# Non small cell lung cancer locally advanced durvalumab (flat dosing) (following chemoradiation)

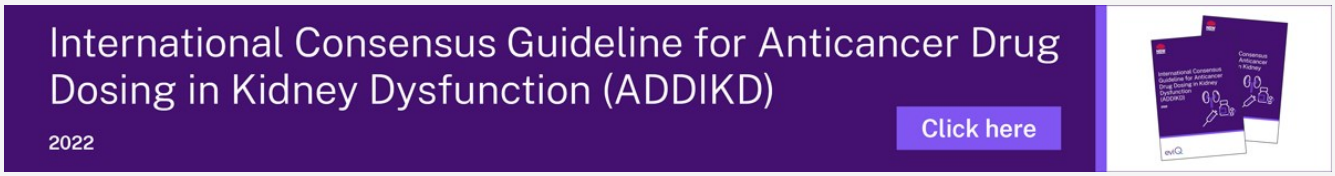
**ID: 4179** v.1 **Endorsed**

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:**

- Non small cell lung cancer locally advanced durvalumab (weight based dosing) (following chemoradiation)
- Non small cell lung cancer locally advanced definitive cARBOplatin and PACLitaxel chemoradiation
- Non small cell lung cancer locally advanced definitive ciSplatin and etoposide chemoradiation

## Treatment schedule - Overview

### Cycle 1 to 13

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

**Frequency:** 28 days

**Cycles:** 13 or until disease progression or unacceptable toxicity

**Notes:**
Patients should commence cycle 1 within 42 days of completing chemoradiation therapy.

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:** Durvalumab is PBS authority

**Cost:** ~ $12,020 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 13

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

Patients should commence cycle 1 within 42 days of completing chemoradiation therapy.

**Frequency:** 28 days

**Cycles:** 13 or until disease progression or unacceptable toxicity

## Indications and patient population

### Indications:

- Stage III non-small cell lung cancer without disease progression following platinum based chemoradiation
- ECOG performance status score 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
- grade 2 or greater pneumonitis.

## Clinical information

| | |
|---|---|
| **Venous access required** | IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment.<br>Read more about central venous access device line selection |
| **Emetogenicity MINIMAL** | No antiemetics should be routinely administered before treatment in patients without a history of nausea and vomiting. If patients experience nausea and/or vomiting, consider using the low antiemetic prophylaxis regimen.<br>Read more about preventing anti-cancer therapy induced nausea and vomiting |

| | |
|---|---|
| **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.<br>Examples of irAEs with high risk of mortality include:<br>• cardiac toxicity: myocarditis<br>• musculoskeletal toxicity: myositis<br>• neurological toxicity: encephalitis, Guillain-Barré syndrome, myelitis, myasthenia gravis<br>• pulmonary toxicity: pneumonitis<br>• skin toxicity: Steven-Johnson syndrome, toxic epidermal necrolysis.<br><br>Examples of irAEs in order of frequency include:<br>• Common<br>◦ endocrinopathies: thyroid dysfunction<br>◦ gastrointestinal toxicity: diarrhoea<br>◦ musculoskeletal toxicity: arthralgia, myalgia<br>◦ skin toxicity: rash, erythema, pruritus<br>• Less common<br>◦ endocrinopathies: hypophysitis, type I diabetes mellitus<br>◦ gastrointestinal toxicity: colitis<br>◦ musculoskeletal toxicity: inflammatory arthritis<br>◦ ocular toxicity: dry eye<br>◦ renal toxicity<br>◦ skin toxicity: vitiligo<br>• Rare<br>◦ endocrinopathies: primary adrenal insufficiency<br>◦ gastrointestinal toxicity: pancreatitis<br>◦ haematological toxicity<br>◦ musculoskeletal toxicity: vasculitis<br>◦ ocular toxicity: uveitis, iritis.<br><br>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.<br>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, serum cortisol, TFTs and BSL at baseline.<br>Repeat FBC, EUC, eGFR, LFTs and BSL prior to each cycle and serum cortisol and TFTs alternate cycles. Check lipase and amylase if symptomatic of pancreatitis.<br>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.<br>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.<br>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** | The safety of having vaccinations during treatment is unknown. Patients in the clinical trials were typically allowed to receive inactivated and recombinant vaccines but not live vaccines.<br>Read more about COVID-19 vaccines and cancer. |
| **Effects of cancer treatment on fertility** | 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.<br>Read more about the effect of cancer treatment on fertility<br>Link to Brahmer et al., 2010 |

## Dose modifications

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)**.

- 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)

## 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*

**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 |

| Durvalumab | | |
|---|---|---|
| | | 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.<br><br>Monitor for signs of organ rejection in transplant recipients. |

## 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.*

### 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.*

The most common side effects with this treatment are immune-related adverse events (irAEs). irAEs can escalate quickly and close monitoring of the patient is required. 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.<br>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.<br>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.<br>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.<br>Read more about Management of immune related adverse events. |
| **Musculoskeletal toxicity** | Inflammatory arthritis, temporal arteritis, arthralgia, myalgia, synovitis, vasculitis, polymyalgia-like syndrome and myositis.<br>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.<br>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.<br>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.<br>Read more about Management of immune related adverse events |
| **Pulmonary toxicity** | Radiographic changes, dyspnoea, new or worsening cough, hypoxia, tachycardia, chest pain or fever.<br>Read more about Management of immune related adverse events. |
| **Renal toxicity** | Increase in serum creatinine, oliguria, haematuria, peripheral oedema and anorexia.<br>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.<br>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.<br>Read more about Management of immune related adverse events |

| Non-immune related adverse events | |
|---|---|
| **Nausea and vomiting** | Read more about prevention of treatment induced nausea and vomiting |
| **Headache** | |
| **Anorexia** | Loss of appetite accompanied by decreased food intake.<br>Read more about anorexia |
| **Constipation** | |
| **Fatigue** | Read more about fatigue |

## Evidence - Flat dosing

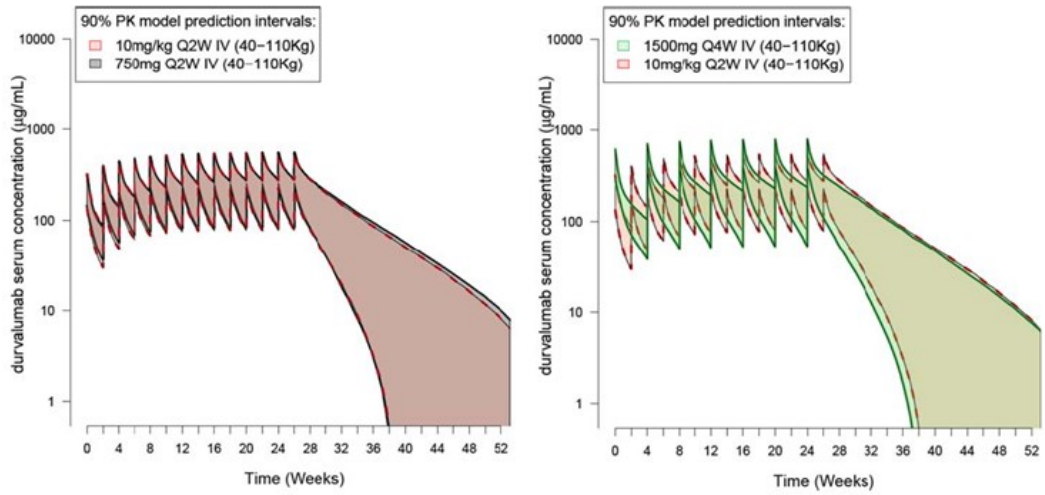
While weight-based dosing (10 mg/kg every 2 weeks) was used in the PACIFIC study for NSCLC, flat dosing has been used in subsequent studies of durvalumab including 4-weekly flat dosing in extensive stage small cell lung cancer.[1, 2]

The evidence for flat as opposed to weight-based dosing for durvalumab comes from a population pharmacokinetic (PK) modelling paper by Baverel et al.[3] This study used pooled data from 1409 patients across two studies: a phase Ib/II study across multiple tumour types, and a phase II study in patients with stage IIIb/IV NSCLC, and aimed to evaluate dosage requirements for special populations and whether a flat-dosing regimen every 2 or every 4 weeks would be comparable to weight-based dosing.[4] The population included in this PK analysis was predominantly male (56.7%), white (71%) or Asian (19%) with median age 62, and median body weight at baseline of 69.8 kg. Lung cancer patients represented the biggest pool (n = 776).

In this paper the authors developed a PK model of durvalumab based on pooled patient data, and then simulated flat dosing and compared the simulated plasma immune checkpoint inhibitor concentrations to actual concentrations corresponding to a body-weight-based dose. In this study simulations of flat-dosing regimens 750 mg every 2 weeks and 1500 mg every 4 weeks vs 10 mg/kg every 2 weeks suggested that all regimens lead to similar median steady-state exposures and variability, with no increased incidence of extreme concentration values with flat dosing.

While multiple baseline patient demographics including body weight (range: 34 to 149 kg) were found to be statistically significant predictors of durvalumab PK, all caused a magnitude of effect on the durvalumab PK of <30%, which was specified *a priori* as a threshold for clinical significance.

**Simulated PK profiles of durvalumab following weight-based dosing regimens (10 mg/kg q2w) compared with flat dosing[3]**




*The area (pink, grey, and green) represents the 90% prediction interval from the semimechanistic time-varying CL model according to three different dosing schemes; they are delimited by the 5th and 95th percentiles of the simulated PK data obtained from a pool of n = 1,000 virtual patients.*



## Evidence

The evidence supporting this protocol is provided by a phase III, multicentre, international, randomised trial (PACIFIC) involving 709 patients comparing the anti-PDL1 antibody durvalumab with placebo as consolidation therapy in patients with stage III, locally

advanced, unresectable NSCLC without disease progression after two or more cycles of platinum-based definitive chemoradiation therapy.[5]

Between May 2014 and April 2016, a total of 473 patients were randomised to receive durvalumab 10 mg/kg every 2 weeks for up to 12 months and 236 patients were randomised to receive placebo, commencing within 42 days of completion of chemoradiation therapy.

The co-primary end points were progression-free survival (PFS) and overall survival (OS). Secondary end points were 12-month and 18-month PFS, objective response rate, duration of response, time to death or distant metastasis, and safety.

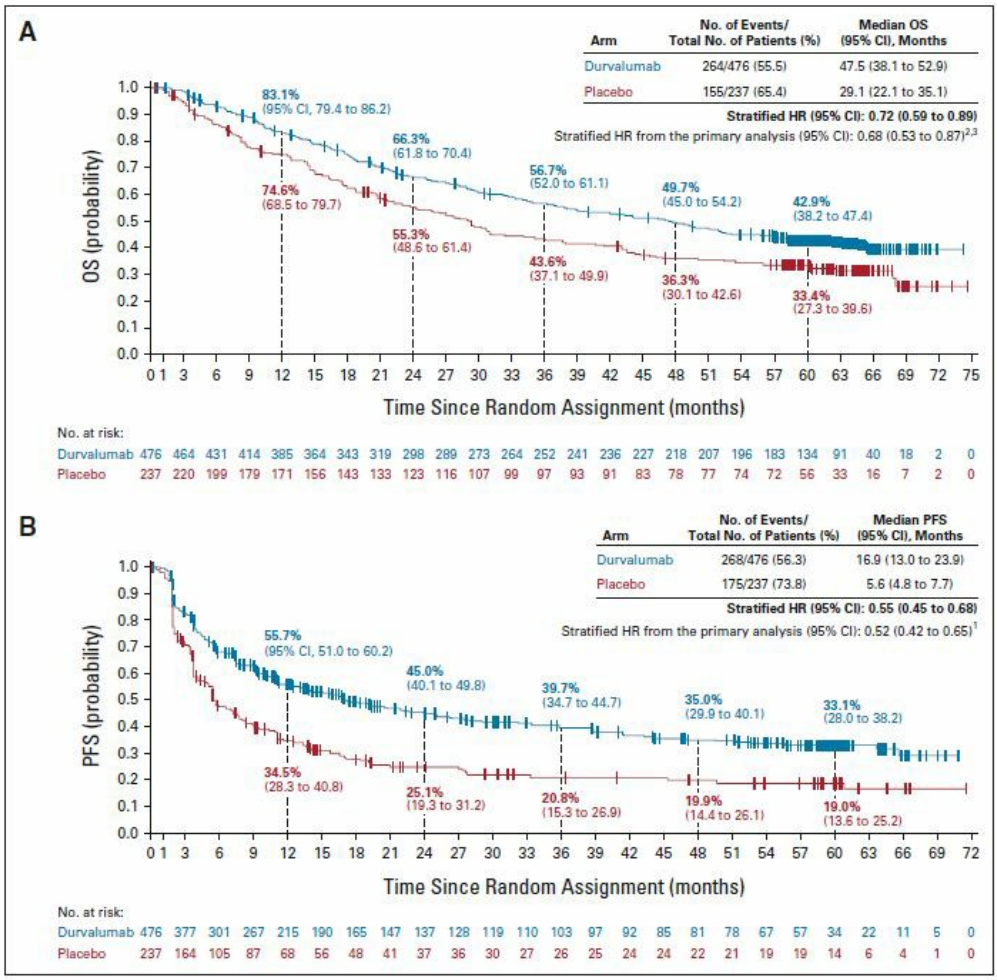
## Efficacy

After a median follow up of 25.2 months, the median OS was not reached in the durvalumab group vs. 28.7 months in the placebo group (HR=0.68; 99.73% CI 0.47 to 0.997; p=0.0025).[6]

Median PFS was 17.2 months (95% CI 13.1 to 23.9) in the durvalumab group vs. 5.6 months (95% CI 4.6 to 7.7) in the placebo group (HR=0.51; 95% CI 0.41 to 0.63).[6]

An updated analysis with median follow-up of 34.2 months demonstrated a median OS of 47.5 months in the durvalumab group vs. 29.1 months in the placebo group (stratified HR= 0.72; 95% CI 0.59 to 0.89).[1] The median PFS was 16.9 months vs. 5.6 months (stratified HR=0.55; 95% CI 0.45 to 0.68) for durvalumab vs. placebo respectively.

**Kaplan-Meier for updated OS and PFS in the intention-to-treat population**[1]






Health related quality of life data was comparable for durvalumab vs. placebo.[7]

## Toxicity

Adverse events of any grade occurred in 96.8% of patients in the durvalumab group and 94.9% of patients in the placebo group. Grade 3 or 4 adverse events occurred in 30.5% of patients in the durvalumab group and 26.1% of patients in the placebo group. The most common adverse events in the durvalumab group were cough (35.2%), pneumonitis/radiation pneumonitis (32.8%), fatigue (24.0%) and dyspnoea (22.3%).[6]

Discontinuation due to adverse events occurred in 15.4% of patients in the durvalumab group and 9.8% of patients in the placebo group. The most frequent adverse events leading to discontinuation of durvalumab and placebo were pneumonitis/radiation pneumonitis (6.1% and 3.9% respectively) and pneumonia (1.1% and 1.3% respectively).[6]

Pneumonitis or radiation pneumonitis of any grade occurred in 32.8% of patients in the durvalumab group and 23.5% of patients in the placebo group. The incidence of grade 3 or 4 pneumonitis/radiation pneumonitis was 3.4% with durvalumab and 2.1% with placebo.[6]

Death due to any adverse events occurred in 4.4% of patients in the durvalumab group and 6.4% of patients in the placebo group.[6] The initial interim analysis listed deaths due to treatment-related adverse events occurred in 7 patients (1.5%) receiving durvalumab (4 with pneumonitis, 1 with each of cardiomyopathy, right ventricular failure, respiratory distress, respiratory failure, increased brain natriuretic peptide and radiation pneumonitis). Death due to treatment-related adverse events occurred in 3 patients (1.3%) receiving placebo.[5] An update on deaths due to treatment-related adverse events was not included in the OS analysis.[6]

**Table S4. Adverse Events of Any Cause Reported in ≥10% of Patients in Either Treatment Group (As- treated Population).**

| Event | Durvalumab (N=475) | | Placebo (N=234) | |
|---|---|---|---|---|
| | Any Grade* | Grade 3 or 4 | Any Grade* | Grade 3 or 4 |
| | *number of patients with event (percent)* | | | |
| Any event | 460 (96.8) | 145 (30.5) | 222 (94.9) | 61 (26.1) |
| Cough | 167 (35.2) | 2 (0.4) | 59 (25.2) | 1 (0.4) |
| Fatigue | 114 (24.0) | 1 (0.2) | 48 (20.5) | 3 (1.3) |
| Dyspnea | 106 (22.3) | 7 (1.5) | 56 (23.9) | 6 (2.6) |
| Radiation pneumonitis† | 96 (20.2) | 7 (1.5) | 37 (15.8) | 1 (0.4) |
| Diarrhea | 88 (18.5) | 3 (0.6) | 46 (19.7) | 3 (1.3) |
| Pyrexia | 72 (15.2) | 1 (0.2) | 22 (9.4) | 0 |
| Nausea | 68 (14.3) | 0 | 31 (13.2) | 0 |
| Decreased appetite | 68 (14.3) | 1 (0.2) | 30 (12.8) | 2 (0.9) |
| Pneumonia | 63 (13.3) | 21 (4.4) | 18 (7.7) | 9 (3.8) |
| Pneumonitis† | 60 (12.6) | 9 (1.9) | 18 (7.7) | 4 (1.7) |
| Arthralgia | 59 (12.4) | 0 | 26 (11.1) | 0 |
| Upper respiratory tract infection | 59 (12.4) | 1 (0.2) | 24 (10.3) | 0 |
| Pruritus | 59 (12.4) | 0 | 12 (5.1) | 0 |
| Rash | 58 (12.2) | 1 (0.2) | 18 (7.7) | 0 |
| Constipation | 56 (11.8) | 1 (0.2) | 20 (8.5) | 0 |
| Hypothyroidism | 55 (11.6) | 1 (0.2) | 4 (1.7) | 0 |
| Headache | 52 (10.9) | 1 (0.2) | 21 (9.0) | 2 (0.9) |
| Asthenia | 51 (10.7) | 3 (0.6) | 31 (13.2) | 1 (0.4) |
| Back pain | 50 (10.5) | 1 (0.2) | 27 (11.5) | 1 (0.4) |
| Musculoskeletal pain | 39 (8.2) | 3 (0.6) | 24 (10.3) | 1 (0.4) |
| Anemia | 36 (7.6) | 14 (2.9) | 26 (11.1) | 8 (3.4) |

Adverse events were graded according to the CTCAE v4.03. Patients with multiple adverse events are counted once at the maximum reported CTCAE grade.
*Grade 5 adverse events of any cause occurred in 21 patients (4.4%) who received durvalumab (4 [0.8%] with pneumonitis, 2 [0.4%] with cardiac arrest, and 1 each [0.2%] with the following: pneumonia, bacterial pneumonia, pneumococcal pneumonia, sepsis, septic shock, cardiomyopathy, cardiopulmonary failure, myocardial infarction, aortic dissection, dyspnea, emphysema, hemoptysis, respiratory distress, respiratory failure, radiation pneumonitis, right ventricular failure, increased level of brain natriuretic peptide, and unknown cause). Grade 5 adverse events of any cause occurred in 14 patients (6.0%) who received placebo (3 each [1.3%] with pneumonitis and pneumonia and 1 each [0.4%] with the following: pneumonia streptococcal, West Nile virus infection, cardiac arrest, eosinophilic myocarditis, hemoptysis, interstitial lung disease, intestinal obstruction, radiation pneumonitis, and unknown cause). Each patient could have had more than one grade 5 adverse event.
†Pneumonitis and radiation pneumonitis were assessed by investigators, with subsequent review and adjudication by the study sponsor.



## References


1 Spigel, D. R., C. Faivre-Finn, J. E. Gray, et al. 2022. "Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer." J Clin Oncol 40(12):1301-1311.

2 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.

3 Baverel, P. G., V. F. S. Dubois, C. Y. Jin, et al. 2018. "Population Pharmacokinetics of Durvalumab in Cancer Patients and Association With Longitudinal Biomarkers of Disease Status." Clin Pharmacol Ther 103(4):631-642.

4 Garassino, M. C., B. C. Cho, J. H. Kim, et al. 2018. "Durvalumab as third-line or later treatment for advanced non-small-cell lung cancer (ATLANTIC): an open-label, single-arm, phase 2 study." Lancet Oncol 19(4):521-536.

5 Antonia, S. J., A. Villegas, D. Daniel, et al. 2017. Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer. N Engl J Med. 377 (20): 1919-1929.

6 Antonia, S. J., A. Villegas, D. Daniel, et al. 2018. "Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC." N Engl J Med.

7 Hui, R., M. Özgüroğlu, A. Villegas, et al. 2019. "Patient-reported outcomes with durvalumab after chemoradiotherapy in stage III, unresectable non-small-cell lung cancer (PACIFIC): a randomised, controlled, phase 3 study." Lancet Oncol 20(12):1670-1680.

## History

### Version 1

| Date | Summary of changes |
|---|---|
| **25/10/2022** | New protocol approved electronically by Medical Oncology Reference Committee and published on eviQ. Review 1 year. |
| **19/06/2023** | Protocol reviewed at the Medical Oncology Reference Committee meeting on 19 May 2023. No changes. Next review in 2 years. |



**First approved:** 25 October 2022
**Last reviewed:** 19 May 2023
**Review due:** 30 June 2025

***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/4179*
*09 Aug 2023*

# Patient information - Lung cancer locally advanced - Durvalumab - flat dosing

**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 anti-cancer drug) that works with your immune system to detect and destroy cancer cells. Immunotherapy can potentially affect any organ of the body.

This treatment may be used to treat different types of cancer. Your doctor will advise you why you are receiving this treatment.

The treatment schedule below explains how the immunotherapy drug is given.

| Durvalumab | | | |
|---|---|---|---|
| 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 | **Durvalumab** (*dur-VAL-u-mab*) | 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

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

**Emergency contact details**

Ask your doctor or nurse from your treating team who to contact if you have a problem

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
- 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

### Treatment delays

There may 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. Your doctor will explain if you need any delays to your treatment and the reason why.

### Blood tests and monitoring

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

### Other medications given during this treatment

- **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. 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.

| Immune related side effects | |
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| **Heart problems** | • You may get:<br>◦ chest pain or tightness<br>◦ shortness of breath<br>◦ swelling of your ankles<br>◦ an abnormal heartbeat.<br>• 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.<br>• Tell your doctor if you have a history of heart problems or high blood pressure.<br>• Before or during treatment, you may be asked to have a test to see how well your heart is working.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.** |

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| **Bowel and stomach inflammation** | • You may get:<br>◦ bowel motions (stools, poo) that are more frequent or more liquid (diarrhoea)<br>◦ blood or mucous in your stool<br>◦ dark, tarry, or sticky bowel motions<br>◦ bloating, cramping, pain or tenderness in your stomach area.<br>• Inform your doctor or nurse immediately if you get diarrhoea<br>• Take your anti-diarrhoeal or steroid medication as directed by your doctor.<br>• Drink plenty of fluids (unless you are on a fluid restriction).<br>• Eat and drink small amounts more often.<br>• Avoid spicy foods, dairy products, high fibre foods, and coffee.<br>• **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.<br>• You may feel dizzy, light-headed, tired, weak and appear more pale than usual.<br>• You may get:<br>• dark, tarry bowel motions (stools, poo)<br>• blood in your urine or not urinating as often<br>• dark-coloured urine<br>• yellowing of the whites of your eyes, and/or your skin<br>• pinpoint red spots on your skin<br>• unexplained bleeding<br>• major bruising<br>• a fever<br>• shortness of breath<br>• a severe headache<br>• confusion<br>• faster heartbeat than normal<br>• **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:<br>◦ fatigue<br>◦ severe nausea and vomiting<br>◦ weight loss<br>◦ bruising or bleeding more easily<br>◦ pain or tenderness on the right side of your stomach area<br>◦ dark coloured urine<br>◦ yellowing of the whites of your eyes and/or your skin<br>◦ itchy skin<br>◦ drowsiness<br>• You will have regular blood tests to check how well your liver is working.<br>• Take your steroid medication as directed by your doctor.<br>• **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:<br>• muscle or joint stiffness, especially after a period of rest<br>• muscle weakness<br>• pain in your muscles or joints<br>• joint swelling<br>• tiredness<br>• headaches<br>• Take your pain relief or steroid medication as directed by your doctor.<br>• **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above.** |

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| **Nervous system problems** | • Nervous system changes are rare, but can be serious.<br>• You may get:<br>◦ headaches<br>◦ fever<br>◦ stiff neck<br>◦ confusion or difficulty concentrating<br>◦ dizziness or drowsiness<br>◦ loss of consciousness<br>◦ muscle weakness or pain<br>◦ numbness or tingling in your hands or feet<br>◦ jerky movements.<br>• Take your steroid medication as directed by your doctor.<br>• **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:<br>◦ eye pain<br>◦ itchy eyes<br>◦ red or swollen eyes<br>◦ blurred or change in vision<br>◦ change in colour vision<br>◦ watery or gritty eyes<br>◦ dry eyes<br>◦ sensitivity to light.<br>• Protect your eyes from the weather (sun and wind) by wearing sunglasses.<br>• Use your eye drops or take your steroid medication as directed by your doctor.<br>• **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.<br>• You may get:<br>◦ headaches<br>◦ tiredness, dizziness or fainting<br>◦ abnormal heartbeat (faster than usual)<br>◦ a feeling of being hot or cold more easily<br>◦ excessive sweating<br>◦ weight changes<br>◦ a deepened voice<br>◦ irregular or absent periods<br>◦ nausea and vomiting<br>◦ thirsty and need to urinate more often than normal<br>◦ high blood sugar levels<br>◦ pain in your stomach area<br>◦ muscle pain or weakness<br>◦ difficulty sleeping<br>◦ agitated more easily<br>◦ changes in your mood or behaviour, such as decreased sex drive or irritability.<br>• Take your hormone or steroid medication as directed by your doctor.<br>• **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.** |

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| **Lung problems** | • You may get:<br>◦ shortness of breath<br>◦ difficulty breathing<br>◦ faster heartbeat than normal<br>◦ chest pain<br>◦ new or worsening cough<br>◦ fever.<br>• Your doctor will monitor how well your lungs are working during your treatment.<br>• Take your steroid medication as directed by your doctor.<br>• **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.<br>• You may get:<br>◦ a feeling of needing to urinate less often than normal<br>◦ blood in your urine<br>◦ swollen hands and feet<br>◦ loss of appetite.<br>• You will have regular blood tests to check how well your kidneys are working.<br>• 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.<br>• Take your steroid medication as directed by your doctor.<br>• **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<br>◦ a red rash<br>◦ a bumpy rash<br>◦ dry and itchy skin<br>◦ skin peeling or blisters.<br>◦ if you have had previous radiation therapy to an area this effect may be worse<br>• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.<br>• Avoid scratching your skin.<br>• Avoid wearing tight fitting clothing<br>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.<br>• Take your antihistamine medication or apply your steroid cream as directed by your doctor.<br>• **Tell your doctor or nurse as soon as possible if you notice any changes to the rash like pain or pus forming.** |

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

| Non-immune related side effects | |
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| **Nausea and vomiting** | • You may feel sick (nausea) or be sick (vomit).<br>• Take your anti-sickness medication as directed even if you don't feel sick.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat small meals more frequently.<br>• Try food that does not require much preparation.<br>• Try bland foods like dry biscuits or toast.<br>• Gentle exercise may help with nausea.<br>• Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment.<br>• **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.** |
| **Headache** | • You can take paracetamol if you have a headache.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.** |
| **Appetite loss (anorexia)** | • You may not feel like eating.<br>• Try to avoid drinking fluids at meal times.<br>• Try to eat small meals or snacks regularly throughout the day.<br>• Try to eat food that is high in protein and calories.<br>• If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian. |
| **Constipation** | • You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass.<br>• You may also get:<br>  ◦ bloating, cramping or pain<br>  ◦ a loss of appetite<br>  ◦ nausea or vomiting.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat plenty of fibre-containing foods such as fruit, vegetables and bran.<br>• Take laxatives as directed by your doctor.<br>• Try some gentle exercise daily.<br>• **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.** |
| **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.<br>• Do not drive or operate machinery if you are feeling tired.<br>• Nap for short periods (only 1 hour at a time)<br>• Prioritise your tasks to ensure the best use of your energy.<br>• Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted).<br>• Try some gentle exercise daily.<br>• Allow your friends and family to help.<br>• **Tell your doctor or nurse if you get any of the symptoms listed above.** |

## General advice for people having cancer treatment

### Blood clot risk

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

### Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal 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.
- 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.

### 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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