BC Cancer Protocol Summary for Adjuvant Treatment of Resected ALK-Positive Non-Small Cell Lung Cancer with Alectinib

Protocol Code:	*LUAJALE*
Tumour Group:	*Lung*
Contact Physician:	*LU Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Resected ALK positive non-small cell lung cancer (NSCLC), and
- Stage IB with tumour size equal to 4 cm to stage III, per AJCC 8th edition, and
- Treatment initiation following surgery

Patients should have:

- Good performance status
- Adequate hematological, hepatic and renal function

Notes:

- Patient who were started on adjuvant chemotherapy prior to 1 November 2025, may switch to LUAJALE provided all other eligibility criteria are met.
- Patients may be retreated with ALK inhibitors if disease recurrence occurs 6 months or more from the last adjuvant alectinib dose

CAUTIONS:

- Baseline symptomatic bradycardia or QTc interval greater than 470 msec
- Patients at risk of gastrointestinal perforation

TESTS:

- Baseline: CBC & Diff, alkaline phosphatase, ALT, total bilirubin, LDH, heart rate, creatine kinase (CK), blood pressure, ECG
- Every 2 weeks for the first 3 months of treatment, then at each visit: CBC & Diff, alkaline phosphatase, ALT, total bilirubin, LDH
- Every 2 weeks for the first month: CK
- If clinically indicated: calcium, potassium, creatinine, CK, ECG, chest radiograph, chest X-ray

PREMEDICATIONS:

- No premedications needed

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
alectinib	600 mg twice daily	PO

Hepatic Impairment: in patients with underlying severe hepatic impairment the recommended starting dose is 450 mg PO twice daily.

Continue until disease progression, unacceptable toxicity up to a maximum of 2 years of treatment.

DOSE MODIFICATIONS:

Dose Levels:

Starting Dose	Dose Level -1	Dose Level -2
600 mg twice daily	450 mg twice daily	300 mg twice daily

1. Hepatic Dysfunction:

Severity	Management
ALT elevation to > 5.0 x ULN with total bilirubin ≤ 2 x ULN	Withhold until recovery of ALT to ≤ 3.0 x ULN or baseline, then resume at lower dose level
ALT elevation to > 3.0 x ULN and concurrent total bilirubin elevation to > 2 x ULN (in absence of cholestasis or hemolysis)	Permanently discontinue

2. Renal Dysfunction:

Severity	Management
Grade 3	Withhold treatment until recover to Grade 1 or baseline, then resume at lower dose level
Grade 4	Permanently discontinue

3. Bradycardia (heart rate less than 60 beats per minute [bpm]):

Severity	Management
Grade 2 or 3 (symptomatic, medical intervention indicated)	• Withhold treatment until recovery to Grade 1 or heart rate increases to greater than or equal to 60 bpm • Evaluate for concurrent contributing bradycardic/hypotensive medications and adjust • Consider referring to cardiology for management • If concurrent contributing medications identified and adjusted, resume at previous dose upon recovery • If no concurrent contributing medications identified or are not adjusted, resume at lower dose level upon recovery
Grade 4 (life-threatening consequences, urgent intervention indicated)	• Permanently discontinue if no concurrent contributing medications identified • If concurrent contributing medications identified and adjusted, resume at lower dose level upon recovery to Grade 1 or baseline • Permanently discontinue in case of recurrence

4. CK Elevation:

Severity	Management
CK greater than 5 x ULN (first occurrence)	Withhold treatment until recovery to baseline or less than or equal to 2.5 x ULN, then resume at same dose
CK greater than 5 x ULN (second or subsequent occurrence)	Withhold treatment until recovery to baseline or less than or equal to 2.5 x ULN, then resume at lower dose level
CK greater than 10 x ULN	Withhold treatment until recovery to baseline or less than or equal to 2.5 x ULN, then resume at lower dose level

5. **Hemolytic Anemia:** For Grade 2 or higher hemolytic anemia with hemoglobin less than100 g/L, withhold until resolution, then resume at lower dose level or permanently discontinue.
6. **Pneumonitis:** Immediately withhold alectinib in patients diagnosed with ILD/pneumonitis and permanently discontinue if no other causes have been identified.
7. **Gastrointestinal perforation:** Permanently discontinue alectinib in patients who develop gastrointestinal perforation.

PRECAUTIONS:

1. **Cardiotoxicity**: Bradycardia, both symptomatic and asymptomatic, has been observed in patients treated with alectinib. Heart rate and blood pressure should be monitored regularly during treatment and co-administration of medications that lower heart rate should be avoided to the extent possible. If avoidance is not possible, patients should be closely monitored. Caution should be exercised in patients with a lower baseline heart rate, history of syncope or arrhythmia, sick sinus syndrome, sinoatrial block, atrioventricular (AV) block, ischemic heart disease, or congestive heart failure. Cardiology consult may be required.
2. **Gastrointestinal Perforation**: Gastrointestinal perforation with fatal outcome, has occurred in <1% of patients treatment with alectinib. Exercise caution in patients at increased risk for gastrointestinal perforation – concomitant use of medications with risk of gastrointestinal perforation, history of diverticulitis, metastases to the gastrointestinal tract. Alectinib should be permanently discontinued in patients who develop gastrointestinal perforation.
3. **Respiratory**: Alectinib has been associated with cases of ILD/pneumonitis. Patients should be regularly monitored throughout treatment for pulmonary symptoms indicative of pneumonitis.
4. **Hepatic Impairment**: Patients with underlying *severe* hepatic impairment should receive a dose reduction of alectinib. Dose adjustment is not required for patients with underlying mild or moderate hepatic impairment. However, for all patients with hepatic impairment, appropriate monitoring is advised.
5. **Hepatotoxicity**: Bilirubin and transaminase elevations have been reported and generally occur within the first three months of treatment. Elevations are usually reversible with treatment interruption/dose reduction. However, biopsy confirmed *drug-induced liver injury* has occurred in some patients. Monitor liver function regularly during treatment and increase test frequency if clinically indicated.
6. **Musculoskeletal**: Myalgia can sometimes be severe and may be associated with elevated CK. Management of symptoms may require alectinib dose modification or temporary discontinuation of treatment.
7. **Photosensitivity**: Photosensitivity has been reported. Prolonged sun exposure should be avoided. If exposure is unavoidable, broad-spectrum sun screen and lip balm of at least SPF 50 should be used during treatment and for seven days after discontinuation of treatment.
8. **Vision disorders**: Diplopia, blurry vision, vitreous floaters, asthenopia, and reduced visual acuity have all been reported. Patients experiencing vision disorders should be cautious when driving or operating machinery.

Contact the LU Systemic Therapy physician at your regional cancer centre or the LU Systemic Therapy Chair with any problems or questions regarding this treatment.

References:

1. Wu YL, Dziadziuszko R, Ahn JS et al. Alectinib in Resected ALK-Positive Non-Small-Cell Lung Cancer. N Engl J Med 2024;390:1265-1276.
2. Alectinib (Alecensaro) CDA-AMC Canada's Drug Agency Reimbursement Recommendation. Canadian Journal of Health Technologies Nov 2024; 4(11): 1-24.