



Positive Quality Intervention: Afatinib Management for Non-Small Cell Lung Cancer (NSCLC)

Description:

This PQI highlights management of common adverse events, patient follow-up, and dose modifications for Afatinib (Gilotrif®) therapy.

Background:

Afatinib is indicated for the first-line treatment of EGFR positive (exon 19 or exon 21) metastatic non-small cell lung cancer (NSCLC). It is also indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy. Proper follow up including patient assessment is essential when new patients start on therapy. Dose adjustments are common and greatly reduced frequency and severity of adverse reactions. In Lux-Lung 3, 43% maintained the 40mg starting dose, 38% reduced to 30mg and 19% further reduced to 20mg. Progression free survival remained consistent in patients with or without dose adjustments. Weekly follow-ups are ideal to assess adverse events.

PQI process:

Day 1 – Initial Patient Counseling

- Educate patients that adverse events, **especially diarrhea and rash/acne** are expected and reassure patients that **dose modifications are common**
- Provide patients with loperamide. Advise patients to take loperamide and call the office at the onset of diarrhea and instruct patients to continue anti-diarrheal until loose stools cease for 12 hours
- Advise patients to call office at the onset and to minimize sun exposure with protective clothing and use of sunscreen due to cutaneous reactions (rash, erythema, acneiform rash and palmar-plantar erythrodysesthesia syndrome)
- Advise patients to immediately report any new or worsening lung symptoms, or any combination of the following symptoms: trouble breathing or shortness of breath, cough, fever
- Advise patients to immediately report any symptoms of a liver problem [e.g., skin or the whites of eyes turn yellow, urine turns dark or brown (tea colored), pain on the right side of stomach, bleeds or bruises more easily than normal, lethargy
- Other: Keratitis, Left Ventricular Dysfunction, Embryo-Fetal Toxicity, Infertility, and do not breastfeed

Days 7, 14, 21, 28– Patient follow-up

- Assess each of the side effects below and discuss each bullet point below
- Assess diarrhea and rash/acne
 - These reactions cause the most dose reductions and typically occur within 14 days.
 - How many bouts of diarrhea have you had since we last spoke? Include any treatment you have taken for diarrhea and describe how it worked.
 - Describe any rashes or acne that may have developed since we last spoke.
- Discuss and manage the other common reactions – Stomatitis and Paronychia
 - Describe changes, if any, you have noticed with any part of your mouth including your tongue.
 - Describe changes, if any, you have noticed to your nails.

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- Discuss and manage less common reactions – Dry skin, Pruritus, Keratitis, Interstitial Lung Disease, Hepatic toxicity
 - Describe any other skin dryness or itching that has started.
 - Describe any eye pain or visual changes you have experienced since starting Afatinib.
 - Describe any new cough or difficulty breathing even at resting that may have developed.
 - Describe any changes to the whites of your eyes or any other skin discoloration.

Afatinib Management:

Hold therapy:

- ≥ grade 3 adverse reactions
- ≥ grade 2 diarrhea (persisting for 2 or more consecutive days while taking anti-diarrheal)
- cutaneous reactions (prolonged, lasting more than 7 days, or intolerable)
- renal impairment

Resume treatment at 10 mg less per day when adverse reaction fully resolves, returns to baseline, or improves to grade 1

Permanently discontinue:

- Life-threatening bullous, blistering, or exfoliative skin lesions
- Confirmed interstitial lung disease (ILD)
- Severe drug-induced hepatic impairment
- Persistent ulcerative keratitis
- Symptomatic left ventricular dysfunction
- Severe or intolerable adverse reaction occurring at a dose of 20 mg per day

Patient Centered Activities:

- Provide Oncology Chemotherapy Education (OCE) sheet
- Counsel patient as described above in PQI Process and follow-up as described
- Supply or advise patient to obtain Anti Diarrheals
- Supply or advise patient to obtain Moisturizing cream
- Supply or advise patient to obtain and utilize Sun Screen

References:

1. Gilotrif® (afatinib) [Prescribing Information]. Boehringer Ingelheim Pharmaceuticals, Inc.: Ridgefield, CT. 12/2019
2. Yang JC, Schuler MH, Yamamoto N, et. al, [LUX-Lung 3: A randomized, open-label, phase III study of afatinib versus pemetrexed and cisplatin as first-line treatment for patients with advanced adenocarcinoma of the lung harboring EGFR-activating mutations.](#) Journal of Clinical Oncology 2012 30:18_suppl, LBA7500-LBA7500

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Supplemental Information: Dosing Modifications by Adverse Event

Diarrhea Management	Grade 1	Grade 2	Grade 3	Grade 4
	< 4 stools	4-6 stools	7 or more stools	Life-Threatening
	Increase of <4 stools per day over baseline, mild increase in ostomy output compared to baseline	Increase of 4-6 stools per day over baseline; not interfering with daily activities; IV fluids indicated ,24 hrs; moderate increase in ostomy output compared to baseline	Increase of 7 or more stools per day over baseline; incontinence; interfering with daily activities; IV fluid fluids ≥ 24 hrs; hospitalization; severe increase in ostomy output compared to baseline	Life-Threatening consequences (eg. hemodynamic collapse)
	Maintain dose	Consider pausing	Pause	Pause
	Continue same dose of GILOTRIF. Stop laxatives and advise patient to drink 8-10 glasses of water or clear fluids per day. Prescribe 4 mg loperamide taken immediately; followed by 2 mg after each loose stool (max. 16 mg/day) until bowel movements cease for 12 hours	Continue same dose of GILOTRIF unless grade 2 diarrhea continues for ≥ 48 hours, in which case GILOTRIF must be paused until reduced to grade 1 or below; follow with dose reduction; see grade 1; continue loperamide; assess for dehydration and electrolyte imbalance; consider IV fluid and electrolyte replacement	Pause GILOTRIF until recovered to grade 1 or below and follow with dose reduction. In addition to grade 2 interventions, an infection process should be ruled out with stool cultures; aggressive IV fluid replacement for ≥ 24 hours; hospitalization to monitor progress; consider prophylactic antibiotics if patient is also neutropenic	See Grade 3
Rash/ Acne Management	Grade 1	Grade 2	Grade 3	Grade 4
	Macular or papular eruptions or erythema without associated symptoms	Macular or papular eruptions with pruritus or other associated symptoms; localized desquamation or other lesions covering <50% of BSA	Severe, generalized erythroderma or macular, papular, or vesicular eruption; desquamation covering ≥ 50% of BSA; associated with pain, disfigurement, ulceration, or desquamation	Generalized exfoliative, ulcerative, or bullous dermatitis
	Maintain dose	Pause	Pause	Permanently Discontinued
	Topical Steroids or tacrolimus ointment alternative. Consider topical antibiotics twice daily. Recommend cream for isolated scattered lesions, and lotion for multiple scattered areas.	Topical steroid treatment as for grade 1 oral antibiotic (6 weeks) e.g. doxycycline 100 mg b.i.d., minocycline hydrochloride 100 mg b.i.d., or, if available, oxytetracycline 500 mg b.i.d. Stop topical antibiotic if being used	Topical and systemic treatment as for grade 2. If Infection suspected (yellow crusts, purulent discharge, painful skin/nares), switch oral antibiotic to broad spectrum/gram negative coverage and consider skin swab for bacterial culture	Permanently discontinue GILOTRIF for life-threatening bullous, blistering, or exfoliative skin lesions

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Paronychia (Nails) Management	Grade 1	Grade 2	Grade 3	Grade 4
	Nail fold edema or erythema; disruption of the cuticle	Localized intervention indicated; oral intervention indicated (e.g. antibiotic, antifungal, antiviral); nail fold edema or erythema with pain; associated with discharge or nail plate separation; limiting instrumental ADL	Surgical intervention or IV antibiotics indicated; limiting self-care activities of daily living (ADL)	N/A
	Maintain dose	Prolonged: Pause	Pause	N/A
	Topical antibiotics/antiseptics, vinegar soaks, and topical ultrapotent steroids	Topical antibiotics, vinegar soaks, silver nitrate application weekly, and topical ultrapotent steroids	Topical antibiotics, vinegar soaks, silver nitrate application weekly/ consider nail avulsion and systemic antibiotics	N/A
Stomatitis Management	Grade 1	Grade 2	Grade 3	Grade 4
	Erythema of the mucosa	Patchy ulcerations or pseudomembranes	Confluent ulcerations or pseudomembranes; bleeding with minor trauma	Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
	Maintain dose	Prolonged: pause	Pause	Pause
	Oral rinses with agents such as non-alcoholic mouthwash, normal saline, diluted salt and baking soda solution	Addition of topical analgesic mouth treatments, topical corticosteroids, antiviral therapy if herpetic infection confirmed, antifungal therapy preferably topical on a case by case basis	Same as for grade 2; institute additional symptomatic therapy (topical or systemic) as clinically indicated	Same as for grade 2; institute additional symptomatic therapy (topical or systemic) as clinically indicated

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