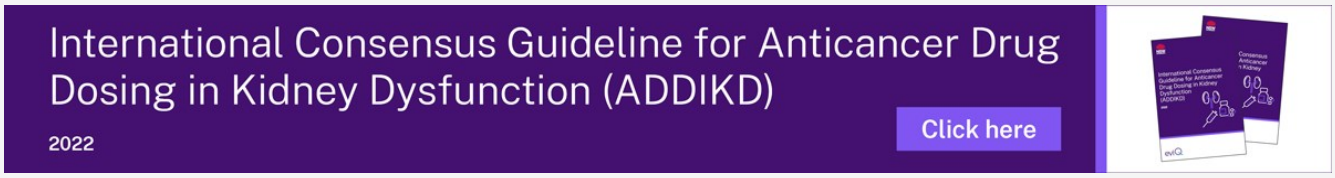
Acute lymphoblastic leukaemia daSATinib

ID: 3506 v.2 **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.



Related pages:

- Acute lymphoblastic leukaemia pONATinib
- Acute lymphoblastic leukaemia Ph+ hyper CVAD and daSATinib part A and B/maintenance overview

Treatment schedule - Overview

Drug	Dose	Route
daSATinib	140 mg ONCE a day *	PO

* Dose may be reduced to 100 mg ONCE a day if combined with chemotherapy.[1, 2]

Continuous as long as there is no evidence of progressive disease or unacceptable toxicity

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

Dasatinib is available as **20 mg**, **50 mg**, **70 mg**, **100 mg** tablets

Cost: ~ $3,760 per month

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		
daSATinib	140 mg (PO)	ONCE a day with or without food *

* Dose may be reduced to 100 mg ONCE a day if combined with chemotherapy.[1, 2]

Continuous as long as there is no evidence of progressive disease or unacceptable toxicity

Indications and patient population

- Philadelphia chromosome (BCR-ABL1) positive relapsed/refractory acute lymphoblastic leukaemia

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
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
Administration details	Long-term suppression of gastric secretions may decrease the absorption of some tyrosine kinase inhibitors (TKIs). Patients should avoid taking H2-receptor antagonists or proton-pump inhibitors while undergoing therapy with this TKI. Antacids may be used instead, but should be avoided within 2 hours of the TKI dose.
Prolongation of QT interval	This treatment may prolong the QT interval and increase the risk of cardiac arrhythmia. Use with caution in patients with a congenital long QT syndrome, patients treated with a high cumulative dose of anthracycline therapy, patients taking medications that may prolong the QT interval and those with electrolyte disturbances. Risk factors (e.g. electrolyte abnormalities) should be corrected, where possible, prior to commencement of treatment and the concurrent use of drugs that may prolong the QT interval should be avoided. Baseline and periodic monitoring of electrocardiogram (ECG) and electrolytes (potassium, magnesium, calcium) should be considered in patients at high risk of QT prolongation. Read more about drugs that may prolong QTc interval at crediblemeds.org (registration required).
Cardiac toxicity	Tyrosine kinase inhibitors have been associated with cardiac complications of varying degrees and severity. Patients, especially those with pre-existing cardiovascular disease, should have a baseline cardiac assessment including an electrocardiogram (ECG) and biochemistry and be closely monitored; consider an echocardiogram (ECHO) as clinically indicated. Cardiac assessment should then be repeated as clinically indicated or when starting new medication which affects the QT interval. Read more about cardiac toxicity associated with anti-cancer drugs
Pulmonary complications	Clinicians should evaluate patients for signs and symptoms of underlying cardiopulmonary disease before starting treatment and during treatment. Pleural effusions are dose dependent events and dose interruption, reduction or steroids should be considered. They are more common with dasatinib than with imatinib and may be bilateral or unilateral. Up to 35 % of patients treated with dasatinib on phase I/II studies developed pleural effusions, most often exudative. Pulmonary arterial hypertension (PAH) is an uncommon but serious complication. Echocardiogram is recommended in symptomatic patients (i.e. dyspnoea, cough, fatigue) and those with pleural effusions. Dasatinib should be withheld during evaluation if symptoms are severe, and permanently discontinued if PAH is confirmed i.e. not rechallenged. Pneumonitis and interstitial lung disease has also been reported.

Fluid retention/oedema	Dasatinib may cause severe fluid retention, including pleural and pericardial effusions, severe ascites, severe pulmonary oedema, and generalised oedema. This may be dose-related. Risk increases in patients greater than 65 years, patients with hypertension or prior cardiac history and those treated with twice daily dosing. (Note: once daily dosing is the recommended dosing schedule for all phases). Monitor regularly for signs and symptoms of fluid retention. Chest x-ray is recommended for symptoms suggestive of pleural effusion (eg. cough, dyspnoea).
Diarrhoea	Consider prescribing prophylactic anti-diarrhoeal (e.g. loperamide) to prevent treatment induced diarrhoea. If severe diarrhoea occurs, discontinue dasatinib until condition improves or resolves. Read more about treatment induced diarrhoea
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
Cytogenetic and molecular tests	Assess cytogenetic responses by bone-marrow aspirate/biopsy every month for the first 3 months and every 3 months thereafter or at the discretion of the clinician.
Molecular testing	RQ-PCR (real-time quantitative polymerase chain reaction test) for BCR-ABL1 transcripts should be performed at baseline and periodically throughout treatment according to clinician discretion. Mutation screening for ABL1 kinase domain mutations is recommended at the time of disease progression and can be considered at baseline.
Blood tests	FBC, EUC, LFTs, calcium, magnesium, phosphate, TSH and BSL at baseline. Repeat FBC weekly for the first two months, then monthly or as clinically indicated. Continue to monitor EUC, LFTs, calcium, magnesium, phosphate, TSH and BSL regularly throughout 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. Pregnancy must be avoided while a female patient is on tyrosine kinase inhibitor (TKI) therapy. There are very few reports of pregnancy outcomes in partners of men receiving second or third-generation TKIs. Although the majority of infants fathered by men taking dasatinib were reported to be without congenital disabilities at birth, the general advice is for couples to avoid pregnancy (Carlier et al., 2017; Cortes et al., 2015). The safety of these drugs has not been proven, and therefore, pregnancy should be avoided. Effective contraception methods and adequate contraception timeframes should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility. Link to Carlier et al. and Cortes et al. references.

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the

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

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

Haematological toxicity	
Dose adjustment is based upon: • **the haematological, cytogenetic and molecular response to therapy and** • **consideration of toxicity (specifically the development of dose-limiting neutropenia or thrombocytopenia).**	
Starting dose 140 mg once daily	
ANC less than 0.5 x 10^9/L and/or platelets less than 10 x 10^9/L	Determine if cytopenia is related to leukaemia via marrow aspirate or biopsy. If cytopenia unrelated to leukaemia, cease dasatinib until recovery to ANC greater than or equal to 1.0 x 10^9/L and platelets greater than or equal to 20 x 10^9/L then resume daily dose at: • First occurrence: 140 mg (i.e. original starting dose) • Second occurrence: 100 mg • Third occurrence: 70 mg If cytopenia related to leukaemia, consider dose escalation to 180 mg once daily.

Note: *The effects of dasatinib on platelet activation may also contribute to bleeding in addition to the thrombocytopenia. The dose modifications above are based on the study by Sugiura et al.[1] and dasatinib PI.*

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

Renal impairment
Dasatinib has not been studied in patients with renal impairment, since renal excretion of unchanged dasatinib and its metabolites is minimal (<4%), a decrease in total body clearance is not expected in patients with renal impairment.

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

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*

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

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 an oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Dasatinib

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

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

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

Discharge information

Dasatinib tablets

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

Antiemetics

- Antiemetics as prescribed.

Antidiarrhoeals

- Antidiarrhoeals 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	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Taste and smell alteration	Read more about taste and smell changes

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Cardiotoxicity	Cardiotoxicity may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, hypertension, cardiac ischaemia and congestive heart failure (CHF). The risk of cardiotoxicity is increased by a number of factors, particularly a history of heart disease and electrolyte imbalances. Read more about cardiotoxicity associated with anti-cancer drugs
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Haemorrhage	
Ototoxicity	Tinnitus and hearing loss may occur due to damage in the inner ear. Tinnitus is usually reversible, while hearing loss is generally irreversible. Hearing loss is dose-related, cumulative and may be worse in those with pre-existing hearing problems. Read more about ototoxicity - tinnitus and hearing loss
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
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 - partial	Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Depression	

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

Philadelphia positive acute lymphoblastic leukaemia (ALL) responds less favourably than Philadelphia negative ALL when treated with chemotherapy alone.[3] Current treatment guidelines recommend the inclusion of tyrosine kinase inhibitors (TKIs). The second-generation TKI, dasatinib, has shown efficacy as a single agent[4, 5] and when combined with HyperCVAD chemotherapy.[2]

The evidence supporting the use of single-agent dasatinib in relapsed/refractory Philadelphia positive ALL is provided by a phase II trial of 36 patients,[4] which was followed by a larger phase III multicentre international open-label randomised trial involving 84 patients comparing two dosing strategies of dasatinib in patients with Philadelphia positive ALL who had resistance or intolerance to initial treatment with imatinib.[5]

Between June 2005 and March 2006, 40 patients were randomised to receive dasatinib 140 mg once daily and 44 patients to receive dasatinib 70 mg twice daily. Treatment was continued until disease progression, unacceptable toxicity or withdrawal at patient or investigator request. No additional therapy was permitted other than hydroxycarbamide (hydroxyurea) for elevated white cell count. Dose increases up to 180 mg daily were permitted for inadequate treatment response.[5]

The primary endpoint was major haematologic response (MaHR), and secondary endpoints were overall haematologic response (OHR), major cytogenetic response (MCyR), progression-free survival (PFS), overall survival (OS) and safety.[5]

There were no significant differences with regards to primary or secondary endpoints between the two dosing strategies.[5]

Efficacy

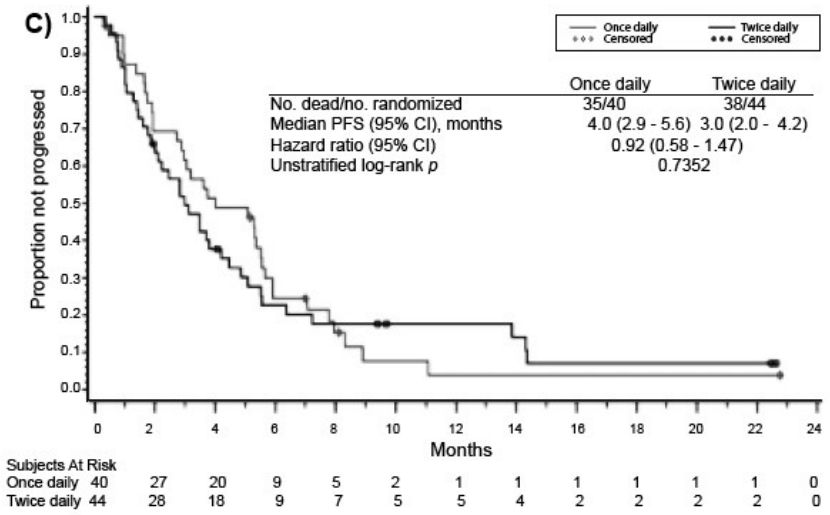
A MaHR was achieved by 22 (55%) and 19 (43%) of patients in the once and twice-daily groups, respectively. MCyR was seen in 28 (70%) and 23 (52%) patients, without significant difference between the two groups.[5]

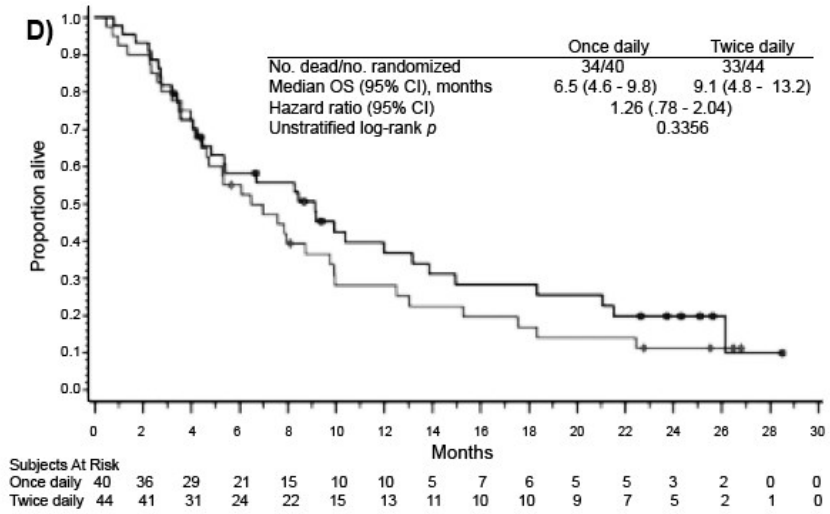
The median PFS was 4.0 months in the once-daily group and 3.1 months in the twice-daily group (p=0.735). The median OS was 6.5 months in the once-daily group and 9.1 months in the twice-daily group (p=0.336). There were no significant differences in outcomes between either once or twice-daily dosing. Only 2 patients in the once-daily group and 3 patients in the twice-daily group were still on therapy at 2-year follow-up, though 5 patients discontinued in order to proceed to transplant.[5]

There did not appear to be a difference in outcome between those patients who failed imatinib due to resistance and those who experienced imatinib intolerance. The three patients with T315I mutation detected had no objective response to dasatinib, as would be expected.[5]

Dasatinib is optimally combined with chemotherapy for efficacy in Philadelphia positive ALL.[1, 2]

Figure 1: Kaplan-Meier analyses[5]





C: Progression-free survival computed on all randomised patients. Patients who neither progressed nor died were censored on the date of last cytogenetic or haematologic assessment.
D: Overall survival computed on all randomised patients. Patients who had not died or who were lost to follow-up were censored on the last date on which they were known to have been alive.
CI, confidence interval; NA, not available.

Toxicity

The incidence and severity of adverse events were similar between the once and twice-daily dosing groups. There was a trend towards less pleural effusions in the once-daily group, which mirrors findings the finding from a study of dasatinib in accelerated phase chronic myeloid leukaemia.[6]

Table 1. Dasatinib-related adverse events[5]

	140 mg once daily (n = 40)		70 mg twice daily (n = 44)	
	All grades	Grade 3/4	All grades	Grade 3/4
Cytopenia, n (%)				
Anemia	39 (100)	14 (35)	43 (98)	16 (36)
Leukocytopenia	33 (85)	21 (53)	35 (81)	30 (70)
Neutropenia	33 (85)	26 (67)	34 (79)	31 (72)
Thrombocytopenia	36 (92)	28 (72)	38 (88)	26 (60)
Fluid retention, n (%)	12 (30)	1 (3)	19 (43)	7 (16)
Pleural effusion	7 (18)[b]	1 (3)[c]	14 (32)[b]	6 (14)[c]
Superficial edema	7 (18)	0	8 (18)	1 (2)
Other fluid-related events	1 (3)	0	7 (16)	2 (5)
Ascites	0	0	1 (2)	0
Generalized edema	1 (3)	0	4 (9)	1 (2)
Pericardial effusion	1 (3)	0	1 (2)	0
Pulmonary edema	0	0	3 (7)	1 (2)
Other adverse events, n (%)[d]				
Diarrhea	14 (35)	2 (5)	12 (27)	2 (5)
Nausea	11 (28)	1 (3)	11 (25)	2 (5)
Vomiting	8 (20)	0	8 (18)	1 (2)
Infection	7 (18)	3 (8)	4 (9)	2 (5)
Hemorrhage	6 (15)	2 (5)	7 (16)	3 (7)
Gastrointestinal bleeding	2 (5)	2 (5)	5 (11)	3 (7)
Central nervous system	0	0	1 (2)	0
Other	4 (10)	0	4 (9)	1 (2)
Pyrexia	6 (15)	0	7 (16)	0
Febrile neutropenia	5 (13)	5 (13)	3 (7)	3 (7)
Musculoskeletal pain	5 (13)	0	3 (7)	1 (2)
Dyspnea	4 (10)	1 (3)	10 (23)	0
Fatigue	4 (10)	0	6 (14)	0
Gastritis	4 (10)	1 (3)	0	0
Headache	4 (10)	0	3 (7)	1 (2)
Anorexia	3 (8)	0	5 (11)	0
Rash	2 (5)	0	8 (18)	0

[a] Graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 3.0. Cytopenia values were based on clinical laboratory measurements on available samples. All other events were based on adverse reaction reports.

[b] $P = 0.207$.

[c] $P = 0.115$.

[d] Adverse events experienced by ≥10% of patients in any group.

References

1 Sugiura, I., N. Doki, T. Hata et al. 2022. "Dasatinib-based 2-step induction for adults with Philadelphia chromosome–positive acute lymphoblastic leukemia". Blood Adv., 6(2):624-636.

2 Benjamini, O., T. L. Dumlao, H. Kantarjian, et al. 2014. "Phase II trial of hyper CVAD and dasatinib in patients with relapsed Philadelphia chromosome positive acute lymphoblastic leukemia or blast phase chronic myeloid leukemia." Am J Hematol 89(3):282-287.

3 Secker-Walker, L. M., J. M. Craig, J. M. Hawkins, et al. 1991. "Philadelphia positive acute lymphoblastic leukemia in adults: age distribution, BCR breakpoint and prognostic significance." Leukemia 5(3):196-199.

4 Ottmann, O., H. Dombret, G. Martinelli, et al. 2007. "Dasatinib induces rapid hematologic and cytogenetic responses in adult patients with Philadelphia chromosome positive acute lymphoblastic leukemia with resistance or intolerance to imatinib: interim results of a phase 2 study." Blood 110(7):2309-2315.

5 Lilly, M. B., O. G. Ottmann, N. P. Shah, et al. 2010. "Dasatinib 140 mg once daily versus 70 mg twice daily in patients with Ph-positive acute lymphoblastic leukemia who failed imatinib: Results from a phase 3 study." Am J Hematol 85(3):164-170.

6 Kantarjian H, Cortes J, Kim DW et al. 2009 " Phase 3 study of dasatinib 140 mg once daily versus 70 mg twice daily in patients with chronic myeloid leukemia in accelerated phase resistant or intolerant to imatinib: 15-month median follow-up."Blood. Jun 18;113(25):6322-9.

History

Version 2

Date	Summary of changes
11/03/2022	Protocol reviewed at 2022 Haematology Reference Committee meeting. Version updated to V.2, for review in 2 years. Updates include: • annotation to reduce dose to 100 mg once a day if combined with chemotherapy • amendments to clinical information regarding fertility • dose reduction to 70 mg for third occurrence of cytopenia and reference added • evidence update

Version 1

Date	Summary of changes
21/09/2018	New protocol taken to Haematology Reference Committee meeting
08/11/2018	Approved and published on eviQ. v.1.
23/10/2020	Protocol reviewed electronically by the Haematology Reference Committee, no changed. Review in 2 years.
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.
21/01/2022	Blood tests updated in clinical information. Pulmonary toxicity added to side effects.

First approved: 8 November 2018
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/3506
28 Jun 2023

Patient information - Acute lymphoblastic leukaemia (ALL) - Dasatinib

Patient's name:

Your treatment

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

Dasatinib		
This treatment is continuous. Your doctor will advise you how long to take the treatment for.		
Day	**Treatment**	**How it is given**
Continuous	**Dasatinib** *(duh-sat-in-nib)*	Take orally ONCE a day, at the same time each day, with or without food. Swallow whole with a large glass of water, do not break, crush or chew. If you are taking an antacid, do not take within two hours as this may interfere with its absorption. If you forget to take a dose or vomit a dose, take your normal dose the next time it is due. 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.

Blood tests and monitoring

You will need to have a blood test before you start treatment and regularly throughout your treatment. Your doctor or nurse will tell you when to have these blood tests.

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.
- **Antidiarrhoeals:** you may be given some medication to treat diarrhoea. Your doctor or nurse will tell you how and when to take your antidiarrhoeal medication.

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.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.
Early (onset days to weeks)	

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Stomach pain	• You may get: ◦ dull aches ◦ cramping or pain ◦ bloating or flatulence (gas). • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have stomach pain that you are unable to control.**
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.
Heart problems	• You may get: ◦ chest pain or tightness ◦ shortness of breath ◦ swelling of your ankles ◦ an abnormal heartbeat. • Heart problems can occur months to years after treatment. • Tell your doctor if you have a history of heart problems or high blood pressure. • Before or during treatment, you may be asked to have a test to see how well your heart is working. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**

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

Hearing changes (ototoxicity)	• You may get ringing in your ears or loss of hearing. • You may have your hearing tested before and during your treatment. • **Tell your doctor or nurse as soon as possible if you notice any changes to your hearing.**

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

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

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)

Depression	• You may find that you:
	  ◦ have a low mood
	  ◦ are tired
	  ◦ don't have much energy
	  ◦ lose interest in everyday activities
	  ◦ have trouble concentrating or making decisions.
	• Keep a diary of how you are feeling once your treatment has started.
	• Let your friends and family know how you are feeling.
	• Tell your doctor or nurse if you get any of the signs or symptoms listed above.

Delayed (onset months to years)	

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

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

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

Other medical and dental treatment

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

Diet and food safety

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

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

Quitting smoking

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

Staying active

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

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

Where to get more information

Telephone support

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

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – aci.health.nsw.gov.au/resources/blood-and-marrow-transplant
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au

- Carers Australia – carersaustralia.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

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

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

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https://www.eviq.org.au/pi/3506
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