

Chemotherapy Protocol

LIVER

SORAFENIB

This protocol may require funding

Regimen

- Hepatocellular carcinoma-Sorafenib

Indication

- Hepatocellular carcinoma where radical resection, liver transplant or locoregional treatment such as transcatheter arterial chemoembolisation (TACE), radio frequency ablation (RFA) or selective internal radiation therapy (SIRT) are not appropriate or where the disease has progressed following locoregional treatment.
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Sorafenib	Palmar-plantar erythrodysaesthesia, hypertension, haemorrhage, cardiac ischaemia, QT interval prolongation, fatigue, hypophosphataemia

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

Monitoring

- FBC, U&Es (including phosphate) and LFTs every 4 weeks for 3 cycles then at least every 8 weeks thereafter
- Blood pressure weekly for the first 4 weeks then every 4 - 8 weeks

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.

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.

Neutrophils (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose Modifications
1 or greater	and	50 or greater	400mg twice a day
0.5 – 0.9	and	50 or greater	400mg once a day
less than 0.5	or	less than 50	Delay until recovery to neutrophils 0.5x10 ⁹ /L or greater and platelets to 50x10 ⁹ /L or greater and then reduce dose to 400mg once a day in the first instance

Hepatic Impairment

The SPC does not recommend dose modifications for patients with Child Pugh A or B hepatic impairment and states that there are no data for use in Child Pugh C hepatic impairment. The following are suggested starting doses from a pharmacokinetic study⁽²⁾. If the patient tolerates the initial dose it may be escalated at the consultant's discretion.

Drug	Bilirubin µmol/L	Albumin g/L	Dose
Sorafenib	less than 26		400mg twice a day
	26 - 51		200mg twice a day
	more than 51		Avoid*
		Less than 25	200mg once a day

Renal Impairment

The SPC does not recommend any dose reductions for patients with renal impairment. The following are suggested starting doses based on a pharmacokinetic study⁽²⁾. If the patient tolerates the initial dose it may be escalated at the consultant's discretion.

Drug	Creatinine Clearance (ml/min)	Dose
Sorafenib	40 or greater	400mg twice a day
	20-39	200mg twice a day
	less than 20	Insufficient data
	haemodialysis	200mg daily

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.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose should then be reduced to 400mg once a day. Patients tolerating the re-introduction of sorafenib may be considered for a dose escalation back to 400mg twice a day.

If there is further toxicity at a dose of 400mg once a day, delay treatment until resolution of the toxicity to NCI-CTC grade 1 or below. On reintroduction of the treatment, the dose should be further reduced to 400mg once a day on alternate days or 200mg once a day.

Hypertension

Sorafenib associated hypertension normally occurs early in treatment and is usually mild to moderate. Hypertension should be treated in accordance with current NICE guidelines. Raised blood pressure is not a reason to stop sorafenib unless it fails to respond to treatment or results in a hypertensive crisis.

Skin

NCI-CTC grade 2 or above palmar-plantar erythrodysesthesia or rash may require a short break in treatment until it resolves to NCI-CTC grade 1 or below. The sorafenib can then be re-introduced at a dose of 400mg once a day and re-escalated as tolerated. Symptomatic measures such as keeping the area well moisturised and cool, avoiding tight fitting socks, tights etc and avoiding activities that place pressure on the hands and feet may help. The patient should be advised to moisturise their hands and feet regularly and to keep them cool.

Regimen

28 day cycle continued as long as clinical benefit is observed or until unacceptable toxicity occurs (6 cycles will be set in Aria)

Drug	Dose	Days	Administration
Sorafenib	400mg twice a day	1-28 inclusive	Oral

Dose Information

- Sorafenib is available as 200mg tablets.

Administration Information

- It is recommended that sorafenib is taken on an empty stomach at least one hour before or two hours after a meal. Swallow whole with a full glass of water.

Additional Therapy

- Emollients according to local trust policy
- 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 sorafenib.
- Sorafenib has the potential to interact with many drugs, a thorough assessment of all concomitant medication is essential.

Coding (OPCS)

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

References

1. J Llovet, S Ricci, V Mazzaferro et al Sorafenib in Advanced Hepatocellular Carcinoma. NEJM 2008; 359 (4): 378-390
2. A Miller, D Murry, K Owzar et al; Phase I Pharmacokinetic Study of Sorafenib in Patients With Hepatic or Renal Dysfunction: CALGB 60301. J Clin Oncol 2009; 27 (11): 1800 -1805
3. National Institute for Health and Clinical Excellence (2010). Hepatocellular carcinoma (advanced and metastatic) – sorafenib (first line). Technology Appraisal 189. London:DOH
4. SPC - Nexavar 200mg film-coated tablets, Bayer Plc, December 2014

REGIMEN SUMMARY

Sorafenib

Day One

1. Sorafenib 400mg twice a day oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Dec 2015	Header changed Mucositis recommendation changed Neutrophil range changed from "0.5-1" to "0.5-0.9" in dose modification table Reference to grapefruit juice removed SPC reference updated Disclaimer added Spelling corrections and formatting changes	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Dec 2012	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Joanna Gale Consultant Medical Oncologist Dr Mathew Wheeler 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.