BC Cancer Protocol Summary for Treatment of Locally Advanced Epidermal Growth Factor Receptor (EGFR) Mutation-Positive Non-Small Cell Lung Cancer (NSCLC) with Osimertinib

Protocol Code: *LULAOSI*

Tumour Group: *Lung*

Contact Physician: *LU Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Unresectable locally advanced stage III NSCLC
- EGFR mutation-positive tumour with exon 19 or L858R mutation, and
- No disease progression during or following prior treatment with platinum-based chemotherapy and radiation (either concurrent or sequential)

Patients should have:

- Treatment initiation within 10 weeks of chemotherapy and radiation treatment completion
- Good performance status
- Adequate hematological, renal and hepatic function

EXCLUSIONS:

Patients must not have:

- Progression on or within 6 months of prior adjuvant EGFR TKI therapy
- History of interstitial lung disease prior to chemoradiation treatment
- Congenital long QT syndrome or a persistent corrected QT interval (QTc) of greater than or equal to 470 msec

TESTS:

- Baseline: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, calcium, potassium, magnesium, ECG
- Baseline, if clinically indicated: MUGA scan or echocardiogram
- During treatment: alkaline phosphatase, ALT, total bilirubin, LDH, potassium, calcium and magnesium at each subsequent visit
- If clinically indicated: CBC & Diff, creatinine, chest x-ray, ECG, MUGA scan or echocardiogram

PREMEDICATIONS:

- No premedications required

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
osimertinib	80 mg once daily	PO

- For patients with difficulty swallowing, or for nasogastric tube administration, please refer to the BC Cancer Drug Manual osimertinib drug monograph

Continue until disease progression or unacceptable toxicity.

DOSE MODICATIONS:

Dose reduction:
Dose level -1: osimertinib 40 mg PO once daily

1. **Renal Impairment:** dose modification is not required in patients with mild or moderate renal impairment. Safety and efficacy has not been established in patients with end-stage renal disease (CrCl < 15 mL/min) or on dialysis.
2. **Hepatic Impairment:** dose modification is not required in patients with mild hepatic impairment. Safety and efficacy has not been established in patients with moderate or severe hepatic impairment.
3. **Interstitial Lung Disease (ILD) and/or Pneumonitis:**

	Severity	Management
ILD/Pneumonitis following definitive platinum-based chemotherapy and radiation	Asymptomatic (Grade 1)	Continue osimertinib treatment, or interrupt and restart as appropriate
	Grade 2 or higher	Permanently discontinue osimertinib
Radiation Pneumonitis	Symptomatic (Grade 2)	▪ Withhold osimertinib until symptoms resolve ▪ If symptoms resolve within 4 weeks, restart osimertinib ▪ If symptoms do not resolve within 4 weeks or recur after restarting, permanently discontinue osimertinib
	Severe or life-threatening (Grade 3 or 4)	Permanently discontinue osimertinib

4. **QT Prolongation:** treatment interruption and subsequent dose reduction is required for development of QTc prolongation (QTc greater than 500 msec on at least two separate ECGs). Withhold osimertinib until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then restart at a reduced dose (40 mg). If QTc interval prolongation with signs/symptoms of serious arrhythmia, permanently discontinue osimertinib.
5. **Left Ventricular Dysfunction/Cardiomyopathy:** treatment interruption is recommended for asymptomatic, absolute decreases in LVEF of 10% from baseline and LVEF below 50%. If LVEF improves, resume osimertinib treatment cautiously and consider dose reduction. If *symptomatic* congestive heart failure occurs at any time, treatment should be permanently discontinued.

PRECAUTIONS:

1. **Cardiomyopathy**: congestive heart failure, pulmonary edema, and decreased ejection fraction have been observed in patients treated with osimertinib. Fatal cardiomyopathy has been reported. LVEF should be assessed regularly during treatment, particularly in patients with known cardiac risk factors, and in patients who develop treatment-related cardiac symptoms.
2. **QT Interval Prolongation**: osimertinib is associated with concentration-dependent QT interval prolongation. Monitor ECG at baseline and correct electrolyte abnormalities prior to treatment. Continued monitoring of ECG and electrolytes is recommended during treatment, particularly in patients with predisposing conditions, and in those receiving concomitant drugs known to prolong the QT interval.
3. **Respiratory**: osimertinib has been associated with severe, life-threatening or fatal treatment-related interstitial lung disease/pneumonitis. Patients should be regularly monitored for pulmonary symptoms indicative of pneumonitis.
4. **Ocular Disorders:** osimertinib has been associated with keratitis, conjunctivitis, blepharitis, and dry eye. Ophthalmologic consultation should be considered for associated symptoms. Contact lens use is known to be an independent risk factor for ocular toxicity, including keratitis. Caution should be exercised when driving or operating machinery.
5. **Drug Interactions**: concurrent use of strong CYP3A inducers should be avoided. If possible, concurrent therapy with drugs that prolong the QTc interval or disrupt electrolyte levels should also be avoided.
6. **Skin Toxicity**: rash, including dermatitis acneiform, drug eruption, folliculitis, rash erythematous and maculopapular are common. They appear on the face, scalp, “v”-shaped area of the chest, upper trunk and less frequently on the extremities, lower back, abdomen and buttocks. Severe rashes may require dose interruption and modification.
7. **Paronychia**: osimertinib is associated with paronychia, which typically occurs later in treatment (e.g., 4 to 8 weeks) and can cause severe pain. Preventative measures and good skin care may help to reduce the frequency and severity of symptoms.

Contact the LU Systemic Therapy Physician at your regional cancer centre or the LU Systemic Therapy Chair with any problems or questions relating to this treatment program.

References:

1. Lu S, Kato T, Dong X et al. Osimertinib after Chemoradiotherapy in Stage III *EGFR*-Mutated NSCLC. N Engl J Med. 2024 Aug 15;391(7):585-597.
2. Osimertinib (Tagrisso) Canada's Drug Agency (CDA-AMC) Reimbursement Recommendation. Canadian Journal of Health Technologies. September 2025; 5(9);1-28.