Systemic Anti Cancer Treatment Protocol

Osimertinib
NSCLC T790M Mutation

PROTOCOL REF: MPHAOSIM
(Version No: 1.3)

The protocol has been temporarily amended – please see the Oral SACT Operational Changes during Covid-19. Amendments may include less frequent blood monitoring, telephone SACT assessments and longer durations of treatment being dispensed.

The approved indication has also been temporarily expanded - please see the SRG Guidelines during COVID-19 Lung Cancer for further details.

Approved for use in:

Histologically or cytologically documented NSCLC that carries an EGFR and a T790M mutation.

Locally advanced or metastatic disease with documented radiological progression following 1st line EGFR TKI treatment with only one TKI and without any further systemic anti-cancer treatment.

Treatment with no more than one prior line of treatment for advanced NSCLC
PS 0 – 1.

Prior chemotherapy in the neo-adjuvant setting must have been completed at least 6 months prior to starting 1st line EGFR treatment.

Dosage:

Drug	Dosage	Route	Frequency
Osimertinib	80mg	Oral	Once daily

Treatment is continuous until unacceptable toxicity or disease progression.

Four weeks supply will be issued at each visit.

Supportive treatments:

Loperamide 2mg as required for management of diarrhoea.

Extravasation risk:

Not applicable: oral formulation

Administration:

Osimertinib should be swallowed whole with water and can be taken irrespective of food intake.

- If the patient is unable to swallow the tablet whole it may first be dispersed in 50ml of non-carbonated water. The tablet should be dropped into water without crushing, stirred until dispersed and immediately swallowed. An additional half glass of water should be added to the empty glass to ensure that no reside remains and then immediately swallowed. No other liquids can be used.
- If administration via the nasogastric tube is required the same process as above should be followed but using 15ml of water for the initial dispersion and 15ml for the residue rinses. The resulting 30ml of liquid should be administered as per the naso-gastric tube manufactures instruction with appropriate flushes.

Drug Interactions

Strong CYP3A4 inducers can decrease the exposure of osimertinib. Osimertinib may decrease the exposure of BCRP substrates.

Please consult SPC for full list of interactions: available via medicines.org.uk or discuss with a pharmacist.

Main Toxicities:

Diarrhoea, rash, dry skin, interstitial lung disease, paronychia, decreased platelets, decreased leucocytes and decreased neutrophils

Investigations and Treatment Plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X	X	X	Every 3 cycles
Nursing Assessment	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every cycle
LDH	x	x	x	x	x	Every cycle--for clinician to review if raised. To be assessed in combination with symptoms and radiological progression
CT scan	X			X*		*CT scan to be carried out prior to cycle 3 then every three months or as clinically indicated
Informed Consent	X					
ECG	X			X		ECG to be carried out at baseline and then on cycle 3 at medical assessment, then as clinically indicated
Blood pressure measurement	X					Repeat if clinically indicated
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Osimertinib causes decreased platelets, decreased leucocytes and decreased neutrophils.

Dose adjustments for Osimertinib are required for CTCAE Grade 3 haematological toxicities (see Table 1).

Non-haematological toxicities

Any patient with grade 3 or 4 toxicity will require a dose reduction as per the table below.

Table 1

CTCAE Grade	Dose Modification
Grade 3 or higher	Withold Osimertinib for up to 3 weeks
If Grade 3 or higher adverse reaction improves to Grade 0-2 after withholding Osimertinib for up to 3 weeks	Osimertinib may be restarted at the same dose (80mg) or lowered dose (40mg)
Grade 3 or higher adverse reaction that does not improve to Grade 0-2 after withholding for up to 3 weeks	Permanently discontinue Osimertinib

Dose adjustment for skin rash:

Rash is a commonly reported adverse effect of Osimertinib, in general it manifests as mild or moderate erythematous and acneiform rash, which may occur or worsen in areas exposed to the sun. Dry skin and pruritis may also occur.

Bullous, blistering and exfoliative skin conditions can occur and treatment should be interrupted or discontinued if severe.

Use of emollients such as Aquamax cream may be used in the case of rash and dry skin for Grade 0-2 toxicities.

Dose adjustment for diarrhoea

Diarrhoea is a common side effect of Osimertinib.

Table 2

Toxicity	Management
Grade 1 or 2	Loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg /day) Encourage fluid intake Continue loperamide until normal bowel function restored for at least 12 hours
Grade 3	Withhold until resolved, see Table 1

Interstitial Lung

Interstitial Lung Disease should be suspected in patients who develop acute onset of new and/or progressive unexplained pulmonary symptoms such as dyspnoea, cough and fever, and should have their Osimertinib interrupted pending diagnostic evaluation.

QT Interval Prolongation

QTc interval prolongation occurs in patients treated with Osimertinib. When possible, avoid use of Osimertinib in patients with congenital long QT syndrome. Caution is required in patients with congestive heart failure, electrolyte abnormalities, or those who are taking medications that are known to prolong the QTc interval. Withhold Osimertinib in patients who develop a QTc prolongation, then resume Osimertinib at a reduced dose as described in Table 1. Permanently discontinue Osimertinib in patients who develop

QTc interval prolongation in combination with any of the following: Torsade de pointes, polymorphic ventricular tachycardia, signs/symptoms of serious arrhythmia.

Hepatic Impairment

Osimertinib is eliminated mainly via the liver.

Treatment should be withheld in patients with AST or ALT more than 2.5 times ULN (unless known liver metastates where 5 times ULN applies) and/or bilirubin more than 1.5 times ULN.

Renal Impairment

No dose adjustments are required in patients with mild to moderate renal impairment. There is limited data for patients with severe renal impairment, and treatment in patients with CrCl <15mL/min is not recommended.

Additional Information

Reporting of all suspected adverse reactions for patients on Osimertinib is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions in accordance with the training provided and the pharmacovigilance protocol.

References:

NICE TA416: Osimertinib for treating locally advanced or metastatic EGFR T790M mutation-positive non-small-cell lung cancer

https://www.medicines.org.uk/emc