Chemotherapy Protocol

Lung cancer - Non-small cell (NSCLC)

OSIMERTINIB

Regimen

- NSCLC - Osimertinib

Indication

- Osimertinib is available as an option within the Cancer Drugs Fund for treating locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small-cell lung cancer in adults whose disease has progressed after first-line treatment with an EGFR tyrosine kinase inhibitor.

- And only if the conditions in the managed access agreement for osimertinib are followed.

Toxicity

Drug	Adverse Effect
Osimertinib	Interstitial lung disease (ILD), diarrhoea, stomatitis, rash, dry skin, paronychia, pruritis, thrombocytopenia, leucopenia, neutropenia.

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- T790M mutation status using a validated test should be performed using either tumour DNA derived from a tissue sample or circulating tumour DNA (ctDNA) obtained from a plasma sample.

- Baseline CT of chest and abdomen. Chest X-ray and CT scan as clinically indicated thereafter.

- Baseline ECG for all patients, then prior to each subsequent cycle of treatment in patients with congestive heart failure, electrolyte abnormalities or those taking QTc interval prolonging medication.

- FBC, LFTs and U&Es at baseline and then prior to each cycle of treatment thereafter.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L).

Neutrophils ($x10^9$/L)		**Platelets ($x10^9$/L**	**Dose Modifications**
less than 1	and / or	less than 50	1.Withold for up to 3 weeks. 2.If recovery to NCI-CTC grade 0-2 occurs within this time, restart osimertinib at 80mg or lower dose of 40mg. 3.If recovery to NCI-CTC grade 0-2 does not occur within 3 weeks, discontinue osimertinib.

Hepatic Impairment

Bilirubin µmol/L		**AST/ALT units**	**Dose (% of original dose)**
less than ULN	and	less than 1.5xULN	No modification generally required, however, consider stopping treatment if the AST levels are elevated to NCI-CTC grade 3 or above irrespective of the bilirubin.
or			
less than 1.5xULN	and	any	
Moderate to severe hepatic impairment			Do not use. Discontinue osimertinib treatment.

Renal Impairment

Creatinine clearance (ml/min)	**Dose Modifications**
Mild to moderate (greater than or equal to 30ml/min)	No dose adjustment necessary
Severe, end stage renal disease or dialysis (less than 29ml/min)	Use with caution

Pulmonary

Severe, life-threatening or fatal ILD or ILD-like adverse reactions (e.g. pneumonitis) have been observed in patients treated with osimertinib in clinical studies. Most cases improved or resolved with interruption of treatment.

Careful assessment of all patients with an acute onset and/or unexplained worsening of pulmonary symptoms (dyspnoea, cough, fever) should be performed to exclude ILD. Whilst investigations are undertaken, osimertinib should be withheld and permanently discontinued if ILD is diagnosed.

Cardiac

QTc interval	Dose Modifications
Greater than 500msec on at least 2 separate ECGs	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

Regimen

28 day cycle until disease progression or intolerance (6 cycles will be set in Aria)

Drug	Dose	Days	Administration
Osimertinib	80mg	1-28 (inclusive)	Oral

Dose Information

- Osimertinib is available as 40mg and 80mg film-coated tablets.

Administration Information

- Osimertinib can be taken either with or without food, at the same time each day.
- If a dose of osimertinib is missed, it should be made up unless the next dose is due within 12 hours.
- Osimertinib should be swallowed whole, with water and not crushed, split or chewed.
- 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.

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to osimertinib.
- It must be made clear to all staff, including those in the community, that osimertinib should only be prescribed under the supervision of a consultant oncologist.

- It is recommended that the concomitant use of strong CYP3A inducers (e.g. phenytoin, rifampicin and carbamazepine) with osimertinib should be avoided. Moderate CYP3A4 inducers (e.g. bosentan, efavirenz, etravirine, modafinil) may also decrease osimertinib exposure and should be used with caution, or avoided where possible. There are no clinical data available to recommend a dose adjustment of osimertinib.

- Concomitant use of St. John's Wort is contraindicated.

Coding

- Procurement – X70.8

- Delivery – X72.9

References

1. National Institute for Health and Care Excellence (2016). Osimertinib for treating locally advanced or metastatic EGFR T790M mutation-positive non-small-cell lung cancer [TA416]. London: National Institute for Health and Care Excellence.
2. Astra Zeneca UK Limited (2017). Tagrisso 40mg and 80mg film-coated tablets Summary of Product Characteristics. Online at http://www.medicines.org.uk/emc/medicine/31496, accessed February 2017.
3. Janne, PA., Chih-Hsin Yang, J., Kim, D-W., Planchard, D., and Ohe, Y., *et al*. (2015). AZD9291 in EGFR Inhibitor–Resistant Non–Small-Cell Lung Cancer. *New England Journal of Medicine*. **372** (18), 1689-1699.

REGIMEN SUMMARY

Osimertinib

Cycle 1 Day 1-28

1. Osimertinib 80mg once a day oral
   Administration Information
   Take either with or without food, at the same time each day.
   Oral chemotherapy.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2017	None	Eleanor Taylor Pharmacist	Dr Judith Cave Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.