Chemotherapy Protocol

RENAL CELL

SUNITINIB

Regimen

- Renal Cell - Sunitinib

Indication

- First line treatment of advanced or metastatic renal cell carcinoma
- WHO Performance status 0, 1
- Palliative intent

Toxicity

Drug	Adverse Effect
Sunitinib	Cardiac failure, hypertension, hypothyroidism, fatigue, skin/hair colour changes, palmar-plantar erythrodysaesthesia, diarrhoea, taste disturbances, oedema, epistaxis, mucositis

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBCs, LFTs and U&Es prior to each cycle for the first three cycles, this may reduce to every other cycle if stable
- Blood pressure weekly for the first 4 weeks then every 6 - 12 weeks
- Thyroid function tests at baseline then every 3 months.
- Ensure adequate cardiac function before starting therapy. Baseline LVEF should be measured in patients with a history of cardiac problems or in the elderly. Repeat every three to six months as clinically indicated.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

For sunitinib dose modifications should occur in 12.5mg steps and are applied based on individual safety and tolerability. Daily dose should not be decreased below 25mg.

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Prior to cycle 1 the following criteria should be met;

Criteria	**Eligible Level**
Neutrophil	$1x10^9$/L
Platelets	$75x10^9$/L

Thereafter;

Neutrophils ($x10^9$/L)	**Dose Modifications**
1 or greater	100%
less than 1	Delay until recovery to $1x10^9$/L or greater. If recovery occurs within 7 days then continue with the last dose dose. If the recovery takes longer than 7 days then reduce dose by 12.5mg.
Platelets ($x10^9$/L)	**Dose Modifications**
75 or greater	100%
Less than 75	Delay until recovery to $75x10^9$/L or greater. If the recovery occurs within 7 days then continue with full dose. If recovery takes longer than 7 days then reduce the dose by 12.5mg.

Hepatic Impairment

Drug	**Child Pugh Class**	**Dose**
Sunitinib	A	50mg daily
	B	50mg daily
	C	No information

There is no information on dosing in patients with an AST or ALT greater than 2.5xULN (or more than 5xULN with liver metastases) as these patients were excluded from clinical trials.

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Sunitinib	N/A	No dose modification required

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Cardiovascular

Hypertension should be treated initially as per the NICE guidelines[(1)]. For persistently high blood pressure of more than 140/90mmHg despite standard hypertensive therapy, reduce the sunitinib dose in 12.5mg steps and continue to monitor. If hypertension persists discontinue the sunitinib.

Gastro-intestinal

Diarrhoea is a frequent complication of sunitinib therapy. Patients should be advised to limit consumption of high fibre or spicy foods, caffeine, alcohol and dairy products. Laxatives should be avoided. For a NCI-CTC grade 1 or 2 diarrhoea continue treatment at the same dose and attempt dietary and dehydration management. Anti-diarrhoeal medicines, such as loperamide, may be necessary. For a NCI-CTC grade 3 adverse reaction reduce the dose by 12.5mg. For a NCI-CTC grade 4 adverse reaction stop the sunitinib until it resolves to at least NCI-CTC grade 2. Treatment may be re-started with a 12.5mg dose reduction in the first instance.

Endocrine

Hypothyroidism can occur and should be managed according to standard medical practice. There is no need to discontinue or dose reduce the sunitinib.

Skin

Palmar-plantar erythrodysaesthesia can occur. Patients should be advised to apply moisturiser to their hands and feet regularly throughout treatment, and to minimise activities that put pressure on feet or hands. Refer to a chiropodist if appropriate.

A NCI-CTC grade 1 reaction should be treated symptomatically. There is no need to interrupt therapy with sunitinib or reduce the dose. For a NCI-CTC grade 2 effect delay treatment with sunitinib until it resolves to at least NCI-CTC grade 1. The sunitinib may be re-started with a 12.5mg dose reduction. The development of palmar-plantar erythrodysaesthesia at NCI-CTC grade 3 should result in treatment being delayed until it resolves to NCI-CTC grade 1. The sunitinib can be re-started with a 12.5 – 25mg dose reduction.

Regimen

42 day cycle until disease progression or unacceptable toxicity occurs (8 cycles will be set in ARIA)

Drug	Dose	Days	Administration
Sunitinib	50mg	1-28 incl.	Oral

Dose Information

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

Additional Therapy

- Mouthwashes according to local or national policy on the treatment of mucositis
- Loperamide 4mg oral after the first loose stool then 2-4mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours).

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to sunitinib.
- It must be made clear to all staff, including those in the community, that sunitinib should only be prescribed under the supervision of an oncologist.

Coding (OPCS)

- Procurement – X71.5
- Delivery – X73.1

References
1. National Institute of Health and Clinical Excellence 2009. Technology Appraisal 169. Sunitinib for the first line treatment of advanced or metastatic renal cell carcinoma.
2.Motzer RJ, Hutson TE, Tomczak P et al. Overall Survival and Updated Results for Sunitinib Compared With Interferon Alfa in Patients With Metastatic Renal Cell Carcinoma. J Clin Oncol 2009; 27: 3584-90.
3.Motzer RJ, Hutson TE, Tomczak P et al. Sunitinib versus Interferon Alfa in Metastatic Renal Cell Carcinoma. N Engl J Med 2007; 356: 115-124.

REGIMEN SUMMARY

Sunitinib

Day One

Take Home Medicines

1. Sunitinib 50mg once a day for 28 days (followed by a 14 day rest period) oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	April 2016	Header changed Mucositis recommendation changed Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Jan 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Joanna Gale Consultant Medical Oncologist Dr Mathew Wheater Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.