Acute myeloid leukaemia azacitidine and venetoclax

ID: 3892 v.2 **Endorsed**

⚠ Warning: Life threatening tumour lysis syndrome with venetoclax:
Tumour lysis syndrome (TLS), which may be life threatening or fatal, has been reported in patients treated with venetoclax.

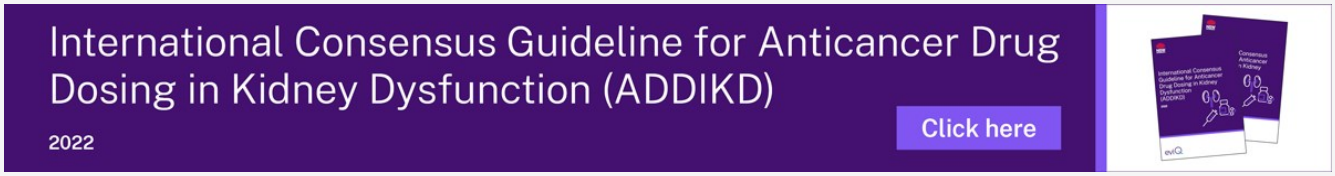
TLS prophylaxis and stringent blood chemistry monitoring is important.

⚠ Venetoclax azole interaction:
Azole antifungals reduce the clearance of venetoclax. If the combination is used, the dose of venetoclax should be adjusted as outlined in the protocol below.

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

This protocol is not exportable and does not have a calculator.

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

Cycle 1

Drug	Dose	Route	Day
Venetoclax	100 mg ONCE a day	PO	1
Venetoclax	200 mg ONCE a day	PO	2
Venetoclax	400 mg ONCE a day	PO	3 to 28
Azacitidine	75 mg/m^2	Subcut *	1 to 7 **

Cycle 2 and further cycles

Drug	Dose	Route	Day
Venetoclax	400 mg ONCE a day	PO	1 to 28
Azacitidine	75 mg/m^2	Subcut *	1 to 7 **

*Azacitidine can also be administered as an intravenous infusion.

**While the dosing schedule for azacitidine is recommended as 7 consecutive days, this is not practical for all cancer units and alternative scheduling may be used e.g. azacitidine for 5 days, followed by 2 day weekend break, followed by azacitidine for 2 days.[1, 2]

Frequency: 28 days

Cycles: **Continuous until disease progression or unacceptable toxicity**

Notes:

- Tumour lysis syndrome (TLS), which may be life threatening or fatal, has been reported in patients treated with venetoclax. TLS prophylaxis, stringent blood chemistry monitoring and adherence to dose modifications for toxicity is imperative. TLS blood monitoring is recommended at baseline and 6-8 hrs after each dose during dose escalation and at 24 hours after maximum intended dose reached. If clinical or biochemical TLS occurs, the next dose of treatment should be held until evidence of TLS resolves.
- Consider initiation as an inpatient during dose escalation with cycle 1.

Drug status: **Azacitidine and Venetoclax:** (PBS authority)

Venetoclax is available as **10 mg, 50 mg** and **100 mg** tablets

Note: all strengths are TGA registered but only 100 mg tablets are available through the PBS for this indication.

Cost: ~ $14,610 per cycle

Treatment schedule - Detail

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

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

Cycle 1

Day 1		
Venetoclax	100 mg (PO)	ONCE a day with food. Swallow tablet(s) whole with a glass of water.
Granisetron	2 mg (PO)	60 minutes before azacitidine
Azacitidine	75 mg/m^2 (Subcut)	Inject subcutaneously*. Roll the syringe between the palms to re-suspend. Rotate the site of injection.

Day 2		
Venetoclax	200 mg (PO)	ONCE a day with food. Swallow tablet(s) whole with a glass of water.
Granisetron	2 mg (PO)	60 minutes before azacitidine
Azacitidine	75 mg/m^2 (Subcut)	Inject subcutaneously*. Roll the syringe between the palms to re-suspend. Rotate the site of injection.

Day 3 to 7		
Venetoclax	400 mg (PO)	ONCE a day with food. Swallow tablet(s) whole with a glass of water.
Granisetron	2 mg (PO)	60 minutes before azacitidine
Azacitidine	75 mg/m^2 (Subcut)	Inject subcutaneously*. Roll the syringe between the palms to re-suspend. Rotate the site of injection.

Day 8 to 28		
Venetoclax	400 mg (PO)	ONCE a day with food. Swallow tablet(s) whole with a glass of water.

Cycle 2 and further cycles

Day 1 to 7		
Venetoclax	400 mg (PO)	ONCE a day with food. Swallow tablet(s) whole with a glass of water.

Day 1 to 7		
Granisetron	2 mg (PO)	60 minutes before azacitidine
Azacitidine	75 mg/m^2 (Subcut)	Inject subcutaneously*. Roll the syringe between the palms to re-suspend. Rotate the site of injection.

Day 8 to 28		
Venetoclax	400 mg (PO)	ONCE a day with food. Swallow tablet(s) whole with a glass of water.

*Azacitidine can also be administered as an intravenous infusion.

Note: While the dosing schedule for azacitidine is recommended as 7 consecutive days, this is not practical for all cancer units and alternative scheduling may be used e.g. azacitidine for 5 days, followed by 2 day weekend break, followed by azacitidine for 2 days.[1, 2]

Frequency: 28 days

Cycles: **Continuous until disease progression or unacceptable toxicity**

Indications and patient population

Indication:

- Acute myeloid leukaemia in patients deemed unfit for intensive chemotherapy.

Exclusions:

- Patients with myelofibrosis-associated AML and acute promyelocytic leukaemia (APML).

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 MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. Note: due to the risk of opportunistic infection daily, dexamethasone which is usually recommended for moderately emetogenic chemotherapy has been omitted in this protocol. For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist is available on the PBS in combination with a 5HT3 antagonist and steroid (which may be omitted). Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Injection site reactions	Injection site reactions are common with subcutaneous azacitidine. Ensure injection sites are rotated and that new injections are at least 2.5 cm from the previous site.
Gastrointestinal toxicity	Both diarrhoea and constipation are common side effects of treatment. Patients should be monitored closely, and prophylactic or symptom control anti-diarrhoeal/laxatives prescribed accordingly.

Tumour lysis risk	Tumour lysis syndrome (TLS), including renal failure requiring dialysis and fatal events, has occurred in patients with high tumour burden or high leukaemic burden being treated with venetoclax. Consider initiating venetoclax treatment as an inpatient for at risk patients. Assessment of TLS risk, prophylaxis and close monitoring is recommended. See Tumour lysis prophylaxis and monitoring during venetoclax treatment . If adverse events occur venetoclax interruption or discontinuation is recommended. See dose modifications section below.
Antifungals and antivirals	There are no specific recommendations for the use of antifungal or antiviral prophylaxis with this treatment. The use of prophylaxis should be at the discretion of the treating clinician and based on patient risk factors and local guidelines. Read more about antifungal and antiviral prophylaxis
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC, eGFR, LFTs, LDH and urate at baseline. TLS prophylaxis and stringent blood chemistry monitoring daily during dose escalation phase of venetoclax and adherence to dose modifications for toxicity is imperative. Repeat FBC, EUC, eGFR, LFTs, LDH and urate prior to each cycle and throughout treatment as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

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

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

Note:

- All dose reductions are calculated as a percentage of the starting dose.
- The haematological dose modifications in this section are based on the study by DiNardo et al.[3] and venetoclax product information.

Tumour lysis syndrome (TLS)	
Blood chemistry suggestive of TLS	Withhold the next day's venetoclax dose, and if resolution occurs within 24 to 48 hours of last dose resume at the same dose
Clinical TLS OR Blood chemistry changes for more than 48 hours	Manage TLS per institutional guidelines and withhold venetoclax dose until recovery. For more information, see Prevention and management of tumour lysis syndrome.

Haematological toxicity	
Bone marrow assessment at the end of cycle	Recommend a bone marrow assessment between days 21-28 of the first cycle. If marrow blasts have been cleared (<5%), withhold venetoclax until commencement of cycle 2. If persistent AML is detected, cycle 2 should commence and an end of cycle bone marrow repeated.
Incomplete count recovery after cycle 1	If the patient has responded to treatment with <5% marrow blasts, withhold the next cycle until ANC ≥0.5 x 10^9/L and platelets ≥50 x10^9/L or up to 14 days after cycle completion. If neutrophils have not recovered by day 35, commence G-CSF three times a week to assist marrow recovery. If haematological recovery has not occurred by day 42, further treatment is at the discretion of the treating haematologist.
Cycle 2 onwards: ANC <0.5 x 10^9/L for ≥1 week (not due to underlying disease)	Withhold venetoclax and commence next cycle when ANC ≥0.5 x 10^9/L and platelets ≥50 x10^9/L. Commence next cycle at the same venetoclax dose level if recovery occurs within 14 days of ceasing venetoclax. If the time to recovery after ceasing venetoclax exceeds 14 days, reduce the duration of venetoclax by 7 days for subsequent cycles (e.g. from 28 days to 21 days to 14 days to 10 days). Venetoclax may be interrupted at the discretion of the haematologist and intermittent G-CSF commenced if ANC <0.2 x 10^9/L until recovery to ANC ≥0.5 x 10^9/L.
Cycle 5 onwards:	
If haematological recovery has not occurred 14 days after completing therapy (ANC <0.5 x 10^9/L or platelets <50 x10^9/L)	Withhold next cycle and monitor and assess counts every 7 days or as needed. If haematological recovery takes > 21 days after completing therapy, consider a reduction in the azacitidine dose according to bone marrow cellularity.

Recovery > 21 days	
Bone marrow cellularity	% dose of azacitidine next cycle
15 to 50%	50%
< 15%	33%

Hepatic impairment	
Hepatic dysfunction	
Severe (Child-Pugh C)	Reduce venetoclax dose by 50% and monitor for signs of toxicity

Hepatic impairment
No formal studies have been conducted in patients with hepatic impairment receiving azacitidine

Renal impairment	
Unexplained clinically significant elevations in serum creatinine or blood urea nitrogen (BUN)	Delay next cycle until values return to normal or baseline and reduce azacitidine by 50% for the next cycle
Unexplained reduction in serum bicarbonate levels to less than 20 mmol/L	Reduce azacitidine by 50% No dose adjustments of venetoclax necessary, however patients are at greater risk of TLS. Intensive TLS monitoring and prophylaxis may be required during venetoclax dose titration phase
Severe renal impairment (creatinine clearance < 30 mL/min)	Azacitidine is contraindicated according to the Australian product information. However, its use has been reported in patients with CrCl < 30mL/min and is associated with a higher incidence of toxicity.[4] There is no data available for venetoclax in patients with severe renal impairment. Updated pharmacokinetic studies included in the product information for venetoclax suggest no dose modifications are required if CrCl >15mL/min.

Concomitant use with CYP3A4 inhibitor or P-gp inhibitor	
Dose escalation phase (Cycle 1 days 1 to 3)	
Strong CYP3A4 inhibitor (e.g. azole antifungals)	Modify dose to: • Day 1: 10 mg • Day 2: 20 mg • Day 3: 50 mg
Moderate CYP3A4 inhibitor or P-gp inhibitor	Reduce daily venetoclax dose by at least 50%
Post escalation phase (Cycle 1 day 4 onwards)	
Strong CYP3A4 inhibitor (e.g. azole antifungals)	Reduce venetoclax dose to 50 mg*
Moderate CYP3A4 inhibitor or P-gp inhibitor	Reduce venetoclax dose by at least 50%

* Note: Consider an early bone marrow assessment on day 21 of cycle 1. Withhold venetoclax if blast clearance is documented, until commencement of cycle 2.

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*

Azacitidine
No formal clinical drug interaction studies with azacitidine have been conducted

Azacitidine		
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Cytidine deaminase (CDA) inhibitors (e.g. cedazuridine)	Potential increased effect/toxicity of azacitidine due to reduced clearance	Avoid combination or monitor for increased effect/toxicity.

Venetoclax		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, fluvoxamine, grapefruit juice, ritonavir, seville oranges etc.)	Increased toxicity of venetoclax and increased risk of TLS at initiation and during dose escalation possible due to increased exposure	Avoid concomitant use with CYP3A inhibitors and consider alternative treatments. If combination must be used, monitor patients closely and reduce venetoclax dose (see Dose modifications table). Any venetoclax dose used prior to initiating a CYP3A4 inhibitor may be resumed 2 to 3 days after discontinuation of the inhibitor. Avoid grapefruit products, seville oranges and starfruit during venetoclax treatment.
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St Johns wort etc.)	Reduced efficacy of venetoclax due to increased clearance	Avoid combination with strong or moderate CYP3A4 inducers, or consider alternative agents with less CYP3A4 induction.
P-glycoprotein inhibitors (e.g. verapamil, ciclosporin)	Increased toxicity of venetoclax possible due to reduced clearance	Avoid combination. If combination must be used monitor patients closely and reduce venetoclax dose (see Dose modifications table).
P-glycoprotein substrates (e.g. digoxin, morphine, topotecan)	Venetoclax may alter the absorption of the substrate	Avoid combination with narrow therapeutic index drugs. If combination must be used administer at least 6 hours before venetoclax
Warfarin	Increased risk of bleeding	Monitor international normalised ratio (INR) closely when used in combination

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.

Days 1 to 7

Approximate treatment time: Consider administering as an inpatient during dose escalation of venetoclax with cycle 1.

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

- daily weight
- daily dipstick urinalysis
- strict fluid balance

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Venetoclax

- administer orally ONCE daily with food on **days 1 to 28** (continuously)
- to be swallowed whole with a glass of water; do not break, crush or chew

Note: if a dose is missed and within 8 hours of the usual dose time, it should be taken as soon as the patient remembers. If it is more than 8 hours the patient should not take the missed dose.

Azacitidine

Prior to administration:

- allow refrigerated drug to warm to room temperature for up to 30 minutes prior to administration
- ensure there is an air bubble of 0.3-1.0 mL in between the syringe plunger and drug to ensure full administration of the desired volume.

Administer azacitidine:

- via subcutaneous injection on days 1 to 7
- vigorously roll the syringe between the palms until a uniform, cloudy suspension is achieved
- rotate sites for each injection (thigh, abdomen, upper arm)
- new injections should be given at least 2.5 cm from the previous site.

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

Days 8 to 28

This is an oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

Chemotherapy - Time out

Venetoclax

- administer orally ONCE daily with food on **days 1 to 28** (continuously)
- to be swallowed whole with a glass of water; do not break, crush or chew

Note: if a dose is missed and within 8 hours of the usual dose time, it should be taken as soon as the patient remembers. If it is

more than 8 hours the patient should not take the missed dose.

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

Discharge information

Venetoclax tablets

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

Antiemetics

- Antiemetics as prescribed.

Antidiarrhoeals

- Antidiarrhoeals as prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

Prophylaxis medications

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

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

Immediate (onset hours to days)	
Headache	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Injection-site reactions	Inflammation of or damage to the tissue surrounding the area where a drug was injected.
Metabolism and electrolyte imbalance	Tumour lysis syndrome, hyperphosphataemia, hyperkalaemia, hypocalcaemia and hyperuricaemia may occur with venetoclax.
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
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
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
Atrial fibrillation	
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Fever	
Respiratory tract infection	

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia

Evidence

Acute myeloid leukaemia (AML) frequently affects older adults who are unsuitable for intensive therapies and is often associated with a poor prognosis and short survival. Azacitidine and venetoclax is a potent combination therapy that offers an opportunity to improve the previously dismal prognosis of these patients.

The evidence supporting this protocol comes from the VIALE-A study[3], a phase 3, multicentre, double blind, randomised controlled trial, involving 431 patients with AML, ineligible for standard induction therapy who had not received prior treatment. Patients with favourable cytogenetics and myelofibrosis associated AML were excluded. Patients of median age 76 years from 134 sites in 27 countries participated from February 2017 to May 2019 and were randomised in a 2:1 ratio to receive azacitidine 75 mg/m^2 subcutaneously or intravenously, and either venetoclax 400 mg target dose (286 patients) or placebo (145 patents) in 28-day cycles. Daily dose escalation of venetoclax was done in cycle 1, following the dosing schedule established in earlier phase 1 trials[5, 6] (100 mg day 1, 200 mg day 2, then the 400 mg target dose from day 3). All patients were hospitalised for tumour lysis prophylaxis consisting of an oral uric acid reducing agent and oral hydration 72 hours prior to venetoclax, intravenous hydration 24 hours before venetoclax commencement.

The primary endpoint was overall survival (OS). Whilst the VIALE-A study had dual primary endpoints of OS and composite complete remission (CRc) / complete remission with incomplete haematological recovery (CRi), the results reported here are from the DiNardo published study.[3] Secondary endpoints included complete remission (CR), event-free survival (EFS) and CRc/CRi.

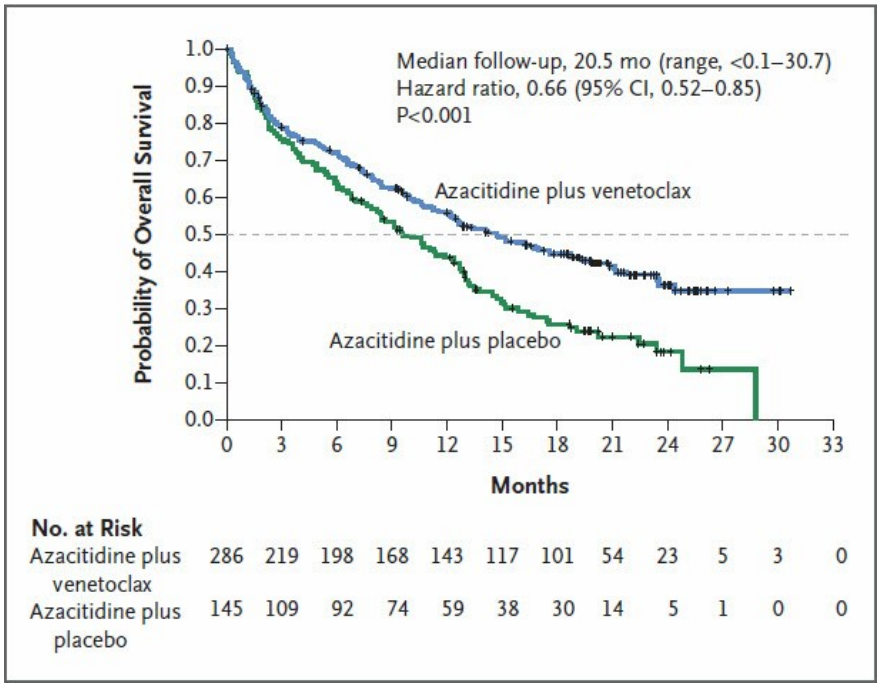
Clinical experience among patients with myelofibrosis associated AML remains minimal. Severe hypoplasia and prolonged pancytopenia has been noted in such patients. Therefore, it is recommended that patients with extensive myelofibrosis are excluded from treatment until more data is published.

Efficacy

Azacitidine and venetoclax therapy is an effective and well-tolerated combination therapy for upfront treatment of elderly AML and has been found to be effective in AML with a variety of mutations. Following preclinical data suggesting synergistic activity between hypomethylating agents and venetoclax, a phase 1b study looked at the safety and preliminary efficacy of azacitidine/decitabine and venetoclax combination therapy in elderly patients over age 65, with previously untreated AML, featuring intermediate or poor risk cytogenetics, unsuitable for standard induction therapy.[6]

DiNardo et al.[3] confirmed the superiority of the azacitidine-venetoclax combination over azacitidine alone. The median duration of follow up was 20.5 months, OS was 14.7 months (95% confidence interval [CI], 11.9 to 18.7) compared to 9.6 months (95% CI, 7.4 to 12.7) and a statistically significant (p<0.001) better remission rate for the combination (hazard ratio (HR) for death, 0.66; 95% CI, 0.52 to 0.85; p<0.001). EFS was 9.8 months (95% CI, 8.4 to 11.8) in the combination group and 7.0 months (95% CI, 5.6 to 9.5) in the group receiving azacitidine alone (HR for disease relapse, treatment failure, relapse, or death, 0.63; 95% CI, 0.50 to 0.80; p<0.001). 36.7% of patients receiving combination therapy achieved CR, compared to 17.9% of the patients receiving azacitidine alone (p<0.001), duration of CR was 17.5 months (95% CI, 15.3 to NR) and 13.3 months (95% CI, 8.5 to 17.6). Treatment continued until disease progression or unacceptable toxicity. Patients receiving combination therapy received a median of 7 cycles, compared to 4.5 in the control group.

Figure 1: Overall survival[3]



Overall, this study and its predecessors provided evidence for an effective treatment for elderly AML patients.[3, 5, 6]

Toxicity

Gastrointestinal toxicity, particularly nausea (in 44% of the patients in the azacitidine-venetoclax group and 35% of those in the control group), constipation (in 43% and 39% patients, respectively), diarrhoea (in 41% and 33% patients, respectively), and vomiting (in 30% and 23% patients, respectively), cytopenias (grade 3 or higher thrombocytopenia in 45% vs. 38%; neutropenia in 42% vs. 28%) and febrile neutropenia (42% vs.19%) were more prevalent with the combination treatment group and, as such, transfusion dependence was more common in the azacitidine-venetoclax combination group. Treatment delays between cycles and reduction in treatment duration from 28 to 21 days happened in 53% of the azacitidine-venetoclax group and 28% of the control group. Tumour lysis presenting as transient biochemical changes requiring simple measures and not interrupting dosing, occurred in 1% of patients during the venetoclax dose escalation phase. Treatment interruption due to adverse events occurred in 72% of patients with the combination treatment compared to 57% in the control group. 30-day mortality was similar at 7% in the azacitidine-venetoclax group and 6% in the control group.

Figure 2: Adverse Events[3]

Event	Azacitidine–Venetoclax Group (N=283)		Azacitidine–Placebo Group (N=144)	
	All Grades†	≥Grade 3‡	All Grades†	≥Grade 3‡
	number of patients (percent)			
All adverse events	283 (100)	279 (99)	144 (100)	139 (97)
Hematologic adverse events	236 (83)	233 (82)	100 (69)	98 (68)
Thrombocytopenia	130 (46)	126 (45)	58 (40)	55 (38)
Neutropenia	119 (42)	119 (42)	42 (29)	41 (28)
Febrile neutropenia	118 (42)	118 (42)	27 (19)	27 (19)
Anemia	78 (28)	74 (26)	30 (21)	29 (20)
Leukopenia	58 (21)	58 (21)	20 (14)	17 (12)
Nonhematologic adverse events				
Nausea	124 (44)	5 (2)	50 (35)	1 (1)
Constipation	121 (43)	2 (1)	56 (39)	2 (1)
Diarrhea	117 (41)	13 (5)	48 (33)	4 (3)
Vomiting	84 (30)	6 (2)	33 (23)	1 (1)
Hypokalemia	81 (29)	30 (11)	41 (28)	15 (10)
Peripheral edema	69 (24)	1 (<1)	26 (18)	0
Pyrexia	66 (23)	5 (2)	32 (22)	2 (1)
Fatigue	59 (21)	8 (3)	24 (17)	2 (1)
Decreased appetite	72 (25)	12 (4)	25 (17)	1 (1)
Infections	239 (84)	180 (64)	97 (67)	74 (51)
Pneumonia	65 (23)	56 (20)	39 (27)	36 (25)
Serious adverse events§	235 (83)	232 (82)	105 (73)	102 (71)
Febrile neutropenia	84 (30)	84 (30)	15 (10)	15 (10)
Anemia	14 (5)	14 (5)	6 (4)	6 (4)
Neutropenia	13 (5)	13 (5)	3 (2)	3 (2)
Atrial fibrillation	13 (5)	10 (4)	2 (1)	2 (1)
Pneumonia	47 (17)	46 (16)	32 (22)	31 (22)
Sepsis	16 (6)	16 (6)	12 (8)	12 (8)

* The safety population included all patients who received at least one dose of azacitidine–venetoclax or azacitidine–placebo.
† Adverse events reported in at least 20% of patients in either treatment group are listed.
‡ Adverse events of grade 3 or higher that were reported in at least 10% of patients in either treatment group are listed.
§ Serious adverse events that were reported in at least 5% of patients in either treatment group are listed.

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4 Batty, G. N., H. Kantarjian, J. P. Issa, et al. 2010. "Feasibility of therapy with hypomethylating agents in patients with renal insufficiency." Clin Lymphoma Myeloma Leuk 10(3):205-210.

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6 DiNardo, C. D., K. W. Pratz, A. Letai, et al. 2018. "Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: a non-randomised, open-label, phase 1b study." Lancet Oncol 19(2):216-228.

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History

Version 2

Date	Summary of changes
15/06/2021	Granisetron added to treatment schedule to align with other azacitidine protocols.
14/06/2022	Protocol reviewed at the Haematology Reference Committee meeting on 11 March 2022, with updates to: • drug status - venetoclax available on the PBS and 50 mg tablets added • indication - added acute promyelocytic leukaemia (APML) to exclusions • dose modifications - added (e.g. azole antifungals) for strong CYP3A4 inhibitors & changed day 3 venetoclax dose to 50 mg. Minor change to wording for BM assessment at D21 of cycle 1. Changed post-escalation phase from C1 D5 to C1 D4. Added updated data from venetoclax PI to renal impairment • evidence - updated to include DiNardo et al study NEJM 2020. Next review in 2 years.

Version 1

Date	Summary of changes
23/10/2020	New protocol presented at Haematology Reference Committee meeting.

First approved: 26 February 2021
Last reviewed: 14 June 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/3892
19 Sep 2023

Patient information - Acute myeloid leukaemia (AML) - Azacitidine and venetoclax

Patient's name:

Your treatment

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

Azacitidine and venetoclax

The first 3 days of treatment is a titration phase where the dose of venetoclax is gradually increased. Azacitidine is usually given for 7 days every 28 days. Each treatment cycle is repeated every 28 days. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
Continuous	**Venetoclax** (*ven-ET-oh-klax*)	Take orally ONCE a day with food. Swallow the tablet(s) whole with a glass of water, do not break, crush or chew. If you vomit a tablet(s), take your normal dose the next time it is due. Do not take an extra dose. If you forget to take a dose, and it is less than 8 hours late, take it as soon as you remember. If it is more than 8 hours late, skip that dose and take your normal dose the next time it is due. Do not take an extra dose.	
1 to 7	**Azacitidine** (*AY-za-SYE-ti-deen*)	By injection under the skin. The injections will be given into your thigh, abdomen or upper arm and the site will be rotated each time to reduce injection site reactions.	About 5 minutes

Note: you may be given azacitidine intravenously by a drip into a vein. While the dosing schedule for azacitidine is recommended as 7 consecutive days, this is not practical for all cancer units and alternative scheduling may be used e.g. azacitidine for 5 days, followed by 2 day weekend break, followed by azacitidine for 2 days. Speak to your doctor or nurse for more information.

When to get help

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

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38ºC or higher • chills, sweats, shivers or shakes • shortness of breath	Daytime:..... Night/weekend:..... Other instructions:.....

- uncontrolled vomiting or diarrhoea
- pain, tingling or discomfort in your chest or arms
- you become unwell.

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- pain, stinging, swelling or redness around the injection site
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Tumour lysis syndrome

Some people having treatment for cancer can develop Tumour Lysis Syndrome (TLS), which results from the fast breakdown of cancer cells especially during the first couple of weeks of treatment. As the cancer cells are destroyed, they break open and the content of the cancer cell (uric acid, potassium, phosphorus) gets into the blood. This can lead to changes in kidney function, sudden kidney failure or even death.

If you do not have any heart or kidney problems, keep your fluids up by drinking at least 8 to 10 glasses of fluid daily. It is also important for you to keep your scheduled appointments for blood tests.

Changes to your dose or treatment delays

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

Blood tests and monitoring

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

Other medications given during this treatment

- **G-CSF:** you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication. Follow this link to read more information on how to give this injection.
- **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.
- **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.
- **Laxatives:** you may be given some medication to prevent or treat constipation. Your doctor or nurse will tell you how and when to take the laxatives.
- **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.**
Injection-site reaction	• At the injection site you may get pain, redness, swelling or bruising. • These symptoms are usually not serious. • **Tell your doctor or nurse immediately if you notice any redness or pain during or after treatment.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
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.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
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 palpitations	• You may get: ◦ chest pain ◦ a pounding or fluttering heart (palpitations) ◦ shortness of breath ◦ dizzy or light-headed ◦ confused ◦ more tired than usual. • Tell your doctor if you have any heart problems or are on any heart medications. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**
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.**
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.**
Fever	• You may feel warm. • Tell your doctor or nurse if you get this symptom.
Chest infection	• You can develop a chest infection whilst receiving this treatment. • **Tell your doctor or nurse as soon as possible if you get any of the following symptoms:** ◦ **shortness of breath** ◦ **difficulty breathing** ◦ **wheezing** ◦ **coughing up mucus**

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.**

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

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

Other medical and dental treatment

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

Diet and food safety

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

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

Quitting smoking

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

Staying active

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

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

Where to get more information

Telephone support

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

Haematology, transplant and cellular therapy information

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

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- Carer Help - carerhelp.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety –

foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx

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

Quit smoking information and support

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

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

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