Lancashire and South Cumbria Cancer Network

Chemotherapy protocol

DRUG REGIMEN
Sorafenib

Indication for use
Unresectable and advanced hepatocellular carcinoma (HCC)

Regimen
Sorafenib 400 mg bd, p.o. continuous until disease progression or intolerable toxicity

(One cycle is 28 days)

Investigation prior to initiating treatment
FBC, differential, platelets, electrolytes, creatinine, total protein, albumin, bilirubin, alkaline phosphatase
MUGA scan or echocardiogram if clinically indicated or if history of cardiac problems

Cautions
History of cardiac problems (significant) and/or known LVEF < 50%. Symptomatic patients with evidence of cardiac dysfunction should have sorafenib discontinued

Moderate to severe liver dysfunction (Child-Pugh Class B and C: sorafenib not recommended)

Sorafenib is predominantly metabolized and excreted through cytochrome P4503A4 in the liver. Potential drug interactions with cytochrome P4503A4 interacting agents must be considered

Patients with hypertension should exercise caution while on Sorafenib. Temporary suspension of sorafenib is recommended for patients with severe hypertension (> 200 mmHg systolic or >110 mmHg diastolic). Treatment with sorafenib may be resumed once hypertension is controlled.

Patients on warfarin should be monitored regularly for changes in INR, PT or clinical bleeding episodes.

Not indicated in pregnancy or during lactation.

Investigations and consultations prior to each cycle
Before each treatment: FBC, differential and platelets, urine analysis, creatinine, uric acid, ALT, bilirubin.

Blood pressure monitoring – every week for first six weeks then monthly thereafter

Acceptable levels for treatment to proceed (if outside these levels defer one week or contact consultant)
Platelets >60, Bilirubin < 2.5 X upper limit of normal, AST <=5 times upper limit of normal, serum creatinine <=1.5 X upper limit of normal

Side Effects
Frequent:
Diarrhoea, fatigue, abdominal pain, weight loss, anorexia, nausea and hand-foot skin reaction

Other Side effects:
Hypertension: Occurred usually within first few weeks of treatment. Monitor BP weekly during the first 6 weeks of treatment. Manage with anti-hypertensives if mild. Discontinue therapy if systolic > 200 mm of Hg or > 110 mg of Hg diastolic.

Increased risk of bleeding (18%)

Cardiovascular ischaemia/infarction (2.7%)

GI Perforation < 1%

Elevation in serum lipase and reduction in serum phosphate can occur with sorafenib

Dose Modification Criteria

1. **Hematological**

ANC ^{9} (x10 /L)	Platelets ^{9} (x10 /L)		Dose
≥ 1.0	and	≥ 50	100%
>0.5 – 1.0	and	≥ 50	Decrease one dose level
≤0.5	or	<50	Delay until ANC > 0.5 and platelets >50 then decrease one dose level. If no recovery after 4 weeks, treatment should be discontinued.

2. **Non-Hematological toxicity:**

CTC-Grade	Dose
1-2	100%
3	Delay until <= Grade 2 then decrease one dose level
4	Discontinue therapy

3. **Renal dysfunction:**

Only a very small percentage of sorafenib and its metabolites are excreted by the kidney. Sorafenib appears safe in patients with mild renal impairment (creatinine ≤ 2x upper limit of normal).

No data exist for sorafenib in patients with moderate to severe kidney failure.

4. **Hepatic dysfunction**:

Sorafenib is mainly metabolized and excreted through the liver. Sorafenib appears safe in patients with mild hepatic impairment (bilirubin ≤ 1.5 x upper limit of normal).

No data exist for Sorafenib in patients with moderate to severe hepatic impairment.

Dose reduction:

Dose level -1: 400 mg **once** a day continuously
Dose level -2: 400 mg **every other day** continuously
If dose level -2 not tolerated then discontinue.

Specific Information on Administration

It is recommended that sorafenib be taken on an empty stomach or with a low or moderate fat meal.

THIS PROTOCOL HAS BEEN DIRECTED BY Dr SIVA, CLINICIAN FOR LIVER CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

DATE January 2013
REVIEW January 2015
VERSION 5