Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

TEPOTINIB

Regimen

- NSCLC - Tepotinib

Indication

Tepotinib as monotherapy for the treatment of adult patients with untreated advanced/metastatic non-small cell lung cancer (NSCLC) harbouring mesenchymal-epithelial transition (MET) exon 14 skipping alterations 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 harbour a mesenchymal-epithelial transition (MET) exon 14 skipping alteration determined on a tumour tissue biopsy or a plasma specimen (liquid biopsy) or both.
- the patient's lung cancer is EGFR wild type and is also negative for both ALK and ROS1 gene rearrangements.
- the patient is treatment-naïve as regards to systemic therapy for the locally advanced or metastatic NSCLC indication
- the patient has not been previously treated with a drug specifically targeting a MET exon 14 skipping alteration unless the patient received tepotinib via the EAMS program 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 tepotinib.
- tepotinib will be used as monotherapy.
- the prescribed is aware of the side effects of tepotinib including the risk of developing oedema, interstitial lung disease and hepatotoxicity.
- the patient will be treated until loss of benefit or excessive toxicity of patient choice to discontinue treatment whichever is the sooner.
- a formal medical review as to how tepotinib is being tolerated will be done before the start of the second month of treatment and the next review to determine whether treatment should continue or not will be scheduled to occur at least by the end of the second month of therapy.

Tepotinib as monotherapy for the treatment of adult patients with previously treated advanced/metastatic non-small cell lung cancer (NSCLC) harbouring mesenchymal-epithelial transition (MET) exon 14 skipping alterations 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 harbour a mesenchymal-epithelial transition (MET) exon 14 skipping alteration determined on a tumour tissue biopsy or a plasma specimen (liquid biopsy) or both.
- the patient's lung cancer is EGFR wild type and is also negative for both ALK and ROS1 gene rearrangements.

- the patient has previously received systemic therapy for the locally advanced or metastatic NSCLC indication;

    a) the only treatment that the patient has received is platinum-based cytotoxic chemotherapy for locally advanced or metastatic NSCLC with or without 2nd line cytotoxic chemotherapy or
    b) the only treatment that the patient has received is 1st line immunotherapy monotherapy for the locally advanced or metastatic NSCLC indication or
    c) the patient has received the 1st line combination treatment of platinum doublet chemotherapy plus immunotherapy for the locally advanced or metastatic NSCLC indication with or without 2nd line cytotoxic chemotherapy or
    d) the patient has received 1st line immunotherapy monotherapy for the locally advanced or metastatic NSCLC indication followed by 2nd line cytotoxic chemotherapy or
    e) the patient has received 1st line platinum-based cytotoxic chemotherapy for locally advanced or metastatic NSCLC followed by 2nd line immunotherapy with or without further cytotoxic chemotherapy

- the patient has not been previously treated with a drug specifically targeting a MET exon 14 skipping alteration unless the patient received tepotinib via the EAMS program 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 tepotinib.
- tepotinib will be used as monotherapy.
- the prescribed is aware of the side effects of tepotinib including the risk of developing oedema, interstitial lung disease and hepatotoxicity.
- the patient will be treated until loss of benefit or excessive toxicity of patient choice to discontinue treatment whichever is the sooner.
- a formal medical review as to how tepotinib is being tolerated will be done before the start of the second month of treatment and the next review to determine whether treatment should continue or not will be scheduled to occur at least by the end of the second month of therapy.

Toxicity

Drug	Adverse Effect
Tepotinib	Hypalbuminaemia, nausea, vomiting, constipation, diarrhoea, abdominal pain, increased transaminases, oedema, fatigue, increased creatinine, hepatotoxicity, interstitial lung disease,

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 prior to day one of treatment of the cycle.
- ROS1, ALK, EGFR and MET exon 14 skipping alteration should be reported before initiating 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.

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80mg/L).

Proceed with the next cycle if neutrophils are greater than or equal to $1.5x10^9$ and platelets greater than or equal to $75x10^9$.

If the neutrophils are less than $1.5x10^9$ and/or platelets less than $75x10^9$ consider withholding tepotinib until recovered and resume at a reduced dose.

If neutrophils are less than $1x10^9$ and/or platelets less than $50x10^9$ withhold tepotinib until resolved, then resume tepotinib at a reduced dose.

If neutrophils are less than $0.5x10^9$ and/or platelets less than $25x10^9$ permanently discontinue tepotinib.

Hepatic impairment

No initial dose adjustments are recommended in patients with mild (Child Pugh class A) or moderate (Child Pugh class B) hepatic impairment. The pharmacokinetics and safety in patients with severe hepatic impairment have not been studied (Child Pugh C).

The following recommendations have been made for treatment related elevations.

Adverse reaction	Severity	Dose modification
Increased ALT and/or AST without increased total bilirubin	Grade 3	Withhold tepotinib until recovery to baseline ALT/AST. If recovered to baseline within 7 days, then resume tepotinib at the same dose; otherwise resume tepotinib at reduced dose.
	Grade 4	Permanently discontinue tepotinib.
Increased ALT and/or AST with increased total bilirubin in the absence of cholestasis or haemolysis	ALT and/or AST greater than 3 times ULN with total bilirubin greater than 2xULN	Permanently discontinue tepotinib.
Increased total bilirubin without concurrent increased ALT and/or AST	Grade 3	Withhold tepotinib until recovery to baseline bilirubin. If recovered to baseline within 7 days, resume tepotinib at a reduced dose, otherwise permanently discontinue.
	Grade 4	Permanently discontinue tepotinib.

Renal Impairment

Drug	Renal impairment	Guidance
Tepotinib	Mild / moderate (CrCl 30-89ml/min)	No dose adjustment required
	Severe (less than 30ml/min)	No information available.

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 tepotinib if ILD suspected. Permanently discontinue tepotinib if ILD confirmed.	
Other adverse reactions	Grade 2	Maintain dose level. If intolerable, consider withholding tepotinib until resolved, then resume tepotinib at a reduced dose.
	Grade 3	Without tepotinib until resolved, then resume at reduced dose.
	Grade 4	Permanently discontinue tepotinib.

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
Tepotinib	450mg once a day	1-28 inclusive	Oral

Dose Information

- Tepotinib is available in 225mg film-coated tablets.

Administration Information

- Tablets should be swallowed whole and taken with food.
- If a daily dose is missed, it can be taken as soon as remembered on the same day, unless the next dose is due within 8 hours.

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to Tepotinib.
- Tepotinib interacts with several medicines (including metformin). Please check for interactions.
- Tepotinib may have a minor influence on the ability to drive or use machinery. During treatment fatigue and asthenia have been reported.

References

1. Merck (2022). Tepmetko 225mg film-coated tablets summary of product characteristics. Available from www.medicines.org.uk. Accessed on 7/7/2022.
2. Paik PK et al. Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 skipping mutations. N Engl J Med (2020); 383: 931-943.

REGIMEN SUMMARY

Tepotinib

Day One

1. Tepotinib 450mg once a day continuous oral
   Administration Instructions
   Take with or just after food. Swallow whole, do not crush or chew.
   Oral SACT

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2022	None	Alexandra Pritchard Pharmacist	Dr Andrew Bates Consultant Clinical 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 Hospital 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.