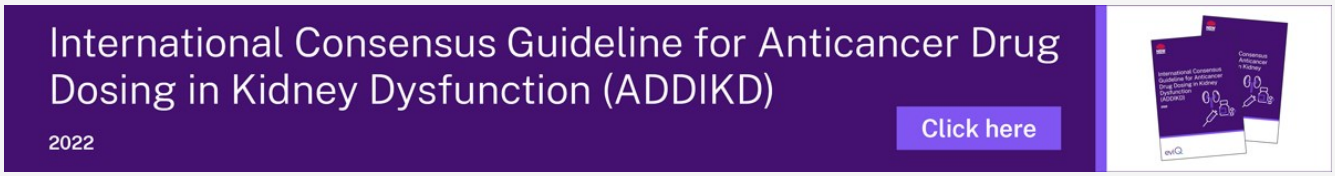
Pancreas metastatic irinotecan nanoliposomal fluorouracil and leucovorin

ID: 3387 v.2 **Endorsed**

⚠ Fluoropyrimidine overdose or overexposure:
Fluoropyrimidine overdose or overexposure may result in severe or life-threatening toxicity. An antidote is available and is highly effective if given within 96 hours. Read more about fluoropyrimidine overdose or overexposure.

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:

- Advanced or metastatic FOLFIRI (modified) (fluorouracil leucovorin irinotecan)

⚠ Do not substitute irinotecan nanoliposomal for or with other drug products containing irinotecan. Irinotecan nanoliposomal is not equivalent to non-liposomal irinotecan formulations and should not be interchanged.

Treatment schedule - Overview

Cycle 1 and further cycles

Drug	Dose	Route	Day
Irinotecan nanoliposomal	70 mg/m^2 *	IV infusion	1
Calcium folinate (Leucovorin)	50 mg **	IV bolus	1
Fluorouracil	2,400 mg/m^2	CIV via pump over 46 hours	1

*For patients known to be homozygous for the UGT1A1*28 allele consider reducing the starting dose of irinotecan nanoliposomal to 50 mg/m^2. If patient does not experience drug related toxicities during the first two weeks of treatment consider increasing the dose to 70 mg/m^2 based on individual patient tolerance. UGT1A1*28 allele testing is available in Australia however is not reimbursed.

** The dose of calcium folinate (Leucovorin®) has been modified in this protocol from the original clinical trial dose of 400 mg/m^2 to 50 mg based on reference committee consensus. Refer to discussion on calcium folinate (Leucovorin®) and evidence section for more information.

Frequency: 14 days

Cycles: Continuous until disease progression or unacceptable toxicity

Drug status: Irinotecan nanoliposomal is TGA approved but not PBS listed for this indication.

Fluorouracil and leucovorin are on the PBS general schedule

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		
Dexamethasone	8 mg (PO)	60 minutes before chemotherapy
Palonosetron	0.25 mg (IV bolus)	30 minutes before chemotherapy
Irinotecan nanoliposomal	70 mg/m^2 (IV infusion)	in a final volume of 500 mL sodium chloride 0.9% over 90 minutes
Calcium folinate (Leucovorin)	50 mg (IV bolus)	over 1 to 2 minutes
Fluorouracil	2,400 mg/m^2 (CIV)	via ambulatory infusion pump over 46 hours

Day 2 and 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on day 2 and 3 may not be required and may be reduced or omitted at the clinicians discretion. *

- For patients known to be homozygous for the UGT1A1*28 allele consider reducing the starting dose of irinotecan nanoliposomal to 50 mg/m^2. If patient does not experience drug related toxicities during the first two weeks of treatment consider increasing the dose to 70 mg/m^2 based on individual patient tolerance.
- The dose of calcium folinate (Leucovorin®) has been modified in this protocol from the original clinical trial dose of 400 mg/m^2 to 50 mg. A discussion regarding the effect of dosing on outcome can be found in the calcium folinate dose document.
- * Link to ID 7 Prevention of chemotherapy induced nausea and vomiting

Frequency: 14 days

Cycles: Continuous until disease progression or unacceptable toxicity

Indications and patient population

Indications:

- Metastatic adenocarcinoma of the pancreas after previous treatment with gemcitabine-based therapy.

Cautions:

- Patients with albumin less than 30 g/L were not included in the trial.

Clinical information

Safety alert fluoropyrimidines	Fluoropyrimidines can be administered by different routes and schedules with each method having associated increased risk of certain side effects. Fluoropyrimidine overdose or overexposure is a rare but potentially life threatening side effect of this drug class and can occur by any route of administration. An antidote is available and highly effective if given within 96 hours. Read more about the medication safety alert for infusional fluorouracil and fluoropyrimidine overdose or overexposure
Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Premedication	Consider atropine 0.3 to 0.6 mg IV or SC prior to irinotecan administration as required to help prevent irinotecan induced cholinergic side effects (atropine should not be used in patients with glaucoma).
Emetogenicity MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist is available on the PBS in combination with a $5HT_3$ antagonist and steroid. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cardiac toxicity	Cardiac toxicity is a serious complication that can occur during treatment with fluorouracil. Patients treated with fluorouracil, especially those with a prior history of cardiac disease or other risk factors, should be carefully monitored during therapy. Read more about cardiac toxicity associated with anti-cancer drugs
Diarrhoea (early onset) and cholinergic syndrome	Early onset diarrhoea and other cholinergic symptoms such as rhinitis, hypersalivation, miosis, lacrimation, diaphoresis, flushing, and abdominal cramping can occur during or within 24 hours of administration of irinotecan. Symptoms may be treated with atropine 0.3 to 0.6 mg IV or SC as needed, repeated up to a maximum dose of 1.2 mg (unless clinically contraindicated). Patients 65 years of age and above should be closely monitored due to a greater risk of early diarrhoea observed in this population. Read more about treatment induced diarrhoea
Diarrhoea (late onset)	Irinotecan induced diarrhoea can be life threatening and requires immediate management. Ensure patients have sufficient antidiarrhoeal (e.g. loperamide) and appropriate instructions should this adverse event occur. Note: If prescribing loperamide, the recommended maximum daily dose of 16 mg of loperamide can be exceeded. Read more about treatment induced diarrhoea
Severe enteropathy associated with fluoropyrimidine	Severe enteropathy has been reported among patients with stage II/III colon cancer treated with fluoropyrimidine chemotherapy with or without oxaliplatin. Patients treated with fluoropyrimidine should be closely monitored for diarrhoea and aggressively managed. Read more about severe enteropathy associated with fluorouracil in colorectal cancer
Dihydropyrimidine dehydrogenase (DPD) enzyme deficiency	Rare, life-threatening toxicities such as mucositis, neutropenia, neurotoxicity and diarrhoea have been reported following administration of fluoropyrimidines (e.g. fluorouracil and capecitabine). Severe unexplained toxicities require investigation prior to continuing with treatment. Testing for DPD enzyme deficiency is available in Australia but not currently reimbursed. Read more about dihydropyrimidine dehydrogenase (DPD) enzyme deficiency

Gilbert's syndrome	Patients with Gilbert's syndrome should have their dose of irinotecan reduced. There is no clear dosing strategy; however based on the area under the concentration-time curve of SN-38, Innocenti et al (2006) recommend a 20% dose reduction of irinotecan. Read more about Gilbert's syndrome
Blood tests	FBC, EUC and LFTs at baseline and prior to each cycle. Consider UGT1A1*28 allele testing as dose reductions may be required (not reimbursed).
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:

- All fluorouracil dose reductions are calculated as a percentage of the starting dose.
- The dose modifications are based on the product information and reference committee consensus.
- For patients who start treatment on 50 mg/m^2 of irinotecan nanoliposomal and do not escalate to 70 mg/m^2, the first dose reduction is to 43 mg/m^2 and the second dose reduction is to 35 mg/m^2.
- The dose of calcium folinate (Leucovorin®) remains fixed at 50 mg and is delayed or omitted if fluorouracil is delayed or omitted.

Haematological toxicity

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
1.0 to less than 1.5	Delay treatment until recovery
less than 1.0	1st occurrence: delay treatment until recovery. Reduce irinotecan nanoliposomal to 50 mg/m^2 and fluorouracil by 25% for subsequent cycles 2nd occurrence: delay treatment until recovery. Reduce irinotecan nanoliposomal to 43 mg/m^2 and fluorouracil by an additional 25% 3rd occurrence: discontinue treatment
Febrile neutropenia	1st occurrence: delay treatment until recovery. Reduce irinotecan nanoliposomal to 50 mg/m^2 and fluorouracil by 25% for subsequent cycles 2nd occurrence: delay treatment until recovery. Reduce irinotecan nanoliposomal to 43 mg/m^2 and fluorouracil by an additional 25% 3rd occurrence: discontinue treatment
Platelets x 10^9/L (pre-treatment blood test)	
50 to less than 100	Delay treatment until recovery
less than 50	1st occurrence: delay treatment until recovery. Reduce irinotecan nanoliposomal to 50 mg/m^2 and fluorouracil by 25% for subsequent cycles 2nd occurrence: delay treatment until recovery. Reduce irinotecan nanoliposomal to 43 mg/m^2 and fluorouracil by an additional 25% 3rd occurrence: discontinue treatment

Renal impairment	
Creatinine clearance (mL/min) at baseline	
30 to 50	Reduce fluorouracil by 25%
less than 30	Reduce fluorouracil by 50%. Insufficient data for irinotecan nanoliposomal in patients with severe renal dysfunction
During treatment	
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: reduce irinotecan nanoliposomal to 50 mg/m^2 and fluorouracil by 25% 2nd occurrence: reduce irinotecan nanoliposomal to 43 mg/m^2 and fluorouracil by an additional 25% 3rd occurrence: discontinue treatment

Hepatic impairment	
Hepatic dysfunction at baseline	
Moderate	Reduce fluorouracil by 25%
Severe	Reduce fluorouracil by 50%
Irinotecan nanoliposomal has not been studied in individuals with hepatic impairment. Use is not recommended if bilirubin greater than 34 umol/L, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) > 2.5 times upper limit of normal (ULN) or > 5 times ULN if liver metastasis is present.	
Hepatotoxicity during treatment	
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows:

Hepatic impairment	
	1st occurrence: reduce irinotecan nanoliposomal to 50 mg/m^2 and fluorouracil by 25% 2nd occurrence: reduce irinotecan nanoliposomal to 43 mg/m^2 and fluorouracil by an additional 25% 3rd occurrence: discontinue treatment

Diarrhoea	
Grade 1 or 2	Delay treatment until toxicity has resolved to Grade 1 or less.
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: reduce irinotecan nanoliposomal to 50 mg/m^2 and fluorouracil by 25% 2nd occurrence: reduce irinotecan nanoliposomal to 43 mg/m^2 and fluorouracil by an additional 25% 3rd occurrence: discontinue treatment

Nausea /vomiting	
Grade 3 or Grade 4 despite optimal antiemetic therapy	Delay treatment until toxicity has resolved to Grade 1 or less, optimise antiemetic therapy and reduce the dose for subsequent cycles as follows: 1st occurrence: reduce irinotecan nanoliposomal to 50 mg/m^2 2nd occurrence: reduce irinotecan nanoliposomal to 43 mg/m^2 3rd occurrence: discontinue treatment

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*

Fluorouracil		
	Interaction	**Clinical management**
Folic acid	Increased toxicity of fluorouracil due to stabilisation of its bond to thymidylate synthetase (folic acid is a precursor of folinic acid/leucovorin)	Advise patients not to take folic acid supplements (inc. multivitamins) around the time of receiving treatment with fluorouracil
Metronidazole, tinidazole	Increased toxicity of fluorouracil due to reduced clearance	Avoid combination or monitor for fluorouracil toxicity
Warfarin and other drugs metabolised by CYP2C9 (e.g. warfarin, phenytoin etc.)	Increased effect/toxicity of these drugs due to inhibition of CYP2C9 by fluorouracil resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity of these drugs (e.g. for bleeding/elevated INR with warfarin, elevated phenytoin serum levels or signs of toxicity such as ataxia, tremor etc.)
Allopurinol	Reduced efficacy of fluorouracil possible due to reduced conversion to the active metabolites	Avoid combination or monitor for reduced fluorouracil efficacy

Irinotecan		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of irinotecan possible due to reduced clearance	Avoid combination or monitor for irinotecan toxicity (Ketoconazole contraindicated and should be discontinued at least 1 week prior to irinotecan)
CYP3A4 and P-gp inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort, dexamethasone etc.)	Reduced efficacy of irinotecan possible due to increased clearance	Avoid combination or monitor for decreased clinical response to irinotecan (St John's wort contraindicated; substituting non-enzyme inducing antiepileptics (e.g. clonazepam, diazepam, lorazepam) at least 1 week prior to irinotecan should be considered)
Atazanavir	Increased toxicity of irinotecan possible due to reduced clearance caused by inhibition of both CYP3A4 and UGT1A1 by atazanavir	Avoid combination or monitor for irinotecan toxicity
Smoking	Reduced efficacy of irinotecan possible due to increased clearance caused by induction of both CYP3A4 and UGT1A1 by smoking	Monitor for decreased clinical response to irinotecan in patients who continue to smoke; no specific dosing recommendations are available

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.

Day 1

Approximate treatment time: 2.5 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Prime IV line(s).

Access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Chemotherapy - Time out

Irinotecan nanoliposomal

- do not use with an in-line filter.

Prior to administration:

- administer atropine premedication if required
- patient vital signs should be closely monitored post atropine administration as atropine can cause tachycardia, heart arrhythmias, hypertension and angina.

Administer irinotecan nanoliposomal (irritant):

- via IV infusion over 90 minutes
- protect from light
- flush with ~ 100 mL of sodium chloride 0.9%
- observe patient for cholinergic symptoms
- if patient develops early onset diarrhoea and other cholinergic symptoms (such as rhinitis, increased salivation, miosis, lacrimation, diaphoresis, flushing) - stop infusion, monitor vital signs and review by medical officer
- observe patient for hypersensitivity
- for severe reactions seek medical assistance immediately and permanently discontinue irinotecan nanoliposomal.

Calcium Folinate (Leucovorin)

- administer by IV bolus via a side port of the IV line over 1 to 2 minutes
- flush with ~ 50mL of sodium chloride 0.9%.

Fluorouracil continuous infusion (irritant)

Connect pump containing fluorouracil and administer over the correct time for the amount of drug in the pump:

- ⚠ safety alert issued for administration of infusional fluorouracil
- verify the correct rate of infusion via the ambulatory infusion pump
- read more information about the different ambulatory infusion pumps.

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

Day 3

Approximate treatment time: 30 minutes

Safe handling and waste management

Disconnection of ambulatory infusion pump/infusor

Verify the ambulatory infusion pump/infusor is complete.

Disconnect the ambulatory infusion pump/infusor as per recommended procedure for type of pump/infusor.

Read more about ambulatory infusion pumps/infusors.

Deaccess TIVAD or CVAD.

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

Discharge information

Antiemetics

- Antiemetics as prescribed.

Antidiarrhoeals

- Antidiarrhoeals (e.g. loperamide) as prescribed with written instructions on how to manage this side effect and 24 hour emergency contact.

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)	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Diarrhoea and cholinergic syndrome (early onset) associated with irinotecan	Cholinergic syndrome can occur during or shortly after commencing the irinotecan infusion, or within 24 hours of administration of the drug. It is characterised by diarrhoea, rhinitis, hypersalivation, miosis, lacrimation, diaphoresis, flushing, and abdominal cramping. Read more about treatment induced diarrhoea
Taste and smell alteration	Read more about taste and smell changes

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
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Diarrhoea (late onset) associated with irinotecan	Late onset of diarrhoea after 24 hours post irinotecan administration can be life threatening and requires immediate treatment. Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
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
Ocular changes	Symptoms may include eye pain, blurred vision, blepharitis, uveitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia.
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
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Actinic keratoses flare	Pre-existing actinic keratoses (AKs) can become more inflamed and scaly as a result of immunosuppression. Read more about actinic keratoses flare

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
Hyperpigmentation	Darkening of an area of skin caused by the overproduction of melanin.
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
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

Due to the lack of conclusive evidence to identify the optimum dose of Leucovorin®, it is the consensus of the eviQ reference committee to adopt flat dosing of Leucovorin® as a 50 mg IV bolus when used with bolus 5FU across all colorectal and upper gastrointestinal protocols. A discussion regarding the effect of dosing on outcome can be found in the calcium folinate

(Leucovorin®) dose document.

The evidence supporting this protocol is provided by a phase III multicentre international randomised trial (NAPOLI-1) involving 417 patients.[1] This study compared nanoliposomal irinotecan and fluorouracil/leucovorin with either nanoliposomal irinotecan or fluorouracil/leucovorin alone in patients with stage IV pancreatic adenocarcinoma (who had previously received gemcitabine containing regimen).

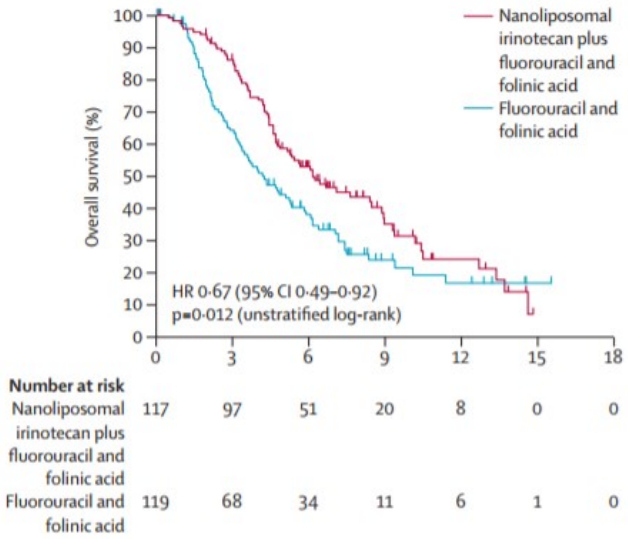
Between January 2012 and September 2013, 117 patients were randomised to receive nanoliposomal irinotecan and fluorouracil/leucovorin fortnightly until progression, 151 patients received nanoliposomal irinotecan alone and 149 patients received fluorouracil/leucovorin alone.

The primary end point was overall survival.

Efficacy

Median overall survival was 6.1 months in the combined therapy arm, (95% CI 4.8–8.9) compared with 4.2 months in the fluorouracil/leucovorin arm (95% CI 3.3–5.3) (unstratified HR 0.67, 95% CI 0.49–0.92; p=0.012).[1]

Median overall survival was 4.9 months (95% CI 4.2–5.6) in the nanoliposomal irinotecan monotherapy arm compared with 4.2 months in the fluorouracil/leucovorin control in that arm of the study (95% CI 3.6–4.9) (unstratified HR 0.99, 95% CI 0.77–1.28; p=0.94).[1]



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There was no difference in quality of life data between the treatment arms, however compliance with self-reported data was low (60% completed pain questionnaires). [1]

Toxicity

Treatment-related deaths were rare in the nanoliposomal irinotecan combined with 5-FU arm and in the comparator, 5FU monotherapy. Of note, the nanoliposomal irinotecan single agent arm was more toxic with treatment-related deaths in 4 out of 147 patients.[1]

Discontinuation due to an adverse event was slightly more common in the combined therapy arm (11%) compared with the 5-FU monotherapy arm (7%). Rates of serious adverse events were similar (48 vs 45%).

Of note, grade 3 and 4 gastrointestinal toxicities and neutropenia were much more common in the combined therapy arm (see table below).

Toxicity[1]	Nanoliposomal irinotecan and fluorouracil (n=117)	Fluorouracil alone (n=134)
Treatment-related deaths	1 (0.9%, death due to septic shock)	0
Serious adverse events	56 (48%)	60 (45%)
Discontinuation due to adverse event	13 (11%)	10 (7%)
Grade 3 and 4 toxicities		
Diarrhoea	15 (13%)	6 (4%)

Toxicity[1]	Nanoliposomal irinotecan and fluorouracil (n=117)	Fluorouracil alone (n=134)
Vomiting	13 (11%)	4 (3%)
Nausea	9 (8%)	4 (3%)
Decreased appetite	5 (4%)	3 (2%)
Fatigue	16 (14%)	5 (4%)
Neutropenia	32 (27%)	2 (1%)
Anaemia	11 (9%)	9 (7%)
Hypokalaemia	4 (3%)	3 (2%)

References

1 Wang-Gillam, A., C. P. Li, G. Bodoky, et al. 2016. "Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomised, open-label, phase 3 trial." Lancet 387(10018):545-557.

History

Version 2

Date	Summary of changes
28/04/2023	Treatment schedule note removed as there is no difference between the European and Australian labelling of irinotecan nanoliposomal. Version number increased to V.2.

Version 1

Date	Summary of changes
16/02/2018	New protocol discussed at Medical Oncology Reference Committee meeting
03/04/2018	Protocol approved and published on eviQ. Review in 1 year
22/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.
25/09/2018	Treatment schedule note and evidence section updated with Leucovorin® dosing information as per reference committee consensus.
20/05/2019	Protocol reviewed electronically by the Medical Oncology Reference Committee. No changes. Review 5 years

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https://www.eviq.org.au/p/3387
15 Jul 2023

Patient information - Irinotecan nanoliposomal, fluorouracil and leucovorin

Patient's name:

Your treatment

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

Irinotecan nanoliposomal, fluorouracil and leucovorin			
This treatment cycle is repeated every 14 days. Your doctor will advise you of the number of treatments you will have.			
Day	**Treatment**	**How it is given**	**How long it takes**
1	**Irinotecan nanoliposomal** (*eye-ri-noe-TEE-kan* na-no-lye-poe-soe-mal) **Calcium folinate (Leucovorin)** *(loo-koe-VOR-in)*	By a drip into a vein	About 2.5 hours
	Fluorouracil (*Flure-oh-YOOR-a-sill*)	Slowly through a pump into a vein	For 2 days (46 hours) by a pump at home
3	**Disconnect pump**		About 30 minutes

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 • leaking from your pump • you become unwell.	Daytime: Night/weekend: Other instructions:

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

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

Other information about your treatment

Changes to your dose or treatment delays

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

Blood tests and monitoring

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.

Pumps and central venous access devices (CVADs)

This treatment involves having chemotherapy through a pump. To have this, you will also need a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information see the eviQ patient information sheets on pumps and CVADs. At home you will need to look at your pump 3 to 4 times a day to check it is working. Your nurse will teach you how to do this.

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 will be given some medication called loperamide to treat the diarrhoea. See the *Side effects* section below for further information about diarrhoea and for instructions on how and when to take the loperamide.

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)	

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

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

Diarrhoea (early onset)	• You may get bowel motions (stools, poo) that are more frequent or more liquid (diarrhoea).
	• You may also get:
	  ◦ bloating, cramping or pain
	  ◦ increased saliva, a runny nose or watery eyes
	  ◦ sweating or flushing.
	• These symptoms are caused by the drug irinotecan. They can occur during or shortly after the drug has been given.
	• **Tell your doctor or nurse immediately if you develop any of these symptoms.**

Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

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.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Diarrhoea (late onset)	• You may get bowel motions (stools, poo) that are more frequent or more liquid (diarrhoea). • You may also get bloating, cramping or pain. • These symptoms are caused by the drug irinotecan. This can become very serious and life threatening if not treated quickly and properly. • Take your antidiarrhoea medication, loperamide, as prescribed: When the diarrhoea starts, take 4 mg (this is 2 tablets/capsules), then take one tablet/capsule (2 mg) every 2 hours during the day and 2 tablets/capsules (4 mg) every 4 hours at night while you still have diarrhoea and until the diarrhoea has stopped for 12 hours. You should not take loperamide at these doses for more than 48 hours. • 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 if you get any of the symptoms listed above.** • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have diarrhoea for more than 24 hours, any blood in your bowel motions, or a temperature of 38°C or higher.**

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.**
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.**
Eye problems	• You may get: ◦ eye pain ◦ red, sore or swollen eyes ◦ blurred vision ◦ watery or gritty eyes ◦ changes in your eyesight ◦ sensitivity to sunlight. • Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you have lost your eyelashes. • **Tell your doctor or nurse if you get any of the symptoms listed above. Eye drops may help with your symptoms.**
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.**

Skin that is more sensitive to the sun (photosensitivity)	• After being out in the sun you may develop a rash like a bad sunburn. • Your skin may become red, swollen and blistered. • Avoid direct sunlight. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin changes	• Your skin may become dry, and you may notice changes to areas of your skin that have been exposed to the sun. • Keep your skin moisturised with a cream such as sorbolene or aqueous cream. • Avoid direct sunlight. • Protect your skin from the sun by wearing a wide-brimmed hat, sun-protective clothing, sunglasses and sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you notice any skin changes.**

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)
Skin colour changes	• You may have darkening of your skin, especially in areas that are exposed to the sun. • You may also notice darkening of your tongue, gums and over your finger joints. • These skin changes may fade over time. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.
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.
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

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

Other medical and dental treatment

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

Diet

- 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

Pancreatic cancer information

- Australian Pancreatic Cancer Genome Initiative – pancreaticcancer.net.au
- Pancare foundation – pancare.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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