Systemic Anti Cancer Treatment Protocol

Afatinib
Non-Small Cell Lung Cancer

PROTOCOL REF: MPHAAFALU
(Version No: 1.1)

This protocol has been temporarily amended-please see the ORAL SACT OPERATIONAL CHANGES DURING COVID -19.

Amendments may include less frequent blood monitoring, telephone SACT assessments and longer durations of treatment being dispensed.

Approved for use in:

First line treatment of locally advanced or metastatic epidermal growth factor receptor (EGFR) mutation positive NSCLC

Treatment of choice for patients with exon 19 deletion

Locally advanced or metastatic NSCLC of squamous histology progressing on or after platinum-based chemotherapy

Dosage:

Drug	Dosage	Route	Frequency
Afatinib	40mg	Oral	Once daily

A dose escalation to 50mg once daily may be considered in patients who tolerate the 40mg once daily dose (with no diarrhoea, skin rash or stomatitis) in the first 3 weeks.

Treatment is supplied every 2 weeks for two months, then every month thereafter.

Treatment is continued until disease progression or unacceptable toxicity.

Supportive treatments:

Loperamide 2 to 4mg four times a day as required for management of diarrhoea.

Emollients such as Aqueous cream, E45 or Diprobase to prevent dry skin

Extravasation risk:

Not applicable

Administration:

Afatinib should be taken with water. Food should not be consumed for at least three hours before or one hour after taking afatinib.

- The tablet can be swallowed whole with some water or if dosing of whole tablets is not possible, tablets may be administered dispersed in water (non-carbonated).
- No other liquids should be used. Without crushing it, the tablet should be dropped in half a glass of drinking water.
- The glass should be swirled occasionally, until the tablet is dispersed (this may take up to 15 minutes).
- The dispersion should be drunk immediately after dispersion is complete (i.e. within 60 minutes).
- The glass should be rinsed with half a glass of water, which should also be drunk.
- The dispersion can also be administered through a naso-gastric or gastrostomy tube.

Drug Interactions:

Concomitant treatment with strong inducers of P-gp may decrease exposure to afatinib.

Please consult SPC for full list of interactions: available via medicines.org.uk or discuss with a pharmacist.

Main Toxicities:

Diarrhoea, rash/acne, stomatitis/mucositis and paronychia

Investigations and Treatment Plan:

	Pre	Cycle 1	Cycle 1 Day 14	Cycle 2	Cycle 2 Day 14	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X	X	X	X	X	Every 3 cycles
Nursing Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X		X		X	X	Every cycle
U&E & LFT	X	X		X		X	X	Every cycle
LDH		X		X		X		Every cycle
CT scan	X					X*		*CT scan to be carried out prior to cycle 3 then every three months or as clinically indicated
Informed Consent	X							
PS recorded	X	X		X		X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X		X		X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Afatinib is not myelosuppressive; however, FBC should be reviewed prior to each cycle.

Non-haematological toxicities

Any patient with a grade 3 or 4 toxicity not controlled by optimum supportive care will require a dose reduction as per the table below.

Level	Afatinib Dose
Increased Dose	50mg daily
Starting Dose	**40mg daily**
1st Reduction	30mg daily
2nd Reduction	20mg daily

If 20mg daily is not tolerated then treatment should be discontinued

Dose adjustment for skin rash:

Rash is a commonly reported adverse effect of afatinib, in general it manifests as mild or moderate erythematous and acneiform rash, which may occur or worsen in areas exposed to the sun. Dry skin and pruritis may also occur.

Bullous, blistering and exfoliative skin conditions can occur and treatment should be interrupted or discontinued if severe.

Treatment with afatinib must be interrupted and dose reduced in the event of any grade 3 rash, grade 2 rash lasting more than 7 days or intolerable grade 2 rash.

Toxicity	Symptoms	Dose modification	Management
Grade 1	Generally localised Minimally symptomatic No sign of infection	None	Simple emollients such as Aqueous cream, E45 or Diprobase with the addition 1% Hydrocortisone cream, and/or 1% Clindamycin lotion
Grade 2	Generalised moderate symptoms No sign of infection	Dose interruption may be required	As for grade 1 plus consider adding doxycycline 100mg daily. Review after 2 weeks
Grade 3	Generalised severe symptoms, potential for infection Significant impact on daily life.	Dose interruption for 7 to 14 days may be required. 50mg dose: reduction required on resuming treatment. Discontinuation may be necessary	As for grade 2 plus oral prednisolone can be given starting at 25mg daily for 1 week then reducing by 5mg per day over 5 days. Review after 2 weeks

Other supportive medicines

Consider adding in antihistamines e.g. chlorphenamine/ hydroxyzine and painkillers, paracetamol/ ibuprofen if itching and or painful.

If there is evidence of photosensitivity, then use sunscreen (SPF30 or above).

Topical retinoids and other acne medications (e.g. benzyl peroxide) are NOT recommended since rash is not acne. Their skin drying effects may exacerbate rash.

Dose adjustment for diarrhoea

Most patients experience some diarrhoea, with grade 3 diarrhoea most frequently occurring within the first 6 weeks of treatment.

Treatment with afatinib must be interrupted and dose reduced in the event of any grade 3 diarrhoea, grade 2 diarrhoea lasting more than 48 hours or intolerable grade 2 diarrhoea.

Toxicity	Dose modification	Management
Grade 1 or 2	None	Loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg /day) Encourage fluid intake Continue loperamide until normal bowel function restored for at least 12 hours
Grade 3	Once resolved to Grade 0/1 then resume at 10mg dose reduction	Continue loperamide Consider other causes Consider octreotide

In more severe or persistent cases of diarrhoea leading to dehydration afatinib treatment must be stopped and appropriate measures should be taken to intensively rehydrate the patients intravenously.

Keratitis

Symptoms such as acute or worsening eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye should be referred promptly to an ophthalmology specialist. If a diagnosis of ulcerative keratitis is confirmed, treatment should be interrupted or discontinued. The benefits and risks of continuing treatment should be carefully considered.

Contact lens use is also a risk factor for keratitis and ulceration.

Dose adjustment for stomatitis

Toxicity	Symptoms	Dose modification	Management
Grade 1	Erythema of the mucosa. Minimally symptomatic	None	Encourage good mouth care, avoid alcohol based mouthwashes. Increase oral intake
Grade 2	Patchy ulcerations or pseudomembranes Generalised moderate symptoms	Interrupt treatment for intolerable stomatitis and consider dose reduction once resolved to Grade 0/1	As above Consider gelclair and pain relief

Grade 3	Confluent ulcerations or pseudomembranes; bleeding with minor trauma. Significant impact on daily life.	Interrupt treatment and dose reduce by one level once resolved to Grade 0/1	As above

Other information

Higher exposure to afatinib has been observed in female patients, patients with lower body weight and those with underlying renal impairment. This could result in a higher risk of developing adverse reactions in particular diarrhoea, rash/acne and stomatitis. Closer monitoring is recommended in patients with these risk factors.

Interstitial Lung Disease

Interstitial Lung Disease (ILD) should be suspected in patients who develop acute onset of new and/or progressive unexplained pulmonary symptoms such as dyspnoea, cough and fever, and should have their afatinib interrupted pending diagnostic evaluation.

Hepatic Impairment

No dose adjustments required for mild to moderate hepatic impairment.
There is limited data on patients with severe hepatic impairment and therefore afatinib should be used with caution.

Renal Impairment

No dose adjustments are required in patients with mild to moderate renal impairment.
There is limited data for patients with severe renal impairment, and treatment in patients with CrCl <30mL/min is not recommended

References:

- https://www.medicines.org.uk/emc
- NICE TA310 Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer

- Guidance for healthcare professionals treating patients with EGFR M+ advanced NSCLC. Giotrif adverse event management guide. Boehringer Ingeleim International.