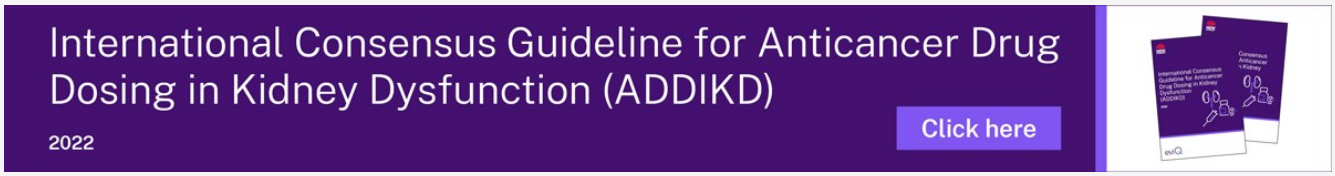
Neuroendocrine pancreatic advanced sUNITinib

ID: 1221 v.5 **Endorsed**

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

For patients with progressive disease, consider referral to or discussion with a centre experienced in NET management.

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:

- Neuroendocrine pancreatic advanced everolimus

- WHO 2019 classification of tumours of the digestive system

Treatment schedule - Overview

Drug	Dose	Route
sUNITinib	37.5 mg ONCE a day *	PO

*Reduce sunitinib dose by 12.5 mg to a minimum of 25 mg if coadministered with a strong CYP3A4 inhibitor.

*Increase sunitinib dose by increments of 12.5 mg to a maximum of 62.5 mg if coadministered with a strong CYP3A4 inducer (link to interactions).

Continuous until disease progression or unacceptable toxicity

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Drug status: **Sunitinib** is PBS authority

Sunitinib is available as **12.5 mg**, **25 mg**, **37.5 mg** and **50 mg** capsules

Cost: ~ $2,330 per month

Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. Select here for recommended doses of alternative antiemetics.*

Continuous treatment		
Metoclopramide	10 mg (PO)	one tablet when necessary (maximum of 30 mg/24

Continuous treatment		
		hours, up to 5 days)
sUNITinib	37.5 mg (PO)	ONCE a day

Reduce sunitinib dose by 12.5 mg to a minimum of 25 mg if coadministered with a strong CYP3A4 inhibitor.

Increase sunitinib dose by increments of 12.5 mg to a maximum of 62.5 mg if coadministered with a strong CYP3A4 inducer (link to interactions).

Continuous until disease progression or unacceptable toxicity

Indications and patient population

Indications:

- Metastatic or unresectable, well-differentiated malignant pancreatic neuroendocrine tumour (pNETs).

Cautions:

- Pre existing cardiac disease.

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Emetogenicity minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cardiac toxicity	Tyrosine kinase inhibitors have been associated with cardiac complications of varying degrees and severity. Patients, especially those with pre-existing cardiovascular disease, should have a baseline cardiac assessment including an electrocardiogram (ECG) and biochemistry and be closely monitored; consider an echocardiogram (ECHO) as clinically indicated. Cardiac assessment should then be repeated as clinically indicated or when starting new medication which affects the QT interval. Read more about cardiac toxicity associated with anti-cancer drugs
Prolongation of QT interval	This treatment may prolong the QT interval and increase the risk of cardiac arrhythmia. Use with caution in patients with a congenital long QT syndrome, patients treated with a high cumulative dose of anthracycline therapy, patients taking medications that may prolong the QT interval and those with electrolyte disturbances. Risk factors (e.g. electrolyte abnormalities) should be corrected, where possible, prior to commencement of treatment and the concurrent use of drugs that may prolong the QT interval should be avoided. Baseline and periodic monitoring of electrocardiogram (ECG) and electrolytes (potassium, magnesium, calcium) should be considered in patients at high risk of QT prolongation. Read more about drugs that may prolong QTc interval at crediblemeds.org (registration required).
Hypertension	Pre-existing hypertension should be adequately controlled prior to commencing treatment. Baseline blood pressure monitoring and repeat weekly for the first 6 weeks then regularly throughout treatment. In severe or uncontrolled hypertension, treatment should be withheld until hypertension is controlled. Dose modification or permanent discontinuation may be necessary.

Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea
Wound healing	Some suggest (Bose et al. 2010- see link to abstract) that antiangiogenic tyrosine kinase inhibitors (TKI's) be interrupted for at least one week (48 hours for agents with short half life) before surgery and not re-initiated until adequate wound healing has occurred. At many institutions, therapy with these agents is held for four weeks after major surgery and for at least two weeks after minor surgery, although there are no prospective data validating this approach. The decision to resume therapy following a major surgical intervention should be based upon clinical judgement of recovery from surgery. Read more about "Vascular endothelial growth factor targeted therapy in the perioperative setting: implications for patient care", Bose et al 2010[1]
Hand-foot syndrome	Hand-foot syndrome (palmar-plantar erythrodysaesthesia) and rash are common adverse effects with this treatment which generally appear during the first 6 weeks of therapy. Read more about hand food syndrome or palmar plantar erythrodysaesthesia (PPE)
Hypothyroidism	Thyroid dysfunction in particular hypothyroidism may occur with this treatment. Monitor for signs and symptoms of thyroid dysfunction and manage as clinically appropriate.
Blood tests	FBC, EUC and LFTs at baseline, repeat at week 2, then every 4 weeks. TFTs at baseline then repeat every 8 to 12 weeks.
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.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

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

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol

has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD).

Note:

- Reduce sunitinib dose by 12.5 mg to a minimum of 25 mg if coadministered with a strong CYP3A4 inhibitor.
- Increase sunitinib dose by increments of 12.5 mg to a maximum of 62.5 mg if coadministered with a strong CYP3A4 inducer (link to interactions).

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
1.0 to less than 1.5	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well.
0.5 to less than 1.0	Delay treatment until ANC 1.5 or greater
less than 0.5	Delay treatment until ANC 1.5 or greater and reduce sunitinib by 12.5 mg for subsequent cycles
Febrile neutropenia	Delay treatment until ANC 1.5 or greater and reduce sunitinib by 12.5 mg for subsequent cycles
Platelets x 10^9/L (pre-treatment blood test)	
50 to less than 100	No dose modification necessary
25 to less than 50	Delay treatment until platelets 50 or greater
less than 25	Delay treatment until platelets 50 or greater and reduce sunitinib by 12.5 mg for subsequent cycles

Renal impairment
No adjustment to starting dose is necessary in mild to severe renal impairment

Hepatic impairment
No adjustment to starting dose is necessary in mild to moderate hepatic impairment Sunitinib has not been studied in patients with severe hepatic impairment

Mucositis and stomatitis	
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce sunitinib by 12.5 mg 3rd occurrence: Discontinue sunitinib
Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce sunitinib by 12.5 mg for subsequent cycles or discontinue sunitinib

Diarrhoea	
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce sunitinib by 12.5 mg 3rd occurrence: Discontinue sunitinib
Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce sunitinib by 12.5 mg for subsequent cycles or discontinue sunitinib

Hand foot syndrome (link to Hand foot syndrome (Palmar-plantar erythrodysaesthesia))	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for

Hand foot syndrome (link to Hand foot syndrome (Palmar-plantar erythrodysaesthesia))	
	subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce sunitinib by 12.5 mg 3rd occurrence: Discontinue sunitinib
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce sunitinib by 12.5 mg for subsequent cycles or discontinue sunitinib

Cardiac toxicity	
Asymptomatic decline in LVEF * (LVEF less than 50% or more than 20% below baseline)	Delay treatment until recovery and consider reducing sunitinib by 12.5 mg for subsequent cycles (If no improvement in LVEF, cease sunitinib)
Symptomatic decline in LVEF	Cease sunitinib

** Left Ventricular Ejection Fraction*

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*

Sunitinib		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of sunitinib and its active metabolite possible due to reduced clearance	Avoid combination or monitor for sunitinib toxicity If concomitant use of strong CYP3A4 inhibitors cannot be avoided, consider reducing sunitinib dose to a minimum of 37.5 mg daily for GIST and MRCC or 25 mg daily for pNET, based on careful monitoring of tolerability
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of sunitinib and its active metabolite possible due to increased clearance	Avoid combination or monitor for decreased clinical response to sunitinib If concomitant use of strong CYP3A4 inducers cannot be avoided, consider increasing sunitinib dose in 12.5 mg increments (up to 87.5 mg per day for GIST and MRCC or 62.5 mg per day for pNET), based on careful monitoring of tolerability
Drugs that may prolong the QTc interval (e.g. azole antifungals, tricyclic antidepressants, antiarrhythmics etc.)	Additive effect with sunitinib; may lead to torsades de pointes and cardiac arrest	Avoid combination or minimise additional risk factors (e.g. correct electrolyte imbalances) and monitor ECG for signs of cardiac arrhythmia
Drugs undergoing P-gp-mediated elimination (e.g. dabigatran, loperamide, phenytoin etc.)	Increased effects/toxicity of these drugs possible due to inhibition of P-gp by sunitinib resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity of interacting drugs
Bevacizumab	Microangiopathic haemolytic anaemia	Monitor for haemolytic anaemia, thrombocytopenia, hypertension, elevated creatinine and neurological symptoms
Levothyroxine	Reduced efficacy of thyroid replacement therapy resulting in hypothyroid symptoms; possibly due to induction of levothyroxine metabolism by sunitinib and subsequent TSH elevation	Monitor closely for signs and symptoms of hypothyroidism, serum thyroxine and TSH levels; increase levothyroxine dose if needed
Temsirolimus	Increased toxicity of sunitinib	Avoid combination or monitor for sunitinib toxicity
Antidiabetic agents	Hypoglycaemia	Monitor blood glucose levels. Adjustment of the dose of antidiabetic medication may be required

General		
	Interaction	**Clinical management**
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

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

product information monographs via the TGA website for further information.

Administration

This is a continuous 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

Sunitinib

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may 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

Sunitinib capsules

- Sunitinib capsules with written instructions on how to take them.

Antiemetics

- Antiemetics as prescribed.

Antidiarrhoeals

- Antidiarrhoeals as prescribed.

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
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
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Palmar-plantar erythrodysaesthesia (PPE) - hand-foot syndrome (HFS)	Bilateral erythema, tenderness, pain, swelling, tingling, numbness, pruritus, dry rash, or moist desquamation and ulceration of the palms and soles. It is also known as hand-foot syndrome (HFS). Symptoms appear to be dose dependent and palms are affected more than soles. Read more about hand-foot syndrome associated with chemotherapy
Skin and tissue discolouration	Discolouration of the skin or hair may be accompanied by other dermatological effects, including dryness, blisters and thickening or cracking of the skin.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Hypertension	High blood pressure is commonly associated with many anti-cancer drugs. Pre-existing hypertension should be controlled prior to initiation of drugs capable of causing hypertension.
Haemorrhage	
Cardiotoxicity	Cardiotoxicity may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, hypertension, cardiac ischaemia and congestive heart failure (CHF). The risk of cardiotoxicity is increased by a number of factors, particularly a history of heart disease and electrolyte imbalances. Read more about cardiotoxicity associated with anti-cancer drugs

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia - partial	Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs. Read more about nail toxicities
Hypothyroidism	

Evidence

The evidence supporting this protocol is provided by a multinational, randomised, double-blind, placebo-controlled phase III trial of sunitinib in patients with advanced, well-differentiated pancreatic neuroendocrine tumours with evidence of disease progression in the previous 12 months.[2]

This pivotal trial has updated progression-free and final overall survival data evaluated five years from trial closure.[3]

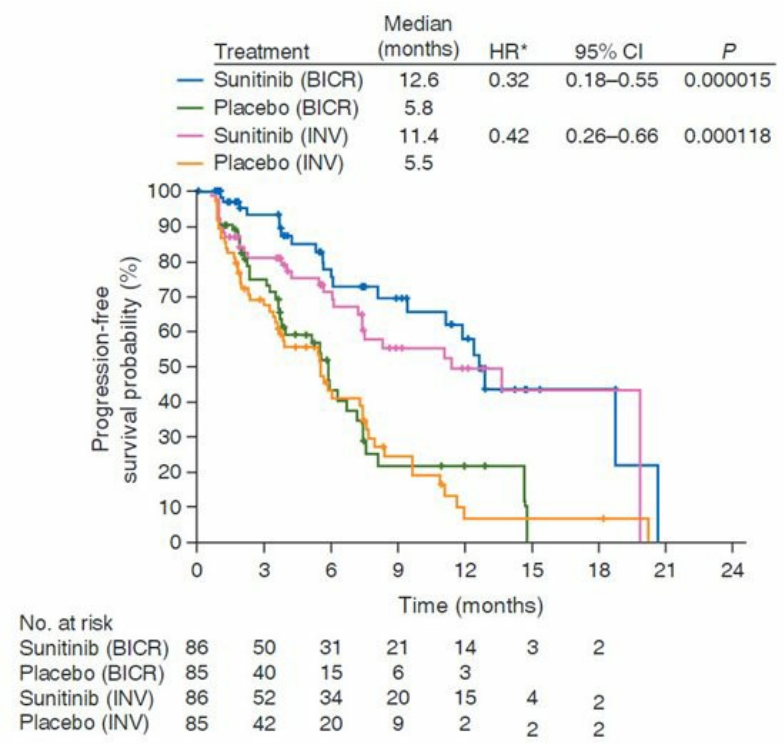
Between June 2007 and April 2009, a total of 171 patients were randomly assigned to receive best supportive care with either sunitinib 37.5 mg per day or placebo.

The primary end point was progression-free survival (PFS); secondary end points included the objective response rate (ORR), overall survival (OS), and safety.

Efficacy

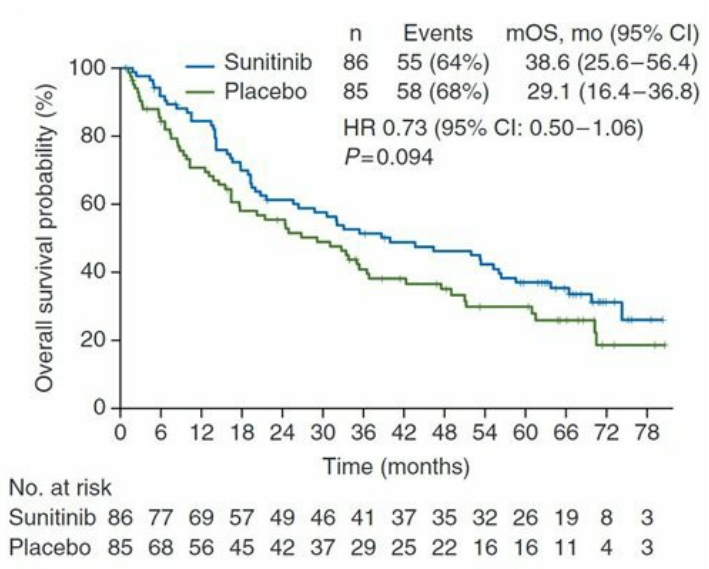
Median PFS was 12.6 months in the sunitinib group as compared with 5.8 months in the placebo group (HR for progression or death, 0.32; 95% CI, 0.18 to 0.55; P<0.001). The ORR was 9.3% in the sunitinib group versus 0% in the placebo group.[2] The median OS was 38.6 months for the sunitinib group and 29.1 months for placebo (HR for death 0.73; 95% CI, 0.50 to 1.05; P=0.09) with 69% of placebo patients having crossed over to sunitinib.[3]

Kaplan-Meier Analysis of Progression-free Survival based on investigator-assessment (INV) versus blinded independence central review (BICR).[3]



Asterisk indicates sunitinib versus placebo.

Kaplan-Meier Analysis of Overall Survival in the Intention-to-Treat Population[3]



The self-administered European Organisation for Research and Treatment of Cancer (EORTC) quality-of-life questionnaire (QLQ-C30, version 3.0) was used to measure patient-reported outcomes. A post-hoc analysis of patient-reported outcomes found that patients in the sunitinib arm had overall clinically and statistically significant worsening of diarrhoea ($p < 0.001$). In this arm there was also a significant trend towards worsening of insomnia ($p = 0.04$) vs placebo. However, in QoL, cognitive, emotional, physical, role, and social functioning domains and other symptoms and scales, there were no overall clinically or statistically significant differences.[4]

The results of a phase IV open-labelled trial conducted in support of phase III study, confirmed initial data. Sixty-one treatment-naive and 45 previously treated patients with advanced/metastatic, well-differentiated, unresectable pancreatic neuroendocrine tumours received sunitinib 37.5 mg per day. Median treatment duration was 11.7 months. Median PFS was 13.2 months (95% CI, 10.9 to 16.7): 13.2 (95% CI, 7.4 to 16.8) in treatment-naive and 13.0 (95% CI, 9.2 to 20.4) in previously treated patients. ORR was 24.5% (95% CI, 16.7 to 33.8) in the total population: 21.3% (95% CI, 11.9 to 33.7) in treatment-naive and 28.9% (95% CI, 16.4 to 44.3) in previously treated patients. Median OS, although not yet mature, was 37.8 months (95% CI, 33.0 to not estimable).[5]

Toxicity

The most frequent adverse events in the sunitinib group were diarrhoea, nausea, vomiting, asthenia, and fatigue.[2]

Updated safety data was presented by Valle et al following two open-label sunitinib extension studies subsequent to original phase III trial. The safety of extended sunitinib treatment (median treatment duration: ~1 year) was consistent with the original phase III study and the known safety profile of sunitinib in pancreatic neuroendocrine tumours.[6]

Toxicity[2]

Table 3. Common Adverse Events in the Safety Population.*

Event	Sunitinib (N=83)			Placebo (N=82)		
	All Grades	Grade 1 or 2	Grade 3 or 4	All Grades	Grade 1 or 2	Grade 3 or 4
	number of patients (percent)					
Diarrhea	49 (59)	45 (54)	4 (5)	32 (39)	30 (37)	2 (2)
Nausea	37 (45)	36 (43)	1 (1)	24 (29)	23 (28)	1 (1)
Asthenia	28 (34)	24 (29)	4 (5)	22 (27)	19 (23)	3 (4)
Vomiting	28 (34)	28 (34)	0	25 (30)	23 (28)	2 (2)
Fatigue	27 (32)	23 (28)	4 (5)	22 (27)	15 (18)	7 (8)
Hair-color changes	24 (29)	23 (28)	1 (1)	1 (1)	1 (1)	0
Neutropenia	24 (29)	14 (17)	10 (12)	3 (4)	3 (4)	0
Abdominal pain	23 (28)	19 (23)	4 (5)	26 (32)	18 (22)	8 (10)
Hypertension	22 (26)	14 (17)	8 (10)	4 (5)	3 (4)	1 (1)
Palmar–plantar erythro-dysesthesia	19 (23)	14 (17)	5 (6)	2 (2)	2 (2)	0
Anorexia	18 (22)	16 (19)	2 (2)	17 (21)	16 (20)	1 (1)
Stomatitis	18 (22)	15 (18)	3 (4)	2 (2)	2 (2)	0
Dysgeusia	17 (20)	17 (20)	0	4 (5)	4 (5)	0
Epistaxis	17 (20)	16 (19)	1 (1)	4 (5)	4 (5)	0
Headache	15 (18)	15 (18)	0	11 (13)	10 (12)	1 (1)
Insomnia	15 (18)	15 (18)	0	10 (12)	10 (12)	0
Rash	15 (18)	15 (18)	0	4 (5)	4 (5)	0
Thrombocytopenia	14 (17)	11 (13)	3 (4)	4 (5)	4 (5)	0
Mucosal inflammation	13 (16)	12 (14)	1 (1)	6 (7)	6 (7)	0
Weight loss	13 (16)	12 (14)	1 (1)	9 (11)	9 (11)	0
Constipation	12 (14)	12 (14)	0	16 (20)	15 (18)	1 (1)
Back pain	10 (12)	10 (12)	0	14 (17)	10 (12)	4 (5)

* Adverse events were defined on the basis of the National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0. Events listed are those of any grade that occurred in more than 15% of patients in either group.

References

1 Bose, D., F. Meric-Bernstam, W. Hofstetter, et al. 2010. "Vascular endothelial growth factor targeted therapy in the perioperative setting: implications for patient care." Lancet Oncol 11(4):373-382.

2 Raymond, E., L. Dahan, J. L. Raoul, et al. 2011. "Sunitinib malate for the treatment of pancreatic neuroendocrine tumors." N Engl J Med 364(6):501-513.

3 Faivre, S., P. Niccoli, D. Castellano, et al. 2017. "Sunitinib in pancreatic neuroendocrine tumors: updated progression-free survival and final overall survival from a phase III randomized study". Annals of Oncology 28:339-343.

4 Vinik, A., Y. Bang, J. Raoul, et al. 2010. "Patient-reported outcomes (PROs) in patients (pts) with pancreatic neuroendocrine tumors (NET) receiving sunitinib (SU) in a phase III trial." ASCO Meeting Abstracts 28(15_suppl):4003.

5 Raymond, E., M. H. Kulke, S. Qin, et al. 2018. "Efficacy and Safety of Sunitinib in Patients with Well-Differentiated Pancreatic Neuroendocrine Tumours." Neuroendocrinology 107(3):237-245

6 Valle, J. W., I. Borbath, B. Rosbrook, et al. 2019. "Sunitinib in patients with pancreatic neuroendocrine tumors: update of safety data." Future Oncol 15(11):1219-1230.

History

Version 5

Date	Summary of changes
08/10/2020	Protocol reviewed electronically by Medical Oncology Reference Committee. Related pages updated to WHO 2019 classification of tumours of the digestive system. Indications and patient population updated based on WHO 2019 classification. Efficacy section updated to substitute the preliminary results with final results from Favire et al and to add Raymond et al study. Toxicity section updated to include safety data from Valle et al. Version number changed to V.5. Next 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.
18/05/2022	Prolongation of QT interval clinical information block added.
20/10/2022	Protocol reviewed electronically by Medical Oncology Reference Committee. No changes. Next review 2 years.
19/05/2023	Wound healing clinical information block updated to align with existing eviQ protocols.

Version 4

Date	Summary of changes
25/11/2011	New protocol taken to Medical Oncology Reference Committee meeting.
13/12/2011	Approved and published on eviQ.
13/09/2013	Protocol reviewed and indications updated as per WHO 2010 classification. Dose modifications updated as per recommendations in the original trial. Next review in 1 year.
01/12/2013	PBS indication updated.
01/04/2015	Protocol reviewed by committee via email survey. No changes and next review in 2 years.
10/11/2016	The following change made post Medical Oncology Reference Committee meeting held on 21 October 2016: link to AGITG and ANZCTR added.
31/05/2017	Transferred to new eviQ website. Version number changed to V.3. Hepatitis B screening changed to NOT recommended.
16/02/2018	Protocol reviewed at Medical Oncology Reference Committee Meeting, evidence updated to include final analysis. Review in 2 years.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.4.

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15 Jul 2023

Patient information - Pancreatic neuroendocrine cancer advanced - Sunitinib

Patient's name:

Your treatment

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

Sunitinib		
This treatment is continuous. Your doctor will advise you how long to take the treatment for.		
Day	**Treatment**	**How it is given**
Continuous	**Sunitinib** *(soo-NI-ti-nib)*	Take orally ONCE a day, at the same time each day with or without food. Swallow whole with a glass of water, do not break, crush or chew. If you forget to take a capsule or vomit a capsule, take your normal dose the next time it is due. Do not take an extra dose.

When to get help

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

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

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.
- **Antidiarrhoeals:** you may be given some medication to treat diarrhoea. Your doctor or nurse will tell you how and when to take your antidiarrhoeal medication.

Side effects

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

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

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

Immediate (onset hours to days)	
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.**
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.**

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.

Hand-foot syndrome (palmar-plantar erythrodysaesthesia)	• The palms of your hands and soles of your feet may become:
	  ◦ red and hot
	  ◦ swollen
	  ◦ painful and tender
	  ◦ blistered.
	• The skin in the area may also peel.
	• Moisturise your hands and feet daily with sorbolene or aqueous cream.
	• Keep your hands and feet clean and dry.
	• Avoid hot water, instead use lukewarm water to bathe.
	• Avoid direct sunlight.
	• Avoid unnecessary walking, jogging or exercise.
	• Wear cotton socks and avoid tight-fitting shoes.
	• **Tell your doctor or nurse as soon as possible if you notice any skin changes on your hands or feet.**

Hair and skin colour changes	• You may notice changes to your hair and skin colour. • This is not harmful and will go away after treatment.
Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**
High blood pressure (hypertension)	• You may not have any signs or symptoms if you have high blood pressure. • If it is severe you may get headaches, shortness of breath or feel dizzy. • Your blood pressure will be taken regularly during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the signs or symptoms listed above.**

Bleeding (haemorrhage)	• Tell your doctor or nurse if you have a wound that does not heal. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **unusual bleeding or bruising** ◦ **bright red or black, tarry bowel motions (stools, poo)** ◦ **stomach pain** ◦ **slurred speech** ◦ **shortness of breath** ◦ **a fast heartbeat.**
Heart problems	• You may get: ◦ chest pain or tightness ◦ shortness of breath ◦ swelling of your ankles ◦ an abnormal heartbeat. • Heart problems can occur months to years after treatment. • Tell your doctor if you have a history of heart problems or high blood pressure. • Before or during treatment, you may be asked to have a test to see how well your heart is working. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)
Nail changes	• Your nails may: ◦ grow more slowly ◦ become darker ◦ develop ridges or white lines ◦ become brittle and flaky • In some cases, you may lose your nails completely. • Keep your nails clean and short. • Avoid things like biting your fingernails, getting a manicure, pedicure or false nails. • Wear gloves when you wash the dishes, work in the garden, or clean the house.
Slow thyroid gland (hypothyroidism)	• You may: ◦ fatigue and low energy levels ◦ depression ◦ slow heart rate ◦ unexplained weight gain ◦ intolerance to cold temperatures ◦ fatigued and aching muscles ◦ dry, coarse skin ◦ puffy face ◦ hair loss ◦ constipation ◦ problems with concentration • You will have regular blood tests to check how well your thyroid is working • **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 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.

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

Neuroendocrine tumour information

- NeuroEndocrine Cancer Australia – neuroendocrine.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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