Small cell lung cancer extensive disease cARBOplatin etoposide and durvalumab

ID: 3921 v.2 **Endorsed**

⚠ ADDIKD Carboplatin dosing:

For dosing carboplatin, ADDIKD recommends that:

- Directly measured glomerular filtration rate (mGFR) is the preferred kidney function value in the Calvert formula, especially where estimated kidney function may be unreliable for accurate therapeutic dosing.
- Where mGFR is unavailable, eGFR adjusted to an individual's body surface area (BSA-adjusted eGFR) is a suitable alternative for use in the Calvert formula.
- Kidney function should not be capped at 125 mL/min for use in the Calvert formula.
- Recalculation of carboplatin doses at each cycle is unnecessary, except when baseline kidney function (e.g., eGFR) alters by > 20% or when there is a change in the clinical status of the patient.

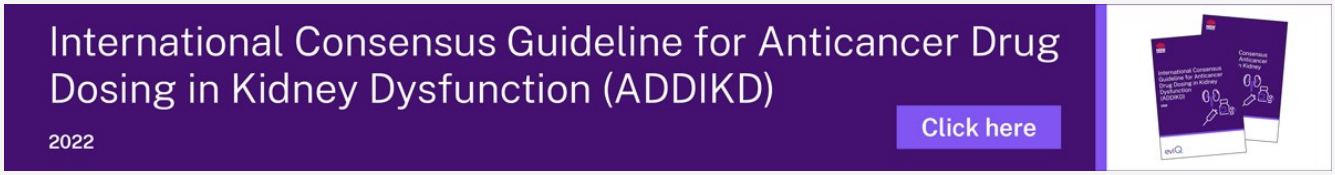
For further information refer the eviQ Factsheet around carboplatin dosing and the carboplatin drug monograph within the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) and carboplatin dose calculators.

Treatment must be initiated and supervised by specialist physicians experienced in the treatment of cancer using immunological agents. Before commencing immunotherapy treatment in any patient, clinicians should have an understanding of the immune-related adverse events (irAEs) associated with immunotherapy treatment and their management.

Check for clinical trials in this patient group. Link to Australian Clinical Trials website

Link to Clinical practice guidelines for the treatment of lung cancer

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:

- Small cell lung cancer extensive disease cARBOplatin and etoposide
- Small cell lung cancer extensive disease cARBOplatin and oral etoposide
- Small cell lung cancer extensive disease cARBOplatin etoposide and atezolizumab

Treatment schedule - Overview

Cycle 1 to 4

Drug	Dose	Route	Day
Durvalumab	1,500 mg	IV infusion	1
cARBOplatin	5 AUC *	IV infusion	1
Etoposide **	100 mg/m^2	IV infusion	1 to 3

*If estimated GFR is greater than 125 mL/min (i.e. 5 AUC doses greater than 750 mg), obtaining direct measurement rather than an estimated renal function and/or dose capping is strongly recommended

**Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.

Frequency: 21 days

Cycles: 4 of chemotherapy combination, followed by continuous treatment with durvalumab until disease progression or unacceptable toxicity

Cycle 5 and further cycles

Drug	Dose	Route	Day
Durvalumab	1,500 mg	IV infusion	1

Frequency: 28 days

Cycles: 4 of chemotherapy combination, followed by continuous treatment with durvalumab until disease progression or unacceptable toxicity

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Notes:
The CASPIAN[1] and KEYNOTE-604 [2] studies permitted either carboplatin or cisplatin as the chemotherapy backbone. For selected patients it may be appropriate to substitute carboplatin with cisplatin.

Oral etoposide may be substituted for intravenous etoposide at the correct conversion dose. There is no evidence to support this but clinical circumstances may justify the use of oral etoposide in this regimen and in this patient population.

The standard oral etoposide dose is approximately twice the effective intravenous etoposide dose i.e. 200 mg/m^2 (*orally*) = 100 mg/m^2 (*intravenously*). Prediction of oral doses based on intravenous doses may be unreliable; it is recommended to titrate the oral dose to achieve maximal effect and minimise toxicity.

In the first few months after the start of immunotherapy, some patients can experience transient tumour flare (termed "pseudo progression" or an immune response). This may manifest as growth of existing lesions or the development of new lesions prior to later tumour regression. While this is rare (~5%), continuing treatment and performing a second scan 4 to 6 weeks later to confirm progression may be considered, particularly if the patient remains well.

Radiation recall has been observed with PD-L1 inhibitors, consideration should be given to the timing when starting this treatment after a prolonged course of radiation therapy

Drug status: Carboplatin and etoposide are on the PBS general schedule

Durvalumab is TGA registered but not PBS listed for this indication

Cost: ~ $12,440 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 to 4

Day 1		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	8 mg (PO)	60 minutes before chemotherapy

Day 1		
Durvalumab	1,500 mg (IV infusion)	in 250 mL sodium chloride 0.9% over 60 minutes
cARBOplatin	5 AUC (IV infusion)	in 500 mL glucose 5% over 30 to 60 minutes (if estimated GFR is greater than 125 mL/min (i.e. 5 AUC dose greater than 750 mg), obtaining direct measurement rather than an estimated renal function and/or dose capping is strongly recommended)
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes *

Day 2 and 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on day 2 and 3 may not be required and may be reduced or omitted at the clinician's discretion **
Etoposide	100 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 30 to 60 minutes *

Frequency: 21 days

Cycles: 4 of chemotherapy combination, followed by continuous treatment with durvalumab until disease progression or unacceptable toxicity

Cycle 5 and further cycles

Day 1		
Durvalumab	1,500 mg (IV infusion)	in 250 mL sodium chloride 0.9% over 60 minutes

*Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.

**Link to ID 7 Prevention of antineoplastic induced nausea and vomiting

Frequency: 28 days

Cycles: 4 of chemotherapy combination, followed by continuous treatment with durvalumab until disease progression or unacceptable toxicity

Indications and patient population

Indications

- First line treatment of small cell lung cancer, extensive disease
- ECOG performance status 0 or 1.

Precautions:

If any of these conditions are present, clinical judgement should be used and individual cases discussed with an expert in the field as indicated:

- significant autoimmune disease (e.g. myasthenia gravis, inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, autoimmune ocular disease)
- organ transplantation
- previous history of viral hepatitis
- HIV/acquired immune deficiency syndrome (AIDS)
- previous radiation to the lungs.

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 etoposide. High risk with carboplatin. Hypersensitivity risk increases with number of cycles of carboplatin. Rechallenge with carboplatin after hypersensitivity carries a high risk of anaphylaxis, and where clinically indicated, should be undertaken with a desensitisation protocol with appropriate supports in place. Refer to local institutional policy. Read more about Hypersensitivity reaction
Emetogenicity MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. Carboplatin AUC $\geq$ 4 is classified by MASCC/ESMO Antiemetic Guidelines 2016 and ASCO Antiemetic Guidelines 2017 as having moderate emetogenicity. However, a NK1 receptor antagonist and a $5HT_3$ receptor antagonist in combination with dexamethasone are available on the PBS for primary prophylaxis of carboplatin induced nausea and vomiting. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Etoposide conversion factor	Note: Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.

Immune-related adverse events (irAEs)	Immune-related adverse events (irAEs) can occur early and escalate quickly in patients receiving immune checkpoint inhibitors. irAEs can also occur after discontinuation of treatment. Fatalities have been reported. Management of irAEs is largely based on expert opinion and consensus guidelines. Examples of irAEs with high risk of mortality include: • cardiac toxicity: myocarditis • musculoskeletal toxicity: myositis • neurological toxicity: encephalitis, Guillain-Barré syndrome, myelitis, myasthenia gravis • pulmonary toxicity: pneumonitis • skin toxicity: Steven-Johnson syndrome, toxic epidermal necrolysis. Examples of irAEs in order of frequency include: • Common ◦ endocrinopathies: thyroid dysfunction ◦ gastrointestinal toxicity: diarrhoea ◦ musculoskeletal toxicity: arthralgia, myalgia ◦ skin toxicity: rash, erythema, pruritus • Less common ◦ endocrinopathies: hypophysitis, type I diabetes mellitus ◦ gastrointestinal toxicity: colitis ◦ musculoskeletal toxicity: inflammatory arthritis ◦ ocular toxicity: dry eye ◦ renal toxicity ◦ skin toxicity: vitiligo • Rare ◦ endocrinopathies: primary adrenal insufficiency ◦ gastrointestinal toxicity: pancreatitis ◦ haematological toxicity ◦ musculoskeletal toxicity: vasculitis ◦ ocular toxicity: uveitis, iritis. Proactive monitoring, patient self-monitoring and early reporting of adverse events is critical. Treatment interruptions/discontinuation, consultation with specialist and administration of corticosteroids and/or supportive care is required to minimise the risk of death. Read more about the management of immune-related adverse events (irAEs)
Baseline investigations	Consider ECG and troponin at baseline. There is no clear evidence regarding the efficacy/value of baseline ECG or troponin in patients receiving immune checkpoint inhibitor therapy. Some cancer specialists obtain baseline testing, and others continue this through the initial period of therapy. Consider urinalysis at baseline, particularly in patients with additional risk factors for developing immune-related acute kidney injury.
Blood tests	FBC, EUC, eGFR, LFTs, calcium, magnesium, serum cortisol, TFTs and BSL at baseline. Repeat FBC, EUC,eGFR, LFTs and BSL prior to each cycle and serum cortisol and TFTs alternate cycles. Calcium and magnesium as clinically indicated. Check lipase and amylase if symptomatic of pancreatitis. Recalculation of carboplatin doses at each cycle is unnecessary, except when baseline kidney function (e.g., eGFR) alters by greater than 20% or when there is a change in the clinical status of the patient. In the absence of suspicion of immune related adverse events less frequent monitoring may be applicable, according to institutional guidelines. Evidence for the frequency of routine blood testing with immunotherapies varies within published studies and guidelines. Read more about immunotherapy blood test monitoring recommendations

Hepatitis and HIV	Hepatitis screening is recommended in all patients who are to receive immune checkpoint inhibitors. Immunotherapy is associated with inflammatory adverse reactions resulting from increased or excessive immune activity and patients are at risk of developing autoimmune hepatitis. It should be used with caution in patients who have a history of chronic hepatic infections (hepatitis B and C), detectable human immunodeficiency virus (HIV) viral load or acquired immune deficiency syndrome (AIDS).
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. The safety of having vaccinations during immunotherapy is unknown. Patients in the clinical trials were typically allowed to receive inactivated and recombinant vaccines but not live vaccines. 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.
Effects of cancer treatment on fertility	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. Studies to evaluate the effects of immune checkpoint inhibitor therapy on fertility have not been performed. Therefore, the effect on male and female fertility is unknown. Limited evidence supports that immune checkpoint inhibitor-related hypogonadism due to orchitis and hypophysitis can impact fertility. Immune checkpoint inhibitors can cause fetal harm when given to pregnant women. A pregnancy test should be considered 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. There is very limited evidence to provide guidance regarding contraception timelines. Some studies have demonstrated PD-1 receptor occupancy for greater than 9 months after anti-PD-1 therapy (Brahmer et al., 2010). As a result, some cancer specialists advise using contraception for at least six months or even as long as two years after treatment finishes. Read more about the effect of cancer treatment on fertility Link to Brahmer et al., 2010

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).

For dosing carboplatin, ADDIKD recommends that:

- Directly measured glomerular filtration rate (mGFR) is the preferred kidney function value in the Calvert formula, especially where estimated kidney function may be unreliable for accurate therapeutic dosing.
- Where mGFR is unavailable, eGFR adjusted to an individual's body surface area (BSA-adjusted eGFR) is a suitable alternative for use in the Calvert formula.
- Kidney function should not be capped at 125 mL/min for use in the Calvert formula.

- Recalculation of carboplatin doses at each cycle is unnecessary, except when baseline kidney function (e.g., eGFR) alters by > 20% or when there is a change in the clinical status of the patient.

*For further information refer the **eviQ Factsheet** around carboplatin dosing and the carboplatin drug monograph within the ADDIKD guideline. To assist with calculations, use the eviQ **Estimated Glomerular Filtration Rate (eGFR)** and **carboplatin** dose calculators.*

Immune checkpoint inhibitor dose modifications

- Dose reduction is not recommended
- No dose adjustment is required in the elderly, mild or moderate renal impairment or mild hepatic impairment. Immune checkpoint inhibitors have not been studied in patients with severe renal impairment or moderate to severe hepatic impairment.

Management of immune-related adverse events (irAEs)

Link to Management of immune-related adverse events (irAEs)

Chemotherapy dose modifications

Note: All dose reductions are calculated as a percentage of the starting dose

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
1.0 to less than 1.5	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well.
0.5 to less than 1.0	Delay treatment until recovery
less than 0.5	Delay treatment until recovery and reduce carboplatin and etoposide by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and reduce carboplatin and etoposide by 25% for subsequent cycles
Platelets x 10^9/L (pre-treatment blood test)	
75 to less than 100	The general recommendation is to delay, however if the patient is clinically well it may be appropriate to continue treatment; refer to treating team and/or local institutional guidelines.
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and reduce carboplatin and etoposide by 25% for subsequent cycles

Renal impairment	
Consider if immune-related adverse event. See Management of immune-related adverse events (irAEs)	
Creatinine clearance (mL/min)	
30 to 50	Reduce etoposide by 25% and recalculate carboplatin dose using Calvert formula
less than 30	Reduce etoposide by 50% and recalculate carboplatin dose using Calvert formula or omit carboplatin

Hepatic impairment	
Hepatic dysfunction	
Consider if immune-related adverse event. See Management of immune-related adverse events (irAEs)	
Mild	Reduce etoposide by 25%
Moderate	Reduce etoposide by 50%
Severe	Omit etoposide

Mucositis and stomatitis	

Mucositis and stomatitis	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce carboplatin and etoposide by 25% 3rd occurrence: Reduce carboplatin and etoposide by 50% 4th occurrence: Omit carboplatin and etoposide
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: Reduce carboplatin and etoposide by 50% 2nd occurrence: Omit carboplatin and etoposide

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*

Carboplatin		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Ototoxic drugs (e.g. aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity	Avoid combination or perform regular audiometric testing
Paclitaxel	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination

Durvalumab		
No formal pharmacokinetic drug interaction studies have been conducted with durvalumab. Since durvalumab is cleared from the circulation through catabolism, no metabolic drug-drug interactions are expected.		
	Interaction	**Clinical management**
Immunosuppressants (inc. corticosteroids)	Reduced efficacy of both immunosuppressants and durvalumab possible due to pharmacodynamic interaction	It is recommended that patients requiring corticosteroids **prior** to treatment receive the lowest possible dose (preferably no greater than 10 mg prednisolone or equivalent steroid per day). **Once started** on durvalumab the use of corticosteroids to treat immune related adverse events (irAEs) does not appear to impact the clinical response to durvalumab. In patients requiring ongoing corticosteroids **post management** of an irAE, the dose should be as low as possible.

Durvalumab		
		Monitor for signs of organ rejection in transplant recipients.

Etoposide and Etoposide Phosphate		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin etc.)	Increased toxicity of etoposide possible due to reduced clearance	Avoid combination or monitor for etoposide toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of etoposide possible due to increased clearance	Avoid combination or monitor for decreased clinical response to etoposide
Glucosamine	Reduced efficacy of etoposide (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II)	Avoid combination or monitor for decreased clinical response to etoposide
Grapefruit juice	Reduced efficacy of oral etoposide possible due to possible alteration of P-gp mediated intestinal transport of etoposide	Avoid combination or monitor for decreased clinical response to etoposide

NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant		
	Interaction	**Clinical management**
Dexamethasone	Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4	Reduce dose of **antiemetic dexamethasone** by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of **antiemetic dexamethasone** has already been taken into account. If **dexamethasone is part of the chemotherapy protocol**, dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover.
Warfarin	Reduced anticoagulant efficacy of warfarin due to increased clearance (aprepitant induces CYP2C9). *Note interaction only applicable to aprepitant/ fosaprepitant	INR should be monitored in the 2 week period, particularly at 7 to 10 days following the administration of aprepitant/ fosaprepitant
Combined oral contraceptive	Reduced contraceptive efficacy due to increased clearance. *Note interaction only applicable to aprepitant/ fosaprepitant	Alternative non-hormonal methods should be used during and for 1 month after stopping aprepitant/ fosaprepitant
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of NK-1 antagonist possible due to increased clearance	Avoid combination or monitor for decreased antiemetic effect. Consider using an alternative antiemetic regimen
CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of NK-1 antagonist possible due to reduced clearance	Avoid combination or monitor for increased adverse effects of NK-1 antagonist (e.g. headache, hiccups, constipation)
Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP3A4 by NK-1 antagonist	Avoid combination or monitor for increased toxicity especially with orally administered drugs

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 cycles 1 to 4

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.

Day 1

Approximate treatment time: 3.5 hours

Safe handling and waste management

Safe administration

General patient assessment and immunotherapy patient assessment prior to each treatment.

Any toxicity 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.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Treatment - Time out

Durvalumab

Administer durvalumab:

- a low protein binding 0.2 or 0.22 micron in-line or add-on filter should be used
- via IV infusion over 60 minutes
- observe for infusion-related reactions
- flush with 50 mL of sodium chloride 0.9%
- do not co-administer other drugs through the same infusion line.

Mild or moderate infusion-related reaction:

- decrease the rate of infusion and monitor closely
- give any further doses with close monitoring.

Severe infusion reaction:

- stop infusion immediately
- medical officer review
- permanently discontinue durvalumab.

Chemotherapy - Time out

Carboplatin

Administer carboplatin (irritant):

- via IV infusion over 30 to 60 minutes
- observe for hypersensitivity reactions
- flush with ~100 mL of sodium chloride 0.9%
- hypersensitivity risk increases with number of cycles administered.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate
- for severe reactions seek medical assistance immediately and do not restart infusion.

Etoposide

Administer etoposide (irritant):

- via IV infusion over 30 to 60 minutes
- rapid infusion may cause hypotension
- observe for hypersensitivity
- flush with ~ 100 mL sodium chloride 0.9%
- if using etoposide phosphate administer in ~ 50 mL sodium chloride 0.9% or glucose 5% over ~15 minutes.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate.
- for severe reactions seek medical assistance immediately and do not restart infusion.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Days 2 and 3

Approximate treatment time: 90 minutes

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Etoposide

Administer etoposide (irritant):

- via IV infusion over 30 to 60 minutes
- rapid infusion may cause hypotension
- observe for hypersensitivity
- flush with ~ 100 mL sodium chloride 0.9%
- if using etoposide phosphate administer in ~ 50 mL sodium chloride 0.9% or glucose 5% over ~15 minutes.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate.
- for severe reactions seek medical assistance immediately and do not restart infusion.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Discharge information

Antiemetics

- Antiemetics as prescribed.

Patient information

- Ensure patient receives patient information sheet.

Administration cycle 5 onwards

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.

Day 1

Approximate treatment time: 90 minutes

Handling of monoclonal antibodies and waste management

Safe administration

Immunotherapy patient assessment prior to each treatment.

Any toxicity may require delay of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Administer antiemetics if required

Treatment - Time out

Durvalumab

Administer durvalumab:

- a low protein binding 0.2 or 0.22 micron in-line or add-on filter should be used
- via IV infusion over 60 minutes
- observe for infusion-related reactions
- flush with 50 mL of sodium chloride 0.9%
- do not co-administer other drugs through the same infusion line.

Mild or moderate infusion-related reaction:

- decrease the rate of infusion and monitor closely
- give any further doses with close monitoring.

Severe infusion reaction:

- stop infusion immediately
- medical officer review
- permanently discontinue durvalumab.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Discharge information

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.

There can be an overlap between the immune-related and chemotherapy-related adverse events with this treatment. Immune-related adverse events (irAEs) can escalate quickly and close monitoring of the patient is required. Immune-related symptoms should improve promptly after the introduction of immunosuppressive therapy. If this does not occur review the diagnosis and seek further specialist advice. Refer to the Management of immune related adverse events document for further information.

Immune related adverse events	
Cardiotoxicity	Cardiotoxicity is a rare but serious side effect, which may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, myocarditis, pericarditis, cardiac fibrosis, hypertension, cardiac ischaemia, congestive heart failure (CHF) and cardiac arrest. Read more about Management of immune related adverse events.
Gastrointestinal toxicity	Colitis, diarrhoea or more bowel movements than usual; blood or mucous in stools; dark, tarry, sticky stools; abdominal pain or tenderness. Read more about Management of immune related adverse events
Haematological toxicity	Autoimmune haemolytic anaemia (AIHA), acquired thrombotic thrombocytopenic purpura (TTP), aplastic anaemia (AA), immune thrombocytopenia (ITP), acquired haemophilia (AH), haemolytic uremic syndrome (HUS) and lymphopenia are rare but potentially serious immune-related adverse events associated with immunotherapy treatment. Read more about Management of immune related adverse events.
Hepatotoxicity	Transaminase and total bilirubin elevation, jaundice, severe nausea or vomiting, pain on the right side of the abdomen, drowsiness, dark urine, bleeding or bruising more easily than normal, anorexia. Read more about Management of immune related adverse events.
Musculoskeletal toxicity	Inflammatory arthritis, temporal arteritis, arthralgia, myalgia, synovitis, vasculitis, polymyalgia-like syndrome and myositis. Read more about Management of immune related adverse events.
Neurological toxicity	Aseptic meningitis, myasthenia gravis, Guillain-Barre syndrome, encephalitis, meningeal symptoms, optic neuritis, neuropathy and acute inflammatory demyelinating polyneuropathy are infrequent but potentially serious immune-related adverse events associated with immunotherapy treatment. Read more about Management of immune related adverse events.
Ocular toxicity	Eye pain, blurred vision, Uveitis/iritis, episcleritis, blepharitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia. Read more about Management of immune related adverse events.
Other endocrinopathies	Type 1 diabetes mellitus, hypophysitis, hypopituitarism and adrenal insufficiency are infrequent but potentially serious immune-related adverse events associated with immunotherapy treatment. Read more about Management of immune related adverse events
Pulmonary toxicity	Radiographic changes, dyspnoea, new or worsening cough, hypoxia, tachycardia, chest pain or fever. Read more about Management of immune related adverse events.
Renal toxicity	Increase in serum creatinine, oliguria, haematuria, peripheral oedema and anorexia. Read more about Management of immune related adverse events.
Skin toxicity	Rash including full thickness, pruritus, skin blisters, ulceration and necrosis. Radiation recall can occur at site of previous radiation therapy. Symptoms include vesiculation, desquamation and ulceration of the skin. Read more about Management of immune related adverse events
Thyroid toxicity	Thyroid toxicity is common with immune checkpoint inhibitors. Hypothyroidism is most frequent however hyperthyroidism can also occur. Read more about Management of immune related adverse events

Chemotherapy immediate (onset hours to days)	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Taste and smell alteration	Read more about taste and smell changes

Chemotherapy 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
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue

Chemotherapy late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling

Evidence

The evidence supporting this protocol is provided by a phase 3, multicentre, international, randomised trial (CASPIAN) involving 537 patients. This protocol is specifically based on the first two arms which have been reported, which compared platinum (carboplatin or cisplatin), etoposide and durvalumab, with platinum (carboplatin or cisplatin) and etoposide alone, in the first line treatment of patients with extensive stage small cell lung cancer (SCLC). The third arm investigates carboplatin, etoposide, durvalumab and tremelimumab in combination and has not yet been reported.[1]

Between March 2017, and May 2018, 537 patients with extensive stage SCLC were randomised 1:1, with 268 receiving durvalumab plus platinum–etoposide and 269 receiving platinum–etoposide alone. Platinum-etoposide consisted of etoposide 80–100 mg/m^2 intravenously on days 1 to 3 with investigator's choice of either carboplatin AUC 5–6 or cisplatin 75–80 mg/m^2 intravenously on day 1 of each 3-week cycle. Patients received up to four cycles of platinum–etoposide plus durvalumab 1500 mg every 3 weeks followed by maintenance durvalumab 1500 mg every 4 weeks in the immunotherapy group or up to six cycles of platinum–etoposide every 3 weeks plus prophylactic cranial irradiation (at investigator discretion) in the platinum–etoposide only group. Maintenance therapy was continued until disease progression or unacceptable toxicity.

The primary endpoint was overall survival (OS) in the intention-to-treat population. Secondary endpoints were progression-free survival (PFS), objective response (OR), OS at 18 months, PFS at 6 and 12 months and safety.

Efficacy

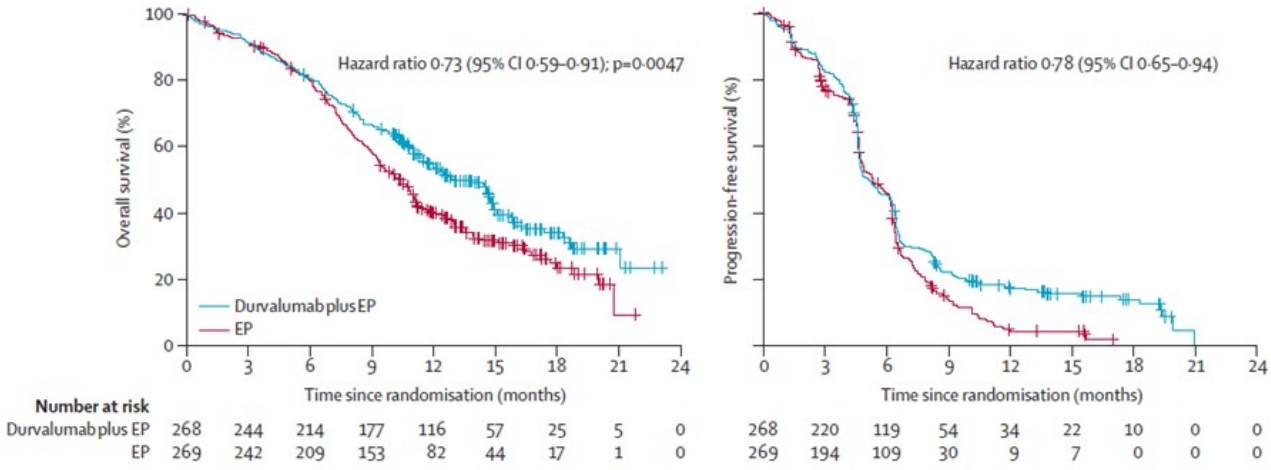
After a median follow up of 14.2 months (interquartile range 11.7–17.0), a significant improvement in OS was demonstrated in the durvalumab plus platinum–etoposide group (HR 0.73 [95% CI 0.59–0.91; p=0.0047]). The median OS was 13.0 months (95% CI 11.5–14.8) in patients receiving durvalumab plus platinum–etoposide, compared with only 10.3 months (95% CI 9.3–11.2) in those

who received platinum–etoposide alone. At median follow-up of 18 months, 34% (95% CI 26.9–41.0) of patients in the durvalumab plus platinum–etoposide group were alive, compared with only 25% (95% CI 18.4–31.6) in those who received platinum–etoposide alone.[1]

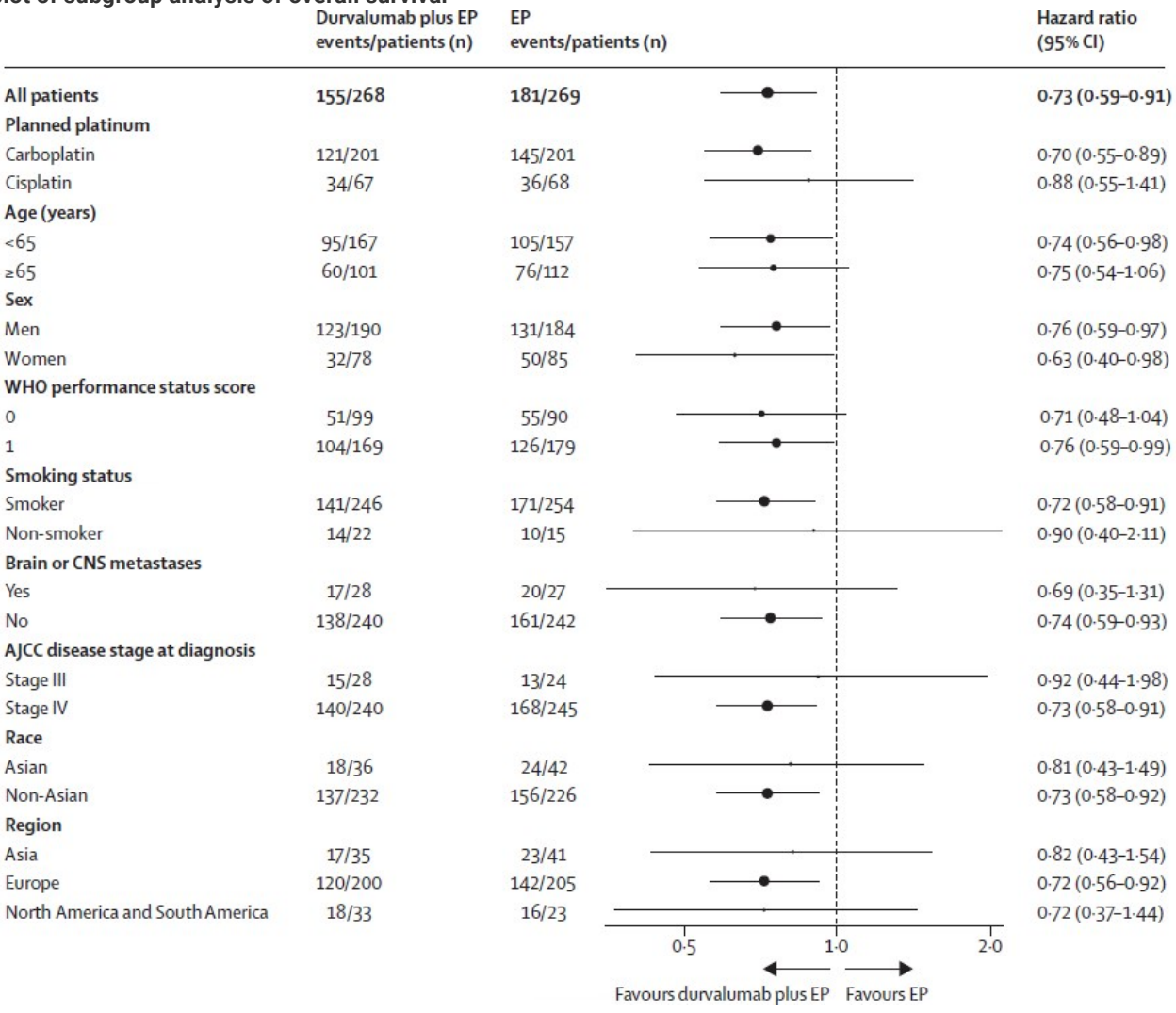
Median PFS was not significantly different between the two groups, measuring 5.1 months (95% CI 4.7–6.2) with durvalumab plus platinum–etoposide and 5.4 months (4.8–6.2) with platinum-etoposide alone. However, the 12-month PFS rates were notably higher in the durvalumab plus platinum–etoposide group, at 18% (95% CI 13.1–22.5) compared with 5% (95% CI 2.4–8.0) in the platinum–etoposide group.[1]

Post hoc analysis demonstrated a confirmed OR in 182 (68%) of the 268 patients who received durvalumab plus platinum–etoposide, compared with 155 (58%) of the 269 patients who received platinum–etoposide alone (OR 1.56 [1.10–2.22]).[1]

Kaplan-Meier curves for overall survival (A) and progression-free survival (B) in the intention to treat population[1]



Forest plot of subgroup analysis of overall survival[1]



Toxicity

Any-cause grade 3 or 4 adverse events occurred in 163 (62%) of the 265 patients treated with durvalumab plus platinum–etoposide and 166 (62%) of the 266 patients treated with platinum–etoposide alone.[1]

Adverse events leading to death occurred in 13 (5%) patients in the durvalumab plus platinum–etoposide group and 15 (6%) in the platinum–etoposide group. Of note, there was no significant group specific mortality identified.

Immune-related adverse events (irAEs) were reported in 52 (20%) of the 265 patients treated with durvalumab plus platinum–etoposide and seven (3%) of the 266 patients treated with platinum–etoposide alone. Most of these events were grade 1 or 2, and grade 3 or 4 irAEs were only identified in 12 (5%) patients in the durvalumab plus platinum–etoposide group and one patient (<1%) in the platinum–etoposide group. Death due to irAEs were from hepatotoxicity in the durvalumab plus platinum–etoposide group and pneumonitis in the platinum–etoposide group, occurring in only one patient in each group. The most common irAEs were grade 1 or 2 thyroid-related events with hypothyroid events affecting 24 patients (9%) treated with durvalumab plus platinum etoposide and two patients (1%) treated with platinum etoposide and hyperthyroid events affecting 14 patients (5%) and none respectively.

Adverse events[1]

	Durvalumab plus platinum–etoposide (n=265)		Platinum-etoposide (n=266)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Any event	260 (98%)	163 (62%)	258 (97%)	166 (62%)
Any serious event	82 (31%)	57 (22%)	96 (36%)	70 (26%)
Any event leading to discontinuation*	25 (9%)	7 (3%)	25 (9%)	7 (3%)
Any event leading to death†	13 (5%)	..	15 (6%)	..
Adverse events with an incidence of at least 10% in any grade category or events of grade 3 or 4 with an incidence of at least 2% in either group‡				
Neutropenia	111 (42%)	64 (24%)	124 (47%)	88 (33%)
Anaemia	102 (38%)	24 (9%)	125 (47%)	48 (18%)
Nausea	89 (34%)	1 (<1%)	89 (33%)	5 (2%)
Alopecia	83 (31%)	3 (1%)	91 (34%)	2 (1%)
Constipation	44 (17%)	2 (1%)	51 (19%)	0
Decreased appetite	48 (18%)	2 (1%)	46 (17%)	2 (1%)
Thrombocytopenia	41 (15%)	15 (6%)	53 (20%)	25 (9%)
Fatigue	48 (18%)	4 (2%)	45 (17%)	3 (1%)
Vomiting	39 (15%)	0	44 (17%)	3 (1%)
Asthenia	40 (15%)	5 (2%)	40 (15%)	3 (1%)
Leucopenia	40 (15%)	17 (6%)	32 (12%)	14 (5%)
Dyspnoea	31 (12%)	5 (2%)	28 (11%)	3 (1%)
Neutrophil count decreased	26 (10%)	17 (6%)	31 (12%)	17 (6%)
Diarrhoea	26 (10%)	3 (1%)	30 (11%)	3 (1%)
Cough	33 (12%)	2 (1%)	18 (7%)	0
Hyponatraemia	26 (10%)	10 (4%)	12 (5%)	7 (3%)
Febrile neutropenia	17 (6%)	14 (5%)	17 (6%)	17 (6%)
White blood cell count decreased	14 (5%)	4 (2%)	17 (6%)	6 (2%)
Platelet count decreased	16 (6%)	4 (2%)	14 (5%)	6 (2%)
Pneumonia	11 (4%)	5 (2%)	18 (7%)	9 (3%)
Hypertension	15 (6%)	8 (3%)	7 (3%)	1 (<1%)
Lipase increased	12 (5%)	9 (3%)	7 (3%)	4 (2%)
Amylase increased	11 (4%)	6 (2%)	2 (1%)	1 (<1%)

Data cutoff was March 11, 2019. Listed are all adverse events that occurred during the treatment period and up to 90 days after the last dose of durvalumab or platinum-etoposide or up to the start of any subsequent therapy (whichever occurred first). Platinum-etoposide=etoposide plus either cisplatin or carboplatin. *Includes patients who permanently discontinued at least one study drug. †Adverse events of any cause leading to death in the durvalumab plus platinum-etoposide group were sudden death in two patients, and acute respiratory failure, aspiration, cardiac arrest, dehydration, hepatotoxicity, hypoxia, pancytopenia, pulmonary artery thrombosis, pulmonary embolism, sepsis, and septic shock in one patient each; adverse events of any cause leading to death in the platinum-etoposide group were pneumonitis and death in two patients each, and acute cardiac failure, acute respiratory failure, cardiac arrest, cardiopulmonary failure, cerebrovascular accident, haematotoxicity, pancytopenia, pneumonia, sudden cardiac death, sudden death, and thrombocytopenia and haemorrhage (in the same patient) in one patient each. ‡The events are listed in descending order of frequency across both treatment groups.

Table 4: Adverse events of any cause (safety population)

References

1 Paz-Ares, L., M. Dvorkin, Y. Chen, et al. 2019. "Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial." Lancet 394(10212):1929-1939.

2 Rudin, C. M., M. M. Awad, A. Navarro, et al. 2020. "Pembrolizumab or Placebo Plus Etoposide and Platinum as First-Line

Therapy for Extensive-Stage Small-Cell Lung Cancer: Randomized, Double-Blind, Phase III KEYNOTE-604 Study." J Clin Oncol:JCO2000793.

History

Version 2

Date	Summary of changes
13/04/2022	Protocol updated based on the consensus gained at immunotherapy reference committee meeting held on 4th of March 2022. The following changes have been made across all immune checkpoint inhibitor protocols: • Clinical information- general irAEs, hepatitis and HIV, and fertility blocks updated. Individual irAE-related blocks removed. New block (baseline investigations) added. • Side effects- preamble wording updated. • Patient information- side effect section preamble wording updated. Pregnancy and breastfeeding block in general advice section updated. Version number increased to V.2.
20/05/2022	Protocol reviewed electronically by Medical Oncology Reference Committee. No change. Next review in 2 years.

Version 1

Date	Summary of changes
22/02/2021	Protocol approved electronically by Medical Oncology Reference Committee.
01/03/2021	Protocol approved and published on eviQ. Review 1 year.

First approved: 1 March 2021
Last reviewed: 20 May 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/3921
09 Aug 2023

Patient information - Lung cancer extensive disease - Carboplatin, etoposide and durvalumab

Patient's name:

Your treatment

It is important to understand that durvalumab is not a traditional chemotherapy drug and has a different way of working. It is an immunotherapy treatment (also called anticancer drug) that works with your immune system to detect and destroy cancer cells.

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

Carboplatin, etoposide and durvalumab cycles 1 to 4

This treatment cycle is repeated every **21 days**. You will have 4 treatments with durvalumab, carboplatin and etoposide followed by durvalumab alone.

Day	Treatment	How it is given	How long it takes
1	**Durvalumab** (*dur-VAL-u-mab*) **Carboplatin** (*carb-o-PLAT-in*) **Etoposide** (*e-TOE-poe-side*)	By a drip into a vein	About 3.5 hours
2 and 3	**Etoposide**	By a drip into a vein	About 1.5 hours

Durvalumab cycle 5 and further cycles

This treatment cycle is repeated every **28 days**. You will have treatment with durvalumab alone after completing 4 cycles of durvalumab, carboplatin and etoposide. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	**Durvalumab**	By a drip into a vein	About 1.5 hours

Prior to your treatment tell your doctor if you are taking any other medicines (e.g. corticosteroids, immunosuppressive therapy), have or ever had chronic liver infections e.g. hepatitis B (HBV) or C (HCV), human immunodeficiency virus (HIV) or an organ transplant.

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	Daytime: Night/weekend: Other instructions:

- you become unwell.

It is important that you tell your doctor or nurse immediately if you develop any of the immune related side effects listed below. If you can't contact your doctor or nurse, go to your nearest hospital Emergency Department.

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

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

Other medications given during this treatment

- **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.
- **Steroids:** you may be given some steroid tablets to help reduce immune-related side effects. Your doctor or nurse will tell you how and when to take the steroids. You may need to monitor your blood sugar levels closely while you are taking steroids. If you have diabetes, your diabetic medication may need to be adjusted because of the effects of steroids. Speak to your diabetes advisor.

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.

Immunotherapy may cause serious immune reactions against your own body. These are called immune-related adverse events. They may occur during your treatment, or after your treatment has ended. Immunotherapy can affect many parts of your body. Some side effects can cause severe or life threatening conditions, so even mild side effects must be reported immediately. Do not try to treat these symptoms yourself without talking to your doctor or nurse first. You will be given an information pack at the start of your treatment. You will be given an information pack at the start of your treatment. This contains an alert card which you should carry with you at all times. Bring this alert card with you to hospital, especially if you are unwell or attending the emergency department.

This treatment uses both chemotherapy and immunotherapy. These drugs work in different ways, but can cause similar side effects.

Immune related side effects	
Heart problems	• You may get: ◦ chest pain or tightness ◦ shortness of breath ◦ swelling of your ankles ◦ an abnormal heartbeat. • Heart problems are uncommon but potentially fatal. If heart problems were to occur, symptoms usually start within the first 3 months of treatment, but can happen at any time even after the treatment has finished. • 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.**
Bowel and stomach inflammation	• You may get: ◦ bowel motions (stools, poo) that are more frequent or more liquid (diarrhoea) ◦ blood or mucous in your stool ◦ dark, tarry, or sticky bowel motions ◦ bloating, cramping, pain or tenderness in your stomach area. • Inform your doctor or nurse immediately if you get diarrhoea • Take your anti-diarrhoeal or steroid medication as directed by your doctor. • Drink plenty of fluids (unless you are on a fluid restriction). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled despite taking anti-diarrhoea medicine, severe stomach pains and bloating, and/or if you feel dizzy or light-headed.**
Blood problems	• Blood problems are infrequent but can be serious. • You may feel dizzy, light-headed, tired, weak and appear more pale than usual. • You may get: • dark, tarry bowel motions (stools, poo) • blood in your urine or not urinating as often • dark-coloured urine • yellowing of the whites of your eyes, and/or your skin • pinpoint red spots on your skin • unexplained bleeding • major bruising • a fever • shortness of breath • a severe headache • confusion • faster heartbeat than normal • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if it has been longer than 12 hours since you have emptied your bladder or if you get any of the symptoms listed above.**

Liver damage	• You may get: ◦ fatigue ◦ severe nausea and vomiting ◦ weight loss ◦ bruising or bleeding more easily ◦ pain or tenderness on the right side of your stomach area ◦ dark coloured urine ◦ yellowing of the whites of your eyes and/or your skin ◦ itchy skin ◦ drowsiness • You will have regular blood tests to check how well your liver is working. • Take your steroid medication as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes or skin look yellow, if you have unexplained bruising or bleeding or if you have severe stomach pain.**
Muscle and joint problems	• You may get: • muscle or joint stiffness, especially after a period of rest • muscle weakness • pain in your muscles or joints • joint swelling • tiredness • headaches • Take your pain relief or steroid medication as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above.**
Nervous system problems	• Nervous system changes are rare, but can be serious. • You may get: ◦ headaches ◦ fever ◦ stiff neck ◦ confusion or difficulty concentrating ◦ dizziness or drowsiness ◦ loss of consciousness ◦ muscle weakness or pain ◦ numbness or tingling in your hands or feet ◦ jerky movements. • Take your steroid medication as directed by your doctor. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**
Eye problems	• You may get: ◦ eye pain ◦ itchy eyes ◦ red or swollen eyes ◦ blurred or change in vision ◦ change in colour vision ◦ watery or gritty eyes ◦ dry eyes ◦ sensitivity to light. • Protect your eyes from the weather (sun and wind) by wearing sunglasses. • Use your eye drops or take your steroid medication as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above.**

Hormone problems	• Hormone changes are infrequent, but can be serious. • You may get: ◦ headaches ◦ tiredness, dizziness or fainting ◦ abnormal heartbeat (faster than usual) ◦ a feeling of being hot or cold more easily ◦ excessive sweating ◦ weight changes ◦ a deepened voice ◦ irregular or absent periods ◦ nausea and vomiting ◦ thirsty and need to urinate more often than normal ◦ high blood sugar levels ◦ pain in your stomach area ◦ muscle pain or weakness ◦ difficulty sleeping ◦ agitated more easily ◦ changes in your mood or behaviour, such as decreased sex drive or irritability. • Take your hormone or steroid medication as directed by your doctor. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you feel confused, weak, dizzy, or faint, or get sudden pain in your lower back or legs.**
Lung problems	• You may get: ◦ shortness of breath ◦ difficulty breathing ◦ faster heartbeat than normal ◦ chest pain ◦ new or worsening cough ◦ fever. • Your doctor will monitor how well your lungs are working during your treatment. • Take your steroid medication as directed by your doctor. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**
Kidney damage	• This treatment can cause changes to how your kidneys work. • You may get: ◦ a feeling of needing to urinate less often than normal ◦ blood in your urine ◦ swollen hands and feet ◦ loss of appetite. • You will have regular blood tests to check how well your kidneys are working. • You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this. • Take your steroid medication as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.**

Skin rash	• You may get
	  ◦ a red rash
	  ◦ a bumpy rash
	  ◦ dry and itchy skin
	  ◦ skin peeling or blisters.
	  ◦ if you have had previous radiation therapy to an area this effect may be worse
	• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.
	• Avoid scratching your skin.
	• Avoid wearing tight fitting clothing
	• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.
	• Take your antihistamine medication or apply your steroid cream as directed by your doctor.
	• **Tell your doctor or nurse as soon as possible if you notice any changes to the rash like pain or pus forming.**

Thyroid problems	Thyroid problems are common with this treatment. The most common problem is an underactive thyroid gland (hypothyroidism), occasionally you may get an overactive thyroid gland (hyperthyroidism).
	• If you have an **underactive** thyroid, you may get:
	  ◦ fatigue and low energy levels
	  ◦ depression
	  ◦ slow heart rate
	  ◦ unexplained weight gain
	  ◦ intolerance to cold temperatures
	  ◦ fatigued and aching muscles
	  ◦ dry, coarse skin
	  ◦ puffy face
	  ◦ hair loss
	  ◦ constipation
	  ◦ problems with concentration
	  ◦ changes in your periods
	• If you have an **overactive** thyroid, you may get
	  ◦ abnormal heartbeat (faster than usual)
	  ◦ a feeling of being hot or cold more easily
	  ◦ excessive sweating
	  ◦ difficulty sleeping
	  ◦ anxiety, nervousness or agitated more easily
	  ◦ diarrhoea
	  ◦ changes in your periods
	• You will have regular blood tests to check how well your thyroid is working.
	• Take your hormone or steroid medication as directed by your doctor.
	• Tell your doctor or nurse if you get any of the symptoms listed above.

Chemotherapy immediate (onset hours to days)	

Allergic reaction	• Allergic reactions are uncommon but can be life threatening.
	• **If you feel unwell during the infusion or shortly after it, or:**
	  ◦ **get a fever, shivers or shakes**
	  ◦ **feel dizzy, faint, confused or anxious**
	  ◦ **start wheezing or have difficulty breathing**
	  ◦ **have a rash, itch or redness of the face**
	
	<u>While you are in hospital:</u> Tell your doctor or nurse immediately.
	<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.

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

Chemotherapy 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.**
Mouth pain and soreness (mucositis)	• You may have: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

Chemotherapy late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program

General advice for patients 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 treatments.
- 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.
- Don't have **any** vaccinations without talking to the doctor who is managing your cancer treatment.
- People you live with should be fully vaccinated, 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

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

Risk of developing a second cancer

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

Quitting smoking

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

Staying active

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

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

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Lung Foundation Australia on 1800 654 301

Lung cancer information

- Lung Foundation Australia – lungfoundation.com.au
- Lungevity – lungevity.org

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
- CHILL Cancer related hair loss - scalpcooling.org
- eviQ Cancer Treatments Online – eviQ.org.au
- 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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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/3921
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