Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

MOBOCERTINIB

Regimen

- NSCLC - Mobocertinib

Indication

Mobocertinib as monotherapy for the treatment of adult patients who have previously received platinum-based chemotherapy for advanced or metastatic non-small cell lung cancer (NSCLC) that is positive for an EGFR exon 20 insertion mutation where:

- The patient has locally advanced or metastatic non-small cell lung cancer.
- The patient has a histologically or cytologically confirmed diagnosis of non-small cell lung cancer that has been shown to have an EGFR exon 20 insertion mutation determined on a tumour tissue biopsy or a plasma specimen (liquid biopsy) or both.
- The patient has previously received platinum-based chemotherapy for the locally advanced or metastatic NSCLC indication.
- The patient has not previously been treated with mobocertinib unless the patient received mobocertinib via a company access scheme and the patient meets all the other treatment criteria on blueteq.
- The patient has an ECOG performance status of 0 or 1.
- The patient either has no known brain metastases or if the patient does have brain metastases then the patient is symptomatically stable before starting mobocertinib.
- Mobocertinib will be used as monotherapy.
- The patient will have evaluation of the QTc interval and assessment of cardiac function including left ventricular ejection fraction before and during treatment with mobocertinib.
- The patient needs ready access to anti-diarrhoeal medicinal products e.g. loperamide and that in patients with continued diarrhoea, electrolyte monitoring is required.
- The patient will be treated until loss of clinical benefit or excessive toxicity or patient choice to discontinue treatment whichever is sooner.
- A formal medical review as to how mobocertinib is being tolerated will be done before the start of the second month of treatment and the next review to determine whether treatment with mobocertinib should continue or not will be scheduled to occur at least by the end of the second month of therapy.

Toxicity

Drug	Adverse Effect
Mobocertinib	Anaemia, thrombocytopenia, leucopenia, anorexia, hypokalaemia, hypomagnesaemia, weight loss, dehydration, ocular toxicity, QT interval prolongation, cardiac failure, hypertension, dyspnoea, cough, rhinorrhoea, interstitial lung disease, diarrhoea, nausea, stomatitis, increased amylase, vomiting, lipase increase, increased transaminases, fatigue, increased blood creatinine, rash, dry skin, alopecia, paronychia, pruritus.

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

Monitoring

- FBC, LFTs and U&Es (including magnesium and calcium) prior to day one of treatment of the cycle. Electrolyte abnormalities (sodium, potassium, calcium and magnesium) should be corrected prior to starting treatment.
- Amylase and lipase prior to starting treatment, after 1 month, then as indicated.
- QTc and LVEF prior to starting treatment and then periodically during treatment.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well. The toxicities below should be read in conjunction with the relevant Summary of Product Characteristics (www.medicines.org.uk).

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Recommended dose reductions

Dose reduction schedule	Dose level
First dose reduction	120mg once daily
Second dose reduction	80mg once daily

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

If neutrophils <1.0 x10^9/L or platelets <50x10^9/L mobocertinib should be withheld until recovery to these levels; then resume at the same dose or at the next lower dose. If neutrophils <0.5x10^9/L or platelets <25xx10^9/L consider permanently discontinuing mobocertinib.

Hepatic impairment

No initial dose adjustments are recommended in patients with mild hepatic impairment (total bilirubin ≤ ULN and AST/ALT > ULN or total bilirubin >1 to 1.5 xULN and any AST/ALT). The recommended dosage in patients with moderate or severe hepatic impairment has not been established and use in these patients is not recommended.

Renal Impairment

Drug	Renal impairment	Guidance
Mobocertinib	Mild / moderate (CrCl ≥30ml/min)	No dose adjustment required
	Severe (<30ml/min)	No information available – not recommended.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

CTCAE grade	Guidance	
Interstitial lung disease / pneumonitis (any grade)	Withhold mobocertinib if ILD or pneumonitis suspected. Permanently discontinue if ILD or pneumonitis confirmed.	
Diarrhoea	Grade 1 or 2	No dose modification is required. Initiate treatment with anti-diarrheal medicinal products e.g. loperamide at first onset of diarrhoea.
	Intolerable or recurrent grade 2 or grade 3	Withhold mobocertinib until recovery to grade 1 or lower; then resume at the same dose or at the next lower dose.
	Grade 4	First occurrence: withhold mobocertinib until recovery to grade 1 or lower. If recovered within 2 weeks, resume at the next lower level. If not recovered to grade 1 or lower within 2 weeks, permanently discontinue. Recurrence: Permanently discontinue.

Amylase/Lipase elevation	Grade 2 (>1.5 to ≤2 xULN) and asymptomatic grade 3 (>5xULN)	Withhold mobocertinib until recovery ≤grade 1. If recovered within 2 weeks, then resume at the same dose or next lower level. If not recovered to ≤grade 1 within 2 weeks, permanently discontinue.
	Symptomatic grade 3 and grade 4	Withhold mobocertinib until recovery ≤grade 1. If recovered within 2 weeks, then resume at the at the next lower level. If not recovered to ≤grade 1 within 2 weeks, permanently discontinue.
Decreased ejection fraction of heart failure	Grade 2 decreased ejection fraction	Withhold mobocertinib until ≤grade 1 or baseline. If recovered to baseline within 2 weeks, resume moboceritinib at the same dose or the next lower dose. If not recovered to baseline within 2 weeks, permanently discontinue.
	≥Grade 2 heart failure or grade 3 or 4 decreased ejection fraction.	Permanently discontinue mobocertinib.
QTc interval prolongation	Grade 2 (QTc interval 481-500 msec)	First occurrence: withhold mobocertinib until ≤grade 1 or baseline. Upon recovery, resume mobocertinib at the same dose. Recurrence: withhold mobocertinib until ≤grade 1 or baseline. Upon recovery, resume mobocertinib at the next lower dose or permanently discontinue.
	Grade 3 (QTc interval ≥501msec or QTc interval >60 msec from baseline)	First occurrence: withhold mobocertinib until ≤grade 1 or baseline. Upon recovery, resume mobocertinib at the next lower dose or permanently discontinue. Recurrence: Permanently discontinue mobocertinib.
	Grade 4 (Torsade de Pointes; polymorphic ventricular tachycardia, signs/symptoms of serious arrythmias)	Permanently discontinue mobocertinib .

Other non-haematological toxicity	Grade 2	No dose modification is required. For intolerable or recurrent grade 2 toxicity withhold mobocertinib until symptoms resolve and resume at the next lower dose.
	Grade 3 or 4	Withhold mobocertinib until recovery to grade 1 or lower, then resume at the same dose or at the next lower dose. For Grade 4 toxicity, consider permanent discontinuation.

Regimen

28 day cycle until disease progression, unacceptable toxicity or patient chooses to stop treatment (12 cycles will be set in ARIA).

Drug	Dose	Days	Administration
Mobocertinib	160mg once a day	1-28 inclusive	Oral

Dose Information

- Mobocertinib is available in 40mg capsules.

Administration Information

- Mobocertinib can be taken with or without food and should be taken at approximately the same time each day.
- Mobocertinib capsules should be swallowed whole. The capsules should not be opened, chewed or the contents dissolved.
- If a dose is missed by more than 6 hours, the patient should not take a dose on that day but should resume the usual dosing the following day at the regularly scheduled time.
- If a patient vomits after taking a dose, the patient should not repeat the dose, but should resume the usual dosing as prescribed on the following day.

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to mobocertinib.
- Mobocertinib interacts with several medicines. Please check for interactions.
- Mobocertinib may have a minor influence on the ability to drive or use machinery. Fatigue has been observed in clinical trials. Patients should be advised not to drive or operate machinery if they experience fatigue.

References
1. Takeda (2022). Exkivity 40mg hard capsules summary of product characteristics. Available from www.medicines.org.uk. Accessed on 11/7/2022.

REGIMEN SUMMARY

Mobocertinib

Day One

1. Mobocertinib 160mg once a day continuous oral
   Administration Instructions
   Swallow whole, do not crush or chew.
   Oral chemotherapy

2. Loperamide 4mg after the first loose stool, then 2-4mg four times a day when required oral
   Administration Instructions
   Maximum 16mg/24hours

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2022	None	Alexandra Pritchard Pharmacist	Dr Judith Cave Consultant 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 should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.