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

Protocol Code: *LUAJOSI*

Tumour Group: *Lung*

Contact Physician: *Dr. Sophie Sun*

ELIGIBILITY:

Patients must have:

- Surgically resected stage IB to IIIB NSCLC (per American Joint Committee on Cancer (AJCC) 8th edition),
- EGFR mutation-positive tumour with exon 19 or L858R mutation, and
- Eligible with or without post-operative chemotherapy:
  - Surgical resection within 12 weeks of starting osimertinib treatment if no adjuvant chemotherapy administered
  - Surgical resection within 28 weeks of starting osimertinib treatment if adjuvant chemotherapy was administered

Patients should have:

- ECOG 0-2

EXCLUSIONS:

Patients must not have:

- Congenital long QT syndrome or a persistent corrected QT interval (QTc) of ≥ 470 msec

TESTS:

- Baseline: CBC & differential, platelets, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, calcium, potassium, magnesium, and ECG
- During treatment: alkaline phosphatase, ALT, total bilirubin, LDH, potassium, calcium and magnesium at each subsequent visit
- As required:
  - CBC & differential, platelets
  - MUGA scan or echocardiogram – if clinically indicated, monitoring of LVEF is recommended at baseline and at 12-week intervals
  - periodic ECG monitoring for QTc prolongation
  - creatinine if clinically indicated
  - chest x-ray for monitoring of dyspnea to rule out development of pneumonitis

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, unacceptable toxicity or a maximum of 3 years of treatment.

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):** permanently discontinue osimertinib for development of any grade of treatment-related ILD/pneumonitis.
4. **QT Prolongation:** treatment interruption and subsequent dose reduction is required for development of QTc prolongation (QTc > 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 *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., 4-8 weeks) and can cause severe pain. Preventative measures and good skin care may help to reduce the frequency and severity of symptoms.

Contact Dr. Sophie Sun or tumour group delegate at (604) 930-2098 or 1-800-663-3333 with any problems or questions relating to this treatment program.

References:

1. Wu YL, Tsuboi M, He J, et al. Osimertinib in Resected EGFR-Mutated Non-Small-Cell Lung Cancer. N Engl J Med. 2020 Oct 29;383(18):1711-1723.
2. Planchard D. Adjuvant Osimertinib in EGFR-Mutated Non-Small-Cell Lung Cancer. N Engl J Med. 2020 Oct 29;383(18):1780-1782.