Oncological Treatment of Lung Cancer

Pathway of Care

Kent & Medway Cancer Collaborative

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1.0 INTRODUCTION AND BACKGROUND

This document has been written to provide guidance on the treatment of lung cancer in the Kent & Medway Cancer Collaborative. Reference should also be made to NICE clinical guideline NG122 March 2019 https://www.nice.org.uk/guidance/ng122

Radiotherapy schedules are as defined in the Kent Oncology Centre Quality System Clinical Protocols.

All patients will be considered for entry into a clinical trial (see appendix A).

See Collaborative chemotherapy prescribing protocols for details of chemotherapy / anti-cancer regimens.

All patients should be discussed within a multidisciplinary team meeting before commencing initial treatment. All patients will be reviewed and assessed and where appropriate (and of adequate performance status), offered chemotherapy and/ or radiotherapy, including Stereotactic Ablative Radiotherapy (SABR).

All chemotherapy regimens listed within this document are delivered at either Maidstone and Tunbridge Wells NHS Trust, Dartford and Gravesham NHS Trust, Medway NHS Foundation Trust or East Kent Hospitals University NHS Foundation Trust.

The thoracic oncologists provide a comprehensive service for NICE approved treatments. For those treatments which are not approved by NICE and are not commissioned locally or via the cancer drugs fund applications may be made where appropriate through the Individual Funding Request route. Some treatments may only be available within an “Additional Private Care” framework.

Please note, some of the drugs / doses recommended within this document are outside of the UK licensed marketing authorisation.

2.0 NON-SMALL CELL LUNG CANCER

2.1 Molecular Testing in NSCLC

The National Genomic Test Directory specifies which genomic tests are commissioned by the NHS in England, the technology by which they are available, and the patients who will be eligible to access a test. This is in development; molecular testing for lung cancer in Kent will evolve in line with this guidance.

Next generation sequencing should be arranged via the genomic hub.

2.2 Adjuvant Treatment

For Stage IB (>4cm) to IIIB completely resected NSCLC with good performance status (WHO 0-1):

- Cisplatin or Carboplatin and oral Vinorelbine for 4 cycles
- Cisplatin or Carboplatin + I.V. Vinorelbine for 4 cycles
- Adjuvant radiotherapy in R1/R2 resection with positive bronchial margin.
- Osimertinib for stage IB to IIIA or N2 only stage IIIB (T3 N2 or T4 N2) tumours with either an EGFR exon 19 deletion or an exon 21 (L858R) substitution mutation. Within 10 weeks following surgery or within 26 weeks of surgery and adjuvant chemotherapy. Maximum of 3 years treatment.
- Atezolizumab for the adjuvant treatment of completely resected stage IIB or IIIA or N2 only IIIB NSCLC which has PD-L1 expression at a level of >/= 50% which has not progressed on adjuvant platinum-based chemotherapy (maximum 4 cycles). The chemotherapy should have been commenced with 12 weeks of the resection. Atezolizumab must be commenced within 12 weeks of the last cycle of adjuvant platinum-based chemotherapy. Maximum of 1 year of treatment.
- Further adjuvant treatments with TKIs and immunotherapy will be considered when commissioned via Blueteq.

2.3 Neo-Adjuvant Treatment

- Neo-adjuvant chemotherapy and immunotherapy is indicated in operable stage IIA-IIIB as per NHSE commissioning criteria.
- A combination of chemotherapy and radiotherapy followed by surgery maybe considered in selected superior sulcus tumours.

2.4 Palliative Treatment

2.4.1 Advanced NSCLC

For guidance on the prescribing in advanced NSLC please refer to NICE guidance:

Overview | Lung cancer: diagnosis and management | Guidance | NICE

NB Please check revision date of this document and refer to Blueteq for the most up to date commissioning criteria.

2.4.2 Subsequent Lines of Therapy

It may be appropriate to offer further lines of therapy in selected patients who remain of good performance status (PS 0/1).

Choice of systemic anti-cancer therapy will be dictated by previous treatment. Some patients may benefit from re-challenging with platinum based chemotherapy.

Selected patients may be candidates for referral to a phase I clinical trial unit.

2.4.3 Palliative Radiotherapy

Palliative radiotherapy is indicated for symptom control. Indications include painful bone metastases, symptomatic intrathoracic disease, and spinal cord compression (impending or developing) as well as intracranial metastases.

2.4.4 Management of Superior Vena Caval Obstruction (SVCO)

In terms of the management of Superior Vena Caval Obstruction (SVCO) radiotherapy is no longer a first-line standard of care. Patients should be assessed for urgent SVC stenting through an appropriate interventional radiologist. Radiotherapy should be reserved for patients who cannot be stented for technical reasons. In the case of SVCO secondary to small cell lung cancer, primary chemotherapy is the treatment of choice.

2.5 Locally Advanced NSCLC

Patients who are potentially suitable for radical treatment should all have a pre-treatment CT (ideally with contrast) and a PET-CT scan within 42 days of the start of treatment, as well as lung function tests and a staging MRI brain.

All chemoradiation patients should have a brain MRI.

If resectable at diagnosis, consider surgery plus adjuvant chemotherapy.

If unresectable at diagnosis or unfit for surgery, patients should be considered for radical radiotherapy or chemoradiation with:

- Vinorelbine + cisplatin
- Weekly paclitaxel + carboplatin

Concurrent chemoradiotherapy will be offered to selected cases of locally advanced inoperable NSCLC, (unresectable stage III and stage II unfit for surgery with PS 0 or 1) (NICE clinical guidance 2019).

All patients receiving chemoradiotherapy should be considered for co-trimoxazole as prophylaxis against PJP infection for the duration of radiotherapy. Refer to trust formulary in cases of allergy.

In some situations, “sequential radical” or “sequential high dose palliative” chemoradiation may be more appropriate.

All potential radical patients should be discussed at the Radical Radiotherapy MDM.

2.5.1 Adjuvant Treatment for Unresectable NSCLC after Chemoradiation

Durvalumab for PDL1 positive patients who have not progressed following platinum based chemoradiation therapy.

2.6 Early Stage Inoperable NSCLC

Where surgery is not possible for early stage disease, radical radiotherapy will be considered.

Stereotactic ablative radiotherapy can be considered for patients T1 N0 M0, T2 (<5cm) N0 M0, T3 (<5cm) N0 M0 NSCLC based on positive histology, positive PET scan or growth on serial CT scan. These patients should be reviewed in the radical peer review meeting to asses suitability.

3.0 SMALL CELL LUNG CANCER GUIDELINES

3.1 Overview

Patients suitable for chemotherapy for SCLC should be prioritised for treatment and commence treatment as soon as possible, ideally within one week of initiation of action sheet.

For patients with bulky disease consider allopurinol for first cycle.

3.2 Extensive Stage (first line)

- Atezolizumab in combination with carboplatin and etoposide for 4 cycles followed by maintenance atezolizumab monotherapy
- Carboplatin + Etoposide for up to 6 cycles
- Cisplatin + Etoposide for up to 6 cycles
- Cisplatin/ carboplatin + irinotecan/ gemcitabine may be considered in rare cases e.g. allergic to etoposide (funding approval required).
- Patients with ES-SCLC who are treated with Chemoimmunotherapy (or chemotherapy alone) should be restaged after completion of the chemotherapy part of treatment. If imaging shows at least stable disease, then patients should be considered for consolidation thoracic radiotherapy (cTRT), 30Gy in 10 fractions, over 2 weeks. Radiotherapy can be given between maintenance immunotherapy cycles.
- It is not clear whether patients with complete response on restaging should receive cTRT; decision is at treating clinician's discretion.
- There is currently no randomised evidence for this situation, but this recommendation is based on a meta-analaysis published 2024. RCT results awaited: NCT04402788 and NCT04462276.
- Responders will also be considered for treatment with prophylactic cranial irradiation (PCI). Patients not proceeding with PCI are offered MRI or CT brain surveillance.

3.3 Limited Stage (first line)

Concurrent or sequential chemoradiation is the treatment of choice.

Sequential chemotherapy regimens include:

- Carboplatin + Etoposide for up to 6 cycles
- Cisplatin + Etoposide for up to 6 cycles
- Cisplatin/ carboplatin + irinotecan may be considered in rare cases e.g. allergic to etoposide (funding approval required)
- Thoracic radiotherapy and PCI after completing chemotherapy (sequential)

A pre-treatment PET and staging MRI brain will be performed prior to radical concurrent chemoradiation.

All patients receiving chemoradiotherapy should be considered for co-trimoxazole as prophylaxis against PJP infection for the duration of radiotherapy. Refer to trust formulary in cases of allergy.

3.4 Further Lines of Chemotherapy on Relapse

Options include:

- CAV for up to 6 cycles
- Oral topotecan for up to 6 cycles (NICE approved if re-treatment with the previous treatment is not considered appropriate and there is a medical reason why the patients cannot have CAV. Other indications funding approval required).
- ACE for up to 6 cycles
- Consider platinum rechallenge in patients who have a durable response to first-line treatment.

4.0 MALIGNANT MESOTHELIOMA

4.1 Overview

Supportive care including optimal management of effusion as per BTS guidelines.

Surgical VATS pleurodesis for effusions.

If localised and of good performance status, consider referral for surgery.

4.1.1 Chemotherapy

Consider systemic treatment.

First line:

- Cisplatin + pemetrexed up to 6 cycles.
- Carboplatin + pemetrexed up to 6 cycles.
- Bevacizumab (funding approval required) may be added to the above protocols.
- Ipilimumab and nivolumab

Other regimens which may be considered as alternative 1st line or as 2nd line include:

- Cisplatin + gemcitabine for up to 6 cycles
- Single agent vinorelbine I.V. or oral
- Nivolumab 2nd line treatment (the option to give nivolumab monotherapy instead of second-line chemotherapy to reduce the risk of immunosuppression only remains in place for patients who started first-line chemotherapy on or before 14 July 2022, when the only first-line option available was chemotherapy).

5.0 MALIGNANT THYMOMA / THYMIC CARCINOMA

5.1 Overview

The management of thymoma is surgical wherever possible. Chemotherapy and radiotherapy may be considered for selected patients following MDT discussion as out-lined below.

5.1.1 Chemotherapy

Chemotherapy with CAP may be indicated as follows: -

- Unresectable disease
- Pre-operative for downstaging.
- Post-operative if R1/R2 resection

5.1.2 Radiotherapy

Radiotherapy may also be considered in both pre and post-operative settings as well as palliatively.

6.0 BISPHOSPHONATES & DENOSUMAB FOR BONE METASTASES

Bisphosphonates reduce skeletal morbidity associated with bone metastases (Hillner et al, 2000; Lipton et al, 2000).

All patients with bone metastases should be considered for treatment, especially those:

- Patients with lytic bone metastases on plain radiographs.
- Patients with symptomatic bone metastases (with appropriate use of palliative radiotherapy and analgesics).
- Patients who have suffered a previous skeletal event (pathological fracture, previous radiation to a painful bone metastasis).

Choice of therapy:

- Pamidronate may be given 3 or 4-weekly (with or without chemotherapy).
- Zoledronic acid is more effective than Pamidronate at reducing skeletal complications (Rosen et al, 2001).
- Denosumab is recommended as an option for preventing skeletal-related events in adults with bone metastases if bisphosphonates would otherwise be prescribed.

7.0 NEUROENDOCRINE TUMOURS OF LUNG ORIGIN

Well differentiated NETs of lung origin will be treated in accordance with the neuroendocrine algorithm / protocols as set out in the Upper GI Oncological Treatment Guidelines.

8.0 APPENDIX A: CLINICAL TRIALS

Refer to the local research team who will provide on request an orientation handbook, list of current trials and associated trial protocols and summaries. We are keen to support any trials supported by the NCRI locally within Kent but also refer to outside centres.

Contact numbers

MTW – Clinical Trials Office	01622 225 033
Darent Valley Hospital – Clinical Trials Office	01322 428 100 ext 4810
Medway Hospital – Clinical Trials Office	01634 825 094
East Kent Hospitals – Clinical Trials Office:	
Solid Tumours	01227 866 393
Gynae Clinical Trials	01843 234343
Haematology Clinical Trials	01227 864129

9.0 APPENDIX B: EGFR TKI THERAPY IN NSCLC

Management of Dermatological Adverse Effects of EGFR Tyrosine-Kinase Inhibitors in NSCLC

General advice

- Provide patient education about prevention and management of skin adverse effects before EGFR TKI treatment starts. Explain that rash is not acne.
- Prevention: moisturise at least twice daily; use emollients (e.g. E45, diprobase cream, epaderm ointment) and soap substitutes (e.g. dermol 500 lotion, oilatum shower gel)
- Protect against excessive exposure to sunlight; use SPF 30 UVA and UVB protective sunscreen.

CTC 4.0 Papulopustular Rash Grading

Grading	Description
0	None
1	Papules and/or pustules covering <10% body surface area (BSA), which may or may not be associated with pruritus or tenderness
2	Papules and/or pustules covering 10-30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL
3	Papules and/or pustules covering >30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; limiting self-care ADL; associated with local superinfection with oral antibiotics indicated
4	Papules and/or pustules covering any % BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection with IV antibiotics indicated; life-threatening consequences

Management of Rash

Severity of rash	Management plan
Grade 1 toxicity (Mild)	• Continue EGFR TKI at current dose • Continue to moisturise regularly (check compliance and change emollient if necessary) • Consider topical antibiotics (1% clindamycin lotion) and/or topical steroids (1% or 2.5% hydrocortisone cream) • Use recommended appropriate shampoos if scalp affected (e.g ketoconazole, betadine or ceanel shampoo)
Grade 2 toxicity (Moderate)	• Continue EGFR TKI at current dose unless intolerable • Continue to moisturise regularly and intensify emollient use • Apply short term topical steroids (hydrocortisone 2.5% cream or pimecrolimus 1% cream as steroid sparing agent) • Apply short-term topical antibiotics (1% clindamycin cream) • Use oral antibiotic course (tetracycline for 2 weeks: oxytetracycline 500mg bd or lymecycline 408mg od) * *Prescribe as per Trust formulary ○ **Note:** Avoid doxycycline as associated with photosensitivity • Consider antihistamines
Grade 3 toxicity (Severe)	• Discontinue EGFR TKI and only reinstate (at reduced dose) when skin has resolved to grade 2 or less. • Manage as for grade 2 • **Seek dermatology advice.** • Fax urgent referral to local Dermatology service.

Produced by Dr Lianne Thomas (CT2 Oncology) and Dr Maher Hadaki (Consultant Clinical Oncologist)

Adapted from Califano et al 2015: Expert Consensus on the Management of Adverse Events from EGFR tyrosine kinase inhibitors in the UK and Thatcher et al 2009: Expert Consensus on the Management of Erlotinib-Associated cutaneous toxicity.

10.0 PERSONNEL AND CONTACT INFORMATION

A comprehensive, up to date list of MDM contact details can be requested by NHS professionals by contacting the Kent & Medway Cancer Collaborative. Their contact telephone number is 01233 651905.

11.0 GLOSSARY

Acronyms in common usage throughout KMCC documentation

BNF	British National Formulary
BOPA	British Oncology Pharmacist Association
CNB	Cancer Network Board
COSHH	Control of substances hazardous to health regulations.
CYP	Children & Young People (in relation to the IOG)
DCCAG	Diagnostic Cross Cutting Advisory Group
DOG	Disease Orientated Group (NSSG/TSSG/TWG)
DVH	Darent Valley Hospital
DGT	Dartford and Gravesham NHS Trust
EK	East Kent
EKHUFT	East Kent Hospitals University Foundation Trust
EPS	Electronic Prescribing System
FP10(HNC)	Prescriptions issued by hospital doctors for dispensing in the community
GP	General Practitioner
HoP	High Level Operational Policy
IOSC	Improving Outcomes: A Strategy for Cancer
IV	Intravenous
K&C	Kent & Canterbury Hospital, Canterbury, (EKHUFT)
KMCC	Kent & Medway Cancer Collaborative
KMCRN	Kent & Medway Cancer Research Network
KOMS	Kent Oncology Management System
LSESN	London & South East Sarcoma Network
MFT	Medway Foundation Trust
MTW	Maidstone & Tunbridge Wells NHS Trust
NHS	National Health Service
NMP	Non-medical prescriber
NPSA	National Patient Safety agency
NOG	Non Surgical Oncology Group *(Permanent oncologist sub group of the DOGs with a specific responsibility for chemo/rad pathways and advice to the DOG, Network and GEOGRAPHICAL LOCATIONs on new drugs)*
PoC	Pathway of Care *(Network agreed disease site specific clinical guidelines)*
QEQM	Queen Elizabeth the Queen Mother Hospital, Margate (EKHUFT)
QoL	Quality of life
QSIS	Quality service information system
QST	Quality Surveillance Team
RAT	Research and Trial Group

	(Permanent sub-group of the DOGs with a specific responsibility for taking forward the clinical trials agenda)
RMH	Royal Marsden Hospital
RNOH	Royal National Orthopaedic Hospital
SACT	Systemic Anti-Cancer therapy
SACT regimen	Systemic Anti-cancer prescription on the electronic prescribing system
SACT protocol	Systemic Anti-cancer protocol on KMCC website
TTO	Treatment to take home
QVH	Queen Victoria Foundation Trust Hospital East Grinstead
UCLH	University College Hospital London
WHH	William Harvey Hospital, Ashford (EKHUFT)
WK	West Kent

12.0 DOCUMENT ADMINISTRATION

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