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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osimertinib</td>
<td>Interstitial lung disease (ILD), diarrhoea, stomatitis, rash, dry skin, paronychia, pruritis, thrombocytopenia, leucopenia, neutropenia.</td>
</tr>
</tbody>
</table>

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).

<table>
<thead>
<tr>
<th>Neutrophils (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 1 and / or 50</td>
<td>less than 50</td>
<td>1. Withhold 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.</td>
</tr>
</tbody>
</table>

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Bilirubin µmol/L</th>
<th>AST/ALT units</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than ULN and less than 1.5xULN</td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>less than 1.5xULN and any</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate to severe hepatic impairment</td>
<td>Do not use. Discontinue osimertinib treatment.</td>
<td></td>
</tr>
</tbody>
</table>

**Renal Impairment**

<table>
<thead>
<tr>
<th>Creatinine clearance (ml/min)</th>
<th>Dose Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate (greater than or equal to 30ml/min)</td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>Severe, end stage renal disease or dialysis (less than 29ml/min)</td>
<td>Use with caution</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>QTc interval</th>
<th>Dose Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than 500msec on at least 2 separate ECGs</td>
<td>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)</td>
</tr>
<tr>
<td>QTc interval prolongation with signs/symptoms of serious arrhythmia</td>
<td>Permanently discontinue osimertinib</td>
</tr>
</tbody>
</table>

Regimen

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osimertinib</td>
<td>80mg</td>
<td>1-28 (inclusive)</td>
<td>Oral</td>
</tr>
</tbody>
</table>

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 nasogastric 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
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.
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.