Chemotherapy Protocol

RENAL CELL

PAZOPANIB

Regimen

- Renal Cell - Pazopanib

Indication

- First line treatment option for people with advanced renal cell carcinoma
- Second line treatment of advanced renal cell carcinoma in those are intolerant of first line sunitinib
- Performance status 0 or 1

Toxicity

Drug	Adverse Effect
Pazopanib	Diarrhoea, hypertension, haemorrhage (rare), fatigue, hair and skin colour changes, hypothyroidism, headache, anorexia, increased transaminases

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

Monitoring

Drugs

- FBC and U&Es every 4 weeks
- LFTs at baseline then week 3, 5, 7 and 9 then every 4 weeks and as clinically indicated
- Blood pressure weekly for the first 4 weeks then every 4 weeks
- ECG at baseline then every 6 – 12 months if patient has relevant cardiac history (e.g. on anti-arrhythmics, history of QT prolongation)
- Thyroid function tests at baseline then every 3 months.
- Urinalysis at baseline and then every 3 months for proteinuria.

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.

Haematological

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

Prior to each cycle the following criteria must be met;

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

If counts fall below these levels during treatment interrupt therapy for 7 days. Once recovered consider a dose reduction (in steps of 200mg).

Hepatic Impairment

Cases of hepatic failure (including fatalities) have been reported during use of pazopanib. Administration of pazopanib to patients with mild or moderate hepatic impairment should be undertaken with caution and close monitoring

On Initiation

Drug	Bilirubin µmol/L	Dose
Pazopanib	less than 1.5ULN	800mg daily
	1.5-3xULN	200mg daily, monitor LFTs weekly increase dose in 200mg increments as tolerated
	greater than 3xULN	Contra indicated

During Treatment

Drug	Bilirubin µmol/L		AST/ALT units/L	Dose (% of original dose)
Pazopanib	less than or equal to 2xULN	and	less than or equal to 3xULN	100%
	less than or equal to 2xULN	and	3-8xULN	Continue on pazopanib but monitor transaminases weekly until they return to less than or equal to 3xULN or baseline
	less than or equal to 2xULN	and	more than 8xULN	Interrupt pazopanib until AST/ALT less than or equal to 3xULN or baseline. If the potential benefit of treatment outweighs the risk of hepatotoxicity, reintroduce pazopanib at a reduced dose and measure LFTs weekly for 8 weeks. If AST/ALT levels return to more than 3xULN then discontinue pazopanib
	More than 2xULN with more than 35% conjugated	and	more than 3xULN	Discontinue pazopanib

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Pazopanib	more than 30ml/min	100%
	greater than or equal to 30ml/min	Clinical decision

Pazopanib and its metabolites have low renal excretion, however there is no data on the use of pazopanib in patients with creatinine clearance of less than 30ml/min.

Other

Blood Pressure

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 pazopanib dose in 200mg steps and continue to monitor. If hypertension persists discontinue the pazopanib.

Gastro-intestinal

Diarrhoea is a reported complication of pazopanib 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 200mg. For a NCI-CTC grade 4 adverse reaction stop the pazopanib until it resolves to at least NCI-CTC grade 2. Treatment may be re-started with a 200mg dose reduction in the first instance.

Endocrine

Hypothyroidism is common. It should be managed according to standard medical practice. There is no need to discontinue or reduce the pazopanib dose.

Skin

For a NCI-CTC grade 1 reaction continue with the pazopanib at the last dose and treat symptomatically. If the reaction is considered to be NCI-CTC grade 2 then delay treatment until it has resolved to at least NCI-CTC grade 1 and re-start the pazopanib with a 200mg dose reduction. For a NCI-CTC grade 3 reaction again delay therapy until it has resolved to NCI-CTC grade 1 and then re-start with a 200-400mg dose reduction.

Proteinuria

If a NCI-CTC grade 4 proteinuria occurs discontinue the pazopanib

Stomatitis

For a NCI-CTC grade 1 reaction continue the pazopanib at the last dose and treat symptomatically. If the reaction is NCI-CTC grade 2 delay the pazopanib until it resolves to at least NCI-CTC grade 1 and then restart treatment with a 200mg dose reduction. For a NCI-CTC grade 3 reaction again delay treatment until resolution to at least NCI-CTC grade 1 and then re-start the pazopanib with a 200-400mg dose reduction.

Regimen

28 day cycle continued as long as clinical benefit is observed or until unacceptable toxicity occurs (10 cycles will be set in ARIA)

Drug	Dose	Days	Administration
Pazopanib	800mg daily	1-28	Oral

Dose Information

- Pazopanib is available as 200mg and 400mg tablets

Administration Information

- Take as a single daily dose on an empty stomach, at least one hour before, or two hours after food
- Swallow whole with a glass of water.

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 pazopanib.
- It must be made clear to all staff, including those in the community, that pazopanib should only be prescribed under the supervision of an oncologist.
- Pazopanib interacts with many medications. Always check for drug interactions

Coding (OPCS)

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

References
1. National Institute for Health and Clinical Excellence (2011). Clinical Guideline 127. Hypertension: Clinical management of primary hypertension in adults. NICE: DOH

2.Sternberg C, Davis I, Mardiak J et al. Pazopanib in Locally Advanced or Metastatic Renal Cell Carcinoma: Results of a Randomized Phase III Trial. J Clin Oncol 2010; 28: 1061 - 1068
3.National Institute for Health and Clinical Excellence (2011). Technology Appraisal 215. Pazopanib for the first line treatment of advanced renal cell carcinoma. NICE: DOH.

REGIMEN SUMMARY

Pazopanib

Day One

Take Home Medicines

1. Pazopanib 800mg once a day oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	April 2016	Header changed LFT monitoring updated Hepatic dose modification guidelines updated Mucositis recommendation changed OPCS codes updated Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Nov 2012	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.