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

Drug	Adverse Effects
Afatinib	Diarrhoea, skin reactions (rash, dermatitis acneiform, acne pustular, pruritis, dry skin, palmar-plantar erythrodysaesthesia), stomatitis, paronychia, anorexia, epistaxis, occular disorders (conjunctivitis, dry eye, keratitis), elevated transaminases, interstitial lung disease.

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

Drug	Dose
Afatinib	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

Renal Impairment

Drug	Dose
Afatinib	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.

Other

NCI-CTC Grade	Action	Dose
1 - 2	Continue treatment	No adjustment
2 (prolonged or intolerable eg more than 48 hours of diarrhoea or 7 days of rash) or 3 or above	Interrupt unto grade 0-1	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

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 alveoltis) 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, afatanib should be discontinued and appropriate treatment initiated.

Skin

Rash usually manifests as a mild or moderate erythematous and acneiform 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)

Drug	Dose	Days	Administration
Afatinib	40mg once a day (maximum 50mg)	Continuous	Oral

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

1. National Institute for Health and Care Excellance. Afatinib for treating epidermal growth factor mutation positive locally advanced or metastatic non0small cell lung cancer. Technology Appraisal 310. DOH:London
2. Yang JC, Wu YL, Schuler M et al. Afatinib versus cisplatin based chemotherapy for EGFR mutation positive lung adenocarcinoma (LUX-Lung 3 and LUX-Lung 6): Analysis of overall survival data from two randomised phase three trials. Lamcer Oncol 2015: 16 (2): 141-151.

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

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	June 2015		Dr Deborah Wright Pharmacist	Dr Andrew Bates Consultant Clinical 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 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.