Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

AFATINIB

**Regimen**

- NSCLC - Afatinib

**Indication**

- Treatment of locally advanced or metastatic non-small cell lung cancer in patients with a positive test for epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation and who have not received prior treatment with an EGFR-TK inhibitor

**Toxicity**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afatinib</td>
<td>Diarrhoea, skin reactions (rash, dermatitis acniform, acne pustular, pruritus, dry skin, palmar-plantar erythrodysaesthesia), stomatitis, paronychia, anorexia, epistaxis, ocular disorders (conjunctivitis, dry eye, keratitis), elevated transaminases, interstitial lung disease.</td>
</tr>
</tbody>
</table>

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

**Monitoring**

- Current CT scan (ideally within 1 month) before starting afatinib and repeat within 3 months of starting treatment, or earlier if necessary
- Chest x-ray should be performed before starting treatment and every 4 weeks
- LFT every two weeks for two months then monthly
- FBC, U&Es every four weeks
- EGFR status before starting treatment

**Dose Modifications**

**Haematological**

In general afatinib is not associated with frequent haematological abnormalities
**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afatinib</td>
<td>Adjustments to the starting dose of afatinib are not necessary in patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Afatinib has not been studied in patients with severe hepatic (Child-Pugh) impairment and treatment is not recommended. Dose interruption may be necessary in patients who experience worsening of liver function. Treatment should be discontinued in patients who develop severe hepatic impairment, discuss with the relevant consultant.</td>
</tr>
</tbody>
</table>

**Renal Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afatinib</td>
<td>No starting dose adjustment is required in patients with CrCl equal to or greater than 30ml/min. No data is available in patients with creatinine clearance of less than 30ml/min so no dosing recommendation can be made for these patients.</td>
</tr>
</tbody>
</table>

**Other**

<table>
<thead>
<tr>
<th>NCI-CTC Grade</th>
<th>Action</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 2</td>
<td>Continue treatment</td>
<td>No adjustment</td>
</tr>
<tr>
<td>2 (prolonged or intolerable eg more than 48 hours of diarrhoea or 7 days of rash) or 3 or above</td>
<td>Interrupt unto grade 0-1</td>
<td>Dose reduce by 10mg decrements. Once a dose reduction has occurred do not re-escalate. Treatment should be discontinued in those unable to tolerate 20mg once a day</td>
</tr>
</tbody>
</table>

**Diarrhoea**

Diarrhoea usually occurs within the first 2 weeks of treatment. NCI-CTC grade 3 diarrhoea most frequently occurs within the first 6 weeks of treatment. Ensure patients have an adequate supply of loperamide and are counselled on how and when to use them. Patients with severe diarrhoea unresponsive to loperamide or who become dehydrated may require IV hydration and interruption, dose reduction or discontinuation of therapy.

**Eye**

Symptoms such as acute or worsening eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and / or red eye should be referred to an ophthalmologist. Treatment should be interrupted or discontinued with a diagnosis of ulcerative keratitis.
Lung

Interstitial lung disease (ILD) and ILD-like adverse reactions (e.g. lung infiltration, pneumonitis, acute respiratory distress syndrome, allergic alveolitis) has been reported in 0.7% of afatinib-treated patients.

If patients experience acute and/or worsening of respiratory symptoms such as dyspnoea, cough and fever, afatinib should be interrupted and the patient assessed. If ILD is confirmed, afatinib should be discontinued and appropriate treatment initiated.

Skin

Rash usually manifests as a mild or moderate erythematous and acniform rash which may occur or worsen on sun exposed areas, advise on protective clothing and use of sunscreen. Bullous, blistering and exfoliative skin reactions have been reported, treatment must be interrupted or discontinued if severe.

Regimen

Continuous (28 day cycle, 12 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>Afatinib</td>
<td>40mg once a day (maximum 50mg)</td>
<td>Continuous</td>
<td>Oral</td>
</tr>
</tbody>
</table>

Dose Information

- Afatinib is available as 50mg, 40mg, 30mg and 20mg tablets
- Dose escalation to 50mg once a day may be considered for patients who tolerate the 40mg dose (i.e. absence of diarrhoea, skin rash, stomatitis and other adverse reactions) in the first 3 weeks. Maximum daily dose is 50mg.
- Take on an empty stomach
- For patients unable to swallow the tablet whole, afatinib can be dispersed in approximately 100ml of non-carbonated drinking water. No other liquids should be used. The tablet should be dropped in the water, without crushing and stirred occasionally for up to 15 minutes until the tablet has broken up into very small particles. The dispersion should be consumed immediately. The glass should then be rinsed with approximately 100ml of water which should also be consumed. The dispersion can also be administered through gastric tubes

Additional Therapy

- Loperamide 4mg oral stat after the first loose stool and then 2-4mg when required for the relief of diarrhoea (maximum 16mg/24 hours)
• Metoclopramide 10mg oral three times a day when required for the relief of nausea and vomiting

**Additional Information**

• Afatinib interacts with a number of other medications

• The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to crizotinib

**Coding**

• Procurement – X70.8

• Delivery – X72.9

**References**


REGIMEN SUMMARY

Afatinib

Day One

1. Afatinib 40mg once a day continuous oral

   Administration Instructions
   This medicinal product should be taken without food. Food should not be consumed for at least 3 hours before and at least 1 hour after taking this product
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 Trust

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