Osimertinib

Indication

Adult patients with locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small-cell lung cancer (NSCLC) who have progressed after first line EGFR TKI therapy

First-line treatment of locally advanced or metastatic epidermal growth factor receptor mutation-positive non-small-cell lung cancer in adults

The adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations

Regimen details

Osimertinib 80 mg oral daily continuously

Cycle frequency

Repeat every 28 days (dispense in packs of 30)

Number of cycles

For locally advanced or metastatic disease, continue treatment until disease progression or unacceptable toxicity

For adjuvant treatment, continue treatment until disease progression, unacceptable toxicity or a total treatment duration of 3 calendar years

Administration

The tablet should be swallowed whole with water and it should not be crushed, split or chewed

It can be taken with or without food at the same time each day

If the patient is unable to swallow the tablet, the tablet may first be dispersed in 50 mL of non-carbonated water. It should be dropped in the water, without crushing, stirred until dispersed and immediately swallowed. An additional half a glass of water should be added to ensure that no residue remains and then immediately swallowed. No other liquids should be added.

If administration via nasogastric tube is required, the same process as above should be followed but using volumes of 15 mL for the initial dispersion and 15 mL for the residue rinses. The resulting 30 mL of liquid should be administered as per the naso-gastric tube manufacturer's instructions with appropriate water flushes. The dispersion and residues should be administered within 30 minutes of the addition of the tablets to water

Pre-medication

Not required

Emetogenicity

Minimal

Additional supportive medication

Provide emollient, steroid cream and loperamide

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
ECG	Baseline
CT chest and abdomen	Baseline

Interstitial lung disease

Past medical history of ILD, drug-induced ILD, radiation pneumonitis that required steroid treatment or any evidence of clinically active ILD were excluded from clinical studies

Osimertinib should be avoided in these patients

QTc prolongation:

Occurs in patients treated with osimertinib. Patients with QTc interval greater than 470 msec were excluded from the studies. ECG should be undertaken every cycle in patients who have congestive heart failure, electrolyte abnormalities and who take medication that prolong QTc interval.

Investigations –pre subsequent cycles

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

Review toxicities closely for 2 weeks after commencing therapy

Medical review every 4 weeks initially

Chest X-ray and CT scans 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	≥ 15 mL/min
Bilirubin	≤ ULN
AST	< 1.5 x ULN

Dose modifications

Target organ	Adverse effect	Dose modification
Lung	Interstitial Lung disease / Pneumonitis	Permanently discontinue Osimertinib
Heart	QTc interval greater than 500 msec on at least 2 separate ECGs with no signs and symptoms of arrhythmia	Withhold Osimertinib until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then restart at a reduced dose (40 mg)
	QTc interval prolongation with signs/symptoms of serious arrhythmia	Permanently discontinue Osimertinib
Other	Other Grade 3 or higher adverse reaction	Withhold Osimertinib for up to 3 weeks
	If Grade 3 or higher adverse reaction improves to Grade 0-2 after withholding of osimertinib for up to 3 weeks	Osimertinib may be restarted at the same dose (80 mg) or a lower dose (40 mg)
	Grade 3 or higher adverse reaction that does not improve to Grade 0-2 after withholding for up to 3 weeks	Permanently discontinue Osimertinib
Liver	Bilirubin < ULN, AST < 1.5 x ULN **OR** Bilirubin <1.5 x ULN and any AST	No modification required
	Moderate to Severe hepatic impairment	Do not use. Discontinue if started,
Renal	Mild to moderate impairment	No modification
	Severe impairment i.e Cr Cl < 15ml/min	Exercise caution

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Myelosupression
Interstitial lung disease
QTc prolongation

- **Frequently occurring side effects**

Diarrhoea – may be severe
Rash, pruritis
Stomatitis

- **Other side effects**

Nail disorders

Significant drug interactions

– for full details consult product literature/ reference texts

CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, St. John's Wort) may decrease efficacy of osimertinib. Avoid co-administration. Concomitant use of St. Johns Wort is contraindicated.

CYP3A4 inhibitors (e.g. itraconazole) may increase plasma levels of osimertinib. Closely monitor for adverse reactions.

Breast Cancer Resistance Protein (BCRP) substrates: osimertinib is a competitive inhibitor of BCRP. If taking BCRP substrates, patients should be closely monitored for tolerability

Additional comments

References

Tagrisso SPC - https://www.medicines.org.uk/emc/product/7615/smpc

SWCN protocol - https://www.swagcanceralliance.nhs.uk/wp-content/uploads/2020/09/Osimertinib-1.pdf

This protocol has been reviewed by the Lancashire & South Cumbria Lung Oncology Consultants' Group and responsibility for the template lies with the Head of Service.

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