CABOZANTINIB

An option in renal cell carcinoma following prior VEGF-targeted therapy

Blueteq registration is required before treatment may start

(N.B. This protocol is not to be used for patients with medullary thyroid cancer)

Drug/Dosage: **Cabozantinib** initiate at 60mg po once daily continuous therapy

Administration: Cabozantinib (Cabometyx) is available as 20mg, 40mg and 60mg tablets, which should be swallowed whole on an empty stomach; no food for at least 2 hours before until 1 hour after taking each dose.
Grapefruit and grapefruit juice should be avoided while on cabozantinib.
If a patient misses a dose, the missed dose should not be taken if it is less than 12 hours before the next dose.

Frequency: clinical review 2 weeks after starting, then every 4 weeks
continue for as long as there is clinical benefit, or unacceptable toxicity.

Main Toxicities: diarrhoea; hand-foot syndrome; hypertension; fatigue; hypothyroidism; constipation; dysphonia

Anti- emetics: mildly emetogenic

Regular:	FBC	every 4 weeks
Investigations:	LFTs	every 4 weeks
	U&Es	every 4 weeks
	Blood pressure	weekly for 1st cycle (ideally via GP, with patient making a record of the readings for the next oncology appointment), then every 4 weeks
	Thyroid function	baseline, then every 3 months
	Urinalysis for proteinuria	baseline, then every 3 months

Comments: Diarrhoea is common, so ensure patients have some loperamide, and ask them to report to hot bleep an increase of 4 - 6 stools per day over baseline.

Patients should be advised to apply moisturiser to their hands and feet regularly throughout treatment, and to minimise activities that put pressure on feet or hands if they start to develop sore hands or feet. Recommended moisturisers are Udderly Smooth or urea-containing moisturisers eg Eucerin.

Interactions: Cabozantinib is a CYP3A4 substrate.
Concomitant use of enzyme inducers (e.g. dexamethasone, phenytoin, St Johns wort) with cabozantinib should be avoided, as this may increase the risk of therapeutic failure.

Co-administration of cabozantinib with enzyme inhibitors (eg itraconazole, clarithromycin, erythromycin, grapefruit juice) should also be avoided, or used with caution and extra monitoring.

Reason for Update: available via the CDF	Approved by Consultant: Dr A Michael
Version: 2	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 1, for compassionate use	Date: 27.7.17
Prepared by: S Taylor	Checked by: C Tucker

Dose Modifications Management of suspected adverse drug reactions may require temporary interruption and/or dose reduction of cabozantinib.
Dose interruptions are recommended for management of Grade 3 or 4 toxicities, or intolerable Grade 2 toxicities.
When dose reduction is necessary, it is recommended to reduce to 40 mg daily, and then to 20 mg daily.

Adverse Reaction	Management
Grade 1, and Grade 2 adverse reactions which are tolerable and easily managed	Dose adjustment is not usually required. Add supportive care as indicated.
Grade 2 adverse reactions which are intolerable and cannot be managed with a dose reduction or symptom management.	Interrupt treatment. Add supportive care as indicated. If toxicity resolves to ≤ Grade 1, consider re-starting at a reduced dose.
Any Grade 3	Interrupt treatment. Add supportive care as indicated. If toxicity resolves to ≤ Grade 1, re-start at a reduced dose.
Any Grade 4	Interrupt treatment. Initiate appropriate medical care. If toxicity resolves to ≤ Grade 1, re-start at a reduced dose. Otherwise, permanently discontinue.

Wound healing: Cabozantinib may adversely affect the wound healing process.
Stop cabozantinib at least 28 days prior to scheduled surgery, including dental surgery. The decision to resume cabozantinib after surgery should be based on clinical judgement of adequate wound healing.

Hypertension: Blood pressure should be well controlled before starting cabozantinib, with baseline blood pressure < 150/100 mmHg.
If hypertension develops, it should be treated (usually by GP) and monitored closely until stabilised. If the hypertension is persistent despite the use of anti-hypertensives, the cabozantinib dose should be reduced.
Cabozantinib should be discontinued if hypertension is severe and persistent despite dose reduction, or if hypertensive crisis.

Hypothyroidism: Manage according to standard medical practice. Cabozantinib treatment may continue.

Proteinuria: Cabozantinib should be discontinued in patients who develop nephrotic syndrome.

Hepatic Impairment: In patients with mild or moderate hepatic impairment, the recommended start dose is 40 mg daily. Cabozantinib is not recommended for use in patients with severe hepatic impairment.

Renal Impairment: Cabozantinib should be used with caution in patients with mild or moderate renal impairment (CrCl 30–59ml/min). Cabozantinib is not recommended for use in patients with CrCl<30ml/min.

Reference: Choueiri et al, Lancet Oncology June 2016, 17 (7): 917-927