Sunitinib

Indication
First line treatment of patients with advanced and/or metastatic renal cell carcinoma

Advanced/Inoperable gastrointestinal tumour after failure of first line treatment or intolerance

Regimen details
Sunitinib 50mg once daily for 4 weeks

Cycle frequency
Every six weeks (i.e. “Four weeks on, two weeks off”)

Number of cycles
Until disease progression

Administration
If a dose is missed or the patient vomits after taking their dose, the patient should not be given an additional dose. The patient should take the usual prescribed dose on the following day.

Pre-medication
None

Emetogenicity
No routine antiemetics required

Additional supportive medication
Nil

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
TFTs	14 days
Blood pressure	14 days
Urinalysis for proteinuria	14 days

ECG if patient has significant cardiac history

Blood pressure must be well controlled before initiating treatment with sunitinib

The use of vascular endothelial growth factor (VEGF) pathway inhibitors in patients with or without hypertension may promote the formation of aneurysms and/or artery dissections. Before initiating sunitinib, this risk should be carefully considered in patients with risk factors such as hypertension or history of aneurysm

Temporary interruption of sunitinib therapy is recommended for precautionary reasons in patients undergoing major

surgical procedures. There is limited clinical experience regarding the timing of reinitiation of therapy following major surgical intervention. Therefore, the decision to resume sunitinib therapy following a major surgical intervention should be based upon clinical judgment of recovery from surgery

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)
TFTs every 12 weeks
Blood pressure weekly for the first cycle then prior to each cycle
ECG if clinically indicated

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 50 x 10^9/L
Creatinine clearance	≥ 30 mL/min
AST/ALT	≤ 1.5 x ULN (or <5 x ULN if liver metastases)

Dose modifications

Haematological toxicity

Toxicity	**Definition**	**Dose adjustment**
Neutropenia	Neutrophils 0.5-0.9 x 10^9 /L	Delay until ≥ 1.0 x 10^9 /L then continue at same dose (repeated occurrence – consider reducing dose by 12.5mg)
	Neutrophils < 10 x 10^9 /L	Delay until ≥ 50 x 10^9 /L then reduce dose by 12.5mg
Thrombocytopenia	Platelets 10-49 x 10^9 /L	Delay until ≥ 50 x 10^9 /L then continue at same dose (repeated occurrence – consider reducing dose by 12.5mg)
	Platelets < 10 x 10^9 /L	Delay until ≥ 50 x 10^9 /L then reduce dose by 12.5mg

Renal impairment

CrCl (ml/min)	**Sunitinib dose**
≥ 30	100%
< 30	No experience of use in patients with CrCl < 30ml/min – discuss with consultant and use with caution

Hepatic impairment
No starting dose adjustment is recommended when administering sunitinib to patients with mild or moderate (Child-Pugh class A and B) hepatic impairment. Sunitinib has not been studied in subjects with severe (Child-Pugh class C) hepatic impairment and therefore its use in patients with severe hepatic impairment cannot be recommended

Hypertension
Initiate standard antihypertensive medication

In the event of resistant hypertension, reduce dose of sunitinib in 12.5mg steps and continue to monitor. If persists discontinue treatment

Other toxicities
Withhold unit resolved and reduce dose by 12.5mg
Also consider “two weeks on, one week off” schedule

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Cardiotoxicity
QT interval prolongation
Thyroid dysfunction
Proteinuria, nephrotic syndrome
Pancreatitis
Arterial thrombotic events
Haemorrhage
Impaired wound healing

- **Frequently occurring side effects**

Diarrhoea, constipation
Nausea and vomiting
Stomatitis and mucositis
PPE
Myelosuppression
Epistaxis
Hypertension

- **Other side effects**

Skin and hair changes
Taste disturbances
Anorexia
Fatigue
Headache

Significant drug interactions

– for full details consult product literature/ reference texts

CYP3A4 inhibitors (e.g. ketoconazole, voriconazole, clarithromycin, ritonavir): avoid co-administration these may increase plasma concentrations of sunitinib.

Grapefruit and grapefruit juice: avoid as an inhibitor of CYP3A4 and may increase plasma concentrations of sunitinib.

Inducers of CYP3A4 (e.g. rifampicin, phenytoin, carbamazepine, St John’s Wort): avoid co-administration as these may reduce exposure to sunitinib. If this is unavoidable, the dose of sunitinib may need to be increased in 12.5mg steps (up to 87.5mg) based on careful monitoring of tolerability

Coumarin anticoagulants, e.g. Warfarin: Avoid if possible as may cause elevation and fluctuation in INR. Consider switching to low molecular weight heparin

Additional comments

Patients should be advised that depigmentation of the hair or skin may occur during treatment with sunitinib

References

Sutent SPC - https://www.medicines.org.uk/emc/product/7966/smpc

South West Clinical Network Cancer Protocols - http://www.swscn.org.uk/guidance-protocols/cancer-protocols/

THIS PROTOCOL HAS BEEN DIRECTED BY DR PARIKH, DESIGNATED LEAD CLINICIAN FOR KIDNEY CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: September 2020
Review: September 2022
VERSION: 9