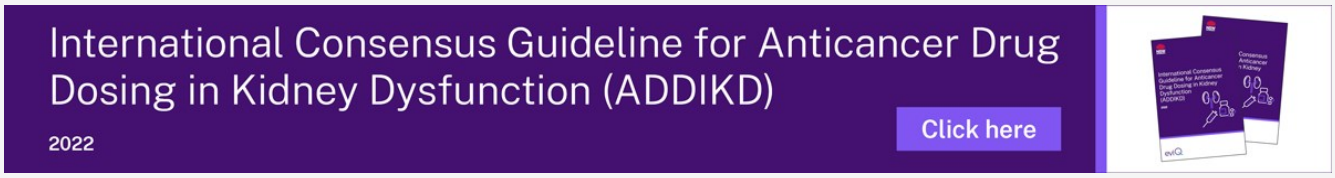
Renal cell metastatic soRAFENib

ID: 323 v.4 **Endorsed**

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

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



Treatment schedule - Overview

Drug	Dose	Route
soRAFENib	400 mg TWICE a day	PO

Continuous until disease progression or unacceptable toxicity

Drug status: **Sorafenib** is PBS authority

Sorafenib is available as **200mg** tablets

Cost: ~ $5,150 per month

Treatment schedule - Detail

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

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

Continuous treatment		
soRAFENib	400 mg (PO)	TWICE a day on an empty stomach one hour before food or two hours after food

Continuous until disease progression or unacceptable toxicity

Indications and patient population

- Advanced renal cell carcinoma (RCC) (both clear cell and papillary cell) after failure of one prior systemic therapy

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Emetogenicity minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cardiac toxicity	Tyrosine kinase inhibitors have been associated with cardiac complications of varying degrees and severity. Patients, especially those with pre-existing cardiovascular disease, should have a baseline cardiac assessment including an electrocardiogram (ECG) and biochemistry and be closely monitored; consider an echocardiogram (ECHO) as clinically indicated. Cardiac assessment should then be repeated as clinically indicated or when starting new medication which affects the QT interval. Read more about cardiac toxicity associated with anti-cancer drugs
Prolongation of QT interval	This treatment may prolong the QT interval and increase the risk of cardiac arrhythmia. Use with caution in patients with a congenital long QT syndrome, patients treated with a high cumulative dose of anthracycline therapy, patients taking medications that may prolong the QT interval and those with electrolyte disturbances. Risk factors (e.g. electrolyte abnormalities) should be corrected, where possible, prior to commencement of treatment and the concurrent use of drugs that may prolong the QT interval should be avoided. Baseline and periodic monitoring of electrocardiogram (ECG) and electrolytes (potassium, magnesium, calcium) should be considered in patients at high risk of QT prolongation. Read more about drugs that may prolong QTc interval at crediblemeds.org (registration required).
Hypertension	Pre-existing hypertension should be adequately controlled prior to commencing treatment. Baseline blood pressure monitoring and repeated weekly for the first 6 weeks then regularly throughout treatment. In severe or uncontrolled hypertension, treatment should be withheld until hypertension is controlled. Dose modification or permanent discontinuation may be necessary - refer to dose modification section for specific recommendations.
Elevations in lipase and amylase	Transient elevations of lipase and amylase have been reported. In some cases, this has been associated with pancreatitis. Monitor patient as clinically indicated.
Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea
Hand-foot syndrome	Hand-foot syndrome (palmar-plantar erythrodysaesthesia) and rash are common adverse effects with this treatment which generally appear during the first 6 weeks of therapy. Read more about hand food syndrome or palmar plantar erythrodysaesthesia (PPE)
Wound healing	Some suggest (Bose et al. 2010- see link to abstract) that antiangiogenic tyrosine kinase inhibitors (TKI's) be interrupted for at least one week (48 hours for agents with short half life) before surgery and not re-initiated until adequate wound healing has occurred. At many institutions, therapy with these agents is held for four weeks after major surgery and for at least two weeks after minor surgery, although there are no prospective data validating this approach. The decision to resume therapy following a major surgical intervention should be based upon clinical judgement of recovery from surgery. Read more about "Vascular endothelial growth factor targeted therapy in the perioperative setting: implications for patient care", Bose et al 2010[1]
Blood tests	FBC, EUC, LFTs, calcium, magnesium and phosphate at baseline, repeat at week 2, then every 4 weeks. INR as clinically indicated.

Hepatitis B screening and prophylaxis	The requirement for routine screening for HBsAg and anti-HBc for patients receiving this treatment is unknown. Clinical judgement and individual patient situations should be taken into consideration. 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:

- the following dose modification recommendations have been adapted from the study Escudier[2] and by consensus of the reference committee.

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
0.5 to less than 1.0	Delay treatment until recovery
less than 0.5	Delay treatment until recovery and consider reducing sorafenib to 200 mg TWICE daily for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing sorafenib to 200 mg TWICE daily for subsequent cycles
Platelets x 10^9/L (pre-treatment blood test)	
10 to less than 100	Delay treatment until recovery

Haematological toxicity	
less than 10	Delay treatment until recovery and consider reducing sorafenib to 200 mg TWICE daily for subsequent cycles

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	Consider starting sorafenib at 200 mg TWICE daily and dose escalate as tolerated * (Monitoring of fluid balance and electrolytes in patients at risk of renal dysfunction is recommended)
less than 30	No recommendations available; use with caution

Hepatic impairment	
Hepatic dysfunction	
Mild	No dose modification necessary
Moderate	Consider starting sorafenib at 200 mg TWICE daily and dose escalate as tolerated *
Severe	Omit sorafenib

Mucositis and stomatitis	
Grade 3	Delay treatment until toxicity has resolved to Grade 2 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce sorafenib to 200 mg TWICE daily 2nd occurrence: Reduce sorafenib to 200 mg ONCE daily 3rd occurrence: Omit sorafenib
Grade 4	Omit sorafenib

Diarrhoea	
Grade 3	Delay treatment until toxicity has resolved to Grade 2 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce sorafenib to 200 mg TWICE daily 2nd occurrence: Reduce sorafenib to 200 mg ONCE daily 3rd occurrence: Omit sorafenib
Grade 4	Omit sorafenib

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 follow: 1st occurrence: No dose reduction 2nd occurrence: Reduce sorafenib to 200 mg TWICE daily 3rd occurrence: Reduce sorafenib to 200 mg ONCE daily 4th occurrence: Omit sorafenib
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follow: 1st occurrence: Reduce sorafenib to 200 mg TWICE daily 2nd occurrence: Reduce sorafenib to 200 mg ONCE daily 3rd occurrence: Omit sorafenib

** These recommendations have been adapted from the study by Miller et al[3] .*

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*

Sorafenib		
	Interaction	**Clinical management**
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of sorafenib possible due to increased clearance	Avoid combination or monitor for decreased clinical response to sorafenib
Drugs that may prolong the QTc interval (e.g. azole antifungals, tricyclic antidepressants, antiarrhythmics etc.)	Additive effect with sorafenib; may lead to torsades de pointes and cardiac arrest	Avoid combination or minimise additional risk factors (e.g. correct electrolyte imbalances) and monitor ECG for signs of cardiac arrhythmia
Paracetamol	Risk of liver toxicity due to inhibition of metabolism of paracetamol by sorafenib	Avoid combination or monitor liver function closely
Neomycin	Reduced efficacy of sorafenib possible due to increased clearance (neomycin interferes with enterohepatic recycling of sorafenib)	Avoid combination or monitor for decreased clinical response to sorafenib

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

Administration

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

product information monographs via the TGA website for further information.

Administration

This is a continuous oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each treatment.

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

Treatment - Time out

Sorafenib

- administer orally TWICE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken on an empty stomach, one hour before or two hours after food
- monitor blood pressure at baseline and regularly throughout treatment.

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

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

Discharge information

Sorafenib tablets

- Sorafenib tablets with written instructions on how to take them.

Antidiarrhoeals

- Antidiarrhoeals as prescribed.

Patient information

- Ensure patient receives patient information sheet.

Side effects

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

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

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Diarrhoea	Read more about treatment induced diarrhoea
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Fatigue	Read more about fatigue
Palmar-plantar erythrodysaesthesia (PPE) - hand-foot syndrome (HFS)	Bilateral erythema, tenderness, pain, swelling, tingling, numbness, pruritus, dry rash, or moist desquamation and ulceration of the palms and soles. It is also known as hand-foot syndrome (HFS). Symptoms appear to be dose dependent and palms are affected more than soles. Read more about hand-foot syndrome associated with chemotherapy
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Hypertension	High blood pressure is commonly associated with many anti-cancer drugs. Pre-existing hypertension should be controlled prior to initiation of drugs capable of causing hypertension.
Haemorrhage	
Cardiotoxicity	Cardiotoxicity may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, hypertension, cardiac ischaemia and congestive heart failure (CHF). The risk of cardiotoxicity is increased by a number of factors, particularly a history of heart disease and electrolyte imbalances. Read more about cardiotoxicity associated with anti-cancer drugs

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

Evidence

The evidence supporting this regimen comes from a phase III randomised controlled trial *(TARGET)* of sorafenib in patients with

advanced clear-cell renal cell carcinoma who had received one prior systemic therapy. 903 patients who had received one prior systemic therapy were randomised to receive either 400 mg sorafenib or placebo twice a day. The primary end point was overall survival. Progression-free survival (single, planned analysis after 363 progressions), best response (RECIST criteria), health-related quality of life (HRQOL), symptom response and adverse events were evaluated as well.[2]

The AXIS trial demonstrated superiority of axitinib in the second line setting for metastatic renal cell carcinoma for progression free survival, there was no difference in overall survival or patient reported outcomes. Median progression free survival was 6.7 months (95% CI 6.3-8.6) with axitinib and 4.7 months (95% CI 4.6-5.6) with sorafenib (HR 0.665, 95% CI 0.544-0.812; p<0.0001).[4]

The INTORSECT trial demonstrated no statistically significant progression free survival advantage for temsirolimus compared with sorafenib (4.3 vs 3.9 months respectively P=0.19) or overall response rate following first line sunitinib. The difference in overall survival advantage was significant in favour of sorafenib (stratified HR 1.31; 95% CI 1.05 to 1.63 two sided P=0.01). Median overall survival in the temsirolimus and sorafenib arms was 12.3 and 16.6 months respectively.[5]

Efficacy

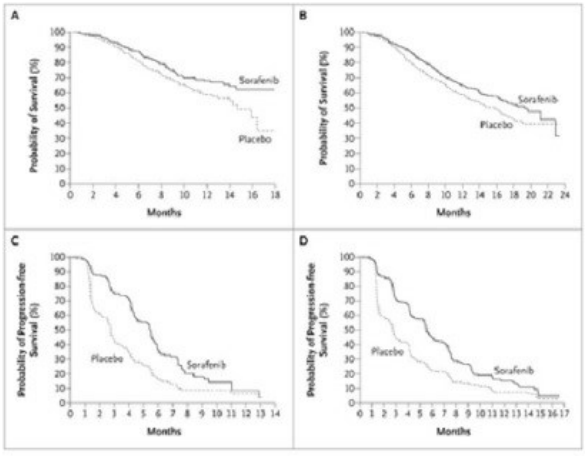
A planned interim analysis on 769 patients was reported. The median overall survival based on 220 deaths revealed a positive trend for the sorafenib group (>18 months), compared to the placebo (14.7 months) with a hazard ratio of 0.72. However, this difference did not reach statistical significance as the threshold for this analysis had been set to a level of 0.0005 (Fleming O'Brian design). In April 2005, 216 of 452 patients (48%) on placebo were crossed over to sorafenib after a positive PFS analysis, which may affect overall survival results.[2]

Median progression-free survival in the sorafenib group doubled against placebo (24 weeks vs 12 weeks, HR 0.44) at 3 months post-randomisation. A statistically significant improvement of patient well being reported by the FACT-G and FACT-KSI-10 scores was seen for sorafenib.[2]

Escudier[2]	Sorafenib (n=384)	Placebo (n=385)	Hazard ratio *p*-value
Median overall survival based on 220 deaths	greater than 18 months	15 months	0.72 (p=0.018)*
Median progression-free survival	24 weeks	12 weeks	0.44(p<0.000001)
Progression free at 3 months post-randomisation	288/384 (75%)	166/385 (43%)	NR
Confirmed partial response (RECIST)	7%	0%	NR

** this difference did not reach statistical significance as the thresh hold for this analysis had been set to a level of 0.0005 (Fleming O'Brien design)*

Kaplan-Meier Analysis of Overall Survival and Progression-free Survival:[2]



Panel A: overall survival among 903 patients in May 2005 when patients receiving placebo were allowed to switch to sorafenib
Panel B: shows the probability of overall survival among the same patients in November 2005
Panel C: shows the probability of progression-free survival among 769 patients in January 2005 (P<0.001)
Panel D: shows the probability of progression-free survival among all 903 patients, according to a review by investigators in May 2005 (P<0.001).

In the final analyses, the OS of patients receiving sorafenib was comparable with that of patients receiving placebo (17.8 vs 15.2 months respectively; HR=0.88; p=0.146); however, when post-cross-over placebo survival data were censored, the difference became significant (17.8 vs 14.3 months respectively; HR=0.78; p=0.029).[6]

Toxicity

Table 3. Adverse Events.*

Adverse Event	Sorafenib (N=451)			Placebo (N=451)			P Value (Grade 3 or 4)†	P Value (Grade 2)‡
	Any Grade	Grade 2	Grade 3 or 4	Any grade	Grade 2	Grade 3 or 4		
	number (percent)							
Cardiac — hypertension§	76 (17)	44 (10)	16 (4)	8 (2)	3 (<1)	2 (<1)	0.001	<0.001
Hematologic — decreased hemoglobin	34 (8)	14 (3)	12 (3)	33 (7)	8 (2)	20 (4)	0.21	0.28
Constitutional								
Fatigue	165 (37)	54 (12)	22 (5)	125 (28)	39 (9)	16 (4)	0.41	0.12
Other symptoms	46 (10)	9 (2)	6 (1)	27 (6)	8 (2)	6 (1)	1.00	1.00
Weight loss	46 (10)	23 (5)	3 (<1)	25 (6)	8 (2)	0	0.25	0.009
Gastrointestinal								
Diarrhea	195 (43)	56 (12)	11 (2)	58 (13)	13 (3)	3 (1)	0.06	<0.001
Nausea	102 (23)	27 (6)	3 (<1)	87 (19)	21 (5)	3 (1)	1.00	0.46
Anorexia	73 (16)	24 (5)	3 (<1)	57 (13)	16 (4)	5 (1)	0.73	0.26
Vomiting	73 (16)	25 (6)	4 (1)	53 (12)	20 (4)	6 (1)	0.76	0.54
Constipation	68 (15)	22 (5)	3 (1)	49 (11)	19 (4)	3 (1)	1.00	0.75
Neurologic — sensory neuropathy	59 (13)	13 (3)	2 (<1)	29 (6)	4 (1)	3 (1)	1.00	0.05
Pain								
Abdominal	49 (11)	22 (5)	7 (2)	41 (9)	16 (4)	9 (2)	0.80	0.41
Headache	47 (10)	18 (4)	1 (<1)	27 (6)	7 (2)	2 (<1)	1.00	0.04
Joint	45 (10)	13 (3)	7 (2)	29 (6)	14 (3)	1 (<1)	0.07	1.00
Bone	34 (8)	18 (4)	3 (1)	35 (8)	12 (3)	15 (3)	0.007	0.35
Tumor	29 (6)	9 (2)	13 (3)	24 (5)	11 (2)	8 (2)	0.38	0.82
Pulmonary								
Cough	60 (13)	21 (5)	1 (<1)	64 (14)	19 (4)	1 (<1)	1.00	0.87
Dyspnea	65 (14)	25 (6)	16 (4)	52 (12)	18 (4)	11 (2)	0.44	0.35
Dermatologic								
Rash or desquamation	180 (40)	59 (13)	4 (1)	70 (16)	9 (2)	1 (<1)	0.37	<0.001
Hand–foot skin reaction	134 (30)	55 (12)	25 (6)	30 (7)	5 (1)	0	<0.001	<0.001
Alopecia	122 (27)	17 (4)	1 (<1)	15 (3)	2 (<1)	0	1.00	<0.001
Pruritus	85 (19)	21 (5)	1 (<1)	29 (6)	2 (<1)	0	1.00	<0.001

* Listed are adverse events of any grade occurring in at least 10% of patients (with a breakdown of grade 2 events) and adverse events of grade 3 or 4 occurring in at least 2% of patients.
† P values are for the comparison between the sorafenib group and the placebo group with respect to grade 3 or 4 adverse events.
‡ P values are for the comparison between the sorafenib group and the placebo group with respect to grade 2 adverse events.
§ Cardiac ischemia or infarction occurred in 12 patients (3%) in the sorafenib group and 2 patients (<1%) in the placebo group (P=0.01).

References

1. Bose, D., F. Meric-Bernstam, W. Hofstetter, et al. 2010. "Vascular endothelial growth factor targeted therapy in the perioperative setting: implications for patient care." Lancet Oncol 11(4):373-382.
2. Escudier, B., T. Eisen, W. M. Stadler, et al. 2007. "Sorafenib in advanced clear-cell renal-cell carcinoma." N Engl J Med 356(2):125-134.
3. Miller, A. A., D. J. Murry, K. Owzar, et al. 2009. "Phase I and pharmacokinetic study of sorafenib in patients with hepatic or renal dysfunction: CALGB 60301." J Clin Oncol 27(11):1800-1805.
4. Rini, B. I., B. Escudier, P. Tomczak, et al. 2011. "Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial." Lancet 378(9807):1931-1939.
5. Hutson, T., Escudier, B. & Esteban, E. 2014. "Randomized Phase III Trial of Temsirolimus Versus Sorafenib As Second-Line Therapy After Sunitinib in Patients With Metastatic Renal Cell Carcinoma." J Clin Oncol 32(8);760-7.
6. Escudier, Bernard, Tim Eisen, Walter M. Stadler, et al. 2009. "Sorafenib for Treatment of Renal Cell Carcinoma: Final Efficacy and Safety Results of the Phase III Treatment Approaches in Renal Cancer Global Evaluation Trial." J Clin Oncol 27(20):3312-3318.

Bibliography

Ratain, M. J., T. Eisen, W. M. Stadler, et al. 2006. "Phase II placebo-controlled randomized discontinuation trial of sorafenib in patients with metastatic renal cell carcinoma." J Clin Oncol. 24(16):2505-2512.

History

Version 4

Date	Summary of changes
17/02/2010	Review, new dose modifications and transferred to eviQ.
01/09/2010	Administration of tablets with reference to a fatty meal was considered confusing and updated to a general statement "taken on an empty stomach, at least 1 hour before or 2 hours after the meal".
21/07/2011	New format to allow for export of protocol information. Protocol version number changed to *V.2.* 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.
12/01/2012	PHC view updated.
30/11/2012	Protocol reviewed at Medical Oncology Reference Committee meeting. No changes and next review in 1 year.
09/05/2014	Protocol reviewed at Medical Oncology Reference Committee meeting. Evidence updated, PHC view removed. Review 2 years.
27/03/2015	Protocol reviewed at Medical Oncology Reference Committee meeting. Wound healing pre clin updated. PBS status updated.
31/03/2017	Protocol discussed and decided to have a 5 year review period. Next due for review in 2019.
31/05/2017	Transferred to new eviQ website. Protocol version number changed to V.3. Hepatitis screening changed to unknown.
27/03/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 15/03/2019. Patient information updated- your treatment and when to get help changed to less chemotherapy focused information. Version number changed to V.4. Next review in 5 years.
09/11/2021	Patient information title changed to "Kidney cancer advanced or metastatic".
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.
18/05/2022	Prolongation of QT interval clinical information block added.

First approved: 19 December 2006
Last reviewed: 15 March 2019
Review due: 30 June 2024

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/323
19 Jun 2023

Patient information - Kidney cancer advanced or metastatic - Sorafenib

Patient's name:

Your treatment

It is important to understand that sorafenib is not a traditional chemotherapy drug and has a different way of working. It works by targeting the cancer cells to stop them growing and spreading. The treatment schedule below explains how the drug for this treatment is given.

Sorafenib		
This treatment is continuous. Your doctor will advise you how long to take the treatment for.		
Day	**Treatment**	**How it is given**
Continuous	**Sorafenib** (*soe-RAF-e-nib)*	Take orally TWICE a day on an empty stomach, at least one hour before or two hours after food. Swallow whole with a glass of water, do not break, crush or chew. If you forget to take a dose or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.

When to get help

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

Emergency contact details

Ask your doctor or nurse from your treating team when you should get help and who to contact if you have a problem

Daytime: .....

Night/weekend: .....

Other instructions: .....

.....

.....

Other information about your treatment

Changes to your dose or treatment delays

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

delays to your treatment and the reason why.

Blood tests and monitoring

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

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Mouth pain and soreness (mucositis)	• You may have: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
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.
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.
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.**

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 rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

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

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

General advice for people having cancer treatment

Blood clot risk

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

Medications and vaccinations

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

Other medical and dental treatment

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

Diet

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- 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

Kidney cancer information

- Kidney Cancer Association – kidneycancer.org/
- Kidney Health Australia – kidney.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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The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/pi/323
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