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Version: Supplemental Material

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Supplementary Material

Organ and Marrow function requirements for inclusion:

Leukocytes $\geq 3,000/\text{mCL}$,

Neutrophils $\geq 1,500/\text{mCL}$,

Platelets $\geq 100,000/\text{mCL}$,

Hemoglobin $> 10 \text{ g/dL}$,

Total bilirubin within institutional upper limit of normal (ULN),

AST/ALT ≤ 5 times ULN,

Creatinine \leq ULN or creatinine clearance $\geq 45 \text{ mL/min/1.73 m}^2$ if creatinine $>$ ULN,

PT-INR/PTT < 1.5 times ULN*

* Patients receiving therapeutic anti-coagulation were permitted provided there was no prior PT-INR/PTT abnormality.

Table 1. Sorafenib dose modification

Toxicity	Severity	Dose Modification for Sorafenib
Diarrhea	Grade 3 or 4 <u>and</u> no improvement with loperamide or diphenoxylate/atropine	If radiated field includes a significant amount of small or large bowel then this is a DLT and the patient should be removed from study. If not bowel is in field then hold until resolves to grade 2 and then resume at 50% of original dose
Skin Rash	Grade 2	Hold until resolves to grade 1 and then resume at 100%
	Grade 3 or 4	Hold until resolves to grade 1 then resume at one dose reduction
Hand-Foot Syndrome	Grade 2	Hold until resolves to grade 1 and then resume at 100%
	Grade 3	Hold until resolves to grade 1 and then resume at 50% of original dose
Hypertension	Grade 2, asymptomatic	Initiate monotherapy (suggest dihydropyridine calcium-channel blocker), monitor blood pressure every two days until stabilized.
	Grade 2 symptomatic/persistent OR Diastolic BP > 100mm/Hg OR grade 3	Add agent(s): Ca++ channel blocker (if not already used), K+ channel opener, beta-blocker, thiazide diuretic)and hold Sorafenib until symptoms resolve and diastolic BP ≤ 100mm/Hg. Monitor blood pressure every two days until stabilized. Resume treatment at 50% original dose.
	Grade 4	Off protocol therapy
Other toxicities	Any grade	At discretion of treating Medical and Radiation Oncologist