Systemic Anti Cancer Treatment Protocol

Gefitinib
Non-Small Cell Lung Cancer

PROTOCOL REF: MPHAGEFILU
(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 non-small cell lung cancer (NSCLC) with activating mutations of EGFR-TK

Note: patient access scheme: the entire course of treatment is paid for at cycle 3

Dosage:

Drug	Dosage	Route	Frequency
Gefitinib	250mg	Oral	Once daily

Tablets will be supplied at 28 day intervals.

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:

- The tablet may be taken orally with or without food, and should be taken at about the same time each day.
- The tablet can be swallowed whole with some water or if dosing of whole tablets is not possible, tablets may be administered as a dispersion 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 20 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.

Interactions:

The patient should be advised to avoid grapefruit and grapefruit juice whilst taking gefitinib.

H2 antagonists and proton-pump inhibitors may reduce bioavailability and reduce efficacy. Therefore review concurrent medications prior to commencing treatment.

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

Main Toxicities:

Dry mouth, skin rash, diarrhoea, ocular disorders, elevated LFT's, interstitial lung disease.

Investigations and Treatment Plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X	X		Every 3 cycles
Nursing Assessment	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	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	Every cycle
Weight recorded	X	X	X	X	X	Every cycle

Repeat CT scan (or other imaging) must be performed prior to prescribing cycle 3 to assess response

Dose Modifications and Toxicity Management:

Haematological toxicity

Gefitinib 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 interruption as per the table below.

Patients with poorly tolerated diarrhoea or skin adverse reactions may be successfully managed by providing a brief (up to 14 days) therapy interruption followed by reinstatement of the 250 mg dose. For patients unable to tolerate treatment after a therapy interruption, gefitinib should be discontinued and an alternative treatment should be considered.

Management for skin rash:

Typical gefitinib rash has the following appearance:

- Acne type appearance usually involving the face, head and upper torso.

Toxicity	Symptoms	Dose modification	Management
Grade 1	Generally localised Minimally symptomatic No sign of infection	Not required	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. Dose reduction required on resuming treatment to alternate days 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.

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.

Management for diarrhoea:

Toxicity	Dose modification	Management
Grade 1 to 2	None Encourage fluid intake	Loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg /day)
3	If unresponsive to anti-diarrhoeal medication for 24 hours then stop drug until resolution to grade <1 and then restart and consider alternate day dosing	As above
4	If unresponsive to anti-diarrhoeal agent for >24 hours then discontinue drug	As above

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

Interstitial lung disease (ILD)

ILD, which may be acute in onset, has been observed in 1.3 % of patients receiving gefitinib, and some cases have been fatal. If patients experience worsening of respiratory symptoms such as dyspnoea, cough and fever, gefitinib should be interrupted and the patient should be promptly investigated. If ILD is confirmed, gefitinib must be discontinued and the patient treated appropriately.

Hepatic Impairment

Patients with moderate to severe liver impairment due to cirrhosis have increased plasma gefitinib levels and should be monitored closely for adverse effects.

Renal Impairment

No dose modifications are required in patients with CrCl > 20mL/min. There is limited data for patients with severe renal impairment.

References:

- https://www.medicines.org.uk/emc
- NICE TA192: Gefitinib for the first line treatment of locally advanced or metastatic NSCLC