Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

DACOMITINIB

Regimen

- NSCLC - Dacomitinib

Indication

Dacomitinib for untreated EGFR-positive non-small-cell lung cancer where the following criteria is met:

- Patient has a histologically or cytologically confirmed diagnosis of non-small cell lung cancer that is either stage IIIB or stage IV
- The patients NSCLC has been shown to express an EGFR-activating mutation as demonstrated by an accurate and validated assay.
- The patient has received no previous EGFR-targeted therapy unless this had to be stopped within 3 months of it start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.
- The patient has not received any previous cytotoxic chemotherapy for locally advanced or metastatic non-small cell lung cancer.
- Dacomitinib will be used as monotherapy.
- The patient has an ECOG performance status of 0 or 1.
- Dacomitinib will be continued until loss of clinical benefit, excessive toxicity or patient choice, whichever is sooner.

Toxicity

Drug	Adverse Effect
Dacomitinib	Decreased appetite, hypokalaemia, conjunctivitis, diarrhoea, stomatitis, vomiting, nausea, interstitial lung disease, rash, palmer-planter erythrodysaesthesia syndrome, skin fissures, dry skin, pruritus, nail disorders, alopecia, fatigue, asthenia, increased transaminases, weight loss

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.
- EGFR 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.

Recommended dose modifications

Dose modifications may be required based on individual safety and tolerability. If dose reduction is necessary, then the dose of dacomitinib should be reduced as per the below table.

Dose level	Dose (once daily)
Recommended starting dose	45mg
First dose reduction	30mg
Second dose reduction	15mg

Haematological

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

Neutrophils should be equal or greater than $1.5x10^9$/L and platelets equal or greater than $100x10^9$/L prior to starting the next cycle.

Hepatic impairment

No starting dose adjustments are required when administering Dacomitinib with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment.

The starting dose of Dacomitinib should be adjusted to 30mg once a day in patients with severe (Child-Pugh class C) hepatic impairment. This dose may be increased to 45mg once a day based on individual safety and tolerability after at least 4 weeks of treatment.

Renal Impairment

No starting dose adjustments are required when administering Dacomitinib to patients with mild or moderate renal impairment (CrCl ≥30ml/min).

Limited data is available in patients with severe renal impairment (CrCl <30ml/min). No data is available in patients requiring haemodialysis. Thus, no dosing recommendations can be made for either patient population.

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.

Adverse reaction	Dose modification
Interstitial lung disease (ILD/Pneumonitis)	• Withhold dacomitinib during ILD/Pneumonitis diagnostic evaluation. • Permanently discontinue dacomitinib if ILD/Pneumonitis is confirmed.
Diarrhoea	• For Grade 1 diarrhoea, no dose modification is required. Initiate treatment with anti-diarrhoeal medicinal products (e.g., loperamide) at first onset of diarrhoea. Encourage adequate oral fluid intake during diarrhoea. • For Grade 2 diarrhoea, if not improved to Grade ≤ 1 within 24 hours while using anti-diarrhoeal medicinal products (e.g., loperamide) and adequate oral fluid intake, withhold dacomitinib. Upon recovery to Grade ≤ 1, resume dacomitinib at the same dose level or consider a reduction of 1 dose level. • For Grade ≥ 3 diarrhoea, withhold dacomitinib. Treat with anti-diarrhoeal medicinal products (e.g., loperamide), and adequate oral fluid intake or intravenous fluids or electrolytes as appropriate. Upon recovery to Grade ≤ 1, resume dacomitinib with a reduction of 1 dose level.
Skin-related adverse reactions	• For Grade 1 rash or erythematous skin conditions, no dose modification is required. Initiate treatment (e.g., antibiotics, topical steroids, and emollients). • For Grade 1 exfoliative skin conditions, no dose modification is required. Initiate treatment (e.g., oral antibiotics and topical steroids). • For Grade 2 rash, erythematous or exfoliative skin conditions, no dose modification is required. Initiate treatment or provide additional treatment (e.g., oral antibiotics and topical steroids). • If Grade 2 rash, erythematous or exfoliative skin conditions persist for 72 hours despite treatment, withhold dacomitinib. Upon recovery to Grade ≤ 1, resume dacomitinib at the same dose level or consider a reduction of 1 dose level. • For Grade ≥ 3 rash, erythematous or exfoliative skin conditions, withhold dacomitinib. Initiate or continue treatment and/or provide additional treatment (e.g., broad spectrum oral or intravenous

	antibiotics and topical steroids). Upon recovery to Grade ≤ 1, resume dacomitinib with a reduction of 1 dose level.
Other	• For Grade 1 or 2 toxicity, no dose modification is required. • For Grade ≥ 3 toxicity, withhold dacomitinib until symptoms resolve to Grade ≤ 2. Upon recovery, resume dacomitinib with a reduction of 1 dose level.

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
Dacomitinib	45mg once a day	1-28 inclusive	Oral

Dose Information

- Dacomitinib is available in 15mg film-coated tablets, 30mg film-coated tablets and 45mg film coated tablets.

Administration Information

- Tablets should be swallowed whole and can be taken with or without food.
- Patients should be encouraged to take their dose at approximately the same time each day. If the patient vomits or misses a dose, an additional dose should not be taken, and the next prescribed dose should be taken at the usual time the next day.

Additional Information

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

References
1. Pfizer Limited. Vizimpro 15mg film-coated tablets summary of product characteristics. Available from www.medicines.org.uk/emc/product/10354/smpc. Last updated 02/04/2019 (Accessed 23/09/2022).

REGIMEN SUMMARY

Dacomitinib

Day One

1. Dacomitinib 45mg once a day continuous oral
   Administration Instructions
   Swallow whole, do not crush or chew.
   Oral SACT

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	September 2022	None	Alexandra Pritchard Pharmacist	Dr Luke Nolan 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 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.