Selpercatinib

Indication
Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) who require systemic therapy

Regimen details
The recommended dose of selpercatinib based on body weight is:

- Less than 50 kg: 120 mg twice daily.

- 50 kg or greater: 160 mg twice daily

Cycle frequency
Dispense monthly

Number of cycles
Treatment should be continued until disease progression or unacceptable toxicity.

Administration
The capsules should be swallowed whole (patients should not open, crush, or chew the capsule before swallowing) and can be taken with or without food.

Patients should take the doses at approximately the same time every day.

Selpercatinib must be accompanied by a meal if used concomitantly with a proton pump inhibitor

Selpercatinib should be administered 2 hours before or 10 hours after H_2 receptor antagonists

If a patient vomits or misses a dose, the patient should be instructed to take the next dose at its scheduled time; an additional dose should not be taken

Pre-medication
None

Emetogenicity
Minimal

Additional supportive medication
Loperamide and metoclopramide

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Calcium	14 days
Magnesium	14 days
Blood pressure	Baseline
ECG	Baseline

Blood pressure should be controlled before starting treatment

Hypokalaemia, hypomagnesaemia and hypocalcaemia should be corrected prior to initiating selpercatinib and during treatment

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST), calcium, magnesium

U&Es and ECG should be checked after 1 week of treatment and at least monthly for the first 6 months

LFTs should be checked every 2 weeks during the first 3 months of treatment, monthly for the next 3 months of treatment and otherwise as clinically indicated

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 10 mL/min
AST	< 3.5 x ULN (see below regarding dose adjustment in hepatic impairment)
Bilirubin	< ULN (see below regarding dose adjustment in hepatic impairment)

Dose modifications

Renal impairment

Dose adjustment is not necessary in patients with mild, moderate or severe renal impairment. There are no data in patients with end stage renal disease, or in patients on dialysis

Hepatic impairment

Close monitoring of patients with impaired hepatic function is important. No dose adjustment is required for patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment. Patients with severe (Child-Pugh class C) hepatic impairment should be dosed with 80 mg selpercatinib twice daily

Dose modification	Adults and adolescents ≥50 Kg	Adults and adolescents <50 Kg
Starting dose	160 mg orally twice daily	120 mg orally twice daily
First dose reduction	120 mg orally twice daily	80 mg orally twice daily
Second dose reduction	80 mg orally twice daily	40 mg orally twice daily
Third dose reduction	40 mg orally twice daily	Not applicable

Adverse drug reaction (ADR)		Dose modification
Increased ALT or AST	Grade 3 or Grade 4	Suspend dose until toxicity resolves to baseline. Resume at a dose reduced by 2 levels. If after at least 2 weeks selpercatinib is tolerated without recurrent increased ALT or AST, increase dosing by 1 dose level. If selpercatinib is tolerated without recurrence for at least 4 weeks, increase to dose taken prior to the onset of Grade 3 or 4 increased AST or ALT. Permanently discontinue selpercatinib if Grade 3 or 4 ALT or AST increases recur despite dose modifications.
Hypersensitivity	All Grades	Suspend dose until toxicity resolves and begin corticosteroids at a dose of 1 mg/kg. Resume selpercatinib at 40 mg twice daily while continuing steroid treatment. Discontinue selpercatinib for recurrent hypersensitivity. If after at least 7 days, selpercatinib is tolerated without recurrent hypersensitivity, incrementally increase the selpercatinib dose by 1 dose level each week, until the dose taken prior to the onset of hypersensitivity is reached. Taper steroid dose after selpercatinib has been tolerated for at least 7 days at the final dose.
QT interval prolongation	Grade 3	Suspend dose for QTcF intervals >500 ms until the QTcF returns to <470 ms or baseline Resume selpercatinib treatment at the next lower dose level.
	Grade 4	Permanently discontinue selpercatinib if QT prolongation remains uncontrolled after two dose reductions or if the patient has signs or symptoms of serious arrhythmia.
Hypertension	Grade 3	Patient blood pressure should be controlled before starting treatment. Selpercatinib should be suspended temporarily for medically significant hypertension until controlled with antihypertensive therapy. Dosing should be resumed at the next lower dose if clinically indicated
	Grade 4	Selpercatinib should be discontinued permanently if medically significant hypertension cannot be controlled.
Haemorrhagic events	Grade 3 or Grade 4	Selpercatinib should be suspended until recovery to baseline. Discontinue selpercatinib for severe or life-threatening haemorrhagic events.
Other adverse reactions	Grade 3 or Grade 4	Selpercatinib should be suspended until recovery to baseline. Discontinue selpercatinib for severe or life-threatening events

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Hypersensitivity
Haemorrhage

- **Frequently occurring side effects**

Hypersensitivity
Decreased appetite
Headache
Dizziness
QT prolongation
Hypertension
Abdominal pain
Diarrhoea
Nausea
Vomiting
Constipation
Dry mouth
Rash
Pyrexia
Fatigue
Oedema
Increased ALT/AST
Decreased platelets
Decreased lymphocyte count
Decrease Magnesium
Increased creatinine
Haemorrhage

- **Other side effects**

Significant drug interactions

– for full details consult product literature/ reference texts

Avoid co-administration with strong CYP3A4 inducers as these may decrease the efficacy of selpercatinib

The current selpercatinib dose should be reduced by 50% if co-administering with a strong CYP3A inhibitor. If the CYP3A inhibitor is discontinued, the selpercatinib dose should be increased (after 3-5 half-lives of the inhibitor) to the dose that was used before starting the inhibitor

Selpercatinib may increase the plasma levels of CYP2C8 substrates (e.g. enzalutamide, paclitaxel, buprenorphine)

Selpercatinib may increase the plasma levels of CYP3A4 substrates (e.g. midazolam, simvastatin)

Selpercatinib has pH dependant solubility. See “Administration” above

Additional comments

References

Retsevmo SPC - https://www.medicines.org.uk/emc/product/12196/smpc

THIS PROTOCOL HAS BEEN DIRECTED BY DR LAU, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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