Acalabrutinib

ID: 3884 v.2 **Endorsed**

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

Patients with lymphoma should be considered for inclusion into clinical trials. Link to ALLG website, ANZCTR website and Lymphoma Australia website.

Treatment schedule - Overview

Drug	Dose	Route
Acalabrutinib	100 mg TWICE a day	PO

Continuous until disease progression or unacceptable toxicity

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Drug status: **Acalabrutinib:** PBS authority for MCL and relapsed/refractory CLL/SLL
TGA registered but not PBS listed for upfront CLL/SLL

Acalabrutinib is available as **100 mg** capsules and tablets

Cost: ~ $8,230 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.*

Continuous treatment		
Acalabrutinib	100 mg (PO)	TWICE a day 12 hours apart, with or without food. Swallow capsule whole with water.

Continuous until disease progression or unacceptable toxicity

Indications and patient population - Chronic lymphocytic leukaemia

- Chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL) who have received at least one prior therapy OR previously untreated patients , including patients with 17p deletion, TP53 mutation or unmutated IGHV gene status

Indications and patient population - Mantle cell lymphoma

- Mantle cell lymphoma that is relapsed or refractory to at least one prior therapy

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
Cardiac toxicity	Acalabrutinib has been associated with atrial fibrillation and flutter, particularly in patients with cardiac risk factors. Patients, especially those with pre-existing cardiovascular disease, should have periodic cardiac assessments and be closely monitored clinically for atrial fibrillation. Patients who develop arrhythmic symptoms or new onset of dyspnoea should be evaluated clinically and if indicated an electrocardiogram (ECG) should be performed. Read more about cardiac toxicity associated with anti-cancer drugs
Haemorrhage	Haemorrhagic events have been reported, both with and without thrombocytopenia. These include minor haemorrhagic events (i.e. contusion, epistaxis, petechiae) and major haemorrhagic events, including fatal events (i.e. gastrointestinal bleeding, intracranial haemorrhage, haematuria). The risk of bleeding may be increased when acalabrutinib is administered with anticoagulants (e.g. warfarin, aspirin) or medications that inhibit platelet function (e.g. fish oil, vitamin E preparations). Avoid concomitant administration. Acalabrutinib should be withheld at least 3 to 7 days pre and post-surgery depending on the risk of bleeding and type of surgery.
Lymphocytosis	A reversible increase in lymphocyte counts has been observed during the first few weeks of acalabrutinib therapy (i.e. greater than or equal to 50% increase from baseline and above absolute count $5x10^9$/L) . Lymphocytosis associated with acalabrutinib should not be considered progressive disease in the absence of other clinical findings. It is often associated with reduction of lymphadenopathy.
Progressive multifocal leukoencephalopathy	Progressive multifocal leukoencephalopathy (PML) have been reported with certain Tyrosine kinase inhibitors (e.g. ruxolitinib, ibrutinib). Patients should be closely monitored for new or worsening neuropsychiatric symptoms suggestive of PML. If PML is suspected treatment should be withheld pending appropriate investigation. Read more about progressive multifocal leukoencephalopthy and Therapeutic Goods Administration Medicines Safety update on progressive multifocal leukoencephalopathy from the Australian Government, Department of Health.
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
PJP prophylaxis	PJP prophylaxis at the discretion of the treating clinician. Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Antifungal prophylaxis	Consider antifungal prophylaxis for at-risk patients. Clinical vigilance and early intervention is recommended in patients with an increased risk of fungal infections. Read more about antifungal prophylaxis drugs and doses.
Blood tests	FBC, EUC, eGFR and LFTs at baseline and repeat monthly during treatment or as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy

Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

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

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

Haematological toxicity	
ANC x 10^9/L	
0.5 to less than 1.5	No dose adjustment necessary
less than 0.5 for more than 7 days or febrile neutropenia	Consider G-CSF support. Delay treatment until recovery (greater than 1.5 or return to baseline) and reinitiate acalabrutinib as follows: 1st or 2nd occurrence: Restart acalabrutinib at 100 mg BD 3rd occurrence: Reduce acalabrutinib to 100 mg daily 4th occurrence: Cease treatment
Platelets x 10^9/L	
25 to 50 with significant bleeding or less than 25	Delay treatment until recovery (greater than 75 or return to baseline) and reinitiate acalabrutinib as follows: 1st or 2nd occurrence: Restart acalabrutinib at 100 mg BD 3rd occurrence: Reduce acalabrutinib to 100 mg daily 4th occurrence: Cease treatment

Renal impairment	
eGFR (mL/min/1.73m^2)	
30 to 50	No dose adjustments necessary

Renal impairment	
Less than 30	There is no data in patients with severe renal impairment

Hepatic impairment	
Hepatic dysfunction	
Mild (Child-Pugh class A)	No dose adjustment necessary
Moderate (Child-Pugh class B)	No dose adjustment necessary
Severe (Child-Pugh class C)	Not recommended

Non-Haematological toxicity	
Greater than or equal to grade 3	Delay treatment until recovery to grade 1 or baseline and reinitiate acalabrutinib for subsequent cycles as follows: 1st or 2nd occurrence: Restart acalabrutinib at 100 mg BD 3rd occurrence: Reduce acalabrutinib to 100 mg daily 4th occurrence: Cease treatment

Concomitant use with CYP3A inhibitor or inducers		
CYP3A inhibitor	Strong CYP3A inhibitor	Avoid concomitant use. If these inhibitors will be used short-term (such as anti-infectives for up to seven days), interrupt acalabrutinib
	Moderate CYP3A inhibitor	Reduce acalabrutinib to 100 mg daily
CYP3A inducer	Strong CYP3A inducer	Avoid concomitant use. If these inducers cannot be avoided, increase acalabrutinib dose to 200 mg twice daily.
Proton pump inhibitors		Avoid concomitant use.

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*

Acalabrutinib		
	Interaction	**Clinical management**
Strong CYP3A4 inhibitors (e.g. itraconazole, posaconazole etc.) **Moderate CYP3A4 inhibitors (e.g. diltiazem, erythromycin, fluconazole, isavuconazole etc.)**	Increased toxicity of acalabrutinib possible due to reduced clearance	Avoid combination with strong CYP3A4 inhibitors. If inhibitor will be used for a short period, interrupt acalabrutinib treatment. If a moderate CYP3A4 inhibitor must be used, reduce acalabrutinib dose to 100 mg once daily.
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St Johns wort etc.)	Reduced efficacy of acalabrutinib due to increased clearance	Avoid combination with strong CYP3A4 inducers. If a strong CYP3A4 inducer must be used, increase the acalabrutinib dose to 200 mg twice a day.
Gastric acid reducing medications (e.g antacids, H2-receptor inhibitors, proton pump inhibitors)	Reduced efficacy of acalabrutinib due to increased clearance	If treatment with a gastric acid reducing agent is required, consider using a H2-receptor antagonist (e.g. famotidine) or an antacid (e.g. calcium carbonate). Take acalabrutinib 2 hours before taking the H2-receptor antagonist For antacids separate dosing by at least 2 hours Avoid co-administration with proton pump inhibitors due to the long lasting effect. Separation of dosing may not eliminate the interaction.

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

Administration

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

Administration

This is a continuous oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

Treatment - Time out

Acalabrutinib

- administer orally TWICE daily, every 12 hours
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food

- administer at least 2 hours prior to H2-antagonists or antacids

Note: if a dose is missed by more than 3 hours, instruct the patient to take the next dose at its regularly scheduled time. Extra doses of acalabrutinib should not be taken to make up for a missed dose.

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

Discharge information

Acalabrutinib capsules or tablets

- Acalabrutinib capsules or tablets with written instructions on how to take them.

Antiemetics

- Antiemetics as prescribed.

Prophylaxis medications

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

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

Immediate (onset hours to days)	
Headache	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
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
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
Dizziness	Feeling faint or lightheaded, weak or unsteady. Advise patients to stand up slowly from sitting down or lying down positions and increase fluid intake if dehydrated.
Fatigue	Read more about fatigue
Fever	
Haemorrhage	
Respiratory tract infection	
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
Progressive multifocal leukoencephalopathy (PML)	A rare opportunistic viral infection of the brain, usually leading to death or severe disability, can occur with monoclonal antibodies (e.g. rituximab, obinutuzumab, ofatumumab, brentuximab vedotin) and other targeted therapies (e.g. ibrutinib, ruxolitinib, idelalisib). Onset may occur up to months after the final dose. Read more about progressive multifocal leukoencephalopathy (PML)

Evidence - Chronic lymphocytic leukaemia

Acalabrutinib is a second-generation Bruton kinase inhibitor, which has activity against chronic lymphocytic leukaemia (CLL) in both the treatment-naïve and relapsed/refractory (R/R) setting. Bruton kinase plays a critical role in B-cell proliferation and survival.

The evidence supporting the protocol in R/R patients comes from the phase 3 multicentre randomised ASCEND trial.[1] This was after a multicentre phase 1/2 trial investigating acalabrutinib monotherapy for R/R CLL/small lymphocytic lymphoma (SLL), which showed an overall response rate (ORR) of 94% and estimated progression-free survival (PFS) at 45 months follow up of 62% (95% CI 51-71%).[2, 3]

In ASCEND, between 2017 and 2018, 310 patients with R/R CLL were randomised to receive either acalabrutinib monotherapy (100mg bd) or investigator's choice. Investigator's choice was either rituximab + bendamustine (bendamustine 70mg/m^2 on day 1 and 2 of a 28-day cycle, for 6 cycles, and rituximab 375 mg/m^2 on day 1 of cycle 1, and 500mg/m^2 on day 1 of cycle 2 through 6) or rituximab + idelalisib (idelalisib 150mg bd until progressive disease (PD) or unacceptable toxicity, with rituximab 375mg/m^2 on day

1 of therapy, followed by 500 mg/m^2 every two weeks for four doses, then every four weeks for three doses). Acalabrutinib was administered until PD or unacceptable toxicity. Crossover to the acalabrutinib arm was allowed for patients with PD on the control arm. The median age of participants was 67, and the median number of prior therapies was one (range one to eight in the treatment arm). 16% of patients harboured del(17p), 24% a TP53 mutation and 19% had unmutated immunoglobulin heavy chain variable (IGHV). Patients with significant cardiovascular disease were excluded, as were those with previous exposure to BTK, BCL2, PI3K or SYK inhibitors.

The primary endpoint was PFS. Secondary endpoints were ORR, duration of response (DOR) and overall survival (OS).

A second phase 3 multicentre international randomised trial (ELEVATE-TN), compared the efficacy of acalabrutinib both as a single agent, and in combination with obinutuzumab, with chlorambucil plus obinutuzumab, in patients with untreated CLL.[4]

Between 2015 and 2017, 535 patients were randomised 1:1:1 to receive acalabrutinib 100mg bd as a single agent, acalabrutinib 100mg bd plus obinutuzumab (day 1 (100mg), day 2 (900mg), day 8 (1000mg) and day 15 (1000mg) of Cycle 2, and 1000mg on day 1 of cycles 3-7) or chlorambucil (0.5mg/kg days 1-15 on cycles 1 to 6, plus obinutuzumab on day 1 (100mg), day 2 (900mg), day 8 (1000mg) and day 15 (1000mg) of cycle 1, and 1000mg on day 1 of cycles 2-6). Acalabrutinib was administered until PD or unacceptable toxicity. Crossover to acalabrutinib was allowed for patients who progressed on the chlorambucil arm.

Eligible patients were aged 65 years or older, or over 18 years and younger than 65 years with a creatinine clearance of 30-69 mL/min, or a Cumulative Illness Rating Scale for Geriatrics score greater than 6. Patients with significant cardiovascular disease were excluded, as well as those taking vitamin K antagonists. The median age of participants was 70. 9% of patients harboured del(17p), 11% a TP53 mutation and 63% had unmutated IGHV (which is higher than the rate of unmutated IGHV typically seen in treatment-naïve CLL[5]).

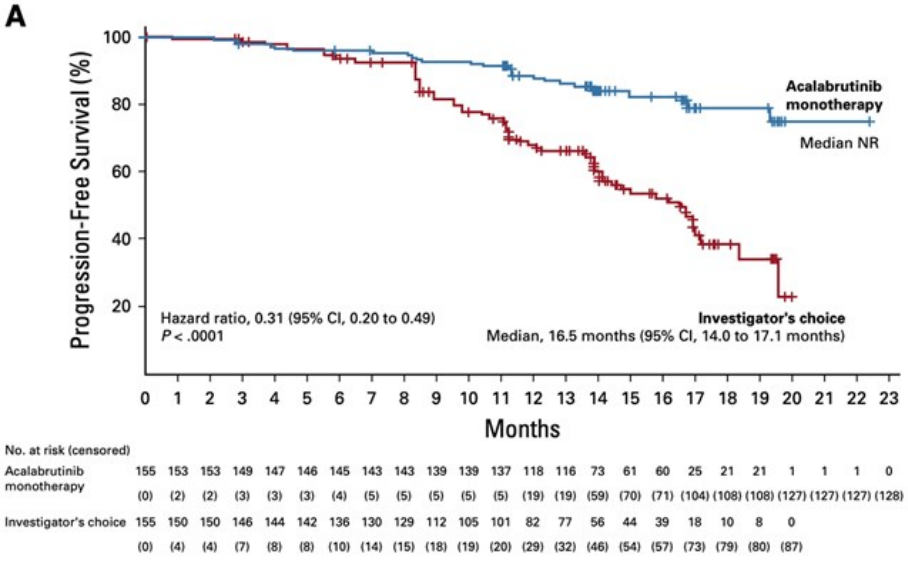
The primary endpoint was PFS, and secondary endpoints were ORR, time to next treatment and OS.

Efficacy

CLL Relapsed/refractory

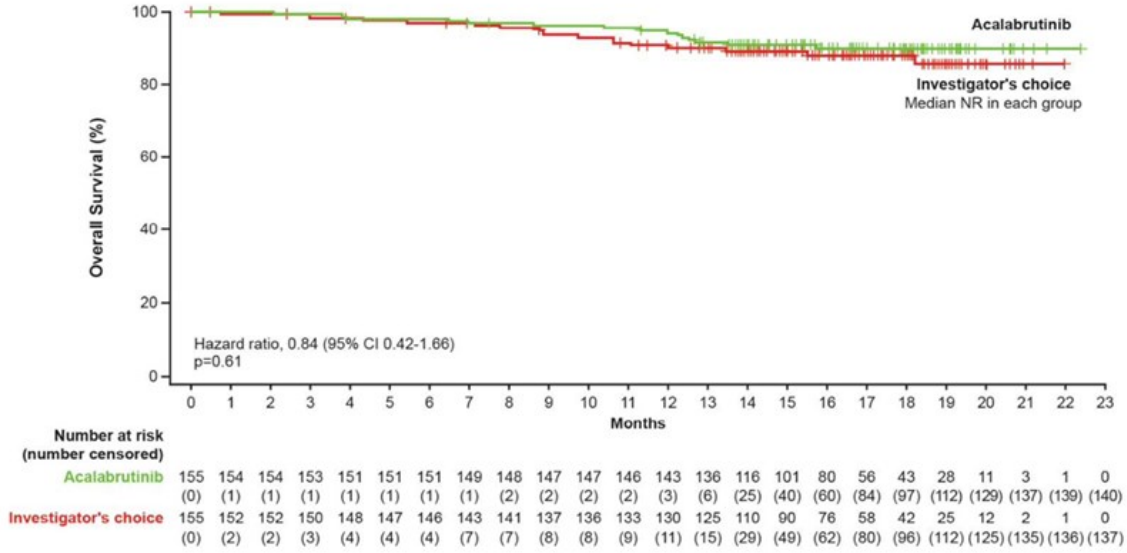
In R/R settings, after a median follow up of 16.1 months, the median PFS was significantly longer with acalabrutinib monotherapy, compared to investigators choice (not reached v. 16.5 months; HR 0.31 95% CI 59-75%) (Figure 1). The estimated 12-month PFS was 88% for acalabrutinib monotherapy (95% CI 81% to 92%), and 68% for investigator's choice (95% CI 59-75%). The PFS benefit was preserved in patients with del(17p), del(11q), TP53 mutations or unmutated IGHV.[1]

Figure 1. Progression-free survival[1]



ORR was not statistically different between the study and control arms. Median DOR was superior in the acalabrutinib arm (NR for acalabrutinib v. 13.6 months (95% CI 11.9 months to NR)) for investigators choice (HR 0.33; 95% CI 0.19 to 0.59; p < 0.0001). Median OS was not reached and was not different between the two study arms (Figure 2).

Figure 2. Overall survival[1]



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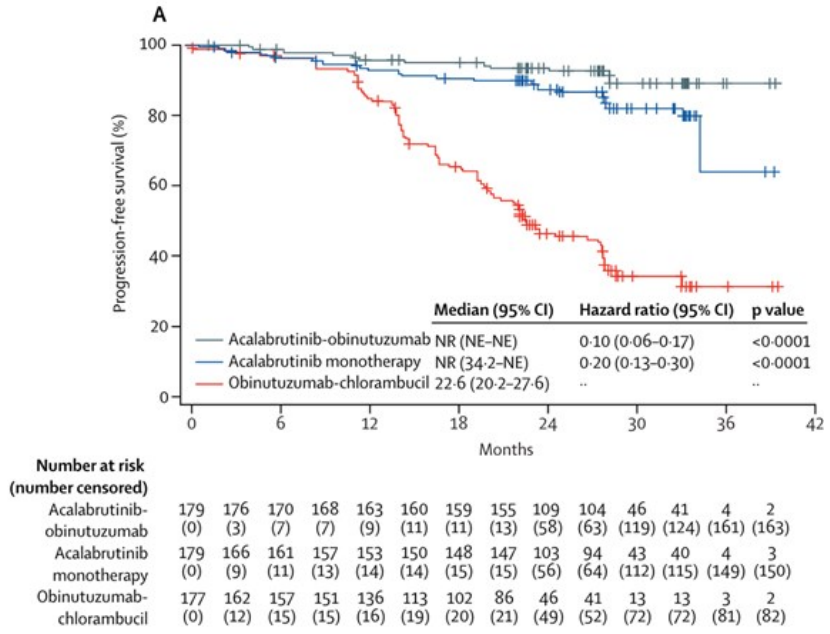
CLL Treatment-naïve

The acalabrutinib arms in patients with untreated CLL in the ELEVATE-TN trial[4], in terms of the primary endpoint, demonstrated superior efficacy over the control arm. After a median follow up of 28.3 months, median PFS was not reached in both acalabrutinib arms, versus 22.6 months in the chlorambucil-obinutuzumab arm (for the acalabrutinib monotherapy arm HR 0.20, p<0.0001) (Figure 3). The 24 month estimated PFS was 87% for acalabrutinib monotherapy (95% CI 81-92%), 93% for acalabrutinib + obinutuzumab (95% CI 87-96%) and 47% for chlorambucil + obinutuzumab (95% CI 39-55%). These results were preserved in patients with del(17p), del(11q), TP53 mutations or unmutated IGHV. Acalabrutinib + obinutuzumab was associated with a reduced risk of progression compared to acalabrutinib monotherapy in a post-hoc analysis (HR 0.49, 85% CI 0.26-0.95).

Figure 3. Progression-free survival[4]



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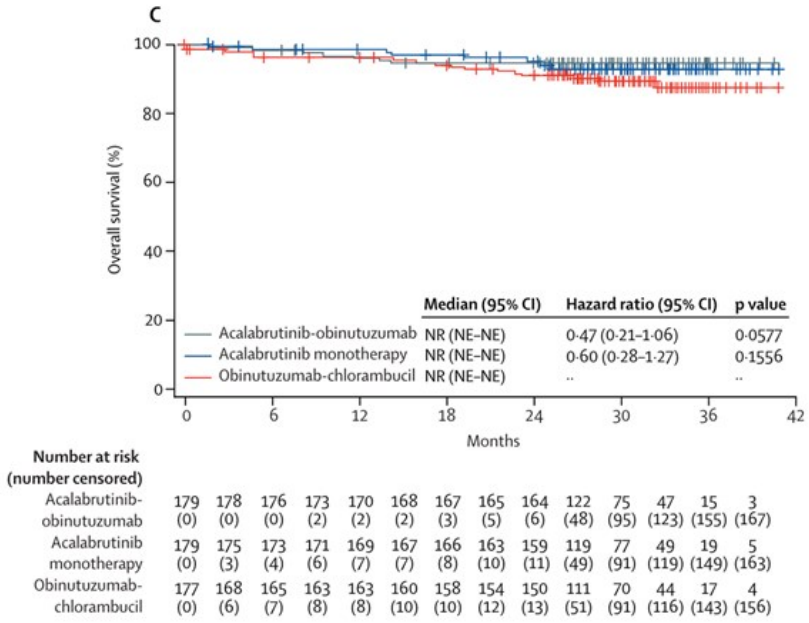
ORR were significantly superior in the acalabrutinib arms, though CR rates were low, in keeping with studies of other BTKi. Median OS was not reached in any arm, with no significant differences between treatments (Figure 4).

Figure 4. Overall survival[4]



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Toxicity

Tabulated summaries from both the ASCEND (Table 1)[1] and ELEVATE-TN (Table 2)[4] trials are shown below. Overall, acalabrutinib had an acceptable toxicity profile.

In ASCEND, ≥ grade 3 adverse events (AEs) occurred in 45% of patients receiving acalabrutinib. The most common ≥ grade 3 AEs were neutropenia (16%), anaemia (12%) and pneumonia (5%). Similar results were seen in the acalabrutinib monotherapy arm in ELEVATE-TN. In the earlier Phase 1/2 trial, ≥ grade 3 AEs were seen in 66% of patients, including infections (23%), neutropenia (14%) and pneumonia (11%).[3]

Rates of ≥ grade 3 major bleeding occurred in 1% of patients receiving acalabrutinib in the ASCEND trial. Rates of ≥ grade 3 bleeding were higher in the acalabrutinib arms in ELEVATE-TN (2.2% to 4.5%, versus 1.8% in the control arm). No cases of pneumocystis jiroveci pneumonia (PJP) were reported in the acalabrutinib arm in ASCEND, with two cases in the control arm (both patients taking idelalisib). It was not reported whether patients were taking PJP prophylaxis or not. ELEVATE-TN did not report on PJP rates.

Second primary malignancies (SPMs) were increased in the acalabrutinib arm in ASCEND (14% v. 5%), as they were in ELEVATE-TN (9-11%). In both trials, these were dominated by non-melanomatous skin cancers. Only one myeloid SPM was diagnosed in each trial in patients taking acalabrutinib.

Atrial fibrillation of any grade was only slightly increased, occurring in 5% of patients on acalabrutinib v. 3% on investigators choice in ASCEND and 3-4% in acalabrutinib-containing arms versus 1% in the control arm in ELEVATE-TN. Rates were higher (7%) in the phase 1/2 trial.

Treatment discontinuation due to treatment-related AEs was similar in both ASCEND and ELEVATE-TN (9-11%). Of interest, this rate was 17% for patients receiving bendamustine + rituximab and 47% receiving idelalisib + rituximab in ASCEND.

Fatal AEs occurred in 4% of patients receiving acalabrutinib in ASCEND, versus 4-6% in the comparator arms. Fatal AEs occurred in 3% of patients receiving acalabrutinib in ELEVATE-TN.

Table 1. Treatment-emergent AEs. ASCEND R/R CLL[1]

TABLE 2. Treatment-emergent AEs observed in ≥10% of patients in any treatment group or grade ≥3 in ≥5% in any treatment group

	Acalabrutinib Monotherapy (n = 154)			Idelalisib Plus Rituximab (n = 118)			Bendamustine Plus Rituximab (n = 35)		
AE	**Grade 1-2**	**Grade 3**	**Grade 4**	**Grade 1-2**	**Grade 3**	**Grade 4**	**Grade 1-2**	**Grade 3**	**Grade 4**
Entire study									
All	68 (44)	48 (31)	22 (14)	11 (9)	59 (50)	42 (36)	11 (31)	8 (23)	7 (20)
Neutropenia	6 (4)	14 (9)	10 (6)	6 (5)	24 (20)	23 (19)	1 (3)	5 (14)	6 (17)
Diarrhea	26 (17)	2 (1)	0	27 (23)	26 (22)	2 (2)	5 (14)	0	0
Pyrexia	18 (12)	1 (1)	0	13 (11)	7 (6)	1 (1)	5 (14)	1 (3)	0
Cough	23 (15)	0	0	17 (14)	1 (1)	0	2 (6)	0	0
Upper respiratory tract infection	19 (12)	3 (2)	0	13 (11)	4 (3)	0	3 (9)	1 (3)	0
Headache	33 (21)	1 (1)	0	7 (6)	0	0	0	0	0
Thrombocytopenia	11 (7)	2 (1)	4 (3)	7 (6)	7 (6)	2 (2)	4 (11)	0	1 (3)
Anemia	5 (3)	16 (10)	2 (1)	2 (2)	8 (7)	0	1 (3)	3 (9)	0
Fatigue	13 (8)	2 (1)	0	10 (8)	0	0	7 (20)	1 (3)	0
Nausea	11 (7)	0	0	14 (12)	1 (1)	0	7 (20)	0	0
Pneumonia	8 (5)	8 (5)	0	4 (3)	10 (8)	0	1 (3)	1 (3)	0
Rash	10 (6)	0	0	12 (10)	4 (3)	0	2 (6)	0	0
Constipation	10 (6)	0	0	9 (8)	0	0	3 (9)	2 (6)	0
Respiratory tract infection	14 (9)	1 (1)	1 (1)	7 (6)	1 (1)	0	0	0	0
ALT increased	1 (1)	2 (1)	0	4 (3)	9 (8)	1 (1)	2 (6)	1 (3)	0
Infusion-related reaction	0	0	0	7 (6)	2 (2)	0	7 (20)	1 (3)	0
AST increased	2 (1)	1 (1)	0	5 (4)	6 (5)	0	1 (3)	1 (3)	0
Neutrophil count decreased	1 (1)	1 (1)	1 (1)	0	3 (3)	6 (5)	0	0	1 (3)
Transaminases increased	0	0	0	1 (1)	6 (5)	0	0	0	0

Table 2. Treatment-emergent AEs. ELEVATE-TN Treatment naïve CLL[4]

	Acalabrutinib–obinutuzumab (n=178)			Acalabrutinib monotherapy (n=179)			Obinutuzumab–chlorambucil (n=169)		
	Any grade	Grade 1–2	Grade ≥3	Any grade	Grade 1–2	Grade ≥3	Any grade	Grade 1–2	Grade ≥3
Summary of adverse events									
Any	171 (96·1%)	46 (25·8%)	125 (70·2%)	170 (95·0%)	81 (45·3%)	89 (49·7%)	167 (98·8%)	49 (29·0%)	118 (69·8%)
Serious	69 (38·8%)	11 (6·2%)	58 (32·6%)	57 (31·8%)	4 (2·2%)	53 (29·6%)	37 (21·9%)	4 (2·4%)	33 (19·5%)
Led to drug discontinuation (any grade)	20 (11·2%)	..	..	16 (8·9%)	..	..	25 (14·1%)	..	..
Most common adverse events									
Headache	71 (39·9%)	69 (38·8%)	2 (1·1%)	66 (36·9%)	64 (35·8%)	2 (1·1%)	20 (11·8%)	20 (11·8%)	0
Diarrhoea	69 (38·8%)	61 (34·3%)	8 (4·5%)	62 (34·6%)	61 (34·1%)	1 (0·6%)	36 (21·3%)	33 (19·5%)	3 (1·8%)
Neutropenia	56 (31·5%)	3 (1·7%)	53 (29·8%)	19 (10·6%)	2 (1·1%)	17 (9·5%)	76 (45·0%)	6 (3·6%)	70 (41·4%)
Fatigue	50 (28·1%)	47 (26·4%)	3 (1·7%)	33 (18·4%)	31 (17·3%)	2 (1·1%)	29 (17·2%)	28 (16·6%)	1 (0·6%)
Contusion	42 (23·6%)	42 (23·6%)	0	27 (15·1%)	27 (15·1%)	0	7 (4·1%)	7 (4·1%)	0
Arthralgia	39 (21·9%)	37 (20·8%)	2 (1·1%)	28 (15·6%)	27 (15·1%)	1 (0·6%)	8 (4·7%)	6 (3·6%)	2 (1·2%)
Cough	39 (21·9%)	39 (21·9%)	0	33 (18·4%)	32 (17·9%)	1 (0·6%)	15 (8·9%)	15 (8·9%)	0
Upper respiratory tract infection	38 (21·3%)	34 (19·1%)	4 (2·2%)	33 (18·4%)	33 (18·4%)	0	14 (8·3%)	13 (7·7%)	1 (0·6%)
Nausea	36 (20·2%)	36 (20·2%)	0	40 (22·3%)	40 (22·3%)	0	53 (31·4%)	53 (31·4%)	0
Dizziness	32 (18·0%)	32 (18·0%)	0	21 (11·7%)	21 (11·7%)	0	10 (5·9%)	10 (5·9%)	0
Back pain	25 (14·0%)	24 (13·5%)	1 (0·6%)	25 (14·0%)	23 (12·8%)	2 (1·1%)	14 (8·3%)	13 (7·7%)	1 (0·6%)
Constipation	25 (14·0%)	25 (14·0%)	0	20 (11·2%)	20 (11·2%)	0	17 (10·1%)	16 (9·5%)	1 (0·6%)
Infusion-related reaction	24 (13·5%)	20 (11·2%)	4 (2·2%)	0	0	0	67 (39·6%)	58 (34·3%)	9 (5·3%)
Vomiting	24 (13·5%)	23 (12·9%)	1 (0·6%)	22 (12·3%)	21 (11·7%)	1 (0·6%)	19 (11·2%)	18 (10·7%)	1 (0·6%)
Pyrexia	23 (12·9%)	23 (12·9%)	0	12 (6·7%)	11 (6·1%)	1 (0·6%)	35 (20·7%)	34 (20·1%)	1 (0·6%)
Thrombocytopenia	23 (12·9%)	8 (4·5%)	15 (8·4%)	13 (7·3%)	8 (4·5%)	5 (2·8%)	24 (14·2%)	4 (2·4%)	20 (11·8%)
Oedema peripheral	22 (12·4%)	21 (11·8%)	1 (0·6%)	16 (8·9%)	15 (8·4%)	1 (0·6%)	12 (7·1%)	12 (7·1%)	0
Pain in extremity	22 (12·4%)	21 (11·8%)	1 (0·6%)	11 (6·1%)	11 (6·1%)	0	7 (4·1%)	7 (4·1%)	0
Urinary tract infection	22 (12·4%)	21 (11·8%)	1 (0·6%)	22 (12·3%)	19 (10·6%)	3 (1·7%)	8 (4·7%)	8 (4·7%)	0
Anaemia	21 (11·8%)	11 (6·2%)	10 (5·6%)	25 (14·0%)	13 (7·3%)	12 (6·7%)	20 (11·8%)	8 (4·7%)	12 (7·1%)
Rash	21 (11·8%)	20 (11·2%)	1 (0·6%)	25 (14·0%)	24 (13·4%)	1 (0·6%)	8 (4·7%)	8 (4·7%)	0
Chills	20 (11·2%)	20 (11·2%)	0	8 (4·5%)	8 (4·5%)	0	14 (8·3%)	13 (7·7%)	1 (0·6%)
Nasopharyngitis	20 (11·2%)	19 (10·7%)	1 (0·6%)	17 (9·5%)	17 (9·5%)	0	7 (4·1%)	7 (4·1%)	0
Pneumonia	19 (10·7%)	9 (5·1%)	10 (5·6%)	13 (7·3%)	9 (5·0%)	4 (2·2%)	5 (3·0%)	2 (1·2%)	3 (1·8%)
Decreased appetite	18 (10·1%)	18 (10·1%)	0	10 (5·6%)	10 (5·6%)	0	13 (7·7%)	12 (7·1%)	1 (0·6%)
Dyspnoea	15 (8·4%)	15 (8·4%)	0	12 (6·7%)	9 (5·0%)	3 (1·7%)	17 (10·1%)	14 (8·3%)	3 (1·8%)

Evidence - Mantle cell lymphoma

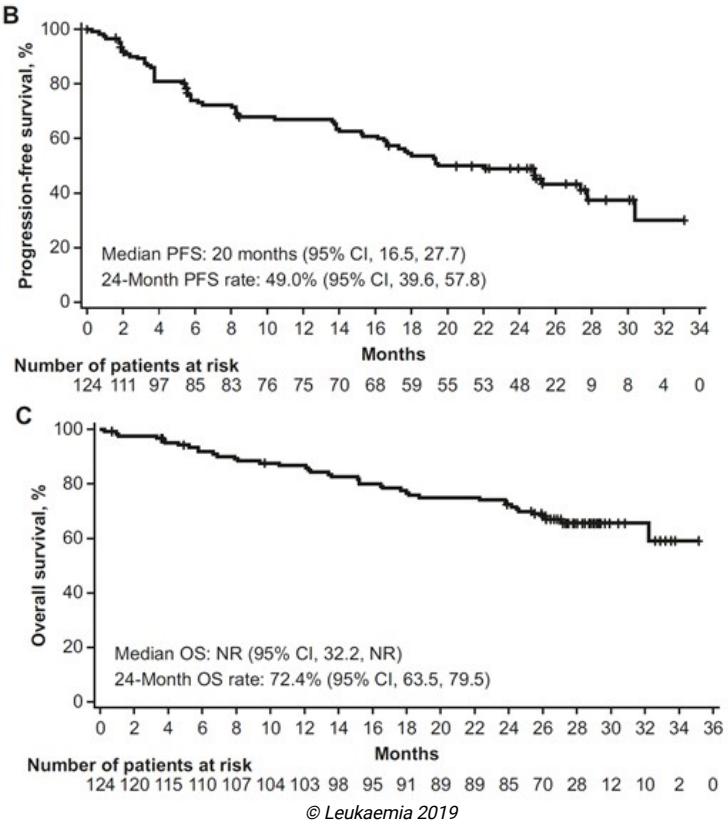
Bruton tyrosine kinase (BTK) has been established as a therapeutic target for mantle cell lymphoma (MCL). Acalabrutinib is a second-generation BTK inhibitor, developed to minimise off-target activity. The expert reference committee supported publication of this protocol based on the information summarised below. The committee was most strongly influenced by the phase II trial (ACE-LY-004) conducted by Wang et al. examining the efficacy and toxicity of acalabrutinib in relapsed/refractory MCL.[6, 7] The trial, conducted across multiple site between 2015 and 2016, included morphological variants such as classical (n=89; 72%), blastoid/pleomorphic (n=26; 21%) and other (n=9; 7%). Of the 96 patients that had Ki-67 data available, 32 (33%) had Ki-67 > 50%.

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trial	Wang et al. 2018[6] Wang et al. 2019[7]	Yes	Yes	Single-arm study; n=124 Median age 68 years Median 2 prior lines of therapy
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	July 2022[8]	Yes	Yes	-
CCO	July 2021	Yes	Yes	-
BCCA	N/A	N/A	-	-

Efficacy

At a median follow-up of 26 months, overall response rate (ORR) was 81% with 43% complete response (CR) rate.[7] Median progression-free survival (PFS) was 20 months. The median overall survival (OS) was not reached, with estimated 24-month OS rate of 72.4%.

Figure 1. Kaplan-Meier curves for progression-free survival (B) and overall survival (C)[7]



The rate of CR was lower in patients who had stage IV disease (27/93, 29%), bone marrow involvement (9/64, 14%) or extranodal disease (25/90, 28%) at initiation of therapy. Median time to best response was 1.9 months, and median time to CR was 3.4 months.

Toxicity

The most frequent adverse events (AEs) included headache (38%), diarrhoea (36%), fatigue (28%), cough (22%) and myalgia (21%).[6, 7] The most common events, headache and diarrhoea, were mostly grade 1-2 and occurred early in treatment. Grade 3-4

anaemia occurred in 11 patients (9%). Grade 3-4 neutropenia occurred in 13 patients (10%). Thirteen patients (10%) had cardiac events, including 4 grade 3-4 events. These events included acute coronary syndrome (thought to be therapy-related), coronary artery disease, acute myocardial infarction and cardiorespiratory arrest, unrelated to therapy. There were no new atrial fibrillation (AF) events in any patient. Bleeding events occurred in 33% of patients. 3 bleeding events were grade 3 major haemorrhages, including gastrointestinal bleeding, haematuria and haematoma. All other bleeding events were grade 1-2, mainly bruising and petechiae. The majority of infections were grade 1-2 and considered unrelated to therapy. Grade 3-4 infections occurred in 15% of patients, most commonly pneumonia. No grade 5 infections occurred. There was one case of CMV viraemia and one case of pneumocystis jirovecii, both grade 2. There were no aspergillus infections. Rashes were infrequent, and majority grade 1-2. Second primary cancers occurred in 10 patients.

Table 1. Incidence of select adverse events by 6-month intervals[7]

Adverse event, *n* (%)	1–6 months (*n* = 124)	7–12 months (*n* = 99)	13–18 months (*n* = 74)	19–24 months (*n* = 65)	>24 months (*n* = 55)
Headache, any grade	42 (34)	2 (2)	0	0	0
Grade ≥3	2 (2)	0	0	0	0
SAE	1 (1)	0	0	0	0
Diarrhea, any grade	31 (25)	8 (8)	3 (4)	5 (8)	5 (9)
Grade ≥3	3 (2)	1 (1)	0	0	0
SAE	0	0	1 (1)	0	0
Infection, any grade	51 (41)	20 (20)	17 (23)	11 (17)	6 (11)
Grade ≥3	11 (9)	4 (4)	2 (3)	2 (3)	1 (2)
SAE	8 (6)	4 (4)	2 (3)	2 (3)	1 (2)
Bleeding events, any grade	31 (25)	14 (14)	5 (7)	4 (6)	0
Major hemorrhage[a]	1 (1)	0	0	2 (3)	0
Atrial fibrillation, any grade[b]	0	0	0	0	0
Rash, any grade	10 (8)	5 (5)	2 (3)	1 (2)	0
Grade ≥3	1 (1)	0	1 (1)	1 (2)	0
SAE	0	0	0	0	0

SAE serious adverse event.

Treatment discontinuation was primarily due to progressive disease (n=54; 44%). However, 10 patients discontinued due to AEs. AEs led to dose delays in 39 patients (31%) and dose reduction to 100 mg daily in 2 patients. There were 43 deaths (35%) - 29 patients due to progressive disease and 6 patients (5%) died due to AEs, including bilateral pulmonary embolism, aortic stenosis with known history, myelodysplastic syndrome, pneumonia, suicide and non-small cell lung cancer.

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8 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) - B-Cell Lymphomas, Version 5.2022

History

Version 2

Date	Summary of changes
11/11/2022	Presented at Haematology Reference Committee meeting. • Reformatted as per eviQ multi-indication protocol standard • New indication and evidence added for mantle cell lymphoma
15/08/2023	Approved and published as version 2, for review in 1 year.

Version 1

Date	Summary of changes
28/10/2020	New protocol developed out of session. v.1. For review in 1 year.
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.
19/05/2022	Clinical information - antifungal prophylaxis block updated.

First approved: 9 November 2020
Last reviewed: 11 November 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/3884
19 Sep 2023

Patient information - Acalabrutinib

Patient's name:

Your treatment

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

Acalabrutinib		
This treatment is taken continuously. Your doctor will advise you how long to take this treatment.		
Day	**Treatment**	**How it is given**
Continuous	**Acalabrutinib** (*A-cal-ah-bru-ti-nib*)	Take orally TWICE a day (every 12 hours) with or without food. Swallow whole with a glass of water, do not break, crush or chew. If you are taking an antacid, do not take within 2 hours as this may interfere with how the drug works. If you vomit after taking a dose, 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 3 hours late, take it as soon as you remember. If it is more than 3 hours late, skip that dose and 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

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.

Surgery and wound healing

This treatment may affect wound healing. Tell your doctor if you are planning to have surgery or have a wound that has not healed.

Other medications given during this treatment

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

Side effects

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

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

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

Immediate (onset hours to days)	
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Early (onset days to weeks)	

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

Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Dizziness or feeling light-headed	• You may feel dizzy or light-headed. • These symptoms may be caused by your treatment, or other problems like dehydration. • If you are feeling dehydrated, drink plenty of fluids (unless you are fluid restricted) as this can be a cause of dizziness. • If you are feeling dizzy, try lying down until the dizziness passes. • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Tell your doctor or nurse if you get any of the symptoms listed above.
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.
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.**

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**
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.**
Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]	• This treatment can affect your central nervous system. This can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms:** ◦ **trouble with your speech or vision** ◦ **confusion or memory loss** ◦ **changes in your personality** ◦ **weakness in your arms and legs** ◦ **poor balance or coordination** ◦ **fits (seizures).**

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.

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.

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.
- Seville oranges, 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)
- 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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