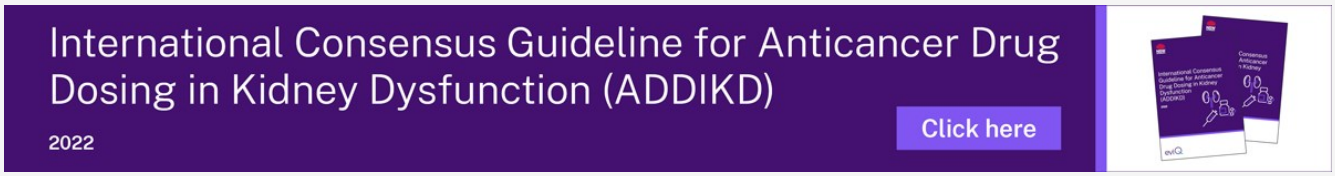
Multiple myeloma Kd (carfilzomib and dexamethasone) twice weekly

ID: 3358 v.3 **Endorsed**

Link to Medical Scientific Advisory Group (MSAG) Clinical Practice Guideline Multiple Myeloma

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

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



Related pages:

- Multiple myeloma Kd (carfilzomib and dexamethasone) weekly

Treatment schedule - Overview

Cycle 1

Drug	Dose	Route	Day
Dexamethasone	20 mg ONCE a day *	IV/PO	1 and 2, 8 and 9, 15 and 16
Carfilzomib	20 mg/m^2 ** (Cap dose at 44 mg)	IV	1 and 2
Carfilzomib	56 mg/m^2 ** (Cap dose at 123 mg)	IV	8 and 9 and 15 and 16
Dexamethasone	20 mg ONCE a day *	IV/PO	22 and 23

Cycle 2 and further cycles

Drug	Dose	Route	Day
Dexamethasone	20 mg ONCE a day *	IV/PO	1 and 2, 8 and 9, 15 and 16
Carfilzomib	56 mg/m^2 ** (Cap dose at 123 mg)	IV	1 and 2, 8 and 9, 15 and 16
Dexamethasone	20 mg ONCE a day *	IV/PO	22 and 23

* Dexamethasone dose and schedule can be adjusted at clinician's discretion.[1]

** Patients with a body surface area > 2.2 m^2 should receive a dose based upon a body surface area of 2.2 m^2. Dose adjustment required when weight changes > 20%.

Frequency: 28 days

Cycles: Continuous until disease progression or unacceptable toxicity.

Notes:
It is the consensus of the reference committee that a 20 mg/week starting dose of dexamethasone should be considered in patients > 75 years.[2]

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

Dexamethasone is on the PBS general schedule

Dexamethasone is available as **4 mg** and **0.5 mg** tablets

Cost: ~ $12,610 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 and 2		
Dexamethasone	20 mg (IV/PO)	ONCE a day on days 1, 2, 8, 9, 15, 16 with or soon after food, 30 minutes to 4 hours before carfilzomib.*
Carfilzomib	20 mg/m^2 (IV) (Cap dose at 44 mg)	in 100 mL glucose 5% over 30 minutes **
Day 8 and 9 and 15 and 16		
Dexamethasone	20 mg (IV/PO)	ONCE a day on days 1, 2, 8, 9, 15, 16 with or soon after food, 30 minutes to 4 hours before carfilzomib.*
Carfilzomib	56 mg/m^2 (IV) (Cap dose at 123 mg)	in 100 mL glucose 5% over 30 minutes **
Day 22 and 23		
Dexamethasone	20 mg (IV/PO)	ONCE a day on days 22 and 23. Take with or soon after food.*

Cycle 2 and further cycles

Day 1 and 2, 8 and 9, 15 and 16		
Dexamethasone	20 mg (IV/PO)	ONCE a day on days 1, 2, 8, 9, 15, 16 with or soon after food, 30 minutes to 4 hours before carfilzomib.*
Carfilzomib	56 mg/m^2 (IV) (Cap dose at 123 mg)	in 100 mL glucose 5% over 30 minutes **
Day 22 and 23		
Dexamethasone	20 mg (IV/PO)	ONCE a day on days 22 and 23. Take with or soon after food.*

* Dexamethasone dose and schedule can be adjusted at clinician's discretion.[1]

** Patients with a body surface area > 2.2 m^2 should receive a dose based upon a body surface area of 2.2 m^2. Dose adjustment required when weight changes > 20%.

Frequency: 28 days

Cycles: Continuous until disease progression or unacceptable toxicity.

Indications and patient population

- Relapsed/refractory multiple myeloma who have received at least one prior therapy

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with carfilzomib. Serious hypersensitivity reactions have been reported with carfilzomib. These reactions can occur immediately following or up to 24 hours after administration of carfilzomib.
Emetogenicity LOW	Antiemetics are not routinely required; however should a patient experience 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 may be administered. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cardiac toxicity	New or worsening cardiac failure (e.g. congestive cardiac heart failure, pulmonary oedema, decreased ejection fraction), myocardial ischaemia and infarction have occurred following administration of carfilzomib. Fatal outcomes associated with cardiac failure and myocardial infarction have been reported in studies. Elderly patients ≥ 75 years are at increased risk of cardiac failure and should be closely monitored throughout treatment. Carfilzomib should be stopped following grade 3 or 4 cardiac events until recovery. Consideration should be given to reducing the dose of carfilzomib by 1 dose level when recommencing carfilzomib, based on an assessment of the benefit/risk.
Carfilzomib hydration	Adequate hydration should be achieved prior to each dose of carfilzomib, particularly during the first cycle. The specific pre and post hydration recommendations should be adjusted according to the treating clinician's assessment of tumour lysis and volume overload/cardiac failure risks.
Reversible posterior leukoencephalopathy syndrome (RPLS)	Reversible posterior leukoencephalopathy syndrome (RPLS) has been reported in patients receiving this treatment and may be fatal. Discontinue drug in patients developing RPLS. Read more about reversible posterior leukoencephalopathy syndrome (RPLS)
Pulmonary hypertension	Pulmonary hypertension has been reported in patients treated with carfilzomib. Evaluate pulmonary hypertension as appropriate. Carfilzomib should be stopped for pulmonary hypertension until resolved or returned to baseline. The decision to restart carfilzomib should be based on a benefit/ risk assessment. Dose modifications and/or delays may be required. For more information see the 'Dose modifications' section below.
Hypertension	Patients may experience an increased incidence of hypertension, including hypertensive crisis with carfilzomib. Pre-existing hypertension should be adequately controlled prior to commencing treatment and blood pressure should be monitored closely throughout treatment and then regularly as clinically indicated. Hypertension should be treated and if not controlled with medical management carfilzomib should be withheld until blood pressure is controlled medically. In severe or persistant hypertension, dose reduction may be necessary or permanent discontinuation should be considered.

Haemorrhage	Patients treated with carfilzomib have an increased risk of haemorrhage, including severe and sometimes fatal haemorrhagic events. Patients should be monitored for signs and symptoms of gastrointestinal, pulmonary and intracranial haemorrhage.
Pulmonary toxicity	Acute respiratory distress syndrome (ARDS), acute respiratory failure, and acute diffuse infiltrative pulmonary disease such as pneumonitis and interstitial lung disease have been reported in patients receiving carfilzomib. Fatal events have occurred. Pulmonary toxicity should be evaluated and carfilzomib should be ceased until resolved. Consideration on whether to restart carfilzomib should be based on a benefit/ risk assessment.
Bone modifying agents	Use of a bone modifying agent (BMA) should be considered in all patients with symptomatic myeloma requiring treatment. For patients with newly diagnosed symptomatic myeloma, zoledronic acid, pamidronate or denosumab should be considered for monthly administration (adjust for kidney dysfunction where appropriate) for up to 2 years. A longer duration of therapy may be appropriate (MRC M IX trial).[3] For more information, please see the following protocols: ID 137 Multiple myeloma zoledronic acid ID 147 Multiple myeloma pamidronate ID 3964 Multiple myeloma denosumab - note denosumab is TGA approved but not PBS reimbursed for this indication.
Bisphosphonates and dental review	Caution should be taken with prolonged use of bisphosphonates due to the risk of osteonecrosis of the jaw (ONJ). A dental review prior to treatment is recommended, and all dental issues treated before the initiation of bisphosphonates. Dental review 6 to 12 monthly during treatment is advisable to minimise risk of ONJ. Concurrent daily oral supplements of calcium 500 mg and vitamin D 400 International Units are recommended. Read more about medication-related osteonecrosis of the jaw (MRONJ)
Peripheral neuropathy	Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Corticosteroids	Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate. Read more about acute short term effects from corticosteroids
Thromboprophylaxis	Thromboprophylaxis should be considered based on an individual benefit/risk assessment and at clinician discretion. Read more about the prophylaxis of venous thromboembolism (VTE) in multiple myeloma
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	PJP prophylaxis is recommended e.g. trimethoprim/sulfamethoxazole 160/800 mg PO one tablet twice daily, twice weekly (e.g. on Mondays and Thursdays) OR one tablet three times weekly (e.g. on Mondays, Wednesdays and Fridays). Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Antiviral prophylaxis is recommended. Read more about antiviral prophylaxis drugs and doses
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC, LFTs, BSL, calcium and magnesium at baseline and prior to each cycle and more frequently (i.e. day 8 and 15) if 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).

Carfilzomib dose level reductions

Carfilzomib dose	1st dose reduction	2nd dose reduction	3rd dose reduction
56 mg/m^2	45 mg/m^2	36 mg/m^2	27 mg/m^{2*}

*If symptoms do not resolve, discontinue carfilzomib treatment.

Haematological toxicity		
ANC x 10^9/L (pre-treatment blood test)		
< 0.5	First episode	Withhold dose Resume at same dose level when ANC ≥ 0.5
	Subsequent episodes	Withhold dose Consider resuming at one dose decrement when ANC ≥ 0.5

Haematological toxicity		
Platelets x 10^9/L (pre-treatment blood test)		
< 10 OR ≤ 30 with evidence of bleeding/bruising	First episode	Withhold dose Resume at same dose level when platelets ≥ 10 and bleeding is controlled
	Subsequent episodes	Resume at one dose decrement when platelets ≥ 10 and bleeding is controlled
Venous thrombosis		
≥ Grade 3	Withhold dose and commence anticoagulation. Resume at same dose level once resolved.	

Renal impairment	
Serum creatinine ≥ 2 x baseline OR CrCl < 15 mL/min OR CrCl decreases to ≤ 50% of baseline OR requiring dialysis	Withhold doses while the cause of renal dysfunction is being assessed If attributable to carfilzomib, resume at one dose decrement when CrCl has recovered to within 25% of baseline If not attributable to carfilzomib, resume the same dose or reduce by one dose decrement, at haematologist's discretion, when CrCl has recovered to within 25% of baseline For patients on dialysis receiving carfilzomib, dose is to be administered after the dialysis procedure.

Note: A pharmacokinetic and safety study of carfilzomib has shown no meaningful differences in PK between patients with normal renal function and end stage renal disease.[4] The carfilzomib dose schedule was not adjusted for baseline renal dysfunction in the ARROW study, but this is at the discretion of the haematologist.[5]

Hepatic impairment	
≥ Grade 3 elevation in LFTs (AST, ALT, or total bilirubin)	Hold carfilzomib dose until return to baseline. If drug induced hepatotoxicity is excluded, resume carfilzomib dose at one dose decrement. If hepatotoxicity is due to carfilzomib, discontinue treatment.

Posterior reversible encephalopathy syndrome (PRES)	
Headaches, altered mental status, seizures, visual loss, and hypertension	If PRES is suspected, withhold carfilzomib. Consider evaluation with neuroradiological imaging for onset of visual or neurological symptoms suggestive of PRES. If the diagnosis of PRES is excluded, resume carfilzomib at the same dose level. If the diagnosis is confirmed, discontinue carfilzomib.

LVEF Reductions	
For resting LVEF < 40% OR reduction of LVEF to < 55% if the drop is greater than 20% from baseline	Withhold carfilzomib dose. Resume carfilzomib at one dose decrement if**: • LVEF returns to ≥ 40% OR • LVEF returns to within 15% baseline (if withheld due to a drop to < 55%)

Other non-haematologic toxicity	
≥ Grade 3	Withhold dose until toxicity has resolved to Grade 2 or less or to baseline grade.

Other non-haematologic toxicity	
	Resume at one dose decrement.
≥ Grade 3 infection	Hold carfilzomib until infection resolves. Resume carfilzomib at same dose.

**Dose reduction should be attempted first to manage treatment-emergent toxicities. Schedule modification may be considered for patients who have persistent toxicities after dose reduction.

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. ***References & Disclaimer***

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

Carfilzomib
No specific clinically significant drug-drug interactions

Dexamethasone		
	Interaction	**Clinical management**
CYP3A4 interactions	Dexamethasone is a substrate of CYP3A4 and a weak to moderate inducer of CYP3A4. The clinical relevance of CYP3A4 induction by dexamethasone is unknown as the mechanism has yet to be established	The effects of the concomitant use of dexamethasone with other CYP3A4 inducers, inhibitors or substrates is variable. If used concomitantly, monitor patients closely for adverse drug reactions
Warfarin	Concurrent use may result in increased risk of bleeding or diminished effects of warfarin	Monitor prothrombin time / INR (especially during initiation or discontinuation) and for signs of drug toxicity during concomitant use; adjust warfarin dose as required
Oral hypoglycaemics	Corticosteroids may cause hyperglycaemia and worsen diabetes control	Monitor blood glucose levels and adjust oral hypoglycaemic dose as required

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 and 2, 8 and 9, 15 and 16

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

Blood pressure should be assessed and monitored closely prior to and throughout treatment.

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

- baseline weight

Pre treatment medication

Dexamethasone

- administer orally ONCE a day in the morning with food **OR**
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%

Note: if a dose is forgotten or vomited, contact treating team.

Dexamethasone is given on days 1, 2, 8, 9, 15, 16, 22 and 23

Infusion reactions can occur immediately following or up to 24 hours after administration of carfilzomib. Dexamethasone must be administered/or taken 30 minutes to 4 hours before carfilzomib is administered

Chemotherapy - Time out

Carfilzomib

Prehydration:

- adequate hydration is required prior to cycle 1, especially in patients at high risk of tumour lysis syndrome
- if required, administer sodium chloride 0.9% over 30 to 60 minutes prior to each dose in cycle 1, or as prescribed
- monitor all patients for evidence of fluid overload, especially in patients with baseline cardiac failure or who are at risk for cardiac failure.

Administer Carfilzomib:

- via IV infusion over 30 minutes
- flush with ~ 100 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

Post-hydration:

- if required, administer sodium chloride 0.9% over 60 minutes or as prescribed.

From cycle 2 onward hydration is at the discretion of the treating team.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Days 22 and 23

This is an oral treatment

Dexamethasone

- administer orally ONCE a day in the morning with food on **days 1, 2, 8, 9, 15, 16, 22 and 23** OR via IV infusion over 15 minutes
- flush with ~ 50 mL sodium chloride 0.9%

Note: if a dose is forgotten or vomited, contact treating team.

Discharge information

Dexamethasone tablets

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

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. PJP prophylaxis, 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)	
Dyspnoea	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Hypertension	High blood pressure is commonly associated with many anti-cancer drugs. Pre-existing hypertension should be controlled prior to initiation of drugs capable of causing hypertension.
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

Early (onset days to weeks)	
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
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
Dizziness	Feeling faint or lightheaded, weak or unsteady. Advise patients to stand up slowly from sitting down or lying down positions and increase fluid intake if dehydrated.
Fatigue	Read more about fatigue
Hyperglycaemia	High blood sugar, an excess of glucose in the blood stream.
Hypokalaemia	Abnormally low levels of potassium in the blood.
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Reversible posterior leukoencephalopathy syndrome (RPLS)	A neurological disorder which may present with headache, seizures, lethargy, confusion, blindness and/or other visual and neurological disturbances. Mild to severe hypertension may also occur. Read more about reversible posterior leukoencephalopathy syndrome (RPLS)
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
Thromboembolism	Thromboembolic events, including pulmonary embolism, deep vein thrombosis and cerebrovascular accidents can occur. Thromboprophylaxis should be considered based on an individual benefit/risk assessment and at clinician discretion. Read more about management of thromboembolism (VTE) in multiple myeloma

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

Delayed (onset months to years)	
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

Carfilzomib is a selective, irreversible proteasome inhibitor which results in more sustained inhibition of the proteasome than the first-generation agent bortezomib.

Evidence supporting this protocol is provided by a randomised, phase 3, open-label, multi-centre trial (ENDEAVOR), involving 929 patients, which compared the combination of carfilzomib and dexamethasone to bortezomib and dexamethasone for the treatment of relapsed or refractory multiple myeloma (rrMM).[6, 7]

Between 2012 and 2014, 464 patients were randomised to receive intravenous carfilzomib (20 mg/m^2 on days 1 and 2 of cycle 1, 56 mg/m^2 thereafter) on days 1-2, 8-9 and 15-16 of a 28-day cycle, together with dexamethasone 20 mg on days 1-2, 8-9, 15-16 and 22-23. The control group of 465 patients were randomised to receive bortezomib 1.3 mg/m^2 by intravenous (IV) or subcutaneous (SC) route on days 1, 4, 8 and 11 of a 21-day cycle, together with dexamethasone 20 mg on days 1-2, 4-5, 8-9 and 11-12. In both arms, cycles were continued until disease progression or unacceptable toxicity.

The primary endpoint was progression free survival (PFS). Overall survival (OS), overall response rate (ORR), duration of response, incidence of grade 2 or higher neuropathy and safety were secondary endpoint/s.

At the first interim PFS analysis, the primary endpoint was met, with significantly higher PFS seen in the carfilzomib compared to the bortezomib group. ORR was also improved for patients receiving carfilzomib. At the time of interim analysis, there was no difference in OS between the two treatment arms.[6] A subsequent interim OS analysis has demonstrated an improvement in survival with the use of carfilzomib.[7]

Carfilzomib has also been investigated in randomised studies as a single-agent,[8] as a weekly 70 mg/m^2 dose on day 1, 8 and 15 in combination with dexamethasone 40 mg on day 1, 8, 15 and 22 (where from cycle 9 onwards the dexamethasone was omitted on day 22) every 28 days,[9] and in combination with lenalidomide and dexamethasone.[10] Single-agent therapy is not currently a TGA-approved indication for carfilzomib. Dexamethasone dose and schedule can be adjusted at clinician's discretion.[1]

Efficacy

After a median follow up of 11.9 months in the carfilzomib and 11.1 months in the bortezomib groups, the median PFS was 18.7 months compared to 9.4 months (HR 0.53, CI 95% 0.44 to 0.65; p<0.0001).

The ORR was also higher in the carfilzomib group at 77% vs 63% (OR 2.03, CI 95% 1.52 to 2.72; p<0.0001). Median treatment durations were 39.9 weeks for carfilzomib and 26.8 weeks for bortezomib with median response duration 21.3 months vs 10.4 months. Quality of life (QOL) data was not reported.[6]

A subsequent interim OS analysis on the same study group in 2017 demonstrated improved outcomes in the carfilzomib-treated group, with median OS 47.6 months (CI 95% 42.5-not evaluable) versus 40.0 months (CI 95% 32.6-42.3) in the bortezomib-treated group (HR 0.791, CI 95% 0.648 to 0.964; p0.010).[7]

Treatment responses in the intention-to-treat population[6]

	Carfilzomib group (n=464)	Bortezomib group (n=465)
Complete response or better†	58 (13%)	29 (6%)
Stringent complete response	8 (2%)	9 (2%)
Complete response	50 (11%)	20 (4%)
Very good partial response or better‡	252 (54%)	133 (29%)
Very good partial response	194 (42%)	104 (22%)
Partial response	104 (22%)	157 (34%)
Minimal response	24 (5%)	53 (11%)
Stable disease	40 (9%)	53 (11%)
Progressive disease	25 (5%)	31 (7%)

Data are n (%) or median (IQR). *Treatment responses were assessed by an independent review committee. †p=0·0010. ‡p<0·0001.

Table 2: **Treatment responses in the intention-to-treat population***

Progression-free survival by independent review committee[6]

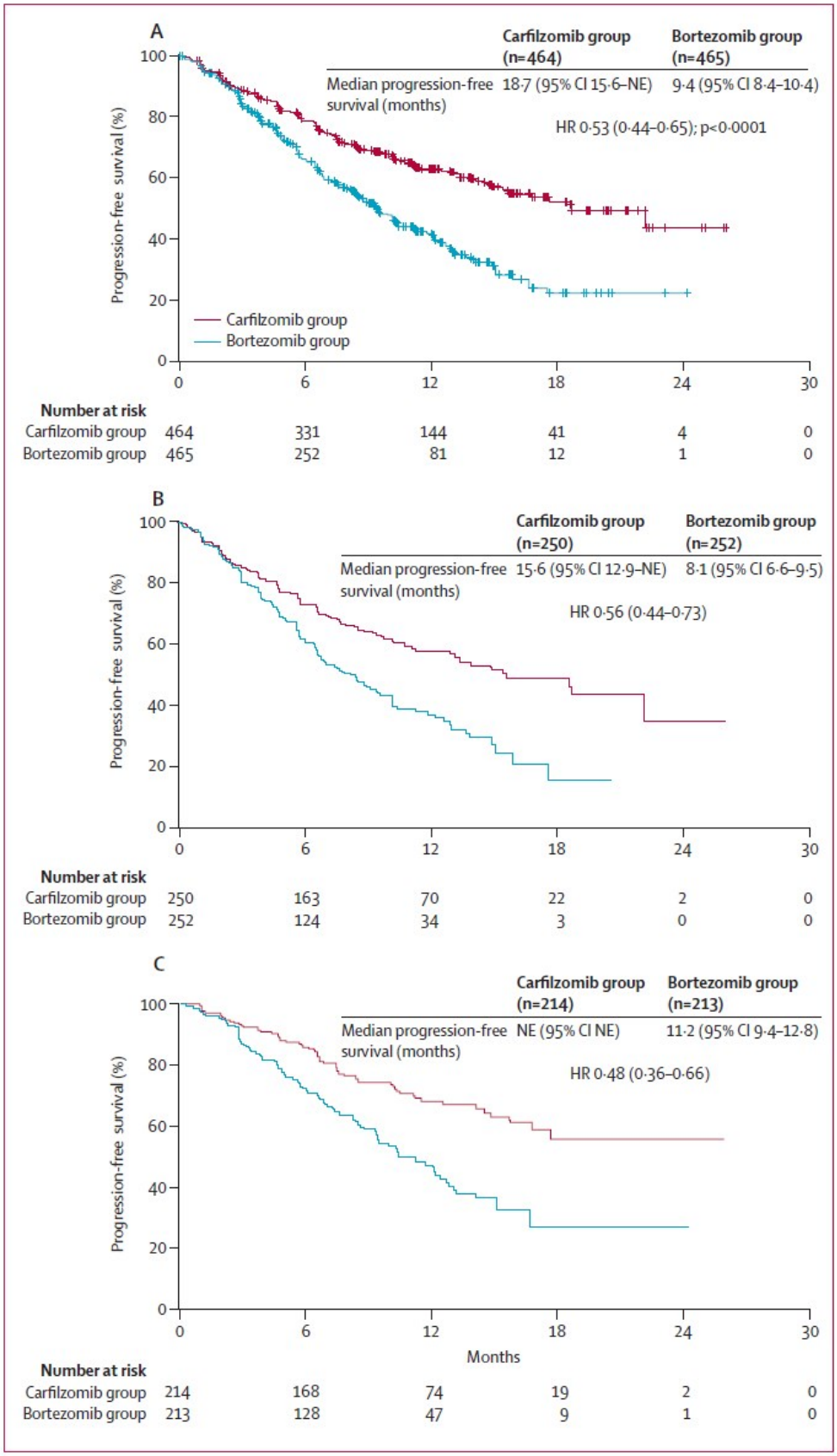


***Figure 2*: Progression-free survival by independent review committee**
Kaplan-Meier curves and median progression-free survival (A) in the intention-to-treat population, (B) in patients with previous bortezomib treatment, and (C) in patients without previous bortezomib treatment. NE=not estimable.

Overall survival[7]

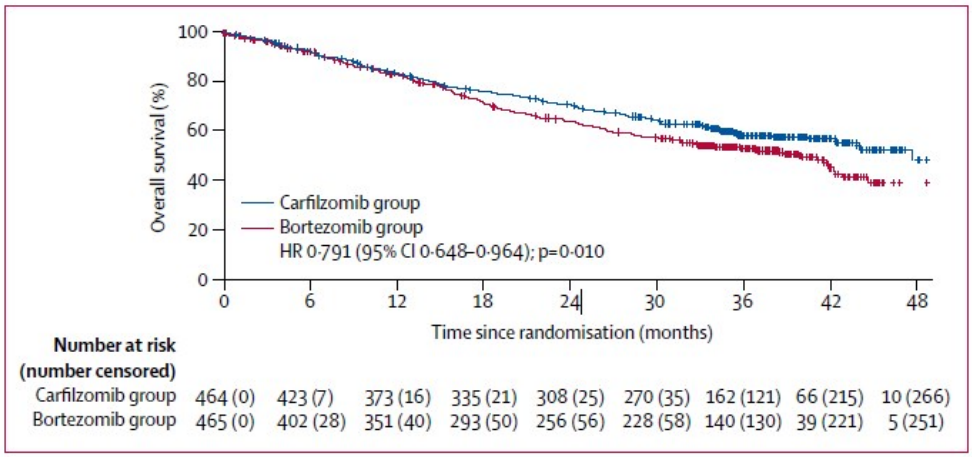


Figure 2: **Overall survival**
HR=hazard ratio.

Furthermore, a secondary analysis of the phase 3 ENDEAVOR study comparing rrMM patients receiving carfilzomib-dexamethasone or bortezomib-dexamethsone in a 1:1 ratio. Patients in the bortezomib arm received either SC or IV bortezomib on days 1,4,8 and 11. A change in the route of bortezomib administration was allowed in the study, but these patients were not included in the secondary analysis. Patient demographics were balanced as per the table below.[11]

Baseline demographics[11]

Table 1. Baseline demographics.

	Kd (SC Vd)[a] ($n=356$)	SC Vd[a] ($n=360$)	Kd (IV Vd)[a] ($n=108$)	IV Vd[a] ($n=75$)
Median age, years (range)	66 (36.0–86.0)	66 (30.0–88.0)	64 (35.0–89.0)	63 (44.0–85.0)
Age ≥65 years, *n* (%)	194 (54.5)	203 (56.4)	47 (43.5)	33 (44.0)
Gender, *n* (%)				
Female	163 (45.8)	188 (52.2)	61 (56.5)	37 (49.3)
Male	193 (54.2)	172 (47.8)	47 (43.5)	38 (50.7)
Number of prior regimens, *n* (%)				
1	182 (51.1)	183 (50.8)	50 (46.3)	34 (45.3)
≥2	174 (48.9)	177 (49.2)[b]	58 (53.7)	41 (54.7)
Prior treatment, *n* (%)				
Bortezomib	196 (55.1)	203 (56.4)	54 (50.0)	33 (44.0)
Lenalidomide	154 (43.3)	151 (41.9)	23 (21.3)	14 (18.7)
Thalidomide	165 (46.3)	198 (55.0)	46 (42.6)	33 (44.0)
Carfilzomib	2 (0.6)	1 (0.3)	0	0
Peripheral neuropathy history, *n* (%)	169 (47.5)	197 (54.7)	46 (42.6)	30 (40.0)
ECOG performance status, *n* (%)				
0	184 (51.7)	192 (53.3)	37 (34.3)	27 (36.0)
1	149 (41.9)	147 (40.8)	62 (57.4)	43 (57.3)
2	23 (6.5)	21 (5.8)	9 (8.3)	5 (6.7)
ISS stage at baseline, *n* (%)				
I	164 (46.1)	161 (44.7)	48 (44.4)	30 (40.0)
II	112 (31.5)	119 (33.1)	26 (24.1)	27 (36.0)
III	80 (22.5)	80 (22.2)	34 (31.5)	18 (24.0)
CrCl,[c] *n* (%)				
<30 mL/min	21 (5.9)	20 (5.6)	7 (6.5)	6 (8.0)
30–50 mL/min	43 (12.1)	59 (16.4)	14 (13.0)	6 (8.0)
50–80 mL/min	146 (41.0)	138 (38.3)	40 (37.0)	28 (37.3)
≥80 mL/min	146 (41.0)	143 (39.7)	47 (43.5)	35 (46.7)
Risk group, *n* (%)[d]				
High risk	74 (25.3)	88 (27.4)	23 (25.8)	19 (31.1)
Standard risk	218 (74.7)	233 (72.6)	66 (74.2)	42 (68.9)

CrCl: creatinine clearance; ECOG: Eastern Cooperative Oncology Group; ISS: International Staging System; IV: intravenous; Kd: carfilzomib and dexamethasone; SC: subcutaneous; Vd: bortezomib and dexamethasone.
[a]SC Vd and IV Vd were based on the actual treatment route of administration in the Vd arm patients, whereas Kd (SC Vd) and Kd (IV Vd) were based on the stratification factor of SC and IV routes of bortezomib administration assigned before randomization, respectively.
[b]One patient randomized to SC Vd had received four prior treatment regimens.
[c]Calculated per the Cockcroft–Gault equation.
[d]Determined via fluorescent *in situ* hybridization. Percentages are calculated as a proportion of the number of patients with known cytogenetic risk status.

PFS was longer for patients treated with carfilzomib-dexamethasone compared with SC or IV bortezomib. The final conclusion was that carfilzomib-dexamethasone was superior therapy to bortezomib-dexamethasone in rrMM regardless of the route of administration of bortezomib or if the patients had received prior bortezomib therapy.[11]

Kaplan-Meier progression-free survival curves for bortezomib-naive patients[11]

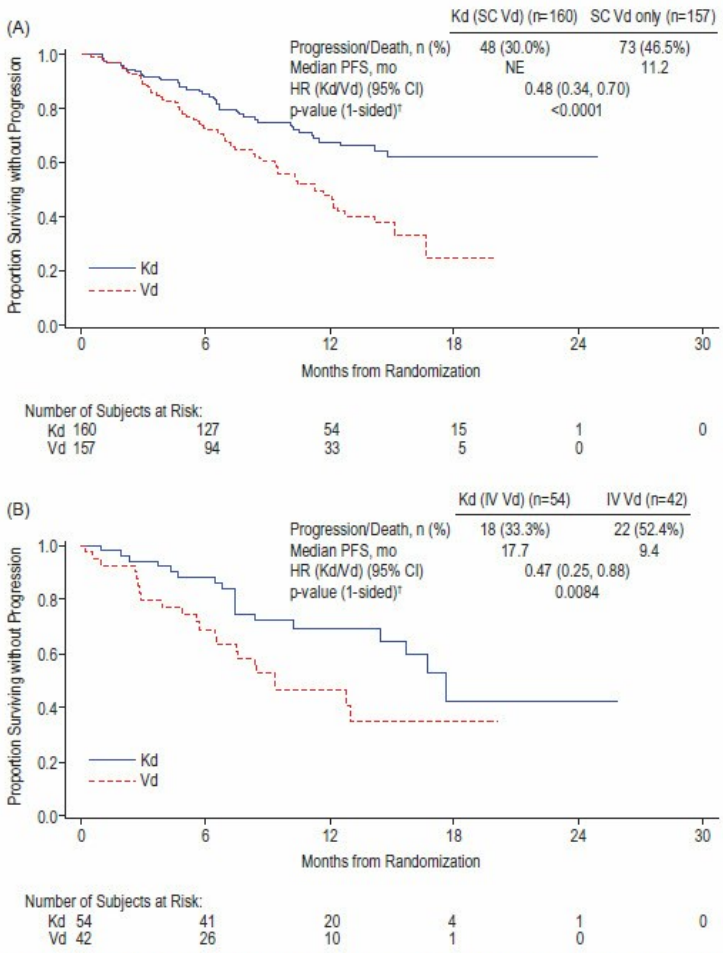


Figure 4. Kaplan–Meier PFS curves for bortezomib-naive patients. (A) Kd (SC Vd) versus SC Vd in the subgroup of bortezomib-naive patients. (B) Kd (IV Vd) versus IV Vd in the subgroup of bortezomib-naive patients. *SC Vd and IV Vd were based on the actual treatment route of administration in the Vd arm patients, whereas Kd (SC Vd) and Kd (IV Vd) were based on the stratification factor of SC and IV routes of bortezomib administration assigned before randomization, respectively. †One-sided *p*-values unadjusted for multiplicity.

Toxicity

In the 2016 Dimopoulos paper, though more serious adverse events were reported in the carfilzomib-treated group (48.4% vs 35.5%), the rate of treatment discontinuation due to adverse events were similar between the two groups (14.0% vs 15.7%).

The main non-haematological adverse events included diarrhea, fatigue, dyspnea, fevers, insomnia, cough and hypertension. The rate of dyspnea, fevers and hypertension was reported as occurring twice as much in the carfilzomib arm.

Significantly fewer patients in the carfilzomib group experienced grade ≥ 2 peripheral neuropathy compared to those treated with bortezomib (6% vs 32%, p<0.0001), which was the most common adverse effect leading to treatment discontinuation.[6]

A meta-analysis indicates higher than expected rates of cardiovascular events associated with carfilzomib exposure. These include hypertension (12.2%), heart failure (4.1%) and ischaemic heart disease 1.8%. Dyspnoea (not necessarily cardiac in aetiology) - is also seen at a high frequency (23.9%).[12]

Tables 3 and 4 - Adverse events[6]

	Carfilzomib group (n=463)				Bortezomib group (n=456)			
	Grade 1 or 2	Grade 3	Grade 4	Grade 5	Grade 1 or 2	Grade 3	Grade 4	Grade 5
Common haematological adverse events (preferred terms)								
Anaemia	115 (25%)	66 (14%)	1 (<1%)	0	78 (17%)	44 (10%)	1 (<1%)	0
Thrombocytopenia	56 (12%)	21 (5%)	18 (4%)	0	35 (8%)	20 (4%)	23 (5%)	0
Common non-haematological adverse events (preferred terms)								
Diarrhoea	127 (27%)	16 (3%)	0	0	141 (31%)	33 (7%)	1 (<1%)	0
Fatigue	111 (24%)	25 (5%)	0	0	98 (21%)	32 (7%)	0	0
Dyspnoea	107 (23%)	25 (5%)	0	0	50 (11%)	10 (2%)	0	0
Pyrexia	119 (26%)	9 (2%)	2 (<1%)	0	59 (13%)	3 (<1%)	0	0
Insomnia	110 (24%)	7 (2%)	0	0	108 (24%)	11 (2%)	0	0
Cough	115 (25%)	0	0	0	63 (14%)	1 (<1%)	0	0
Hypertension	74 (16%)	41 (9%)	0	0	28 (6%)	12 (3%)	0	0
Peripheral oedema	97 (21%)	4 (<1%)	0	0	75 (16%)	3 (<1%)	0	0
Asthenia	78 (17%)	16 (3%)	0	0	61 (13%)	13 (3%)	1 (<1%)	0
Upper respiratory tract infection	85 (18%)	9 (2%)	0	0	64 (14%)	3 (<1%)	0	0
Nausea	84 (18%)	6 (1%)	0	0	79 (17%)	3 (<1%)	0	0
Back pain	78 (17%)	7 (2%)	1 (<1%)	0	59 (13%)	12 (3%)	0	0
Muscle spasms	85 (18%)	1 (<1%)	0	0	24 (5%)	3 (<1%)	0	0
Headache	75 (16%)	4 (<1%)	0	0	43 (9%)	3 (<1%)	0	0
Bronchitis	66 (14%)	10 (2%)	0	0	37 (8%)	4 (<1%)	0	0
Constipation	66 (14%)	2 (<1%)	0	0	114 (25%)	9 (2%)	0	0
Nasopharyngitis	66 (14%)	0	0	0	50 (11%)	1 (<1%)	0	0
Vomiting	59 (13%)	6 (1%)	0	0	34 (7%)	6 (1%)	0	0
Pain in extremity	45 (10%)	2 (<1%)	0	0	46 (10%)	3 (<1%)	0	0
Peripheral neuropathy	37 (8%)	6 (1%)	0	0	97 (21%)	23 (5%)	1 (<1%)	0
Decreased appetite	36 (8%)	4 (<1%)	0	0	52 (11%)	5 (1%)	0	0
Dizziness	36 (8%)	1 (<1%)	0	0	64 (14%)	3 (<1%)	0	0
Paraesthesia	35 (8%)	1 (<1%)	0	0	72 (16%)	2 (<1%)	0	0
Peripheral sensory neuropathy	26 (6%)	1 (<1%)	0	0	61 (13%)	6 (1%)	0	0
Neuralgia	6 (1%)	3 (<1%)	0	0	63 (14%)	7 (2%)	0	0

Data are n (%). Adverse events (preferred terms) of grades 1–2 occurring in at least 10% of patients in either treatment group are listed. All grade 3 or higher adverse events not shown here are reported in the appendix. On-study deaths due to adverse events occurred in 18 (4%) of 464 patients in the carfilzomib group and in 16 (3%) of 465 patients in the bortezomib group.

Table 3: **Adverse events in the safety population**

	Carfilzomib group (n=463)				Bortezomib group (n=456)			
	Grade 1 or 2	Grade 3	Grade 4	Grade 5	Grade 1 or 2	Grade 3	Grade 4	Grade 5
Peripheral neuropathy*	77 (17%)	10 (2%)	0	0	198 (43%)	36 (8%)	1 (<1%)	0
Acute renal failure†	19 (4%)	15 (3%)	3 (<1%)	1 (<1%)	10 (2%)	11 (2%)	1 (<1%)	0
Cardiac failure‡	16 (3%)	17 (4%)	3 (<1%)	2 (<1%)	5 (1%)	5 (1%)	1 (<1%)	2 (<1%)
Pneumonia	9 (2%)	30 (6%)	1 (<1%)	1 (<1%)	12 (3%)	33 (7%)	1 (<1%)	2 (<1%)
Ischaemic heart disease§	4 (<1%)	5 (1%)	3 (<1%)	0	2 (<1%)	3 (<1%)	1 (<1%)	3 (<1%)
Pulmonary hypertension‖	3 (<1%)	3 (<1%)	0	0	0	1 (<1%)	0	0

Data are n (%). *Peripheral neuropathy included (in descending order of frequency): peripheral neuropathy, peripheral sensory neuropathy, neuralgia, decreased vibratory sense, polyneuropathy, sensory loss, amyotrophy, peripheral motor neuropathy, peripheral sensorimotor neuropathy, sensory disturbance, and toxic neuropathy. †Acute renal failure included (in descending order of frequency): acute renal failure, renal failure, renal impairment, acute prerenal failure, anuria, oliguria, and prerenal failure. ‡Cardiac failure included (in descending order of frequency): cardiac failure, ejection fraction decreased, pulmonary oedema, acute cardiac failure, congestive cardiac failure, acute pulmonary oedema, acute left ventricular failure, chronic cardiac failure, cardiopulmonary failure, hepatojugular reflex, right ventricular failure, and left ventricular failure. §Ischaemic heart disease included (in descending order of frequency): angina pectoris, acute coronary syndrome, myocardial infarction, increased troponin T, coronary artery disease, increased troponin I, acute myocardial infarction, myocardial ischaemia, and cardiomyopathy stress. ‖Pulmonary hypertension included (in decreasing order of frequency): pulmonary hypertension, right ventricular failure, and pulmonary arterial hypertension.

Table 4: **Adverse events of interest in the safety population**

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History

Version 3

Date	Summary of changes
24/08/2020	Protocol reviewed and updated with the following changes: • Title changed to include 'twice-weekly' dosing in title. • Dose modifications updated to align with once-weekly protocol (ID 3830).

Date	Summary of changes
	• Side effects updated to include 'dizziness'. • Version change to v.3. • For review in 1 year.
30/04/2021	Protocol reviewed at Haematology Reference Committee Meeting. Updates included: • Changing thromboprophylaxis to the clinician's discretion. • Recommending PJP prophylaxis. • Recommending antiviral prophylaxis. • Adding a sentence into the evidence section of toxicity. Review in 2 years.
20/01/2022	Interactions updated.
24/01/2022	Pulmonary toxicity added to side effects.
21/11/2022	The following changes have been made with the consensus agreement of the eviQ Haematology Reference Committee: • Name updated to include acronym to align with other carfilzomib protocols on eviQ • Bone modifying agents block added to clinical information, related note removed from treatment schedule and linked pages removed • Link to Medical Scientific Advisory Group (MSAG) guidelines updated • Febrile neutropenia advice removed from Dose modifications section • Note regarding dexamethasone reduction in specific patient populations added to treatment schedule notes • Volume of pre and post-carfilzomib hydration removed • Blood pressure added to assessments in Administration section • Administration details specified for day 22 and 23

Version 2

Date	Summary of changes
29/11/2019	Protocol reviewed at the Haematology Reference Committee meeting. Discussion continued over email and protocol approved with the following changes: • Clinical information: thromboprophylaxis, PJP prophylaxis and blood test recommendations updated. • Dose modifications updated: note regarding maximum dose interruption remove. • Evidence section updated. • Version change to v.2. • Review in 5 years.

Version 1

Date	Summary of changes
24/11/2017	New eviQ protocol presented at Haematology Reference Group meeting.
26/02/2018	New protocol published in eviQ

First approved: 26 February 2018
Last reviewed: 30 April 2021
Review due: 31 December 2023

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/3358
13 Jun 2023

Patient information - Multiple myeloma - Kd (carfilzomib and dexamethasone) twice weekly

Patient's name:

Your treatment

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

Kd (carfilzomib and dexamethasone) twice weekly			
This 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**
1 and 2, 8 and 9, 15 and 16, 22 and 23	**Dexamethasone** *(dex-a-meth-a-sone)*	Take orally ONCE a day 30 minutes to 4 hours before carfilzomib, with food on days 1, 2, 8, 9, 15 and 16. Take orally ONCE a day in the morning with food on days 22 and 23.	
1 and 2, 8 and 9, 15 and 16	**Carfilzomib** *(car-fill-zo-mib)*	By drip into a vein	About 30 minutes

Missed doses:

- **Dexamethasone:** if you forget to take your tablets or vomit your tablets, contact your treating team.

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 • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime: Night/weekend: Other instructions:

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

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Changes to your dose or treatment delays

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

Blood tests and monitoring

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

Central venous access devices (CVADs)

This treatment may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the eviQ patient information sheets on CVADs.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication.

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)	
Shortness of breath	• You may have a cough. • You may feel short of breath. • **Tell your doctor or nurse immediately if you feel you have a cough or feel short of breath.**
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.**
High blood pressure (hypertension)	• You may not have any signs or symptoms if you have high blood pressure. • If it is severe you may get headaches, shortness of breath or feel dizzy. • Your blood pressure will be taken regularly during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the signs or symptoms listed above.**
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)	
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.**

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.
Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Dizziness or feeling light-headed	• You may feel dizzy or light-headed. • These symptoms may be caused by your treatment, or other problems like dehydration. • If you are feeling dehydrated, drink plenty of fluids (unless you are fluid restricted) as this can be a cause of dizziness. • If you are feeling dizzy, try lying down until the dizziness passes. • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Tell your doctor or nurse if you get any of the symptoms listed above.
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.**
High blood sugar level (hyperglycaemia)	• You may feel thirsty and need to urinate more often than normal. • You may get repeated infections, especially thrush. • If you are a diabetic you will need to have your blood sugar levels checked more often. You may also need to have your diabetes medication increased. • **Tell your doctor or nurse if you get any of the signs or symptoms listed above.**

Low blood potassium levels (hypokalaemia)	• This may be found from your routine blood tests and treated by your doctor.
	• If it is severe you may get:
	  ◦ muscle cramps or twitches
	  ◦ constipation
	  ◦ confusion
	  ◦ an irregular heartbeat.
	• **Tell your doctor or nurse as soon as possible if you get any of the signs or symptoms listed above.**

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

Changes in the way your brain works [reversible posterior leukoencephalopathy syndrome (RPLS)]	• This treatment can have an effect on your brain, but this is rare. • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **headaches or vision problems** ◦ **nausea and vomiting** ◦ **tiredness** ◦ **confusion** ◦ **fits (seizures)** ◦ **high blood pressure.**
Side effects from steroid medication	• Steroid medication may cause: ◦ mood swings and behaviour changes ◦ an increased appetite ◦ weight gain ◦ swelling in your hands and feet ◦ stomach upsets ◦ trouble sleeping ◦ fragile skin and bruising ◦ an increase in your blood sugar level ◦ weak and brittle bones (osteoporosis) • Take your steroid medication with food to reduce stomach upset • If you have diabetes, your blood sugar levels may be tested more often. • Tell your doctor or nurse if you get any of the symptoms listed above.

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**

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

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.

- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

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

Other medical and dental treatment

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

Diet and food safety

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

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

Quitting smoking

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

Staying active

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

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

Where to get more information

Telephone support

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

Haematology, transplant and cellular therapy information

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

General cancer information and support

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

Quit smoking information and support

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

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

Additional notes:

First approved: 26 February 2018
Last reviewed: 30 April 2021
Review due: 31 December 2023

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/pi/3358
13 Jun 2023