



Colorectal metastatic QUASAR (modified) fluorouracil and leucovorin weekly

ID: 98 v.4 Endorsed Essential Medicine List

▲ 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 <u>may</u> 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 <u>eviQ Estimated Glomerular Filtration Rate (eGFR) calculator</u>.

International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD)

Click here



Related pages:

2022

· Colorectal metastatic Roswell Park (modified) fluorouracil and leucovorin weekly

Treatment schedule - Overview

Cycle 1 and further cycles

Drug	Dose	Route	Day
Calcium folinate (Leucovorin)	50 mg *	IV bolus	1
Fluorouracil	370 mg/m ²	IV	1

^{*} This is a 'modified' QUASAR regimen as the dose of calcium folinate (Leucovorin®) in this protocol has been modified from the original clinical trial dose of either 175 mg/m 2 or 25 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: 7 days

Cycles: Continuous until disease progression or unacceptable toxicity

Drug status: All drugs in this protocol are on the PBS general schedule

Cost: ~ \$60 per cycle

Treatment schedule - Detail

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

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

Cycle 1 and further cycles

Day 1		
Metoclopramide	10 mg (P0)	one tablet when necessary (maximum of 30 mg/24 hours, up to 5 days)
Calcium folinate (Leucovorin)	50 mg (IV bolus)	over 1 to 2 minutes
Fluorouracil	370 mg/m ² (IV)	over 3 to 5 minutes

This is a 'modified' QUASAR regimen as the dose of calcium folinate (Leucovorin®) in this protocol has been modified from the original clinical trial dose of either 175 mg/m² or 25 mg/m² to 50 mg based on reference committee consensus. Refer to discussion on calcium folinate (Leucovorin®) and evidence section for more information.

Frequency: 7 days

Cycles: Continuous until disease progression or unacceptable toxicity

Indications and patient population

· Metastatic colorectal cancer.

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
Emetogenicity LOW	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. 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
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

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
Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea
Blood tests	FBC, EUC and LFTs at baseline and prior to each treatment. INR as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
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 dose reductions are calculated as a percentage of the starting dose.
- The dose of calcium folinate (Leucovorin®) remains fixed at 50 mg and is delayed or omitted if fluorouracil bolus is delayed or omitted.

Haematological toxicity

ANC x 10⁹/L (pre-treatment blood test)

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

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	Reduce fluorouracil by 25%
less than 30	Reduce fluorouracil by 50%

Hepatic impairment		
Hepatic dysfunction		
Mild	No dose modifications necessary	
Moderate	Reduce fluorouracil by 25%	
Severe	Reduce fluorouracil by 50%	

Mucositis and stomatitis		
Grade 2	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 fluorouracil by 25% 3rd occurrence: Reduce fluorouracil by 50% 4th occurrence: Omit fluorouracil	
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 fluorouracil by 50% 2nd occurrence: Omit fluorouracil	

<u>Diarrhoea</u>		
Grade 2	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 fluorouracil by 25% 3rd occurrence: Reduce fluorouracil by 50% 4th occurrence: Omit fluorouracil	
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: 1 st occurrence: Reduce fluorouracil by 50% 2 nd occurrence: Omit fluorouracil	

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

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

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

Day 1

Approximate treatment time: 30 minutes

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Ochemotherapy - Time out

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

• If using cryotherapy commence ~ 5 minutes prior to administering fluorouracil and continue for ~ 30 minutes post.

Administer fluorouracil (irritant):

- over 3 to 5 minutes
 - o via a minibag OR
 - by IV bolus via a side port of a freely flowing IV infusion
- flush with ~ 100 mL of sodium chloride 0.9%.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Discharge information

Antiemetics

· Antiemetics as prescribed.

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 day	ys)
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Cardiotoxicity	Coronary artery spasm is a temporary, sudden narrowing of one of the coronary arteries that may present at any time during treatment with fluoropyrimidines. It most commonly manifests as angina.
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
Diarrhoea	Read more about treatment induced diarrhoea
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
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
Fatigue	Read more about fatigue
Ocular changes	Symptoms may include eye pain, blurred vision, blepharitis, uveitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia.
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	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Hyperniamontation	Darkening of an area of skin caused by the overproduction of melanin.
Hyperpigmentation	
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.

Evidence

Due to the lack of conclusive evidence to identify the optimum dose of calcium folinate (Leucovorin®), it is the consensus of the eviQ reference committee to adopt flat dosing of calcium folinate (Leucovorin®) as a 50 mg IV bolus when used with bolus 5FU

Read more about nail toxicities

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.

Prior to the availability of irinotecan, oxaliplatin and bevacizumab, single agent weekly fluorouracil was the preferred treatment option for patients with metastatic colorectal cancer. Combination therapies which include fluorouracil have improved response rates and survival compared with weekly fluorouracil. For this reason, combination therapy is usually the treatment of choice for first line therapy in patients with good performance scores.

Capecitabine is an alternative to intravenous fluorouracil. Two trials have compared capecitabine with 5FU/Leucovorin (Mayo regimen) in first line metastatic setting. ^{1, 2} These studies showed higher response rates in capecitabine arms and no signficant difference in TTP, PFS and OS. There was less grade 3/4 stomatitis, neutropenia, diarrhoea, nausea and vomiting and more hand and foot syndrome in the capecitabine arms.

The weekly fluorouracil (5-FU) plus leucovorin QUASAR regimen, is sometimes used instead of the Roswell Park regimen. The highest level of evidence supporting the activity of weekly fluorouracil (5-FU) plus leucovorin (QUASAR) comes from studies conducted in the adjuvant setting.³ It is this evidence that is used to support the use of QUASAR in the metastatic setting.

Between May 1994 and October 1997, a total of 4927 patients were enrolled and randomly assigned to receive 5-FU 370 mg/m² and either high-dose (175 mg/m²) or low-dose (25 mg) folinic acid and either levamisole or placebo.

The schedule of administration was determined by the clinician as either a 5 days, every 4 weeks for 6 cycles or weekly for 30 weeks.

The primary end point of the study was all- cause mortality and secondary end points included death from colorectal cancer and recurrence.

Patel et al., 2004⁴

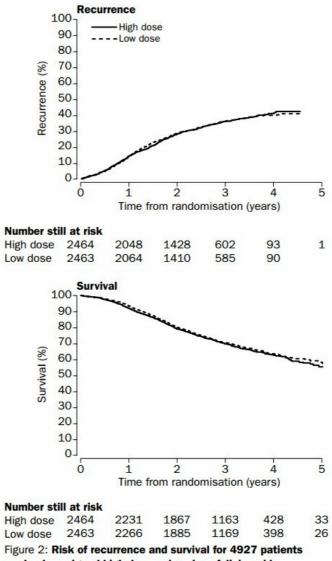
Patel et al., 2004 presented data for the use of a weekly fluorouracil (5-FU) and folinic acid (FA) regimen that was aimed to provide moderately dose-intense treatment with low toxicity.

Between November 1999 and February 2003, a total of 162 patients received weekly 5-FU 425 mg/m² with FA 45 mg for 24 weeks.

Efficacy

At 3 years, survival was similar with high-dose and low-dose folinic acid (70.1% versus 71%; p=0.43) as were recurrence rates (36% versus 35.8%; p=0.94).³

Risk of recurrence and survival for high-dose versus low-dose folinic acid³



randomly assigned high-dose or low-dose folinic acid

© Lancet 2000

Patel et al., (2004)4

Dose intensity (DI) was used to evaluate the efficacy of this weekly 5-FU/FA regimen. Median DI was 96% of planned (407 mg/m²/week) during treatment, and 91% of planned (385 mg/m²/week) over the full 24 week treatment plan. Compared to the QUASAR's 5-day monthly schedule, this weekly 5-FU/FA regimen was found to deliver a similar DI.

Toxicity

The toxicity data is summarised in the table below. The only significant difference in toxic effects seen between the high-dose and low-dose folinic acid groups was stomatitis. There was only 0.1% treatment related mortality seen, showing that the QUASAR regimens were safe.3

Numbers of toxic events reported by treatment³

	Folinic-acid dose comparison			Levamisole comparison		
	High-dose	Low-dose	Odds ratio (95% CI)	Levamisole	Placebo	Odds ratio (95% CI)
Diarrhoea	362	338	1.08 (0.92–1.27)	337	356	0.93 (0.80-1.10)
Stomatitis	216	158	1.40* (1.13-1.74)	181	191	0.95 (0.77-1.17)
Vomiting/nausea	169	150	1.14 (0.91-1.43)	173	143	1.23 (0.98-1.55)
Any haematological	111	116	0.95 (0.73-1.25)	109	117	0.93 (0.71-1.22)
Dermatological	95	79	1.21 (0.89-1.64)	110	63	1.79† (1.30-2.45)
Cardiovascular	42	37	1.14 (0.73-1.78)	39	40	0.98 (0.63-1.52)
Neurological	22	22	1.00 (0.55-1.81)	25	19	1.32 (0.73-2.41)
Other or unspecified	327	285	1.17 (0.99-1.39)	325	283	1.17 (0.99-1.39)
Any fluorouracil dose reduction	33%	30%	1.14 (0.99-1.30)	32%	31%	1.06 (0.92-1.21)
Completion of chemotherapy	69%	70%	0.99 (0.93-1.06)	68%	70%	0.96 (0.90-1.03)
Completion of levamisole	67%	68%	0.95 (0.83-1.09)	65%	70%	0.77* (0.68-0.89)

p>0.05 for all comparisons except: *p=0.002; †p<0.0001.

Table 2: Numbers of toxic events reported by treatment

Patel et al., 2004⁴

Treatment was generally well-tolerated, with only 20% patients experiencing any toxicity greater or equal to grade 3 and only 2% experiencing any grade 4 toxicity. Most common was diarrhoea, which occurred in 14% of patients.

Maximum toxicities per patient4

Table 2. Maximum toxicities per patient (National Cancer Institute common toxicity criteria version 2.0) (n = 162 patients)

	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)
Diarrhoea	36	12	12	2
Mucositis	17	1	_	-
Lethargy	45	32	7	100
Nausea	44	12	2	-
Hand-foot	28	9	2	100
Watery eyes	28	5	2	-
Leucocytes	6	1	1	100
Granulocytes	3	16	1	-
Platelets	10	1	-	_

© Annals of Oncology 2004

Dose reductions were made in 35% of patients (although only 21 % required 20 % or more reduction); and a decision to stop treatment before 24 weeks because of toxicity was 16 % of patients.

References

- 1 Cassidy, J., C. Twelves, E. Van Cutsem, et al. 2002. "First-line oral capecitabine therapy in metastatic colorectal cancer: a favorable safety profile compared with intravenous 5-fluorouracil/leucovorin." Ann.Oncol 13(4):566-575.
- Van Cutsem, E., C. Twelves, J. Cassidy, et al. 2001. "Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study." J Clin Oncol 19(21):4097-4106.
- **3** QUASAR Collaborative Group. 2000. "Comparison of flourouracil with additional levamisole, higher-dose folinic acid, or both, as adjuvant chemotherapy for colorectal cancer: a randomised trial." Lancet. 355(9215):1588-1596
- 4 Patel, K., D. A. Anthoney, et al. 2004. "Weekly 5-fluorouracil and leucovorin: achieving lower toxicity with higher dose-intensity in adjuvant chemotherapy after colorectal cancer resection." Ann.Oncol 15(4): 568-573.

History

Version 4

Date	Summary of changes
01/05/2007	Patient information updated.
03/12/2007	BWI information and hepatitis screening added.
25/08/2009	Review and transferred to eviQ.
01/07/2010	Haematological dose modifications updated (20% changed to 25% dose reduction).

Date 25/01/2011	New format to allow for export of protocol information. Protocol version number changed to <i>V.2</i> . Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.
04/04/2012	Protocol reviewed at reference committee meeting 25/11/11. "QUASAR Modified" added to the title. This was done to distiguish this weekly fluorouracil and leucovorin protocol with the Roswell Park regimen (ID 1275) has been created. (link to Roswell Park protocol). The dose of 5FU changed (was 400 mg/m²) to reflect the dose that was used in the orginal QUASAR trial.
04/04/2012	PHC OMIS view updated.
13/09/2013	Protocol reviewed at medical oncology reference committee. Group consensus not to supersede as protocol is still being used. No changes and next review in 2 years.
25/08/2014	PHC view removed.
18/02/2016	Discussion with medical oncology reference committee Chairs and protocol to be reviewed every 5 years. Next review due in 3 years.
16/10/2016	Patient information sheet updated to include more fluorouracil toxicity symptom warnings.
09/11/2016	The following changes made post medical oncology reference committee meeting held on 21 October 2016. Link to AGTIG and ANZCTR added. Sentence in dose modifications regarding omitting leucovorin if fluorouracil is delayed or omitted changed to specify fluorouracil bolus.
31/05/2017	Transferred to new eviQ website. Version number change to V.3. Hepatitis screening changed to not required.
16/02/2018	Protocol reviewed electronically by medical oncology reference committee. Fluoropyrimidine warning added. Review in 5 years.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.4.
25/09/2018	Treatment schedule note and evidence section updated with Leucovorin® dosing information as per reference committee consensus.
20/10/2022	Protocol reviewed electronically by Medical Oncology Reference Committee. No changes. Next review 4 years.

The information contained in this protocol is based on the highest level of available evidence and consensus of the eviQ reference committee regarding their views of currently accepted approaches to treatment. Any clinician (medical oncologist, haematologist, radiation oncologist, medical physicist, radiation therapist, pharmacist or nurse) seeking to apply or consult this protocol is expected to use independent clinical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use is subject to eviQ's disclaimer available at www.eviQ.org.au

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https://www.eviq.org.au/p/98

16 Jul 2023

NSW COVERNMENT COVERNMENT

Patient information - Bowel cancer metastatic - QUASAR modified (fluorouracil and leucovorin)

Patient's name:

Your treatment

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

QUASAR modified (fluorouracil and leucovorin)					
This treat	This treatment cycle is repeated every 7 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	Calcium folinate (Leucovorin) (loo-koe-VOR-in) Fluorouracil (flure-oh-YOOR-a-sill)	By a drip into a vein	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 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. Tell your doctor if you are on an anticoagulant (medication used to treat or prevent blood clots) e.g. warfarin. You may need to have additional 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 da	ays)
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.
Heart problems	 You may get: chest pain or tightness shortness of breath an abnormal heartbeat Tell your doctor if you have a history of heart problems or high blood pressure. Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.
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
 - o 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.

Diarrhoea

- You may get bowel motions (stools, poo) that are more frequent or more liquid.
- You may also get bloating, cramping or pain.
- Take your antidiarrhoeal medication as directed by your doctor.
- Drink plenty of fluids (unless you are fluid restricted).
- · Eat and drink small amounts more often.
- Avoid spicy foods, dairy products, high fibre foods, and coffee.
- Ask your doctor or nurse for eviQ patient information Diarrhoea during cancer treatment.
- Tell your doctor or nurse immediately, or go to your nearest hospital Emergency
 Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions
 per day, and if you feel dizzy or light-headed.

Mouth pain and soreness (mucositis)

- You may have:
 - bleeding gums
 - mouth ulcers
 - o a white coating on your tongue
 - o 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:
 - o 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.

Hand-foot syndrome (palmar-plantar erythrodysaesthesia)

- The palms of your hands and soles of your feet may become:
 - o red and hot
 - swollen
 - o painful and tender
 - o 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.

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.

Eye problems

- · You may get:
 - eye pain
 - red, sore or swollen eyes
 - blurred vision
 - watery or gritty eyes
 - o 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.

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

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.
- 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

Bowel cancer information

- Australian Council of Stoma Associations australianstoma.com.au
- Australian Government Bladder and Bowel bladderbowel.gov.au
- Australian Government Department of Health & Ageing Stoma appliance scheme health.gov.au/internet/main/publishing.nsf/Content/Stoma+Appliance+Scheme-1
- Bowel Cancer Australia bowelcanceraustralia.org
- National Public Toilet map toiletmap.gov.au
- Recovering after Pelvic Radiation Therapy: A guide for women https://www.targetingcancer.com.au/useful-resources/recovering-after-pelvic-radiation-therapy-a-guide-for-women/

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

Additional notes:	

This document is a guide only and cannot cover every possible situation. The health professionals caring for you should always consider your individual situation when making decisions about your care. Contact your cancer clinic staff or doctor if you have any questions or concerns about your treatment, or you are having problems coping with side effects. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use of this document is subject to eviQ's disclaimer available at www.eviQ.org.au

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