	1 (0.4)	15 (13.8)	0	0
Dyspnea	58 (23.6)	10 (4.1)	10 (4.1)	7 (6.4)	3 (2.8)	2 (1.8)
Blood alkaline phosphatase increased	56 (22.8)	7 (2.8)	1 (0.4)	2 (1.8)	0	0

* The events shown are limited to adverse events that had a difference in incidence of more than 2 percentage points between the treatment groups. The safety population comprised all the patients who had received at least one dose of trial treatment.

References

1 Perl, A. E., G. Martinelli, J. E. Cortes, et al. 2019. "Gilteritinib or Chemotherapy for Relapsed or Refractory FLT3-Mutated AML." N Engl J Med 381(18):1728-1740.

History

Version 1

Date	Summary of changes
20/01/2021	New protocol presented at the Haematology reference committee meeting and approved for publication. For review in 1 year.
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.
24/01/2022	Pulmonary toxicity added to side effects.
11/03/2022	Protocol reviewed at Haematology Reference Committee meeting; minor change to dose modifications (add a note re: liver biopsy for deranged LFTs). Review in 2 years.

First approved: 20 January 2021
Last reviewed: 11 March 2022
Review due: 30 June 2024

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/3907
19 Sep 2023

Patient information - Acute myeloid leukaemia (AML) - Gilteritinib

Patient's name:

Your treatment

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

Gilteritinib		
This treatment is taken continuously. Your doctor will advise you how long to take the tablets.		
Day	**Treatment**	**How it is given**
Continuous	**Gilteritinib** *(gil-te-ri-ti-nib)*	Take orally ONCE a day, at about the same time with or without food. Swallow the tablets whole with a glass of water, do not break, crush or chew. If you vomit the tablets, take your normal dose the following day. Do not take an extra dose. If you forget to take a dose, and it is less than 12 hours late, take it as soon as you remember. If it is more than 12 hours late, skip that dose and take your normal dose the next time it is due (the following day). Do not take an extra dose.

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:

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.

You will need to have a blood test before you start treatment. Your doctor or nurse will tell you when to have the blood test.

Medications for blood pressure

This medication may lower your blood pressure. Tell your doctor if you are taking any blood pressure medications. Your doctor may advise you to adjust or temporarily stop your blood pressure medications whilst you are on this treatment.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.

Side effects

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

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

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

Immediate (onset hours to days)	
Headache	• You can take paracetamol 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.**
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<u>While you are in hospital:</u> Tell your doctor or nurse immediately.** **<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
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.**
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.**
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.
Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**

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.**
Dizziness or feeling light-headed	• You may feel dizzy or light-headed. • These symptoms may be caused by your treatment, or other problems like dehydration. • If you are feeling dehydrated, drink plenty of fluids (unless you are fluid restricted) as this can be a cause of dizziness. • If you are feeling dizzy, try lying down until the dizziness passes. • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Tell your doctor or nurse if you get any of the symptoms listed above.
Shortness of breath	• You may have a cough. • You may feel short of breath. • **Tell your doctor or nurse immediately if you feel you have a cough or feel short of breath.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**

Liver problems	• You may get:
	  ◦ yellowing of your skin or eyes
	  ◦ itchy skin
	  ◦ pain or tenderness in your stomach
	  ◦ nausea and vomiting
	  ◦ loss of appetite
	• You will have regular blood tests to check how well your liver is working.
	• **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**

Low blood pressure (hypotension)	• You may get low blood pressure from this treatment. • You may feel dizzy or light-headed. • Tell your doctor if you are taking blood pressure medication. • Your doctor will monitor your blood pressure regularly while you are on this treatment. • Drink plenty of fluids (unless you are fluid restricted). • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Do not drive or operate machinery if you feel dizzy or light-headed. • Tell your doctor or nurse if you get any of the signs or symptoms listed above.

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.**
Heart changes	• You may get chest pain, shortness of breath, an abnormal heartbeat or swelling in your arms or legs. • Before, during or after treatment you may be asked to have tests to see how well your heart is working. • You will also have other blood tests to check your electrolyte levels. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department, if you get any of the symptoms listed above.**

Delayed (onset months to years)	

Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment.
	• You may get:
	  ◦ shortness of breath
	  ◦ fever
	  ◦ dry cough
	  ◦ wheezing
	  ◦ fast heartbeat
	  ◦ chest pain.
	• Your doctor will monitor how well your lungs are working during your treatment.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don’t stop or start any medications during treatment without talking to your doctor and pharmacist first.

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

Other medical and dental treatment

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

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/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

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

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

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https://www.eviq.org.au/pi/3907
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