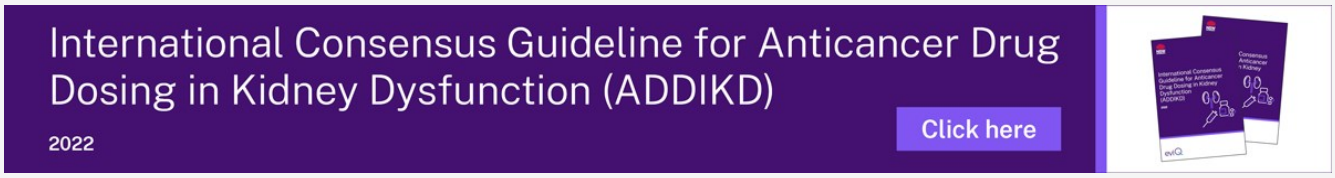
Breast metastatic palbociclib

ID: 3369 v.4 **Endorsed**

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

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



Related pages:

- Breast metastatic anastrozole
- Breast metastatic letrozole
- Breast metastatic fulvestrant
- Breast metastatic ribociclib
- Breast metastatic abemaciclib

Treatment schedule - Overview

Cycle 1 and further cycles

Drug	Dose	Route	Day
Palbociclib	125 mg ONCE a day	PO	1 to 21 *

*palbociclib is taken daily for 3 weeks followed by 1 week break

Frequency: 28 days

Cycles: Continuous until disease progression or unacceptable toxicity

Notes:
Palbociclib is given in combination with hormonal therapy. See Indications and patient population section below

Drug status: Palbociclib is PBS authority

Palbociclib is available as **75 mg**, **100 mg** and **125 mg** capsules or tablets

Cost: ~ $4,250 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 and further cycles

Day 1 to 21		
Palbociclib	125 mg (PO)	ONCE a day (capsules with food; tablets with or without food)

- palbociclib is taken daily for 3 weeks followed by 1 week break
- palbociclib is given in combination with hormonal therapy. See Indications and patient population section below

Frequency: 28 days

Cycles: Continuous until disease progression or unacceptable toxicity

Indications and patient population

- Hormone receptor (HR) positive, HER-2 negative advanced or metastatic breast cancer **in combination with**:
  - a non-steroidal **aromatase inhibitor** as initial endocrine-based therapy, OR
  - **fulvestrant** in patients who have received prior endocrine-based therapy.
- Patients must be post-menopausal. Pre- or perimenopausal patients should receive a GnRH agonist (e.g. goserelin), starting 4 weeks prior to commencing palbociclib.
- ECOG performance status score 0 to 2

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Emetogenicity minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Pneumonitis	Pneumonitis, including some fatal cases, has been reported in a small number of patients receiving this treatment. Monitor patient for new or worsening respiratory symptoms such as dyspnoea, cough and fever, or a radiological abnormality. If pneumonitis is suspected, this treatment should be withheld and prompt investigation initiated. If pneumonitis is confirmed, this treatment should be discontinued.
Radiation therapy or surgery	The interaction of CDK4/6 inhibitors with radiation therapy is unknown. Consider interrupting CDK4/6 inhibitor treatment during palliative radiation therapy, stopping 1 day before and resuming treatment 1 week after finishing radiation therapy. Caution is advised for any surgical procedures required during CDK4/6 inhibitor treatment. Consider interrupting CDK4/6 inhibitor treatment prior to surgery and reinitiating postoperatively once satisfactory wound healing has occurred.
Blood tests	FBC, EUC and LFTs at baseline. Repeat FBC prior to each cycle for the first 6 cycles and as clinically indicated. Consider repeating FBC on day 15 of the first 2 cycles. If neutropenia grade ≥ 3 has not occurred after the first 6 cycles, repeat FBC every 3 months (prior to the beginning of a cycle) and as clinically indicated. Repeat EUC and LFTs as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy

Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.

Dose modifications

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

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

Note: dose modifications have been adapted from the clinical trials and the palbociclib product information.

Palbociclib dose modifications for adverse events

Dose level	Dose
Recommended dose	125 mg/day
First dose reduction	100 mg/day
Second dose reduction	75 mg/day*

**If further dose reduction below 75 mg/day is required, consider discontinuing palbociclib treatment or review scheduling*

Haematological toxicity	
ANC x 10^9/L	
0.5 to less than 1.0	**On day 1 of cycle:** withhold palbociclib until ANC ≥ 1.0, then start cycle at the same dose* **On day 15 of first 2 cycles:** continue palbociclib at current dose to complete the cycle. Repeat FBC on day 22 *Consider dose reduction if recurrent neutropenia or prolonged recovery
less than 0.5	Withhold palbociclib until ANC ≥ 1.0, then resume palbociclib at the next lower dose
Febrile neutropenia	Withhold palbociclib until ANC ≥ 1.0 and fever resolved, then resume palbociclib at the next lower dose
Platelets x 10^9/L	
25 to less than 50	**On day 1 of cycle:** withhold palbociclib until platelets ≥ 50, then start cycle at the same dose* **On day 15 of first 2 cycles:** continue palbociclib at current dose to complete the cycle. Repeat FBC on day 22

Haematological toxicity	
	*Consider dose reduction if recurrent thrombocytopenia or prolonged recovery.
less than 25	Withhold palbociclib until platelets ≥ 50, then resume palbociclib at the next lower dose

Renal impairment	
Mild to moderate (CrCl > 30 mL/min)	No dose modifications necessary
Severe (CrCl < 30 mL/min)	Palbociclib has not been studied in patients with severe renal impairment

Hepatic impairment	
Hepatic dysfunction (at baseline)	
Mild	No dose modifications necessary
Moderate or severe	Palbociclib has not been studied in patients with moderate or severe hepatic impairment
Hepatotoxicity (during treatment)	
Grade 1 or Grade 2	No dose modifications necessary
Grade 3 or Grade 4	If persisting despite medical treatment, withhold palbociclib until toxicity has resolved to Grade 1 or less (or Grade 2 or less if not considered a safety risk for the patient) and resume at the next lower dose

Mucositis and stomatitis	
Grade 1 or Grade 2	No dose modifications necessary
Grade 3 or Grade 4	If persisting despite medical treatment, withhold palbociclib until toxicity has resolved to Grade 1 or less (or Grade 2 or less if not considered a safety risk for the patient) and resume at the next lower dose

Diarrhoea	
Grade 1 or Grade 2	No dose modifications necessary
Grade 3 or Grade 4	If persisting despite medical treatment, withhold palbociclib until toxicity has resolved to Grade 1 or less (or Grade 2 or less if not considered a safety risk for the patient) and resume at the next lower dose

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*

Palbociclib		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of palbociclib possible due to reduced clearance	Avoid combination or monitor for palbociclib toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of palbociclib possible due to increased clearance	Avoid combination or monitor for decreased effect of palbociclib
Drugs metabolised by CYP3A (e.g. ciclosporin, fentanyl, quinidine, ergotamine, pimozide, sirolimus, tacrolimus etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP3A by palbociclib resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity of interacting drugs

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 to 21

This is an oral treatment

Safe handling and waste management (reproductive risk only)

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.

Treatment - Time out

Palbociclib

- administer orally ONCE a day on **days 1 to 21**
- to be swallowed whole with a glass of water; do not break, crush or chew
- capsules to be taken with food; tablets to be taken with or without food.

Note: missed doses should not be replaced, if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

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

Discharge information

Palbociclib capsules or tablets

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

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

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

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Asthenia	Physical weakness characterised by loss of strength or lack of energy.
Diarrhoea	Read more about treatment induced diarrhoea
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
Headache	
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

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

Evidence

The evidence supporting this protocol is provided by two separate phase III multicentre international randomised trials, PALOMA-2 and PALOMA-3. These trials respectively evaluated the effectiveness and safety of palbociclib and letrozole as first line therapy in HER 2 negative, hormone receptor positive advanced breast cancer and the safety and efficacy of palbociclib and fulvestrant following progression after prior endocrine therapy in this patient group.

PALOMA-2[1]

PALOMA-2 was a double blinded phase III trial in women with advanced ER positive, HER-2 negative breast cancer who had not received prior therapy for advanced disease. Between February 2013 and July 2014, 666 post-menopausal women were randomised 2:1 to either letrozole 2.5 mg daily plus palbociclib 125mg in 4 weekly cycles (3 weeks on 1 week off for palbociclib) or letrozole 2.5mg daily plus matching placebo. Prior adjuvant or neoadjuvant aromatase inhibitor therapy was allowed unless disease had recurred whilst receiving therapy or within 12 months of completing adjuvant therapy.

The primary end point was investigator assessed recurrence free survival. Secondary end points included overall survival, objective response, duration of response, clinical benefit response and safety.

PALOMA-3[2, 3, 4]

PALOMA 3 was a randomised, double-blind, placebo-controlled phase 3 trial of fulvestrant with or without palbociclib in women with HER-2 negative, hormone receptor positive metastatic breast cancer whose disease had progressed after previous endocrine therapy. Women were eligible for this study regardless of menopausal status.

Between October 7 2013 and August 26 2014 527 patients were randomised 2:1 to receive 500 mg of fulvestrant on day 1 and 15 (cycle 1), then on day 1 of every 28 day cycle and palbociclib 125 mg on day 1 to 21 of a 28 day cycle versus matched placebo. All pre or peri menopausal women also received luteinising hormone releasing hormone agonist (goserelin) at least 4 weeks prior to

randomisation and then monthly timed with fulvestrant administration during the study.

The primary end point was investigator assessed recurrence free survival. Secondary end points included confirmed objective response, clinical benefit (complete response, partial response and stable disease at 24 weeks), tissue biomarkers and safety.

Efficacy

PALOMA-2

The PALOMA-2 study met its primary end point by showing an improved progression free survival of 24.8 months (95% CI, 22.1 to not estimable) compared to 14.5 months (95% CI, 12.9 to 17.1) in the letrozole-placebo group with a hazard ratio for disease progression or death, 0.58, 95% CI, 0.46 to 0.72; two sided P<0.001.

Data on overall survival were immature at the time of analysis of the primary end point and final overall survival analysis will be performed when a total of 390 deaths occur per protocol.

Kaplan-meier analysis of progression-free survival

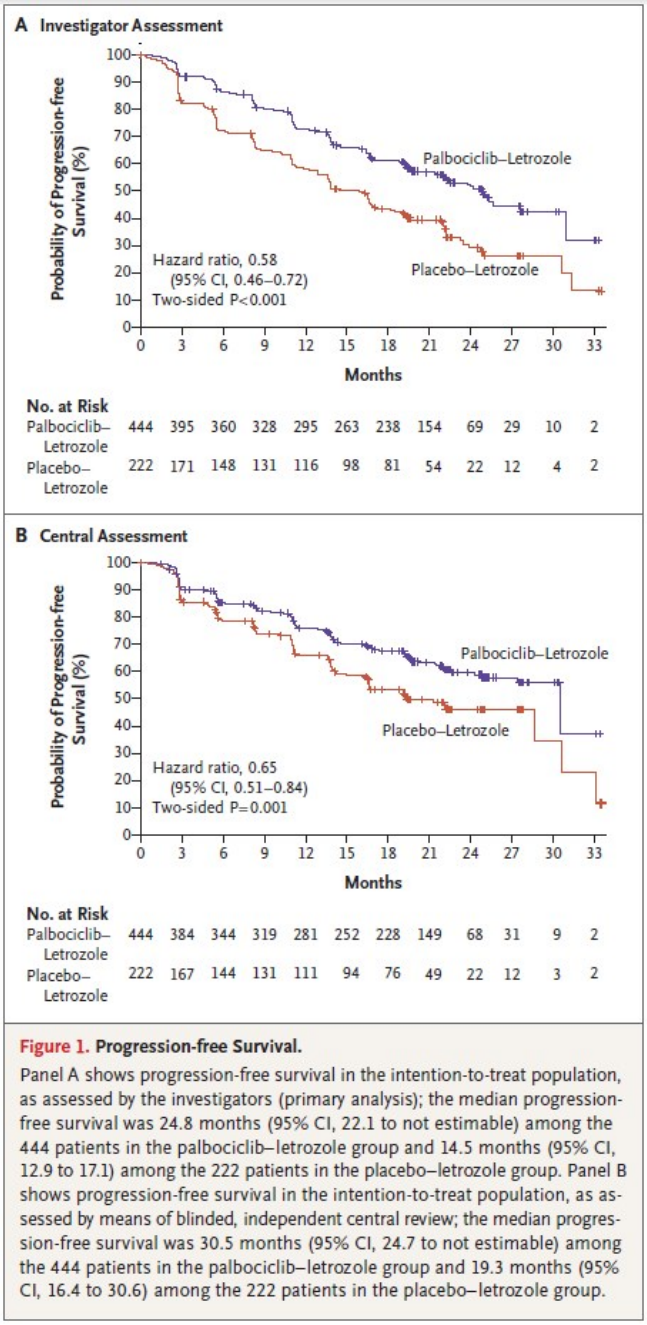


Figure 1. Progression-free Survival.

Panel A shows progression-free survival in the intention-to-treat population, as assessed by the investigators (primary analysis); the median progression-free survival was 24.8 months (95% CI, 22.1 to not estimable) among the 444 patients in the palbociclib–letrozole group and 14.5 months (95% CI, 12.9 to 17.1) among the 222 patients in the placebo–letrozole group. Panel B shows progression-free survival in the intention-to-treat population, as assessed by means of blinded, independent central review; the median progression-free survival was 30.5 months (95% CI, 24.7 to not estimable) among the 444 patients in the palbociclib–letrozole group and 19.3 months (95% CI, 16.4 to 30.6) among the 222 patients in the placebo–letrozole group.

Subgroup analyses of progression-free survival according to baseline characteristics and stratification factors, showed a consistent benefit of palbociclib plus letrozole across all subgroups..

Best overall response (in the intention-to-treat population)

Table 3. Best Overall Response in the Intention-to-Treat Population.

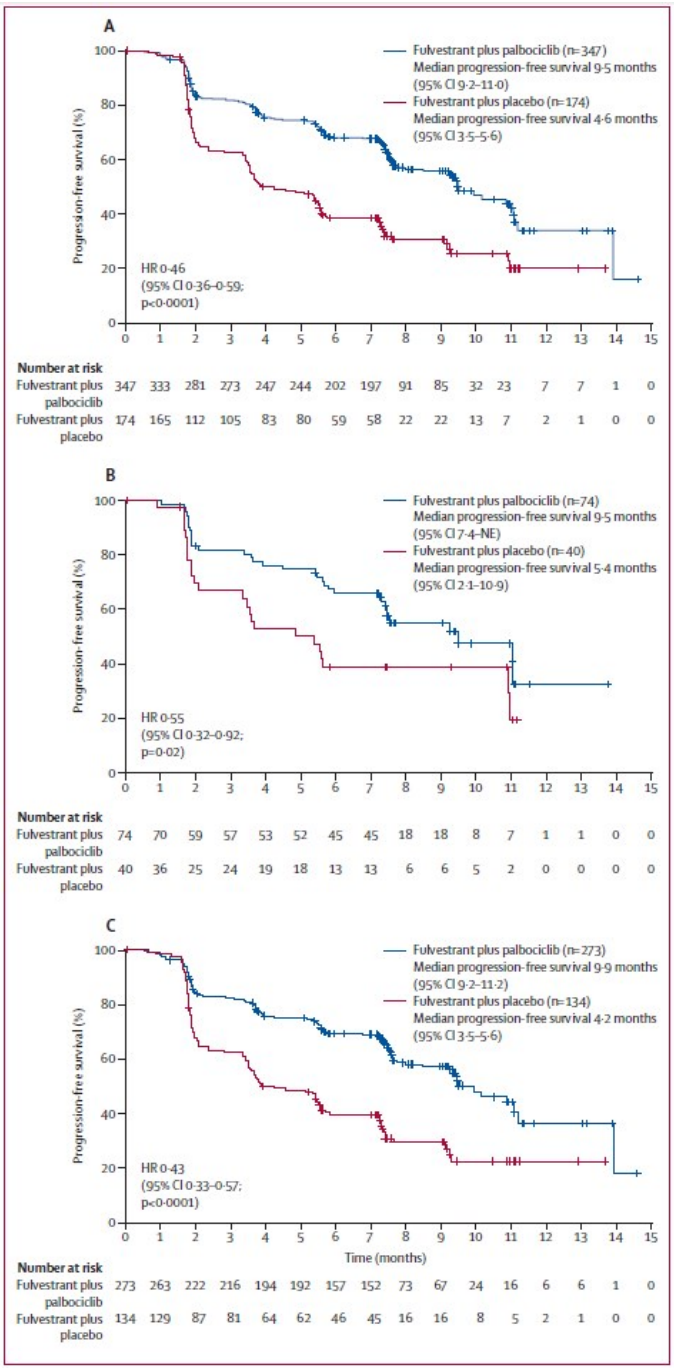
Variable	Palbociclib–Letrozole (N=444)	Placebo–Letrozole (N=222)	Odds Ratio (95% CI)	P Value
All randomly assigned patients — no.	444	222		
Rate of objective response — % (95% CI)*	42.1 (37.5–46.9)	34.7 (28.4–41.3)	1.40 (0.98–2.01)	0.06
Rate of clinical benefit response — % (95% CI)†	84.9 (81.2–88.1)	70.3 (63.8–76.2)	2.39 (1.58–3.59)	<0.001
Median duration of response — mo (95% CI)	22.5 (19.8–28.0)	16.8 (14.2–28.5)‡		
Patients with measurable disease — no.§	338	171		
Rate of objective response — % (95% CI)*	55.3 (49.9–60.7)	44.4 (36.9–52.2)	1.55 (1.05–2.28)	0.03
Rate of clinical benefit response — % (95% CI)†	84.3 (80.0–88.0)	70.8 (63.3–77.5)	2.23 (1.39–3.56)	<0.001
Median duration of response — mo (95% CI)	22.5 (19.8–28.0)	16.8 (15.4–28.5)		

* Rate of objective response was defined as the percentage of patients who had a confirmed complete response or a partial response.
† Rate of clinical benefit response was defined as the percentage of patients who had a confirmed complete response, a partial response, or stable disease for 24 weeks or more.
‡ One patient with bone-only disease at baseline was included; all other patients had measurable disease at baseline.
§ Measurable disease was defined according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1.[8]

PALOMA-3

In the PALOMA-3 study the median progression free survival was 9.5 months (95% CI, 9.2 - 11.0) in the palbociclib plus fulvestrant group compared with 4.6 months (95% CI, 3.5 - 5.6) in the fulvestrant plus placebo group (HR 0.46, 95% CI, 0.36 – 0.59, two sided p<0.0001).

Kaplan-meier analysis of progression free survival



A) intention to treat population, B) patients who had received neoadjuvant or adjuvant therapy but no previous systemic therapy for metastatic breast cancer, C) patients who received at least one previous systemic therapy for metastatic breast cancer.
Note: previous systemic therapy means chemotherapy or endocrine therapy, or both. HR = hazard ratio, NE = not estimable
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Subgroup analyses of progression-free survival were generally consistent with the results from the overall population.

Best overall tumour response by treatment and according to PIK3CA mutation status in the intention-to-treat population[3]

	Intention to treat					PIK3CA positive					PIK3CA negative				
	Fulvestrant plus palbociclib		Fulvestrant plus placebo		p value	Fulvestrant plus palbociclib		Fulvestrant plus placebo		p value	Fulvestrant plus palbociclib		Fulvestrant plus placebo		p value
	n	% (95% CI)*	n	% (95% CI)*		n	% (95% CI)*	n	% (95% CI)*		n	% (95% CI)*	n	% (95% CI)*	
Intention to treat															
Population	347	..	174	..	..	85	..	44	..	..	180	..	86	..	..
Complete response†	0	0	4	2%	..	0	0	0	0	..	0	0	4	5%	..
Partial response†	66	19%	11	6%	..	13	15%	7	16%	..	53	29%	12	14%	..
Stable disease	213	61%	94	54%	..	54	64%	21	48%	..	91	51%	38	44%	..
Progressive disease	58	17%	57	33%	..	16	19%	15	34%	..	32	18%	28	33%	..
Indeterminate	10	3%	8	5%	..	2	2%	1	2%	..	4	2%	4	5%	..
Objective tumour response	66	19% (15·0–23·6)	15	9% (4·9–13·8)	..	13	15% (8·4–24·7)	7	16% (6·6–30·1)	..	53	29% (22·9–36·7)	16	19% (11·0–28·4)	..
Odds ratio		2·47 (1·36–4·91)	..	..	0·0019	..	1·16 (0·38–3·95)	..	..	0·98	..	1·78 (0·92–3·66)	..	..	0·090
Clinical benefit	231	67% (61·3–71·5)	69	40% (32·3–47·3)		51	60% (48·8–70·5)	16	36% (22·4–52·2)		129	72% (64·5–78·1)	34	40% (29·2–50·7)	
Odds ratio		3·05 (2·07–4·61)	..	..	<0·0001	..	2·17 (0·93–5·04)	..	..	0·078	..	4·21 (2·35–7·76)	..	..	0·00010

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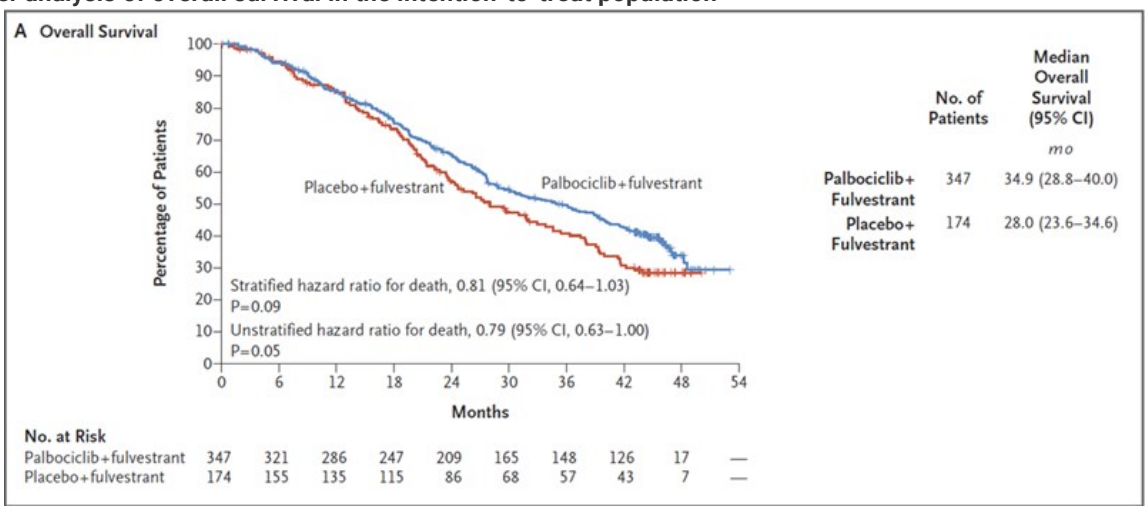
Median overall survival was 34.9 months (95% CI, 28.8-40.0) in the palbociclib plus fulvestrant group and 28.0 months (95% CI, 23.6-34.6) in the fulvestrant plus placebo group (HR 0.81, 95% CI 0.64-1.03, P=0.09).[4]

Kaplan-meier analysis of overall survival in the intention-to-treat population[4]



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Toxicity

PALOMA-2

The median relative dose intensity was 93% for palbociclib and 100% for letrozole in the palbociclib and letrozole group versus 100% for both in the placebo and letrozole group. The dose of palbociclib was reduced according to protocol in 160 of the 444 patients (36%) in the palbociclib-letrozole group whereas matching placebo was reduced in 3 of the 222 patients (1.4%) in the placebo-letrozole group. Permanent discontinuation of the study treatment due to adverse events occurred in 9.7% in the palbociclib-letrozole group and 5.9% in the placebo-letrozole group. Permanent discontinuation of palbociclib or matching placebo occurred in 7.4% of patients in the palbociclib-letrozole group and 4.5% in the placebo-letrozole group.[1]

The most common grade 3/4 adverse events in the palbociclib-letrozole group were neutropenia, leucopenia, anaemia, asthenia and fatigue.

Table 2. Adverse Events from Any Cause That Occurred in at Least 10% of the Patients in Either Study Group in the As-Treated Population.

Adverse Event	Palbociclib–Letrozole (N = 444)			Placebo–Letrozole (N = 222)*		
	Any Grade	Grade 3	Grade 4†	Any Grade	Grade 3	Grade 4
	number of patients (percent)					
Any adverse event	439 (98.9)	276 (62.2)	60 (13.5)	212 (95.5)	49 (22.1)	5 (2.3)
Neutropenia‡	353 (79.5)	249 (56.1)	46 (10.4)	14 (6.3)	2 (0.9)	1 (0.5)
Leukopenia§	173 (39.0)	107 (24.1)	3 (0.7)	5 (2.3)	0	0
Fatigue	166 (37.4)	8 (1.8)	0	61 (27.5)	1 (0.5)	0
Nausea	156 (35.1)	1 (0.2)	0	58 (26.1)	4 (1.8)	0
Arthralgia	148 (33.3)	3 (0.7)	0	75 (33.8)	1 (0.5)	0
Alopecia¶	146 (32.9)	0	0	35 (15.8)	0	0
Diarrhea	116 (26.1)	6 (1.4)	0	43 (19.4)	3 (1.4)	0
Cough	111 (25.0)	0	0	42 (18.9)	0	0
Anemia‖	107 (24.1)	23 (5.2)	1 (0.2)	20 (9.0)	4 (1.8)	0
Back pain	96 (21.6)	6 (1.4)	0	48 (21.6)	0	0
Headache	95 (21.4)	1 (0.2)	0	58 (26.1)	4 (1.8)	0
Hot flush	93 (20.9)	0	0	68 (30.6)	0	0
Constipation	86 (19.4)	2 (0.5)	0	34 (15.3)	1 (0.5)	0
Rash**	79 (17.8)	4 (0.9)	0	26 (11.7)	1 (0.5)	0
Asthenia	75 (16.9)	10 (2.3)	0	26 (11.7)	0	0
Thrombocytopenia††	69 (15.5)	6 (1.4)	1 (0.2)	3 (1.4)	0	0
Vomiting	69 (15.5)	2 (0.5)	0	37 (16.7)	3 (1.4)	0
Pain in extremity	68 (15.3)	1 (0.2)	0	39 (17.6)	3 (1.4)	0
Stomatitis	68 (15.3)	1 (0.2)	0	13 (5.9)	0	0
Decreased appetite	66 (14.9)	3 (0.7)	0	20 (9.0)	0	0
Dyspnea	66 (14.9)	5 (1.1)	0	30 (13.5)	3 (1.4)	0
Insomnia	66 (14.9)	0	0	26 (11.7)	0	0
Dizziness	63 (14.2)	2 (0.5)	0	33 (14.9)	0	0
Nasopharyngitis	62 (14.0)	0	0	22 (9.9)	0	0
Upper respiratory tract infection	59 (13.3)	0	0	25 (11.3)	0	0
Dry skin	55 (12.4)	0	0	13 (5.9)	0	0
Pyrexia	55 (12.4)	0	0	19 (8.6)	0	0
Myalgia	53 (11.9)	0	0	20 (9.0)	0	0
Urinary tract infection	53 (11.9)	5 (1.1)	0	17 (7.7)	0	0
Abdominal pain	50 (11.3)	4 (0.9)	0	12 (5.4)	0	0
Peripheral edema	50 (11.3)	0	0	14 (6.3)	0	0
Dysgeusia	45 (10.1)	0	0	11 (5.0)	0	0
Dyspepsia	41 (9.2)	0	0	27 (12.2)	1 (0.5)	0
Anxiety	36 (8.1)	0	0	25 (11.3)	0	0

PALOMA-3

Serious adverse events occurred in 13% of patients in the fulvestrant plus placebo group and 17% in the fulvestrant plus placebo group. 54% of patients in the fulvestrant plus palbociclib group had a dose interruption due to an adverse event, 36% had a cycle delay and 34% had at least one dose reduction compared to 6%, 2% and 3% respectively in the fulvestrant plus placebo group. Discontinuations due to adverse events occurred in 4% of patients in the fulvestrant plus placebo group and 2% in the fulverstrant plus placebo group. No deaths occurred in either treatment group as a result of treatment related toxicity.[3]

The most common grade 3/4 adverse event was neutropenia which was reported in 65% of patients in the palbociclib group and 1% in the placebo group. Febrile neutropenia was uncommon in both groups (3 patients vs 1 patient). [3]

Infections, fatigue, nausea, anaemia, thromboctopenia, alopecia, rash and stomatitis were also more common in the palbociclib group. [3]

References

1 Finn, R. S., M. Martin, H. S. Rugo, et al. 2016. "Palbociclib and Letrozole in Advanced Breast Cancer." N Engl J Med 375(20):1925-1936.

2 Turner, N. C., J. Ro, F. Andre, et al. 2015. "Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer." N Engl J Med 373(3):209-219.

3 Cristofanilli, M., N. C. Turner, I. Bondarenko, et al. 2016. "Fulvestrant plus palbociclib versus fulvestrant plus placebo for

treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial." Lancet Oncol 17(4):425-439.

4 Turner, N. C., D. J. Slamon, J. Ro, et al. 2018. "Overall Survival with Palbociclib and Fulvestrant in Advanced Breast Cancer." N Engl J Med 379(20):1926-1936.

History

Version 4

Date	Summary of changes
19/11/2019	Pulmonary toxicity added to side effects. Version increase to V4.
18/02/2020	Blood test recommendations updated- FBC frequency reduced if neutropenia grade ≥ 3 has not occurred after the first 6 cycles, EUC and LFTs at baseline and as clinically indicated.
18/11/2020	ID 3379 Breast metastatic ribociclib and ID 3625 Breast metastatic abemaciclib added as related pages.
13/08/2021	Protocol reviewed electronically by Medical Oncology Reference Committee. Nil changes. Review in 2 years.
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.
10/01/2022	Tablet formulation added to treatment schedule, administration and patient information sections.
01/08/2022	Drug status updated- now PBS listed for all combinations.

Version 3

Date	Summary of changes
03/11/2017	New protocol taken to Medical Oncology Reference Committee meeting
18/01/2018	Protocol approved and published on eviQ. Review protocol in 1 year.
30/01/2019	Protocol electronically reviewed by Medical Oncology Reference Committee. Evidence section updated to include final overall survival data. Version number change to V.2. Review in 2 years.
23/09/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 30/08/2019. Drug status updated to PBS in combination with an aromatase inhibitor. ECOG performance status score added to indications. Combination with anastrozole added to patient information. Pneumonitis added to clinical information. ID 1302 Breast metastatic anastrozole added as related page. Version number change to V.3. Next review in 2 years.

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Patient information - Breast cancer metastatic - Palbociclib

Patient's name:

Your treatment

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

Palbociclib		
This treatment cycle is repeated every 28 days. Your doctor will advise you how long to take the treatment for.		
Day	**Treatment**	**How it is given**
1 to 21	**Palbociclib** *(PAL-boe- SYE-klib)*	Take orally ONCE a day at the same time each day. Take capsules with food, or tablets with or without food. Swallow whole with a glass of water. Do not break, crush or chew. If you forget to take a dose or vomit a dose, take your normal dose the next time it is due. Do not take an extra dose.
22 to 28	**Do not** take palbociclib capsules or tablets from day 22 to day 28	

- Palbociclib is used in combination with hormonal therapy. This will either be an injection (called fulvestrant) or a tablet (called an aromatase inhibitor e.g. anastrozole or letrozole). Your doctor with discuss your treatment plan with you.

When to get help

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

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime:..... Night/weekend:..... Other instructions:..... ....

Other information about your treatment

Changes to your dose or treatment delays

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

treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

Blood tests and monitoring

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

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.

Side effects

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

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

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

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

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Physical weakness and lack of energy (asthenia)	• You may feel very weak, have no energy and need to sleep a lot • You may have difficulty concentrating and may 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.
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.**

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.**
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

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

General advice for people having cancer treatment

Blood clot risk

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

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.

- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

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

Diet

- 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.

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.

Breast cancer information

- Australasian Lymphology Association – lymphoedema.org.au
- Australasian Menopause Society – menopause.org.au
- Breast Cancer Network Australia – bcna.org.au
- National Breast Cancer Foundation – nbcf.org.au
- YWCA Encore breast cancer exercise program – ywcaencore.org.au

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
- 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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