**Systemic Anti Cancer Treatment Protocol**

# Alectinib

**PROTOCOL REF: MPHAALECLU**
**(Version No: 1.1)**

**This protocol has been temporarily amended-please see the ORAL SACT OPERATIONAL CHANGES DURING COVID -19.**

**Amendments may include less frequent blood monitoring, telephone SACT assessments and longer durations of treatment being dispensed.**

## Approved for use in:

- 1st line treatment for patients with anaplastic lymphoma kinase (ALK) positive advanced non-small cell lung cancer
- Must be stage IIIb or IV disease
- **Blueteq registration required: https://www.blueteq-secure.co.uk/Trust/**

## Dosage:

| Drug | Dosage | Route | Frequency |
|---|---|---|---|
| Alectinib | 600mg | Oral | Twice daily |

Treatment is continuous until unacceptable toxicity or disease progression.

Four weeks supply will be issued at each visit.

## Extravasation risk:

Not applicable: oral formulation

## Administration:

Alectinib should be swallowed whole with food. Capsules must not be opened or dissolved.

## Drug Interactions

The list below is not exhaustive, consult SPC for further details

- CYP3A4 inducers and inhibitors: no dose adjustment to alectinib is required. Appropriate monitoring is recommended for patients taking concomitant strong CYP3A inhibitors and inducers. Examples include but not limited to carbamazepine, phenobarbital, phenytoin, St John's Wort, rifampicin, ketoconazole, itraconazole, voriconazole, ritonavir. Discuss with pharmacist
- Avoid grapefruit and Seville oranges
- P-gp subtrates: Alectinib has potential to increase plasma concentrations of P-gp substrates (e.g. digoxin, dabigatran, topotecan, sirolimus, everolimus and lapatinib), appropriate monitoring is recommended.
- BRCP substrates: Appropriate monitoring is recommended due to the risk of increased plasma concentrations of BRCP substrates (e.g. methotrexate, mitoxantrone)
- CYP substrates: The effectiveness of concomitant administration of oral contraceptives may be reduced

## Main Toxicities:

Constipation, oedema (eyelid, periorbital and peripheral), nausea, myalagia, anaemia and rash were the most common adverse drug reactions. Interstitial lung disease/pneumonitis, hepatotoxicity and bradycardia have been reported in clinical trials- please see "dose modification and toxicity management" for advice.

## Investigations and Treatment Plan:

| | Pre | Cycle 1 | Cycle 1 D15 | Cycle 2 | Cycle 2 D15 | Cycle 3 | Cycle 3 D15 | Cycle 4 | Ongoing |
|---|---|---|---|---|---|---|---|---|---|
| Medical Assessment | X | | | X | | X | | X | Every 3 cycles |
| Nursing Assessment | X | X | | X | | X | | X | Every cycle |
| FBC | X | X | X | X | X | X | X | X | Every cycle |
| U&E & LFT (including creatine kinase (CK)) | X | X | X | X | X | X | X | X | Every cycle |
| Lipid profile | | X | | X | | X | | X | Can reduce frequency if lipids stabilised |
| LDH | | X | | X | | X | | X | Every cycle |
| CT scan | X | | | | | X* | | | *CT scan to be carried out prior to cycle 3 then every three months or as clinically indicated |
| ECG | X | | | | | X | | | ECG to be carried out at baseline and then on cycle 3 at medical assessment, then as clinically indicated |
| Blood pressure and heart rate measurement | X | X | | X | | | | | Repeat if clinically indicated |
| Informed Consent | X | | | | | | | | |
| PS recorded | X | X | X | X | X | X | X | X | Every cycle |
| Toxicities documented | X | X | X | X | X | X | X | X | Every cycle |
| Weight recorded | X | X | X | X | X | X | X | X | Every cycle |

## Dose Modifications and Toxicity Management:

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 150mg twice daily based on tolerability. Alectinib treatment should be permanently discontinued if patients are unable to tolerate the 300mg twice daily dose.

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

**Haematological toxicity**

**Proceed on day 1 if:**

| | |
|---|---|
| Plt ≥ 100 x $10^9$/L | ANC ≥ 1.0 x $10^9$/L |

**Hepatic Impairment**

No dose adjustment is required in patients with mild hepatic impairment. Alectinib has not been studied in patients with moderate to severe hepatic impairment. Therefore, alectinib is not recommended in patients with moderate to severe hepatic impairment. Please see dose modification table for guidance on ALT/AST/Bilirubin elevation.

**Renal Impairment**

No dose adjustment is required in patients with mild or moderate renal impairment. Alectinib has not been studied in patients with severe renal impairment. However, since alectinib elimination via the kidney is negligible, no dose adjustment is required in patients with severe renal impairment.

**Dose modification advice for specific toxicities:**

| CTCAE Grade | Dose Modification |
|---|---|
| Interstitial lung disease (ILD) / pneumonitis of any severity grade | ILD should be suspected in patients who develop acute onset of new and/or progressive unexplained pulmonary symptoms such as dyspnoea, cough and fever. 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 upper limit of normal (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 (heart rate less than 60 beats per minute) grade 2 or 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.<br><br>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.<br>If no contributing concomitant medicinal product is identified, or if contributing concomitant medicinal products are not discontinued or dose modified, resume at reduced dose (see Table 1) upon recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm. |

| | |
|---|---|
| Bradycardia (heart rate less than 60 beats per minute) grade 4 (life-threatening consequences, urgent intervention indicated) | Permanently discontinue if no contributing concomitant medicinal product is identified.<br>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.<br>Permanently discontinue in case of recurrence. |
| CK elevation > 5 times ULN | Temporarily withhold until recovery to baseline or to ≤ 2.5 times ULN, then resume at the same dose. |
| CK elevation > 10 times ULN or second occurrence of CK elevation of > 5 times ULN | Temporarily withhold until recovery to baseline or to ≤ 2.5 times ULN, then resume at reduced dose. |

## Additional Information

- Photosensitivity to sunlight has been reported with alectinib administration. Patients should be advised to avoid prolonged sun exposure while taking alectinib, and for at least 7 days after discontinuation of treatment. Patients should also be advised to use a broad-spectrum Ultraviolet A (UVA)/ Ultraviolet B (UVB) sun screen and lip balm (SPF ≥50) to help protect against potential sunburn.

## References:


- SPC available via: https://www.medicines.org.uk/emc/
- NICE TA Alectinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer