

Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

CERITINIB

Regimen

- NSCLC – Ceritinib

Indication

- Ceritinib is recommended, within its marketing authorisation, as an option for untreated anaplastic lymphoma kinase (ALK)-positive advanced non-small-cell lung cancer in adults.
- The treatment of ALK+ve advanced or metastatic non-small cell lung cancer as second or subsequent line treatment post first line treatment with crizotinib.

Toxicity

Drug	Adverse Effects
Ceritinib	Interstitial lung disease, QT interval prolongation, hepatotoxicity, hyperglycaemia, diarrhoea, nausea, raised lipase / amylase and pancreatitis

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- Current CT scan (ideally within 1 month) before starting ceritinib and repeat within 3 months of starting treatment, or earlier if necessary
- Chest x-ray should be performed before starting treatment and every 4 weeks, as appropriate
- LFT every two weeks for one month then monthly thereafter (more frequent monitoring can be considered during the first three months. The SPC recommends every two weeks for the first three months of treatment)
- FBC, U&Es every four weeks

Dose Modifications

Temporary dose interruption and/or dose reduction of ceritinib may be required based on individual safety and tolerability. If dose reduction is required due to an adverse drug reaction (ADR) not listed, then this should be achieved by decrements of 150 mg daily. Early identification and management of ADRs with standard supportive care measures should be considered.

Ceritinib should be discontinued in those who cannot tolerate a dose of 150mg once a day with food.

Haematological

Any haematological toxicity (except lymphopenia)	Dose Modification Algorithms
NCI-CTC Grade 1 or 2	Continue treatment at same dose; monitor as clinically indicated.
NCI-CTC Grade 3	Step 1. Interrupt treatment until toxicity reduced to NCI-CTC grade 2 or below Step 2. Restart treatment at same dose.
NCI-CTC Grade 4 (first and second occurrence)	Step 1. Interrupt treatment until toxicity reduced to NCI-CTC grade 2 or below Step 2. Restart treatment with lower dose
NCI-CTC Grade 4 (further recurrence)	Discontinue permanently

Hepatic Impairment

Drug	Dose
Ceritinib	Ceritinib is largely eliminated via the liver. No dose adjustment is required in those with mild hepatic impairment. It is not recommended in those with moderate to severe hepatic impairment.

Ceritinib can also cause liver abnormalities, adjust doses according to the table below.

Liver	Dose Modification Algorithms
AST or ALT greater than 5xULN, and bilirubin less than 2xULN	Step 1. Interrupt treatment until toxicity reduced to NCI-CTC grade 1 or baseline. Step 2. Restart treatment with lower dose (reduce by 150mg)
AST or ALT greater than 3xULN, and bilirubin greater than 2xULN (in the absence of cholestasis or haemolysis)	Discontinue permanently

Renal Impairment

Drug	Dose
Ceritinib	No starting dose adjustment is required in patients with mild to moderate renal impairment

Other

Adverse Effect	Dosing
Severe or intolerable nausea, vomiting or diarrhoea despite optimal anti-emetic or anti-diarrhoeal therapy	Withhold ceritinib until improved, then reinitiate treatment with dose reduced by 150mg.
Persistent hyperglycaemia greater than 250mg/dl despite optimal anti-hyperglycaemic therapy	Withhold ceritinib until hyperglycaemia is adequately controlled, then reinitiate treatment with dose reduced by 150mg. If adequate glucose control cannot be achieved with optimal medical management, permanently discontinue ceritinib
Lipase or amylase elevation grade greater than or equal to NCI-CTC grade 3	Withhold ceritinib until lipase or amylase returns to NCI-CTC grade 1, then reinitiate with dose reduced by 150mg.

Pneumonitis

Ceritinib has been associated with severe, life-threatening, or fatal treatment-related pneumonitis in clinical trials. All of these cases occurred within two months after the initiation of treatment. Patients with pulmonary symptoms indicative of pneumonitis should be monitored and treatment withheld if pneumonitis is suspected. Other causes of pneumonitis should be excluded, and ceritinib should be permanently discontinued in patients diagnosed with treatment-related pneumonitis.

Cardiac

QTc prolongation has been observed, which may lead to an increased risk for ventricular tachyarrhythmias (e.g., Torsade de Pointes) or sudden death. The risk of QTc prolongation may be increased in patients concomitantly taking antiarrhythmics and in patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances (e.g., secondary to diarrhoea or vomiting). Ceritinib should be administered with caution to patients who have a history of or predisposition for QTc prolongation, or who are taking medicinal products that are known to prolong the QT interval.

Cardiac	Dose Modification Algorithms
QT corrected for heart rate (QTc) greater than 500msec on at least two separate electrocardiograms (ECGs)	Withhold ceritinib until recovery to baseline or to a QTc 480msec or lower, check and if necessary correct electrolytes, then reinstate with dose reduced by 150mg.
QTc greater than 500msec or greater than 60msec change from baseline and torsade de pointes or polymorphic ventricular tachycardia or signs / symptoms of serious arrhythmia	Permanently discontinue
Bradycardia with a heartbeat of less than 60 beats per minute (symptomatic, may be severe and medically significant, medical intervention indicated)	<p>Withhold ceritinib until recovery to asymptomatic bradycardia or to a heart rate of 60 beats per minute (bpm) or above.</p> <p>Evaluate concomitant medicinal products known to cause bradycardia, as well as anti-hypertensive medicinal products.</p> <p>If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, reinstate ceritinib at the previous dose upon recovery to asymptomatic bradycardia or to a heart rate of 60bpm or above.</p> <p>If no contributing concomitant medicinal product is identified, or if contributing concomitant medicinal products are not discontinued or dose modified, reinstate ceritinib with dose reduced by 150mg upon recovery to asymptomatic bradycardia or to a heart rate of 60bpm or above.</p>
Bradycardia (life-threatening consequences, urgent intervention indicated)	<p>Permanently discontinue ceritinib if no contributing concomitant medicinal product is identified.</p> <p>If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, reinstate ceritinib with dose reduced by 150mg upon recovery to asymptomatic bradycardia or to a heart rate of 60bpm or above, with frequent monitoring</p>

[Regimen](#)

Continuous (28 day cycle)

Drug	Dose	Days	Administration
Ceritinib	450mg once a day	Continuous	Oral

Ceritinib should be discontinued in those who cannot tolerate a dose of 150mg once a day with food.

[Administration Information](#)

- Ceritinib is available as 150mg capsules
- If a dose is missed, the patient should make up that dose, unless the next dose is due within 12 hours
- If vomiting occurs during the course of treatment, the patient should not take an additional dose, but should continue with the next scheduled dose
- The capsules should be taken with food
- Swallow whole, do not chew or crush.

[Additional Therapy](#)

- Loperamide 4mg oral stat after the first loose stool and then 2-4mg when required for the relief of diarrhoea (maximum 16mg/24 hours)
- Metoclopramide 10mg oral three times a day when required for the relief of nausea and vomiting

[Additional Information](#)

- Ceritinib interacts with a number of other medications. Always check for drug interactions.
- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to ceritinib.

[Coding](#)

- Procurement – X71.5
- Delivery – X73.1

[References](#)

1. Shaw AT, Kim DW, Mehra R et al. Ceritinib in ALK re-arranged non-small cell lung cancer. N Engl J Med 2014; 370 (13): 1189-1197.
2. National Institute for Health and Clinical Excellence. Technology Appraisal 500 (Jan 2018). Ceritinib for untreated ALK positive non-small cell lung cancer. NICE:DOH.
3. National Institute for Health and Clinical Excellence. Technology Appraisal 395 (June 2016). Ceritinib for previously treated ALK positive non-small cell lung cancer. NICE:DOH.

REGIMEN SUMMARY

CERITINIB

Day One

1. Ceritinib 450mg once a day continuous oral

Administration Instructions

The capsules must be taken with food.

Swallow whole, do not chew or crush.

If a dose is missed, the patient should make up that dose, unless the next dose is due within 12 hours

2. Metoclopramide 10mg three times a day when required for the relief of nausea

Administration Instructions

Please supply an original pack of 28 tablets per 28 days of treatment.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	June 2018	None	Dr Deborah Wright Pharmacist	Dr Luke Nolan Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

- Hampshire Hospitals NHS Foundation Trust
- NHS Isle of Wight
- Portsmouth Hospitals NHS Trust
- Salisbury Hospitals NHS Foundation Trust
- University Hospital Southampton NHS Foundation Trust
- Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines. These protocols are only one source of information. They should be read in conjunction with the latest Summary of Product Characteristics and published information.