Afatinib

Indication
Locally advanced or metastatic non-small-cell lung cancer which is EGFR-TKI sensitising mutation positive and where the patient has not previously been treated with an EGFR-TK inhibitor

Regimen details
Afatinib 40mg orally daily

Cycle frequency
Treatment is continuous, dispensed every month

Number of cycles
Until disease progression or unacceptable toxicity

Administration
Afatinib is available as 50mg, 40mg, 30mg and 20mg tablets.

The dose should be taken once daily at least one hour before and at least three hours after food.

If patients cannot swallow the tablets they may be dispersed in 100mL non-carbonated water. The tablet should be dropped into the water (not crushed) and stirred until it has dispersed into very small particles. The dispersion should be drunk immediately. Patients should be advised to then rinse the glass in approximately 100mL of water and also consume this. Afatinib may also be administered via a gastric tube following this method

Pre-medication
N/A

Emetogenicity
No routine antiemetics required

Additional supportive medication
Prophylactic TTO with Loperamide 2mg prn (up to 20mg/d), emollient / topical steroids
Patients should be advised to use emollient cream regularly and use sun screen with at least SPF15

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Calcium	14 days

Investigations –pre subsequent cycles
FBC, U+E (including creatinine), LFT (including AST)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 3 x ULN
AST	≤ 5 x ULN

Dose modifications

Dose escalation:

A dose escalation to a maximum of 50mg/day may be considered in patients who tolerate a 40mg/day dose (i.e. absence of diarrhoea, skin rash, stomatitis, and other adverse reactions with CTCAE Grade > 1) in the first 3 weeks. The dose should not be escalated in any patients with a prior dose reduction. The maximum daily dose is 50 mg

Dose reduction:

CTCAE[a] Adverse reactions	Recommended dosing	
Grade 1 or Grade 2	No interruption	No dose adjustment
Grade 2 (prolonged or intolerable) or Grade ≥ 3	Interrupt until Grade 0/1	Resume with dose reduction by 10mg decrements

If patients cannot tolerate 20mg/day then drug should be discontinued

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Stevens-Johnson syndrome/toxic epidermal necrosis
Interstitial lung disease
Left ventricular dysfunction

- **Frequently occurring side effects**

Diarrhoea – may be severe
Rash
Stomatitis
Epistaxis
Anorexia
Fatigue
Elevated LFTs

- **Other side effects**

Keratitis
Nail infections

Significant drug interactions

– for full details consult product literature/ reference texts

P-gp inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, St. John's wort) may decrease exposure to afatinib. Increased risk of therapeutic failure. Avoid co-administration.

Strong P-gp inhibitors (e.g. ritonavir, cyclosporine A, itraconazole, erythromycin, verapamil, quinidine, tacrolimus, nelfinavir, saquinavir, amiodarone): use staggered dosing, preferably 12 hours apart from afatinib (for once daily drugs) or 6 hours apart from afatinib (for twice daily drugs).

BCRP: afatinib is a substrate and an inhibitor of the transporter BCRP. Afatinib may increase the bioavailability of orally administered BCRP substrates (e.g. rosuvastatin and sulfasalazine)

Additional comments

References

Giotrif SPC - https://www.medicines.org.uk/emc/product/7699/smpc

SWCN protocol - http://www.swscn.org.uk/guidance-protocols/cancer-protocols/

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

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