North West Coast
Strategic Clinical Networks

Chemotherapy Protocol

DRUG REGIMEN
Alectinib

Indication for use
First-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC)

Regimen
Alectinib 600 mg (four 150 mg capsules) taken twice daily with food (total daily dose of 1200 mg)
Treatment is continued until disease progression or unacceptable toxicity

Hepatic Impairment
No starting dose adjustment is required in patients with underlying mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Patients with underlying severe hepatic impairment (Child-Pugh C) should receive a starting dose of 450 mg taken twice daily. For all patients with hepatic impairment, appropriate monitoring (e.g. markers of liver function) is advised

Investigation prior to initiating treatment
FBC, U&Es, LFTs, HR, BP, ECG, CPK

Investigations and consultations prior to each cycle
FBC, U&Es, LFTs, every 2 weeks for first three months
Creatine phosphokinase (CPK) levels
Heart rate and Blood pressure
ECG prior to cycle one and subsequently if HR drops to <60/min

Acceptable levels for treatment to proceed (if outside these levels contact consultant and see table below)

ALT or AST < 3 times the upper limit of normal (ULN) AND Bilirubin <2 times ULN
Haemoglobin >=9
CPK <= 2.5 times ULN
HR >60

Side Effects
Interstitial lung disease (ILD)/pneumonitis, hepatotoxicity, myalgia, bradycardia, rash, photosensitivity, constipation, oedema, anaemia, nausea, vomiting, diarrhoea, visual disorders

Dose Modification Criteria
Management of adverse events may require dose reduction, temporary interruption, or discontinuation of treatment with alectinib. The dose of alectinib should be reduced in steps of 150 mg twice daily based on tolerability. Alectinib treatment should be permanently discontinued if patients are unable to tolerate the 300 mg twice daily dose. Management of adverse events may require dose reduction, temporary interruption, or discontinuation of treatment with alectinib. The dose of alectinib should be reduced in steps of 150 mg twice daily based on tolerability. Alectinib treatment should be permanently discontinued if patients are unable to tolerate the 300 mg twice daily dose.

Dose reduction schedule	
Starting dose	600 mg twice daily
First dose reduction	450 mg twice daily
Second dose reduction	300 mg twice daily

CTCAE grade	**Alectinib treatment**
ILD/pneumonitis of any severity grade	Immediately interrupt and permanently discontinue alectinib if no other potential causes of ILD/pneumonitis have been identified
ALT or AST elevation of Grade ≥ 3 (> 5 times ULN) with total bilirubin ≤ 2 times ULN	Temporarily withhold until recovery to baseline or ≤ Grade 1 (≤ 3 times ULN), then resume at reduced dose
ALT or AST elevation of Grade ≥ 2 (> 3 times ULN) with total bilirubin elevation > 2 times ULN in the absence of cholestasis or haemolysis	Permanently discontinue alectinib.
Bradycardia Grade 2 or Grade 3(symptomatic, may be severe and medically significant, medical intervention indicated)	Temporarily withhold until recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm. Evaluate concomitant medicinal products known to cause bradycardia, as well as anti-hypertensive medicinal products. If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, resume at previous dose upon recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm. If no contributing concomitant medicinal product is identified, or if contributing concomitant medicinal products are not discontinued or dose modified, resume at reduced dose upon recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm.
Bradycardia Grade 4 (life-threatening consequences, urgent intervention indicated)	Permanently discontinue if no contributing concomitant medicinal product is identified. If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, resume at reduced dose upon recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm, with frequent monitoring as clinically indicated. Permanently discontinue in case of recurrence
CPK elevation > 5 times ULN	Temporarily withhold until recovery to baseline or to ≤ 2.5 times ULN, then resume at the same dose
CPK elevation > 10 times ULN or second occurrence of CPK elevation of > 5 times ULN	Temporarily withhold until recovery to baseline or to ≤ 2.5 times ULN, then resume at reduced dose

Specific Information on Administration
If a planned dose of alectinib is missed, patients can make up that dose unless the next dose is due within 6 hours. Patients should not take two doses at the same time to make up for a missed dose.
If vomiting occurs after taking a dose of alectinib, patients should take the next dose at the scheduled time.

Drug Interactions
Alectinib is an inhibitor of P-gp, BCRP. Appropriate monitoring is recommended when alectinib is co-administered with P-gp or BCRP substrates

The effectiveness of concomitant administration of oral contraceptives may be reduced

THIS PROTOCOL HAS BEEN DIRECTED BY DR MIRZA, CLINICIAN FOR LUNG CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

DATE **June 2018**
REVIEW **June 2020**
VERSION **2**