

REFERRAL AND CLINICAL GUIDELINES FOR LUNG CANCER

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REFERRAL PROCESS

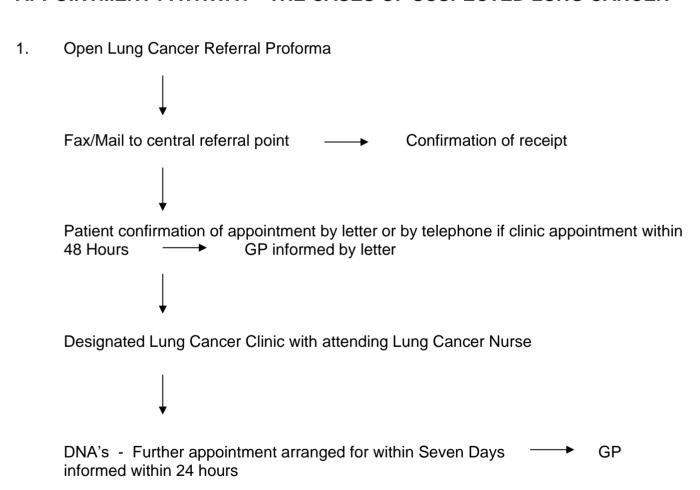
>	Appointment Pathway
>	Suspicious X-Ray Policy
>	Clinical Assessment
>	Fitness for Investigation/Treatment
>	Bronchoscopy/PCNB/Mediastinoscopy/Interventional bronchoscopy Procedures
>	Radiology Protocols
>	Follow-Up Arrangements
>	Histology/Cytology Protocols
>	MDTM Arrangements
>	Surgery
>	Radiotherapy
>	Chemotherapy

General Practitioner Information Arrangement

REFERRAL PROCESS

- 1. Central information point providing telephone, fax, e-mail facilities
- 2. General Practice Generic or Fast Track Lung Cancer Forms to be used
- 3. Hospital: In-house referrals from the Wards, Out-Patients or Casualty to be notified through the Central Referral System

APPOINTMENT PATHWAY - THE CASES OF SUSPECTED LUNG CANCER



SUSPICIOUS X-RAY POLICY

The following procedure is to be undertaken when a report of a **routine** chest x-ray raises the possibility of lung cancer.

Radiology Department

- 1. Inform the patient's General Practitioner by fax or phone by the next working day of the unsuspected finding
- 2. Post the full confirmatory written report to the General Practitioner
- 3. Copy the report to the Chest Physician and the Chest Clinic and cancer data team if appropriate
- 4. In some cases, it will be appropriate to arrange urgent CT scan, before, or on the day of, chest clinic appointment

General Practitioner

The General Practitioner will initiate the referral under the **14 Day Rule**.

Chest Clinic

The Chest Clinic or cancer data team will number, and check referrals received against the copy x-ray reports.

FIRST CLINIC VISIT

1. Clinical Assessment

- a) History including smoking habits, employment history (for suspected mesothelioma)
- b) Examination Height/Weight
- c) Performance Status

2. <u>Investigations</u>

- a) Spirometry
- b) Chest X-Ray
- c) Bloods FBC/Serum Biochemistry/LFT's/Bone Profile/LDH
- d) CT thorax/upper abdo to be arranged urgently or on same day (if not already done)
- e) Bronchoscopy to be arranged if appropriate

3. Patient Information

Provision of literature and contact arrangements by Lung Cancer Nurse

FITNESS FOR INVESTIGATION/TREATMENT

All patients should be considered for investigations to obtain histological or cytological confirmation of their disease.

Patients who after the initial assessment are deemed too seriously ill for further investigation should be discussed at the MDTM for registration and consideration for supportive care without a confirmatory histological diagnosis.

Patients who decline investigations or treatment should similarly be reviewed and a management strategy documented.

BRONCHOSCOPY

1. Consent

Informed consent to be obtained by the Operator

2. Patient Information

Arrangements for the procedure to be explained by the Chest Clinic staff and with accompanying literature which should include a contact telephone number for any subsequent enquiries.

3. Follow-up

Follow-up arrangements to be initiated at the first visit for next results clinic after bronchoscopy or following CT/Histology/MDTM review.

CT Guided Lung Biopsy

- 1. **Suitability.** Most lung and mediastinal lesions (mediastinal lesions? Does this need to be modified? Anterior mediastinal?) can be considered for CT Guided Lung biopsy However peripheral lesions >10mm are most suitable (to be discussed with the radiologist performing the test). As per local MDT protocols, PET scan can be done before CT guided biopsy.
- 2. **Fitness.** Resting hypoxia and impaired lung function (FEV1 < 1 litre, or <40%) are relative contraindications. Cognitive impairment which renders the patient uncooperative is a near absolute contraindication.
- 3. **Consent**. Outline consent should be obtained in the OPC, and written consent obtained by the operator on or before the day of procedure. Patient information literature should be given at the first opportunity.

REFERRAL GUIDELINES FOR IMAGING IN LUNG CANCER

CT Scan Referral

- 1. Requests received on a standard CT request card or by electronic referral.
- 2. Consultant Radiologist vets request to determine the appropriate protocol and level of urgency
- 3. Scans are booked on the next available urgent slot. Where possible and appropriate, scans will be performed on or before the day of clinic attendance. All scans are reported by a Consultant Radiologist or designated Registrar.
- 4. Where confirmed histology is available, a report should contain the following features:
 - Tumour site and maximum dimension
 - Multiplicity or satellite lesions
 - o Evidence of pleural or fissural involvement
 - Evidence of pericardial involvement
 - Presence of associated pneumonitis or collapse
 - Presence of ipsilateral or contralateral lung nodules (T3/N3/M1a)
 - Evidence of mediastinal invasion, and comment on whether only mediastinal fat invaded
 - o Proximity to the main carina or carina of the main bronchi
 - Location and short axis diameter of nodes
 - Evidence of distant metastasis
- 5. From this, a TNM stage will be offered, or alternative TNM stages dependent upon further investigation and a radiological tumour stage.
- 6. If there is a doubt as to histology no definite TNM stage is offered. A provisional TNM stage contingent upon histology may be offered if possible. In this instance, protocol indicating tumour stage should be confirmed at the MDT once histology is confirmed.
- 7. If reports identify a previously unsuspected lung cancer, a report should be faxed to the GP within 24 hours of the report being typed and a copy of the report sent to the MDT secretary.
- 8. Patient for radical treatment should have a recent scan (within 4 weeks) available for planning.

HISTOLOGICAL PATHWAYS FOR LUNG CANCER

The sample (cytology, biopsy or resected tumour) is reported as promptly as possible i.e., ideally a provisional working diagnosis provided within 48 hours for biopsies and cytology and 5 working days for resected specimens. It is recognised that if extended immunohistochemistry or external opinion is required it will take longer to report the resection specimens.

A report is then sent to the requesting clinician so that details of the specimen are available at the weekly MDT. In addition, a copy report of the resected specimen should be sent to the respective lung cancer nurse to facilitate further discussion at the MDT

The vast majority of malignant tumours will be either small cell, squamous or adenocarcinoma and it is recognised that H and E staining alone will be sufficient to categorise most tumours appropriately. In difficult cases immunohistochemical and mucin staining may be required including a neuroendocrine panel (chromogranin, synaptophysin and CD56) as well as CK7, TTF1 and CK5/6. The reporting of resected tumours will be based on the Pathology Lung Cancer National Minimal Data Set (enclosed in appendix 6).

The adenocarcinoma cases, discussed at MDT, should be sent for EGFR, ALK and PD-L1 assay. These patients will usually be those with adenocarcinoma and little smoking history. The appropriate cases with diagnosis of squamous cell carcinoma will be sent for PD-L1 testing after MDT discussion.

POST INVESTIGATION FOLLOW-UP

1. Bronchoscopy

Follow-up appointment to be made at the first visit for the next results clinic, or appointment to be made subsequently when the MDTM/Histology/CT results are available.

2. CT Scan

Copies to Clinicians and Lung Cancer Nurses for urgent attention.

3. PCNB/Pleural Biopsy/Mediastinoscopy/VAT Biopsy

Appointment to be given to the patient after the procedure for the next clinic or the Lung Cancer Nurse to be contacted to arrange further supervision.

4. Histology/Cytology Report

Copies to Clinicians and Lung Cancer Nurses.

GENERAL PRACTITIONER COMMUNICATION

The General Practitioner must be informed by the end of the following working day of all patients who have been informed of their diagnosis of lung cancer.

1. Out-Patients

The General Practitioner/Surgery would be notified by telephone on the next working day that the patient had been informed of the diagnosis. The Clinician should ensure that a full report is available to the General Practitioner by the end of the following working day.

2. <u>In-Patients</u>

The medical team/Consultant office is responsible for telephone/fax confirmation of the patient information.

The record of date/time/author of the fax/telephone information should be recorded in the patient's notes.

Multi-Disciplinary Team (MDT)

Once investigations have been completed all patients should be discussed at the weekly MDT meeting where individual treatment options will be determined. The completed MDT proforma would be an accepted referral letter for surgery/oncology/palliative care. All patients deemed suitable for radical treatment (surgery, radiotherapy or chemoradiation) should be referred for a PET scan via the electronic referral form.

PET/CT SCANNING - REFERRAL STRATEGY

Clinical Indications in respiratory cancers

Following detailed discussion and taking into account current evidence base the following clinical indications were agreed.

- 1. Evaluation of solitary pulmonary nodules
- 2. Staging of non-small cell lung cancer
- 3. Patients for radical intent treatment

Patients meeting the above criteria are discussed in the local MDT. Referral should be made on the electronic request form, which must be fully completed, or it will be returned. This is in order to comply with IRMER regulations and the requesting process. Particular care should be taken in giving a full relevant clinical history and noting whether a patient is diabetic.

Brain scanning before radical treatment including surgery / radical radiotherapy

- 1.Do not offer dedicated brain imaging to people with clinical stage I NSCLC who have no neurological symptoms and are having treatment with curative intent.
- 2. Offer contrast-enhanced brain CT to people with clinical stage II NSCLC who are having treatment with curative intent. If CT shows suspected brain metastases, offer contrast-enhanced brain MRI.
- 3. Offer contrast-enhanced brain MRI for people with stage III NSCLC who are having treatment with curative intent.

Smoking Cessation:

Smoking cessation carries a number of benefits including improvements in response rate to treatment, reduced rates of toxicity and improved survival. Overview | Tobacco: preventing uptake, promoting quitting and treating dependence | Guidance | NICE

- Patients should be educated in the harms of smoking and encouraged to stop smoking.
- Patient (and family) are referred to smoking cessation services.
- Nicotine replacement therapy, varenicline and or bupropion are prescribed appropriately.

GUIDELINES ON INDICATIONS FOR SURGERY FOR LUNG CANCER

Surgery for stage I-IIIA should be considered if patient has the necessary respiratory reserve and is deemed medically fit for major surgery. There is a customised surgical referral form (Appendix 7) available (with bundle of information) for referral to cardiac.referral@bfwhospitals.nhs.uk

Based on the BTS Guidelines and NICE guidelines- See Links

https://thorax.bmj.com/content/thoraxjnl/56/2/89.full.pdf

Lung cancer: diagnosis and management (nice.org.uk)

FITNESS

a) Age:

- i) Perioperative morbidity increases with advancing age. Elderly patients undergoing lung resection are more likely to require intensive perioperative support. Preoperatively, a careful assessment of co-morbidity needs to be made.
- ii) Age over 80 alone is not a contraindication to lobectomy or wedge resection for clinically stage I disease.
- ii) Pneumonectomy is associated with a higher mortality risk in the elderly. Age should be a factor in deciding suitability for pneumonectomy.

b) Cardiovascular Fitness:

Previous MI – interval of 6 weeks + cardiological opinion Previous CABG – no increased risk if asymptomatic Previous CVA – Doppler for carotid artery stenosis Murmur – ECHO Angina or SOB due to cardiac disease – exercise test

c) Performance status:

WHO 0,1 or 2

The Medical and fitness optimisation checklist should be referred before referring for surgery (Appendix 9)

d) Further Assessment and Planning of Patients for Surgery (Based on NICE Guidance 2011,2019)

- Perform spirometry and Diffusion studies (TLCO,KCO) in all patients being considered for treatment with curative intent.
- Offer patients surgery if they have an FEV1, TLCO within normal limits and good exercise tolerance.
- When considering surgery perform a segment count to predict postoperative lung function.

- Offer patients with predicted postoperative FEV₁ or T_LCO below the recommended limit of 30% the option of undergoing surgery if they accept the risks of dyspnoea and associated complications.
- Consider using shuttle walk testing (using a distance walked of more than 400 m as a cutoff for good function) or 6 Min walk test to assess fitness of patients with moderate to high risk of postoperative dyspnoea.
- Consider cardiopulmonary exercise testing to measure VO₂ max and assess lung function in patients with moderate to high risk of postoperative dyspnoea, using more than 15 ml/kg/minute as a cut-off for good function.
- Offer patients with NSCLC who are medically fit and suitable for treatment with curative intent, lobectomy (either open or thoracoscopic) as the treatment of first choice. For patients with borderline fitness and smaller tumours (T1a-b, N0, M0), consider lung parenchymal-sparing operations (segmentectomy or wedge resection) if a complete resection can be achieved.
- Offer more extensive surgery (bronchoangioplastic surgery, bilobectomy, pneumonectomy) only when needed to obtain clear margins.
- Perform hilar and mediastinal lymph node sampling or en bloc resection for all patients undergoing surgery with curative intent.

e) Special Situations:

- 1. Advanced local disease: consider for surgery only if N0/N1
- Chest wall invasion: Potentially operable if T3N0. Pain is a good predictor. CT 90% accurate. MRI may be indicated. High resolution Ultrasound is also a useful modality.
- ii) Adherence to vertebral column: surgery may be contemplated in individual cases. Erosion = inoperable. MRI may be indicated.
- iii) **Superior sulcus tumours:** Horner's syndrome, invasion of brachial plexus and subclavian vessels or vertebrae = inoperable. In this situation induction treatment with chemotherapy and radiotherapy might be attempted to downsize the tumour with subsequent surgery as an option for very selected patients
- 2. N2 diseases: Surgery should be considered in all single station N2 patient, the selection should depend on the potential of curability and overall fitness of patient
- **3. Small cell lung cancer:** for stage I only (T1N0, T2N0)

Following resection patients should be discussed at the MDT for consideration of adjuvant treatment (see under radiotherapy/chemotherapy section).

4. Reinvestigation and selection of patients for surgery after Neo adjuvant chemotherapy

A complete re-staging needs to be done as per protocol after Neo adjuvant chemotherapy and re-discuss in MDT. The modality for re-staging should be individualised and plan agreed on before the start of Neo adjuvant chemotherapy to prevent delay.

5. Oligometastasis

Fit patients with single curable metastasis and potentially curable local diseases should be considered for radical curative surgery.

L&SC Lung Network Second Opinion Guidance

Cardiothoracic Surgery

1) Internal (High risk Thoracic Surgery MDT at Blackpool Victoria Hospital)

It is felt that referral to Thoracic surgeons outside the network will rarely be necessary, as a full range of techniques and procedures are now available from the surgeons based at Blackpool Victoria Hospital. However, it is recognised that in difficult, complex or borderline fitness cases, the opinion of more than one surgeon may be valuable. Should a referring MDT feel that a particular patient requires discussion with a second surgeon, a referral should be made in writing on the High-risk thoracic surgery MDT form (Appendix 8) to the thoracic surgery nurse specialist at: cardiac.referral@bfwhospitals.nhs.uk

2) External

Referrals for Cardiothoracic surgical opinions outside the network should, it is envisaged, be only occasional, however should a referring MDT deem this necessary, then a referral should be made to the clinician of your choice. The external referral should be done only after the internal second opinion route has been explored. The core surgical member of the MDT should be aware about such referral, - for reference purposes this should be copied to the chair of the Lung NSSG together with a note of the outcome, if any. It is emphasised that the referring MDT retains clinical responsibility for the patient at all times.

INTERVENTIONAL BRONCHOSCOPY/THORACOSCOPY SERVICES

Among the many areas of respiratory medicine which have been revolutionised by technological advances, bronchoscopy is one of the most obvious examples. Parallel to the development of ever finer flexible bronchoscopes and working tools, there has been considerable expansion in the diagnostic and therapeutic techniques that can be practised via the bronchoscope, particularly in lung cancer. Diagnostic flexible bronchoscopy available in all centres of the network.

Therapeutic Flexible (Service available at Preston) and Rigid Bronchoscopy (Service available at Thoracic surgery, Blackpool)

Tracheo-bronchial obstruction due to malignant processes can lead to recurrent pneumonia, respiratory insufficiency and death. Curative resection is not possible in the majority of cases, and treatment instead is focussed upon palliation. Techniques available for treatment of tracheobronchial obstruction include electrocautery, argon plasma coagulation, airway stents, laser therapy, cryotherapy, brachytherapy, balloon dilatation and photodynamic therapy. At Preston, we are able to offer majority of these techniques.

Endobronchial Electrocautery (Diathermy), Cryotherapy and Argon Plasma Coagulation (Service available at Preston)

Endobronchial Nd:Yag Laser debulking (<u>Service available at Thoracic surgery</u>, <u>Blackpool</u>)

Indications: These techniques are particularly useful when there is clear evidence of endobronchial disease and the patient presents with one of the following:

- 1. Marked volume loss such as lobar or extensive lung collapse.
- Stridor.
- 3. Worsening dyspnoea.
- 4. Post-obstructive pneumonia.
- 5. Haemoptysis caused by an accessible, visible lesion.

The following points are worth noting with regard to diathermy and argon plasma coagulation.

- 1. The more central the obstruction in the bronchus, the greater the likelihood of palliation. For more distal obstruction, benefit achieved is small. However, treatment of tracheal lesions carries a slightly greater risk.
- 2. These techniques are best considered after the more established treatment options have been looked at, such as surgery, radiotherapy and chemotherapy.
- 3. Diathermy is not indicated in the presence of massive haemoptysis, as adequate visualisation is essential to this technique, and in that situation surgical help with rigid bronchoscopy or interventional vascular radiology input would be needed.

Tracheobronchial Stenting (<u>Service available at Preston and Thoracic surgery Blackpool)</u>

The ultraflex (Nitinol) stent can be placed to relieve acute or sub-acute obstruction of the central airways, in patients who present with stridor, marked volume loss, increasing dyspnoea and post-obstructive pneumonia. This technique is useful essentially where the lesion is 'extrinsic' causing obstruction. Also, they are most effective where there is a relatively short segment of stenosis in the mid/lower trachea, right main and intermediate bronchi, and the left main bronchus (in rare situations where there is a combination of localised intrinsic and extrinsic obstruction, diathermy, laser debulking can be followed up with stenting).

Stenting can also be effective in the presence of a localised tracheo-oesophageal fistula, where double stenting may be required, that is tracheal followed by oesophageal stent.

Stent placement through the flexible bronchoscope is not possible when:

- (a) There is a high tracheal lesion.
- (b) The obstruction extends from the lower trachea into both main bronchi where rigid bronchoscopy and an inverted Y stent is indicated.
- (c) When the mucosa is involved by an extremely vascular, fragile process.

Transbronchial Needle Aspiration (TBNA) (<u>Service available at Preston, Blackpool, Lancaster and Blackburn)</u>

Over the last decade, TBNA has improved the diagnostic yield and extended the role of flexible bronchoscopy in the evaluation of mediastinal pathology and the diagnosis and staging of lung cancer, although it has been largely superseded by EBUS-TBNA

Indications:

- 1. Peri-bronchial disease-causing extrinsic compression.
- Sub-mucosal disease.
- 3. Necrotic, haemorrhagic endobronchial lesions.
- 4. Mediastinal and/or hilar lymphadenopathy to help diagnose malignant and benign lesions.

TBNA is particularly safe and carries a high yield when the abnormality is in the sub-carinal, right para-tracheal or right hilar region.

EBUS-Guided TBNA (Service available at Preston, Blackpool, Lancaster and Blackburn)

Endobronchial ultrasound-guided transbronchial needle aspiration is a new technique which has largely superseded TBNA in majority of situations. This is a procedure using a dedicated bronchoscope with a convex ultrasound probe at the tip. Real time ultrasound images of mediastinal nodes are obtained, along with Doppler flow to differentiate blood vessels from the lymph nodes. Through a side port, a needle can be advanced into the lymph node and targeted samples can be obtained. With practice, this technique has a greater than 90% positive yield

and samples can be aspirated from a variety of lymph nodes including sub-carinal, right paratracheal, left paratracheal, right hilar and left hilar regions. With the advantage of dynamic ultrasound guidance, larger samples are acquired, and the procedure carries a very low risk of bleeding.

Therefore, any patient with unexplained or malignant appearing mediastinal/ hilar adenopathy can be referred for this procedure. In addition, peribronchial lesions can be diagnosed and mediastinal staging can be completed.

Radial EBUS miniprobe guided biopsy-with or without Fluoroscopy and Navigation (Service available at Preston)

This technique utilises radial EBUS miniprobe guidance to sample parenchymal lung lesions which are not accessible via CT guided biopsy, VATS biopsy or second generation EBUS guided TBNA, especially if the lesion is more than 2 cm in size and there is a 'CT Bronchus' sign (please discuss with your radiologist. The diagnostic yield ranges between 60% and 80%, and it is important to explain this to the patient prior to referral.

Semi-Rigid Medical Thoracoscopy (Service available at Preston)

The technique involves a single incision of just over a centimetre in the mid-axillary line under local anaesthesia and standard sedation. It is performed in the Endoscopy Suite and the patient is usually required to stay overnight after the procedure.

Indications

- 1. Undiagnosed unilateral, exudative pleural effusion drainage, pleural biopsy and if appropriate TALC pleurodesis can be performed in one sitting
- 2. Hydropneumothorax or pneumothorax when an underlying parietal pleural pathology is suspected.
- 3 Early cases of empyema.

All such patients should have normal clotting, liver and renal function, and a contrast enhanced CT scan of the thorax, besides a recent chest x-ray prior to the procedure.

Guidelines for Referrals (based on the Preston services)

- 1. If the indication for the procedure is obvious, as outlined above, please email a referral and arrange for the images to be uploaded to LTHT PACS.
- 2. It is essential that the patient's clotting profile, renal and hepatic function are satisfactory. If the patient is on warfarin, this will need to be discontinued for about seven days before the procedure. The same applies to Clopidogrel.
- 3. In cases of therapeutic bronchoscopy, the patient and relatives need to be aware that the treatment is purely for palliation of symptoms/obstruction. Also, the risk of bleeding and other usual complications of bronchoscopy needs to be mentioned. Further details of the possible complications of the specific procedure will be outlined when the patient is seen.
- 4. The patient will often need to stay overnight after the procedure on the respiratory ward.
- 5. Patients referred for stenting will occasionally have to stay for a few days in the hospital, as the stents may have to be measured and ordered after the initial assessment, and the patient may require a further bronchoscopy after the stent is deployed.

Referral contact details

BTHT	ELHT	LTHTR	UHMBT
TBNA & EBUS-TBNA	TBNA	ALL SERVICES	Tel: 01524 511979 01524 512249
Tel: 01253 956706	Tel: 01254 734360	Tel: 01772 522416	
Dr Bhatta Dr Mirakhur	Dr Wilson	01772 522412 01772 522189	Fax: 01524 583981
	EBUS-TBNA		
T/B STENTING			
	Tel: 01254 734338	Dr Munavvar	
Tel: 01253 951466	Dr Zaman		
Mr Duncan			
Mr Bittar	Fax for all:		
	01254 735910		

Management and Investigation of Unilateral Pleural Effusions

• Take a full history and perform a clinical examination

Clinical assessment can be used to identify transudative effusions which will not require sampling and can therefore be managed medically.

Perform pleural aspiration

Collect a 50 ml sample of the pleural fluid using a 21G (green) needle. Note the colour and odour of the fluid; if it is turbid, collect an additional sample using an ABG syringe and analyse it immediately using the ABG machine.

• Request appropriate analysis of the pleural fluid

Add 10 ml to two universal containers (for cytology and AAFB/gram stain/TB culture), 10 ml to each of anaerobic and aerobic blood culture bottles and the remainder to citrate (yellow, for glucose), gel (brown, for LDH/protein) tubes. If the fluid is frankly blood-stained, add 2 ml to an EDTA (red) tube to measure the haematocrit. Ensure the sample is analysed within 4 hours.

Apply Light's Criteria to the results received from the laboratory

The fluid is an exudate if [protein]_p \div [protein]_s > 0.5 or [LDH]_p \div [LDH]_s > 0.6

• Interpret the results

• pH < 7.2 with evidence of infection or positive gram stain

Empyema requiring prompt tube drainage; refer to the Respiratory team

Transudate

Drain only if there is respiratory distress; treat the underlying cause.

Exudate

Request a contrast-enhanced CT of the thorax optimised for pleural assessment and refer to the Respiratory Team.

RESPIRATORY PHYSICIANS

O Discuss

The contrast-enhanced CT scan of the thorax should be reviewed ASAP with a radiologist or discussed in the next Chest Radiology meeting.

Direct as necessary for tissue diagnosis or case review Thoracoscopy

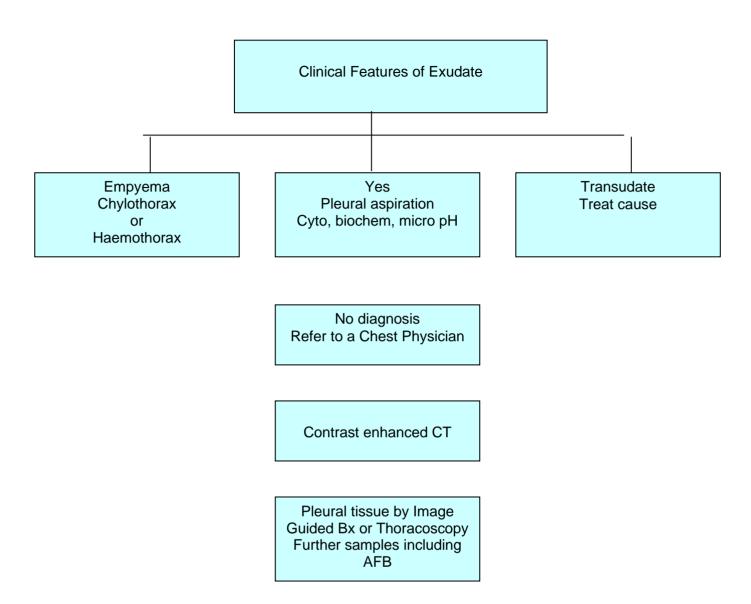
Direct visualisation of any pleural lesions. Sampling, drainage and talc poudrage performed in one sitting. Semi-rigid thoracoscopy (minimally invasive, under LA and sedation (Important note: Please try, if possible, to avoid complete therapeutic drainage of effusion prior to referral, as it can potentially cause adhesions and prevent safe access to the pleural cavity for thoracoscopy)

Image guided Pleural biopsy- Ultrasound or CT guided- discuss with Consultant Radiologist

VATS

Requires GA and single lung ventilation- discuss with Cardio-thoracic Surgeon

Algorithm for investigation of Pleural Effusion





<u>Thymic epithelial tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up (annalsofoncology.org)</u>

WORKUP

Imaging and diagnostic tests

- Thymoma is the first diagnosis to consider when facing a mediastinal mass associated with autoimmune disease.
- The diagnosis of any thymic epithelial tumour relies on making the differential diagnosis with other anterior mediastinal tumours and non-malignant thymic lesions.
- Standard imaging for Thymic tumours is i.v. contrast-enhanced (CT) scan of the thorax
- MRI is recommended to differentiate thymic tumour from hyperplasia whenever CT scan is doubtful, or in case of cystic lesion.
- PET scan is generally not recommended to assess thymic masses.
- Therapeutic intervention is usually not required if the lesion is <30 mm, given a low risk of progression or thymic malignancy.
- Systematic immunological check-up is recommended, including complete blood cells count with reticulocytes and serum protein electrophoresis, as well as anti-acetylcholine receptor and anti-nuclear antibodies tests.

Need for a biopsy

- Pre-treatment biopsy is not required if the diagnosis of thymic epithelial tumour is highly suspected and upfront surgical resection is achievable.
- Biopsy is required in all other clinical situations; approaches may consist of percutaneous core-needle biopsy or incisional surgical biopsy through mediastinotomy or mini-thoracotomy.
- Fine-needle aspiration is not recommended

Diagnosis

- Thymic epithelial tumours are classified according to the WHO histopathological classification.
- Although designed for surgical resection specimen, the WHO classification may be used for small biopsies.
- Immunohistochemistry with anti-CD117/KIT and anti-CD5 antibodies is useful to establish the thymic primary nature of a mediastinal carcinoma.
- Each component of heterogeneous tumours may be quantified by 10% increments.
- Consultation with a second pathologist or referral of the case to a thymic tumour pathology panel is recommended whenever there is any diagnostic difficulty.
- Ontogenetic assessment should be carried out in case of familial thymic epithelial tumour, looking especially at MEN1.

Paraneoplastic syndromes associated with thymic neoplasms

Neurologic and neuromuscular	Myasthenia gravis, polymyositis, sensory neuropathy, stiff person syndrome, neuromyelitis optica, Isaacs syndrome (neuromyotonia), Lambert-Eaton myasthenic syndrome, hemichorea	
Hematologic	Pure red cell aplasia, agranulocytosis, hemolytic anemia, pernicious anemia	
Dermatologic	Alopecia areata, pemphigus, scleroderma, oral lichen planus, vitiligo	
Endocrine	Addison's disease, Cushing syndrome, panhypopituitarism, thyroiditis	
Miscellaneous Acquired hypogammaglobulinemia, myocarditis, nephrotic syndron rheumatoid arthritis, sarcoidosis, hepatitis, gastrointestinal pseudoobstruction, ulcerative colitis		

Classification of thymic epithelial tumors

Levine and Rosai*	Müller-Hermelink, et al [¶]	WHO∆	
Thymoma	Thymoma	Thymoma	
Encapsulated	Medullary type	Type A	
	Mixed type	Type AB	
Malignant type I (invasive)	Predominantly cortical	Type B1	
	Cortical type	Type B2	
	Well-differentiated carcinoma	Type B3	
Malignant type II	Thymic carcinoma	Thymic carcinoma (Type C thymoma)	

Clinical staging of thymic epithelial tumors

Masaoka's clinical st	age ^[1]
Stage I: Macroscopically	completely encapsulated and microscopically no capsular invasion
Stage II: Macroscopic inv	asion into surrounding fatty tissue or mediastinal pleura, or microscopic invasion into
Stage III: Macroscopic in	vasion into neighboring organs (ie, pericardium, great vessels, or lung)
Stage IVa: Pleural or peri	cardial dissemination
Stage IVb: Lymphogenou	is or hematogenous metastasis

Tumors of the thymus TNM staging AJCC UICC 8th edition

Primary tumor (T)*¶		
T category	T description	
TX	Primary tumor cannot be assessed	
T0	No evidence of primary tumor	
T1	Tumor encapsulated or extending into the mediastinal fat; may involve the mediastinal pleura	
T1a	Tumor with no mediastinal pleura involvement	
T1b	Tumor with direct invasion of mediastinal pleura	
T2	Tumor with direct invasion of the pericardium (either partial or full thickness)	
Т3	Tumor with direct invasion into any of the following: Lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall, or extrapericardial pulmonary artery or veins	
T4	Tumor with invasion into any of the following: Aorta (ascending, arch, or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus	

^{*} Involvement must be microscopically confirmed in pathological staging, if possible.

[¶] T categories are defined by "levels" of invasion; they reflect the highest degree of invasion regardless of how many other (lower-level) structures are invaded. T1, level 1 structures: thymus, anterior mediastinal fat, mediastinal pleura; T2, level 2 structures: pericardium; T3, level 3 structures: lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall, hilar pulmonary vessels; T4, level 4 structures: aorta (ascending, arch, or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus.

Regional lymph nodes (N) [∆]			
N category N description			
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Metastasis in anterior (perithymic) lymph nodes		
N2	N2 Metastasis in deep intrathoracic or cervical lymph nodes		
Δ Involvement mi	ust be microscopically confirmed in pathological staging, if possible.		

Distant metastasis (M)

M category	M description	
M0	No pleural, pericardial, or distant metastasis	
M1	Pleural, pericardial, or distant metastasis	
M1a	Separate pleural or pericardial nodule(s)	
M1b	Pulmonary intraparenchymal nodule or distant organ metastasis	

When T is	And N is	And M is	Then the stage group is
T1a,b	NO	MO	I
T2	N0	MO	II
T3	N0	MO	IIIA
T4	N0	MO	IIIB
Any T	N1	MO	IVA
Any T	N0, N1	M1a	IVA
Any T	N2	M0, M1a	IVB
Any T	Any N	M1b	IVB

[♦] R0: no residual tumor; R-any: any type of resection (no residual tumor, microscopic residual tumor, or macroscopic residual tumor at the primary cancer site or regional nodal sites).

Meneshian A, Giaccone G, Olivier KR. Clinical presentation and management of thymoma and thymic carcinoma. In: UpToDate, Post TW (James R Jett JR and others), UpToDate, Waltham, MA. (Accessed on November 21, 2021).

Masaoka-Koga staging and treatment recommendations:

Stage I Thymoma 100% 5-year survival	Surgery
IIA, IIB Thymoma	Surgery
86-95% 5-year survival	OR Surgery with or without radiation therapy (PORT) in high-risk cases stage
30 33/03 year sarvivar	IIB (close surgical margins, WHO type B or, large tumour size)
Resectable III Thymoma	Surgery + probably PORT
56-69% 5-year survival	Sanger, productive control
Potentially resectable III Thymoma	Neoadjuvant Chemotherapy followed by surgery (if operable) and radiation
Up to 50% 5-year survival	therapy
	OR Chemotherapy followed by radiation therapy (if it remains inoperable)
	Chemotherapy alone is not considered a curative option.
Resectable IVA Thymoma (limited	Surgery +/- PORT +/- chemotherapy
pleural disease)	OR Chemo followed by surgery +/-PORT
Thymoma:	Chemotherapy followed by radiation therapy
Unresectable stage III	Chemotherapy alone
IVA (disseminated pleural disease)	Palliative RT
IVB	BSC (if not fit for Chemo)
R0 resection	Observation for stage I or II Thymoma
	Consider for high risk IIB Thymoma
	Consider RT for stage III, IV Thymoma
	RT+Chemo for thymic carcinoma
R1 resection	RT for thymoma
	OR RT+/-chemo if thymic carcinoma
R2 resection	RT+/-Chemo for thymoma
	OR RT+/-chemo if thymic carcinoma
Relapse/Progression	Salvage surgery (isolated recurrence)
	RT
	Chemo.
	BSC

Risk assessment

• The management of autoimmune syndromes should be integrated in the oncological management.

Management of resectable disease

- The treatment strategy for thymic epithelial tumour is primarily based on whether the tumour may be resected upfront or not
- Complete respectability should be the aim; it is recommended to discuss indications for surgery in a multidisciplinary tumour board setting
- If complete resection is deemed to be achievable upfront, surgery represents the first step of the treatment

Surgery principles

- Standard approach is median sternotomy
- Complete thymectomy including the tumour, the residual thymus gland and perithymic fat, is preferred
- Thymomectomy alone—leaving residual thymic tissue and perithymic fat behind—is an option in stage I tumours in non-myasthenic patients
- If the tumour is widely extensive invasive (stage III/IV), en bloc removal of all affected structures, including lung parenchyma (usually through limited resection), pericardium, venous great vessels, nerves should be carried out
- Areas of uncertain margins are marked with clips to allow precise delivery of postoperative radiotherapy
- Phrenic nerve preservation does not affect OS but increases the risk of local recurrence.
- Frozen sections to assess tumour involvement of resection margins are not recommended.
- Minimally invasive surgery is an option for presumed stage I–II tumours
- The choice for minimally invasive resection should not jeopardise or change the principles that are deemed
 - appropriate for an open approach, especially the achievement of complete resection that may ultimately Require switching to an open procedure.
- Minimally invasive surgery is not recommended for stage III tumours.
- There should be agreed protocol for lymph node managements for Thymic carcinoma (in process).

Systemic therapy Options:

First Line	Platinum based chemotherapy	PE or CAP as neoadjuvant, adjuvant, first line palliative. PE or Carboplatin paclitaxel for concurrent chemoradiation.	PE=Platinum etoposide. CAP=cyclopho sphamide, Adriamycin, cisplatin.
Second Line	A wide range of chemotherapeutic agents has been used when disease progresses. They include: Rechallenge with platinum-based regimen, Etoposide, ifosfamide, pemetrexed, octreotide, 5FU (FU) plus leucovorin, gemcitabine with or without capecitabine, and paclitaxel.	We do not offer immunotherap y to patients with thymoma or those with autoimmune disease due to concerns about irAEs	
Subject to Funding:	VEGF inhibitor therapy with sunitinib or lenvatinib		
Subject to Funding:	Immunotherapy for thymic carcinoma		

Radiotherapy protocols:

Indication	Dose fractionation	
Postoperative	50Gy in 25 fractions	
	60Gy in 30 fractions	
Primary radiotherapy	60Gy in 30 fractions	
Pre-operative radiotherapy	45Gy in 25 fractions	
Palliative Radiotherapy, this is a radiosensitive	As per lung cancer protocols	
disease		

Follow-up

History, physical examination, and CT q6 months for 2 years, then annually for 5 years for thymic carcinoma.

Follow up for thymomas to continue to 10 years.

MESOTHELIOMA

WORKUP

All Cases

- History and physical examination
- Thoracocentesis for cytology assessment
- Pleural biopsy for pathologic confirmation (e.g., VATS, Abrams needle, CT-guided core biopsy, open biopsy)
- Pulmonary function tests
- Imaging-CT chest and abdomen with contrast, PET/CT
- Labs-FBC, LDH
- Clinicians should consider carrying out a Rockwood Clinical Frailty Scale Analysis and also a Charlson Comorbidity Index (without including the malignancy in the Charlson Scale) for patients with ECOG PS 2 or worse.

Considerations

- Chest MRI
- Mediastinoscopy/EBUS and FNA for pathologic evaluation of mediastinal nodes
- VATS and/or laparoscopy if concern of contralateral or peritoneal disease
- Talc pleurodesis or indwelling pleural catheters if recurrent effusion
- Cardiac stress test (surgical evaluation)

.

TREATMENT RECOMMENDATIONS

I to IIIA epithelioid	Pleurectomy / decortication can be considered in selected cases up to T3N1M0 epithelioid mesothelioma as of multimodality therapy. OR Chemo
IIIB or IV epithelioid	Observation
OR sarcomatoid or biphasic type	OR Chemo
OR medically inoperable	OR Palliative RT (e.g., chest wall, scar, skin,
	bone metastases)
	Or Ipilimumab + nivolumab immunotherapy (if
	funding available) for non-epithelioid
	mesothelioma.
	OR best supportive care (PS 3-4)

Stage	MST Epithelioid vs	2-year survival
	Non-E	Epithelioid vs Non-E
IA	23.3 vs.19	48% vs. <mark>41%</mark>
IB	21.1 vs.15.5	46% vs. <mark>27%</mark>
II	21.6 vs.12.9	41% vs. <mark>25%</mark>
IIIA	15.4 vs.13.2	33% vs. <mark>22%</mark>
IIIB	16.6 vs.10.8	31% vs. <mark>14%</mark>
IV	10.7 vs. <mark>8.7</mark>	17% vs.15%

Overall survival according to overall stage

CHEMOTHERAPY FOR MESOTHELIOMA

		First Line	Second Line
Epitheloid	PS0-1	Platinum Pemetrexed	Pemetrexed platinum if not used in first line or rechallenge following good durable response Single agent immunotherapy with nivolumab or pembrolizumab (irrespective of PDL1 status) Single agent chemotherapy with vinorelbine or gemcitabine Cisplatin gemcitabine in selected patients Motivated patients could be considered for clinical trials
	PS2	Single agent Vinorelbine or Gemcitabine	
Non Epitheloid	PS 0-1	●Pemetrexed and Platinum combination. ●Nivolumab + Ipilimumab (nivolumab 3mg / kg 2 weekly and ipilimumab 1mg/kg 6 weekly, up to 2 years maximum duration). PSO-1 patients. [If funding available]	Pemetrexed platinum if not used in first line or rechallenge following good durable response Nivolumab + Ipilimumab (if not used first line) (nivolumab 3mg / kg 2 weekly and ipilimumab 1mg/kg 6 weekly, up to 2 years maximum duration). PSO-1 patients. (if funding is available. Cisplatin gemcitabine in selected patients single agent vinorelbine or gemcitabine Motivated patients could be considered for clinical trials
	PS2	single agent vinorelbine or gemcitabine but priority is best supportive care.	

RADIOTHERAPY IN MESOTHELIOMA

Indication	Dose fractionation	
Palliative chest wall pain	As per lung cancer guidelines	
Prophylactic radiotherapy	 This is not routinely used for biopsy sites. Prophylactic radiotherapy may be offered to scar of Pleurectomy/ decortication 	

Follow up

Frequent follow up with CXR, CT chest, history, and physical examination indefinitely.

SMALL CELL LUNG CANCER

WORKUP

All Cases

- History and physical examination (including weight loss and performance status)
- Smoking cessation
- MRI brain
- PET/CT
- Labs- FBC, Electrolytes, LFTs, Ca, LDH, BUN, Creatinine
- Pathologic confirmation
- Clinicians should consider carrying out a Rockwood Clinical Frailty Scale Analysis and a Charlson Comorbidity Index (without including the malignancy in the Charlson Scale) for patients with ECOG PS 2 or worse
- (Pre-) Rehabilitation focusing on comorbidities, nutrition, exercise, and wellbeing is strongly encouraged.

Considerations

- Pathologic evaluation of mediastinal nodes only if T1-2 N0 and patient is surgical candidate.
- Thoracocentesis with cytology for pleural effusions
- Bone scan if PET unavailable and relevant symptoms
- SIADH in previously untreated patients: These patients should be managed actively in liaison
 with endocrinologists. Pharmacological options to correct low sodium include demeclocycline
 and tolvaptan. Ideally sodium should be >125 before starting chemotherapy.
- Pulmonary function tests.

Prognostic factors: Each adverse feature scores +1

- 1. LD vs ED
- 2. KP > 60 vs \leq 60
- 3. Serum Na (low vs normal)
- 4. Serum LDH (normal vs high)
- 5. Serum alk phos (normal vs high)
- Scores of 0 and 1 have better prognosis

TREATMENT RECOMMENDATIONS

Operable IA or IB (T1-T2a, N0, M0)	Surgery followed by chemotherapy and PCI OR (concurrent) ChemoRT followed by PCI OR surgery followed by ChemoRT followed by PCI
IA inoperable, IB inoperable, IIA, IIB, IIIA, IIIB. (Fit patients and radiotherapy volume feasible)	Concurrent ChemoRT followed by PCI
Unable to tolerate concurrent or tumour (radiotherapy) volume not suitable for concurrent	Sequential Chemo-RT followed by PCI
IV	Chemo followed by PCI and possible thoracic RT if good response to chemo. Chemo-IO +/- PCI
Unfit for Chemo	BSC, Palliative Radiotherapy, rarely radical radiotherapy is an option.
Recurrent disease	Chemo / Chemo-IO OR Palliative Radiotherapy Palliative Care

Staging	Median OS	5-y survival
Limited	20 months	20%
Extensive	12 months	1%

1.Limited Stage Disease, good Manchester Score (0/1) T1-4 N0-3 M0

- Stage 1 (T1-2a, N0, M0) may be considered for <u>surgical resection</u> (followed by adjuvant chemoand radiotherapy).
- Concurrent chemo-irradiation: Fit patients with disease encompassable in radical radiotherapy portals should be offered concurrent chemoradiation with Cisplatin 80mg/m2 day1 and iv Etoposide 100-120mg/m2 day 1-3 x 4-6 cycles (oral Etoposide 200mg/m2 can be substituted for days 2-3). Radiotherapy will start ideally by cycle 2. Carboplatin can be substituted for cisplatin in case of renal impairment or poor tolerance to cisplatin.
 - A dose of 45Gy in 30 fractions twice daily over 3 weeks will be given to the involved areas. Alternatively, once daily radiotherapy to 60-66 Gy in 30-33 fr (with minimum over 50Gy in 25 fractions) can be utilised.
 - o Prophylactic co-trimoxazole should be considered in concurrent chemoradiotherapy.
- <u>Sequential Chemo-irradiation:</u> Patients with initial disease volume too large to be treated with radical radiation should be reassessed after induction chemotherapy (as above) with platinum-based chemotherapy and could be offered sequential radiotherapy with a dose of 40Gy/15 fr; 55Gy/20fr; 66Gy/33fr or 45Gy/30Fr twice daily. A palliative radiotherapy dose (30Gy in 10 fr or

- 39Gy 13 fr may be employed if there is extensive residual disease that is not amenable to a more radical dose).
- <u>PCI</u>: For patients who have not progressed, with good PS (0-2) should be considered for prophylactic cranial irradiation (25Gy/10#). This may be withheld in patients over age 75.
 - The Premer Trial 2021 demonstrated the significant benefit of hippocampal sparing PCI IMRT, and this is suggested to be rapidly adopted in L&SC.
 - o MRI brain surveillance can be utilised instead of PCI

2. Limited stage, poor Manchester Score OR Extensive stage, good Manchester Score

(Patients should receive primary prophylaxis with GCSF).

<u>Chemo-IO</u>: In PS 0-1 extensive stage patients. Combination chemotherapy with Carboplatin AUC5 day1 and Etoposide 100mg/m2 day 1-3 (oral Etoposide 200mg/m2 can be substituted for days 2-3) up to 4 cycles. Atezolizumab starts with cycle 1 chemo and continues as maintenance post chemo.

Patients with brain metastases do not benefit from IO.

<u>Chemotherapy alone:</u> Combination chemotherapy with Carboplatin AUC5 day1 and Etoposide 100mg/m2 day 1-3 (oral Etoposide 200mg/m2 can be substituted for days 2-3) up to 6 cycles.

<u>Thoracic consolidation radiotherapy</u> (usually non radical dose) should be considered for these patients. Impower 133 trial did not utilise thoracic consolidation radiotherapy in chemo-IO arm.

 <u>PCI</u> should be considered in patients who have responded (PR or CR). This may be withheld in patients over age 75. The use of hippocampal avoidance techniques is recommended. MRI brain surveillance can be utilised instead of PCI.

3.Extensive Stage Disease, poor Manchester score

Treatment with single agent Carboplatin AUC5 could be considered as alternative to combination treatment initially. However, as soon as the performance status improves patients should be reassessed for use of combination chemotherapy.

- PCI is considered in patients who have responded (PR or CR). This may be withheld in patients over age 75 or of poor PS. The use of hippocampal avoidance techniques is recommended.
- Radiotherapy may also be used for symptom control e.g., lung, bone, brain skin metastases.

4.Second Line Chemotherapy

Patients who recur more than 3 months after completion of 1st line treatment should be considered chemosensitive and may be offered further chemotherapy with a platinum rechallenge, CAV or oral topotecan. Their overall prognosis is however poor and median survival is months.

• Radiotherapy may also be used for symptom control e.g., lung, bone, brain skin metastases.

Follow-up

First 2 years q 3 months

+2 years q 6 months

History and physical examination.

Blood tests only if clinically indicated

CT +/- brain imaging (MRI preferred) recommended at least 6 monthly

Guidelines for Radiotherapy and Chemotherapy in

NON-SMALL CELL LUNG CANCER

Appropriate treatment choice for individual patients depends largely on the stage of disease at presentation, their performance status and presence of driver mutations / PDL1 status. Comorbidities should be optimised and prehabilitation considered particularly for patients whose disease is suitable for curative treatment. Investigations and actions to address these should be performed prior to referral to a surgeon or an oncologist.

Clinicians should consider carrying out a Rockwood Clinical Frailty Scale Analysis and also a Charlson Co-morbidity Index (without including the malignancy in the Charlson Scale) for patients with ECOG PS 2 or worse.

Work up:

All cases:

1-History and Examination (including weight loss and performance status)

2-smoking cessation assistance.

3-pulmonary function tests (including spirometry and transfer factor).

4-PET/CT.

5-Tissue diagnosis: CT-guided biopsy, bronchoscopic and EBUS directed biopsy, Bronchial lavage, Mediastinoscopy, VATS, or chamberlain for LN biopsy if indicated

6-MRI brain/CT brain with contrast

7-Molecular markers (All specimens should be checked for biomarkers at diagnosis ideally via DNA and RNA NGS platforms.

Currently available tests are:

DNA NGS: EGFR, BRAF, KRAS, MET
RNA NGS: ALK, ROS1, RET, NTRK 1/2/3

IHC: PDL1

The guidelines below do not deal with surgical issues:

Early / Locally Advanced Disease

Radical Radiotherapy

A] Chemoradiotherapy +/- Durvalumab IO

- Consider chemoradiotherapy for people with stage II or III NSCLC that are not suitable for or decline surgery.
- Vinorelbine/Cisplatin (or Carboplatin for patients unsuitable for Cisplatin) concurrent for NSCLC.
- Weekly Carboplatin Taxol x 6 for NSCLC is also utilised particularly in less fit patients.
- Consider co-trimoxazole in concurrent chemoradiotherapy.
- --Durvalumab monotherapy is recommended for use within the Cancer Drugs Fund as an option for treating locally advanced unresectable NSCLC in adults whose tumours express PD-L1 on at least 1% of tumour cells and whose disease has not progressed after platinum-based chemoradiation only.
- --For people with operable stage IIIa-N2 NSCLC who can have surgery and are well enough for multimodality therapy, consider neoadjuvant and /or adjuvant therapy. However, we have not done neoadjuvant Chemoradiotherapy pre surgery at L&SC.

B] Radiotherapy alone

- For people with stage I-IIa (T1a-T2b, N0, M0) NSCLC who decline lobectomy or in whom it is contraindicated, offer radical radiotherapy with SABR (or sublobar resection).
- For people with stage I-IIa (T1a-T2b N0, M0) NSCLC who decline surgery or in whom any surgery is contraindicated, offer SABR. If SABR is contraindicated, offer either conventional or hypofractionated radiotherapy.
- For eligible people with stage IIIa NSCLC who cannot tolerate or who decline chemoradiotherapy (with or without surgery), consider radical radiotherapy (either conventional or hypofractionated).
- For eligible people with stage IIIb NSCLC who cannot tolerate or who decline chemoradiotherapy, consider radical radiotherapy (either conventional or hypofractionated).

If conventionally fractionated radical radiotherapy is used, offer either:

- 55 Gy in 20 fractions over 4 weeks or
- 60-66 Gy in 30-33 fractions over 6-6½ weeks.

C] Postoperative radiotherapy

Indications:

- Patients with incompletely resected disease
- Patients who are N2 and have had inadequate lymph node dissection / sampling. N2 disease per se is no longer an indication for adjuvant radiotherapy.

Post-operative radiotherapy (50Gy in 25# over 5 weeks) +/- adjuvant sequential / concurrent chemotherapy if their PS is good.

Concurrent chemoradiation to be considered only in the setting of positive margins / macroscopic residual disease.

D] Stereoablative Body Radiotherapy (SABR):

This involves high intensity radiotherapy to a small focal area of the lung.

Peripheral Tumours

- ITV ≥ 2.0cm from proximal bronchial tree (PBT), trachea, oesophagus, heart, great vessels, spinal cord,

brachial plexus, phrenic nerve, recurrent laryngeal nerve

- Dose 18Gy x 3# or 11Gy x 5#

Central Tumours

- Tumours which do not satisfy the criteria for peripheral tumours (as above) **and** are **not** ultra-central (as below)
- Dose 7.5Gy x 8#

Ultra-central Tumours should not be treated

- ITV < 1.0 cm from PBT or
- PTV directly contacting or overlapping the trachea, oesophagus, pulmonary vein or pulmonary artery

Early / Locally Advanced Disease

Systemic Therapy

A] Neoadjuvant chemotherapy

- Neoadjuvant chemotherapy is generally not advised outside the context of a clinical trial in Stage I and II patients.
- Selected Stage III patients may be suitable for chemotherapy x 2-4 cycles prior to considering surgical resection or radical radiotherapy. A cisplatin-based doublet such as cisplatin vinorelbine (or appropriate for histology is recommended). Carboplatin (AUC5) can be considered in place of cisplatin in patients in less fit patients and / or with poor renal function. Gemcitabine is a strong radiosensitiser and its use prior to radiotherapy must be approved by a clinical oncologist.

The patient fitness for possible surgery / radical radiotherapy should be assessed.

The restaging plan for surgery (post neoadjuvant chemotherapy) should be in place before starting neo adjuvant chemotherapy.

B] Adjuvant Systemic therapy

1] Adjuvant chemotherapy with Vinorelbine and Cisplatin x 4 cycles should be offered. Histology specific platinum doublet can be used.

Carboplatin (AUC5) can be considered in place of cisplatin in less fit patients or patients with poor renal function.

- Offer to fit patients with size over 4cm disease, Stage III and or Node +ve
- Consider in fit patients if they have: LVSI+ve, high grade, visceral pleural involvement, non-well differentiated neuroendocrine tumours.

2]Adjuvant <u>osimertinib</u> to be offered (if no contraindications) to EFGR sensistising mutation positive patients (exon 19 deletions or exon 21 L858R mutation) for 3 years either with or without prior chemotherapy.

3]Adjuvant <u>atezolizumab</u> (post adjuvant chemo) for completely resected stage II-IIIA NSCLC whose tumour express PDL1_>50% and whose disease has not progressed following platinum-based adjuvant chemotherapy.

C] Future Considerations:

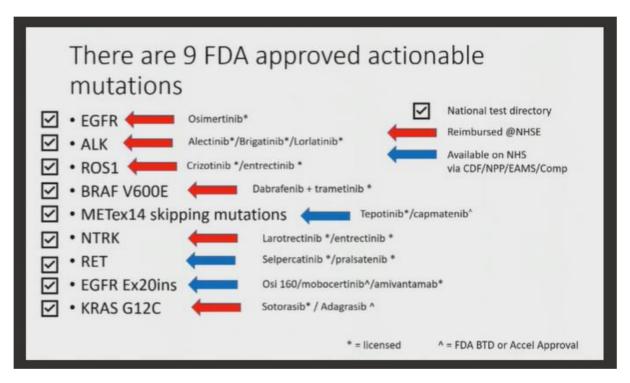
The use of (chemo)-immunotherapy with checkpoint inhibitors is actively explored in the neoadjuvant setting. This is to be reviewed as an interim measure as National Guidance evolves.

Advanced Disease

Patients with Stage III/IV disease unsuitable for radical treatment who have PS 0-2 should be considered for palliative systemic therapy. Further lines of therapy depend on previous response and duration of response to treatment, fitness, biomarkers and are at the discretion of the treating clinician.

(Pre-) Rehabilitation focusing on comorbidities, nutrition, exercise and wellbeing is strongly encouraged to be set up in each Trust. Clinicians should consider carrying out a Rockwood Clinical Frailty Scale Analysis and also a Charlson Co-morbidity Index (without including the malignancy in the Charlson Scale) for patients with ECOG PS 2 or worse.

A] Targeted therapy against driver mutations:



Rivaz Shah BTOG 2022

This is a fast-moving field that users need to stay up to date (beyond this guidance).

EGFR sensitising mutation positive such as Exon 19 deletion or L858R mutation:

- Preferred osimertinib first line.
- Other first options include: erlotinib, afatinib (for non-common mutations), gefitinib, dacomitinib

EGFR exon 20 insertion mutation positive

- First line: systemic therapy
- Second line: Amivantamab-vmjw or Mobocentric in trials or as available. Osimertinib can be used.

Kras G12c mutation positive:

• First line: systemic therapy

• Second line: sotorasib

ALK rearrangement positive:

• Available agents are: Brigatinib, Alectinib, Lorlatinib, Ceritinib. Useful occasionally: crizotinib

NICE:

• First Line: Brigatinb

• Second Line: Lorlatinib (Brigatinib post crizotinib)

• Third Line: Lorlatinib post Brigatinib post crizotinib

ROS1 rearrangement positive:

• Preferred First Line: crizotinib or entrectinib. Other recommended cetirinib

• Second Line: Lorlatinib or entrectinib

BRAF V600E mutation positive:

• Preferred First Line: Dabrafenib and trametinib

NTRK Fusion positive:

• Larotrectinib or Entrectinib

MET ex14 Skipping mutation

• Preferred First Line: Tepotinib or Capmatinib

• Can be useful: crizotinib

RET rearrangement positive:

• Preferred: selpercatinib or Pralsetinib

• Useful in certain circumstances: Cabozantinib or Vandetanib

B. Patients negative for actionable mutations.

Pre-amble on chemo:

- Chemotherapy for non-squamous histology should be a Platinum/Pemetrexed combination (or non-pemetrexed platinum regimen that is followed by maintenance pemetrexed). Patients with non-squamous histology who had at least stable disease after 4 cycles of platinum-based chemotherapy should be offered maintenance treatment with Pemetrexed every 3 weeks until disease progression.
- Chemotherapy for squamous cell carcinoma is carboplatin doublet with Gemcitabine, Taxane or Vinorelbine.
- Patients with PS 2 or worse (without actionable mutation) should have treatment tailored to their comorbidities and functional status. Single agent systemic therapy, best supportive / palliative care and palliative radiotherapy to be utilised appropriately.

B1] PDL-1 expression positive >50% and negative for actionable mutations and no contraindications to Immunotherapy. PS 0-1

Adenocarcinoma, Large cell carcinoma or NSCLC NOS:

First line Options include:

- Pembrolizumab single agent 2 years
- Platinum + pemetrexed + pembrolizumab. Maintenance Pemetrexed and pembrolizumab
- Atezolizumab single agent (also allowed if >10% tumour infiltration by immune cells and not subject to stopping rules at 2 years)
- (Chemotherapy alone if IO is contraindicated).

Second and subsequent Line therapy:

Patients with non-squamous histology who do not respond to, progress or relapse after 1st line chemotherapy and whose PS is 0-2 should be considered for 2nd line systemic therapy. Options include:

- Pemetrexed platinum regimen (if not previously received pemetrexed)
- Docetaxel 75mg/m2 every 3/52 for 4 cycles +/- Nintedanib or
- Pembrolizumab for maximum 2 years (if they have not previously received immunotherapy).
- Atezolizumab if no previous immunotherapy (also allowed if >10% tumour infiltration by immune cells and not subject to stopping rules at 2 years)

Squamous cell carcinoma, PDL1 >50%, PS 0-1

First Line options include:

- Pembrolizumab
- Carboplatin + Paclitaxel + Pembrolizumab with maintenance pembrolizimab to 2 years

- Atezolizumab (also allowed if >10% tumour infiltration by immune cells and not subject to stopping rules at 2 years)
- Non-pemetrexed platinum doublet (if immunotherapy is contraindicated)

Second and subsequent Line therapy:

- Platinum doublet chemotherapy (if chemo naïve) with gemcitabine, vinorelbine or taxane
- Docetaxel 75mg/m2 every 3/52
- Pembrolizumab for maximum 2 years (if they have not previously received immunotherapy).
- Atezolizumab if no previous immunotherapy (also allowed if >10% tumour infiltration by immune cells and not subject to stopping rules at 2 years)

B2] PDL-1 expression <50% and negative for actionable mutations and no contraindications to Immunotherapy. PS 0-1

Adenocarcinoma, Large cell carcinoma or NSCLC NOS:

First line Options include:

- Platinum + pemetrexed + pembrolizumab. Maintenance Pemetrexed and pembrolizumab.
- Carboplatin + Paclitaxel + Bevacizumab + Atezolizumab. Maintenance Bevacizumab and atezolizumab to maximum 2 years. (This regiment to be considered particularly for fit mutation positive patients who have exhausted targeted therapy, or fit patients with liver metastases). PDL-1 eligibility: 0-49%
- Chemotherapy without immunotherapy. Platinum/Pemetrexed combination (or non-pemetrexed platinum regimen that is followed by maintenance pemetrexed). Patients with non-squamous histology who had at least stable disease after 4 cycles of platinum-based chemotherapy should be offered maintenance treatment with Pemetrexed every 3 weeks until disease progression.

Second and subsequent Line therapy:

Options include:

- pemetrexed regimen (if not previously received pemetrexed),
- Docetaxel 75mg/m2 every 3/52 for 4 cycles +/- Nintedanib
- Chemotherapy with gemcitabine, vinorelbine or taxane either as single agent (or in combination with carboplatin depending on platinum free interval).
- Pembrolizumab for maximum 2 years (if they have not previously received immunotherapy).
 PDL1 >1%.
- Atezolizumab if no previous immunotherapy for maximum 2 years. PDL1 can be 0%.

Nivolumab for maximum 2 years (if they have not previously received immunotherapy). PDL1
 >1%.

Squamous cell carcinoma, PDL1 <50%, PS 0-1

First Line options include:

- Carboplatin + Paclitaxel + Pembrolizumab with maintenance pembrolizimab to 2 years
- Platinum doublet if immunotherapy is contraindicated. Chemotherapy for squamous cell carcinoma with Gemcitabine, Taxane or Vinorelbine and Carboplatin.

Second and subsequent Line therapy:

- Docetaxel 75mg/m2 every 3/52
- Chemotherapy with gemcitabine, vinorelbine or taxane either as single agent (or in combination with carboplatin depending on platinum free interval).
- Pembrolizumab for maximum 2 years (if they have not previously received immunotherapy).
 PDL1 ≥1%.
- Atezolizumab for maximum 2 years if no previous immunotherapy. PDL1 can be 0%.
- Nivolumab for maximum 2 years if no previous immunotherapy. PDL1 can be 0%.

Stage	IA	IB	IIA	IIB	IIIA	IIIB	IV
Clinical	76-92%	67%	60%	33-50%	17-34%	9-22%	1-20%
Pathological	81-92%	74%	65%	51-61%	34-40%	24-30%	1-20%

Overall survival at 5 years.

RADIOTHERAPY FOR NSCLC

Indication	Dose fractionation
Medically inoperable T1–3 (≤5 cm) N0: SABR	54Gy in 3 fractions over 5–8 days
	• 55Gy in 5 fractions over 10–14 days
	60Gy in 8 fractions over 10–20 days
Medically inoperable stage I and II	54Gy in 36 fractions treating thrice
	daily over 12 consecutive days
	continuous, hyperfractionated,
	accelerated radiotherapy (CHART)
	55Gy in 20 fractions
Concurrent Stage III	• 55Gy in 20 fractions over 4 weeks
	60-66Gy in 30-33 fractions over 6-6.5 weeks
Sequential stage III	 55Gy in 20 fractions over 4 weeks
	• 60Gy-66Gy in 30-33 fractions over 6-6.5
	weeks
	54Gy in 36 fractions treating thrice
	daily over 12 consecutive days (CHART)
Radiotherapy alone	54Gy in 36 fractions treating thrice
	daily over 12 consecutive days (CHART)
	66Gy in 33 fractions over 6.5 weeks
	55Gy in 20 fractions over 4 weeks
Pancoast tumours (T3–4 N0–1)	45Gy in 25 fractions over 5 weeks with
	chemotherapy such as cisplatin and
D. H. C. DT. C. C. C. D. LDC	etoposide followed by surgery
Palliative RT in patients with good PS	39Gy in 13 fractions over 2.5 weeks
	with cord dose limited to 36Gy
	36Gy in 6 fractions 48 hours apart over 2 weeks
	36Gy in 12 fractions over 2.5 weeks 30Gy in 10 fractions over 3 weeks
	30Gy in 10 fractions over 2 weeks 30Gy in 5 fractions over 1 week
Palliative PT in patients with page PC	20Gy in 5 fractions over 1 week
Palliative RT in patients with poor PS	10Gy in 1 fraction 20Gy in 5 fractions
	20Gy in 5 fractions 16 17Gy in 3 fractions even 8 days
	16-17Gy in 2 fractions over 8 days

Follow up:

Individualised depending on clinical setting to 5 years.



Stage Grouping for the 8th Edition of the TNM Classification for Lung Cancer

CTACE	-		
STAGE	T	N	M
Occult carcinoma	TX	No	Mo
0	Tis	No	Mo
IA1	T1mi	No	Mo
	Tia	No	Mo
IA2	T1b	No	Mo
IA3	Tic	No	Mo
IB	T2a	No	Mo
IIA	T2b	No	Mo
IIB	Tia	N1	Mo
	T1b	N1	Mo
]	T1c	N1	Mo
	T2a	N1	Mo
1	T2b	N1	Mo
1	T3	No	Mo
IIIA	Tia	N2	Mo
1	T1b	N2	Mo
1	Tic	N2	Mo
1	T2a	N2	Mo
1	T2b	N2	Mo
1	T3	N1	Mo
1	T4	No	Mo
1	T4	N1	Mo
IIIB	Tia	N3	Mo
1 1	T1b	N3	Mo
1	Tic	N3	Mo
1	T2a	N3	Mo
1	T2b	N3	Mo
1	T3	N2	Mo
1	T4	N2	Mo
IIIC	T3	N3	Mo
	T4	N3	Mo
IVA	Any T	Any N	M1a
	Any T	Any N	M1b
IVB	Any T	Any N	M1c

References

- Rami-Porta R, Bolejack V, Gloux DJ et al. The IASLC Lung Cancer Staging Project: the new database to inform the 8th edition of the TMM classification of lung cancer. J Thorac Oncol 2014; 9: 1618-1624.
- Rami-Porta R, Bolejack V, Crowley J et al. The IASUC Lung Cancer Staging Project: proposals for the revisions of the T descriptors in the forthcoming 8th edition of the THM classification for lung cancer. J Thorac Oncol 2015; 10: 990-1003.
- Asamura H, Chansky K, Crowley J et al. The IASLC Lung Cancer Staging Project: proposals for the revisions of the N descriptors in the forthcoming 8th edition of the TNM classification for lung cancer J Thorax Oncol 2015; 10: 1675-1684.
- Eberhardt WEE, Mitchell A, Crowley J et al. The IASIC Lung Cancer Staging Project: proposals for the revisions of the Midescriptors in the forthcoming 8th edition of the THM classification for lung cancer. J Thorac Oncol 2015; 10: 1515-1522.
- Goldstraw P, Chansky K, Crowley J et al. The IASIC Lung Cancer Staging Project: proposals for the revision of the stage grouping in the forthcoming (Rth) edition of the TMM classification of lung cancer. J Theres Concol 2015; 11:39-51.
- Hicholson AG, Chansky K, Crowley J et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the dinical and pathologic staging of small cell lung cancer in the forthcoming eighth edition of the TNM classification for lung cancer. J Thoroconcol 2016; 11: 200, 201
- Travis WD, Asamura H, Bankter A et al. The IASIC Lung Cancer Staging Project: proposals for coding T categories for subsolid nodules and assessment of tumors lae in part-solid tumors in the forthcoming eighth edition of the TMM classification of lung cancer. J Thoroc Oncol 2016; 11: 1204-1223.

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UICC TNM 8, which should be used for all tumours diagnosed after 1 January 2018.

Primary tumour (T)

- TX Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualised by imaging or bronchoscopy
- To No evidence of primary tumour
- Tis Carcinoma in situ; Tis (AIS) for adenocarcinoma in situ, Tis (SCIS) for squamous cell carcinoma in situ
- T1 Tumour 30 mm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus^a
 - T1mi Minimally invasive adenocarcinomab
 - T1a Tumour 10 mm or less in greatest dimension^a
 - T1b Tumour more than 10 mm but not more than 20 mm in greatest dimension^a
 - T1c Tumour more than 20 mm but not more than 30 mm in greatest dimension^a
- Tumours more than 30 mm but not more than 50 mm in greatest dimension; or tumours with any of the following features:
 - involves the main bronchus
 - invades the visceral pleura
 - associated with atelectasis or obstructive pneumonitis that extends to the hilar region, either involving part of the lung or the whole lung.

T2 tumours with these features are classified as T2a if 40 mm or less, or cannot be determined, or T2b if more than 40 mm but not more than 50 mm^c

- T2a Tumour more than 30 mm but not more than 40 mm in greatest dimension
- T2b Tumour more than 40 mm but not more than 50 mm in greatest dimension
- Tumour more than 50 mm but not more than 70 mm in greatest dimension, or one that directly invades one of the following: parietal pleura (PL3), chest wall (including superior sulcus tumours), phrenic nerve, parietal pericardium; or associated separate tumour nodule(s) (intra-pulmonary metastases) in the same lobe as the primary
- Tumour more than 70 mm or one of any size that directly invades one of the following: diaphragm, mediastinum, heart, great vessels, recurrent laryngeal nerve, carina, trachea, oesophagus, vertebra; or separate tumour nodule(s) (intra-pulmonary metastases) in a different ipsilateral lobe to that of the primary

Regional lymph nodes (N)

- NX Regional lymph nodes cannot be assessed
- No regional node involvement
- N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar nodes and/or intrapulmonary nodes (node stations 10–14), including involvement by direct extension
- N2 Metastasis in ipsilateral mediastinal and/or subcarinal node(s) (node stations 1–9)
- N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene or supraclavicular nodes

Distant metastasis (M)

M1 Distant metastasis

M1a Separate tumour nodule(s) in a contralateral lobe; tumour with pleural nodules or malignant

pleural or pericardial effusion^d

M1b Single extrathoracic metastasis in a single organ and involvement of a single distant (non-

regional) lymph node^e

M1c Multiple extrathoracic metastases in one or several organs

*Small cell carcinomas: Staging via TNM 8 is now recommended, especially for those with limited

disease

*Carcinoid tumours: Staging via TNM 8 is now recommended for all cases

^aThe uncommon superficial spreading tumour of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.

^bSolitary adenocarcinoma (not more than 3 cm in greatest dimension), with a predominantly lepidic pattern and not more than 5 mm invasion in greatest dimension in any one focus.

°T2 tumours with these features are classified as T2a if 4 cm or less, or if size cannot be determined, and T2b if greater than 4 cm but not larger than 5 cm.

^dMost pleural (pericardial) effusions with lung cancer are due to tumour. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumour, and the fluid is non-bloody and is not an exudate. Where these elements on clinical judgement dictate that the effusion is not related to tumour, the effusion should be excluded as a staging descriptor.

eThis includes involvement of a single non-regional node.



Stage Grouping for the 8th Edition of the TNM Classification for Lung Cancer

STAGE	T	N	M
Occult carcinoma	TX	No	Mo
0	Tis	No	Mo
IA1	T1mi	No	Mo
	Tia	No	Mo
IA2	T1b	No	Mo
IA3	T1c	No	Mo
IB	T2a	No	Mo
IIA	T2b	No	Mo
IIB	Tia	N1	Mo
	T1b	N1	Mo
	T1c	N1	Mo
	T2a	N1	Mo
]	T2b	N1	Mo
	T3	No	Mo
IIIA	Tia	N2	Mo
	T1b	N2	Mo
	Tic	N2	Mo
1	T2a	N2	Mo
-	T2b	N2	Mo
1	T3	N1	Mo
	T4	No	Mo
-	T4	N1	Mo
IIIB	Tia	N3	Mo
	Tib	N3	Mo
	Tic	N3	Mo
1	T2a	Nз	Mo
1	T2b	N3	Mo
	T3	N2	Mo
	T4	N2	Mo
IIIC	T3	N3	Mo
	T4	N3	Mo
IVA	Any T	Any N	M1a
	Any T	Any N	M1b
IVB	Any T	Any N	M1c

References

- Rami-Porta R, Bolejack V, Gloux: DJ et al. The IASIC Lung Cancer Staging Project: the new database to inform the 8th edition of the TMM classification of lung cancer. J Thorax Oncol 2014; 9: 1618-1624.
- Rami-Porta R, Bolejack V, Crowley J et al. The USUC Lung Cancer Staging Project: proposals for the revisions of the T descriptors in the forthcoming 8th edition of the THM classification for lung cancer. J Thorac Oncol 2015; 10: 990–1003.
- Asamura H, Chansky K, Crowley J et al. The IASLC Lung Cancer Staging Project: proposals for the revisions of the H descriptors in the forthcoming 8th edition of the TMM classification for lung cancer. J Thorac Oncol 2015; 10: 1675-1684.
- Eberhardt WEE, Mitchell A, Crowley J et al. The IASIC Lung Cancer Staging Project: proposals for the revisions of the Midescriptors in the forthcoming 8th edition of the THM classification for lung cancer. J Thorac Oncol 2015; 10: 1515-1522.
- Goldstraw P, Chansley K, Crowley J et al. The IASIC Lung Cancer Staging Project: proposals for the revision of the stage grouping in the forthcoming (Rth) edition of the TAM classification of lung cancer. J Thereo: Oncol 2015; 11:39-51.
- Nicholson AG, Chansky K, Crowley J et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the dividal and pathologic staging of small cell lung cancer in the forthcoming eighth edition of the TNM classification for lung cancer. J Thorac Oncol 2016; 11: 300-311.
- Travis WD, Asamura H, Bankier A et al. The IASIC Lung Cancer Staging Project: proposals for coding T categories for subsolid nodules and assessment of tumors be in part-solid tumors in the forthcoming eighth edition of the TMM classification of lung cancer. J Thoroc Oncol 2016; 11: 1204-1223.

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Performance Status

KP		WHO
100	Normal, no complaints, no evidence of disease	0
90	Able to carry on normal activity; minor signs or symptoms of disease	
80	Normal activity with effort, some signs and symptoms of disease	1
70	Cares for self but unable to carry on normal activity or do work	
60	Requires occasional assistance but is able to care for most personal needs	2
50	Requires considerable assistance and frequent medical care	
40	Disabled; requires special care and assistance	3
30	Severely disabled; hospitalisation indicated; death no imminent	
20	Very ill; hospitalisation and active supportive care necessary	4
10	Moribund	
0	Dead	

Small Cell Lung Cancer Staging

Small Cell Lung Cancer Staging should be done <u>according to the TNM staging</u> The description of limited/extensive stage disease not in use anymore

<u>Limited stage</u> – disease confined to one hemithorax (can include ipsilateral SCF and contralateral hilar nodes but excludes pleural effusion)

Extensive stage – disease beyond one hemithorax

Prognostic factors

- o LD vs ED
- o KP >60 vs ≤ 60
- Serum Na (low vs normal)
- Serum LDH (normal vs high)
- Serum alk phos (normal vs high)
- Each adverse features scores +1

Scores of 0 and 1 have better prognosis

Calculation of predicted post-operative FEV1 (ppoFEV1)

If any obstructed segments:

ppoFEV1 = pre FEV1 x
$$(19 - a) - b)$$

19 - a

a = no of obstructed segmentsb = no of obstructed segments to be resected

Right upper lobe	= 3	Left upper lobe	= 3
Middle lobe	= 2	Lingula	= 2
Right lower lobe	= 5	Left lower lobe	= 4

Appendix 6

Dataset for Lung Cancer Histopathology reports (3rd edition)

Histopathology reporting proforma for lung cancer resection specimens

Surname	Forenames	Date	of birth	Sex
Hospital	Hospital no	NHS/	CHI no	
Date of receipt	Date of reporting	Repo	rt no	
Pathologist	Surgeon/physician	Lab n	0	
Previous treatment (neoadj	juvant chemotherapy	/radiotherapy)	Yes 🗆	No 🗆
Specimen type				
Right lung		VATS		
Left lung		VATS converted to o	pen 🗆	
		Open \square		
Single wedge resection		Pneumonectomy (ex	tra-pericardial)	
Multiple wedge resections		Pneumonectomy (int	tra-pericardial)	
Segmentectomy				
Lobectomy/bi-lobectomy		Other \square (specify)		
Other surgical procedures				
Sleeve resection		Other (e.g., chest wa	all)	
Macroscopic features				
Main bronchus within 20 mm	of carina (T3) (if know	n) 🗆		
Main bronchus more than 20	mm from carina (T2)			
Location of tumour:				
Hilar/endobronchial/central				
Right upper lobe	Right middle lo	obe 🗆	Right lower lol	be 🗆
Left upper lobe	Left lower lobe		Not assessabl	le 🗆
Tumour sizemm (ma (T1a =<20 mm; T1b 21–≥30	•	· T2b 51–≤70 mm· T3	Not assessabl	le 🗆
Distance of tumour (or staple margin:mm			,	resection
Extent of atelectasis/obstruct	ive pneumonia:	None/less than the to	wo categories be	elow 🗆

lı	nvolving hilar region	but not whole lung (T2	2) 🗆
	nvolving whole lung	(T3)	
Microscopic features			
Histological type			
Squamous cell carcinoma Large cell undif	ferentiated	Small cell carcinoma	1 🗆
Adenocarcinoma			
Adenocarcinoma-in-situ			
Minimally invasive adenocarcinoma (invasive con	nponent less than 5	mm) 🗆	
Predominant pattern (lepidic, acinar, p	apillary, micropapilla	ry, solid)	
Mucinous			
Non-mucinous □			
Mixed mucinous/non-mucinous (>10% of each)			
Combined tumours $\ \ \Box$ (specify		.)	
Other tumour $\ \square$ (specify, e.g., carcinoid, etc.		.)	
Local invasion			
Visceral pleura (T2)			
Parietal pleura/chest wall (T3)			
Mediastinal pleura (T3)			
Pericardium (T3)			
Diaphragm (T3)			
Great vessel (aorta, central pulmonary artery or vein)	(T4) \Box		
Atrium, heart (T4)			
Malignant pleural effusion (M1a)			
Satellite nodules			
Satellite tumour nodules in same lobe (T3)			
Satellite tumour nodules in different ipsilateral lobe (T	-4)		
Satellite tumour nodules in contralateral lobe (M1a)			
Pleural invasion			
PL0 (no pleural involvement)			
PL1 (breaching of the outer layer of the visceral pleur	a but no extension t	o the pleural surface)	
PL2 (breaching of the outer layer of the visceral pleur		,	
PL3 (involvement of the parietal pleura)		•	

Lymph node spread Ipsilateral hilar/intrapulmonary (node stations 10–14) Submitted □ Involved (N1) □						
Ipsilateral medias	tinal (node static	Submitted □	Involved (N2)			
Contralateral med	liastinal, hilar no	des		Submitted	Involved (N3)	
Ipsilateral or contr	alateral scalene	or supraclavio	cular nodes	Submitted	Involved (N3) □	
Margins						
Bronchial	Clear	Involved		I/A □		
Mediastinal	Clear	Involved		I/A □		
Vascular	Clear	Involved		I/A □		
Chest Wall	Clear	Involved		I/A □		
Other pathology	•					
Emphysema	No 🗆	Yes 🗆	•	degree(mild/mode	•	
Interstitial fibrosis	No 🗆	Yes 🗆		ause (if known)		
Other	Details:					
Metastases						
Unknown (MX)	Absent (M	0) □ Pre	sent (M1a)	□ (M1b) □		
Details:	,		(_ (2)		
Ancillary data						
Epidermal growth			No [ssed 🗆	
Other genetic data	a (specify)					
Summary of path	nological stagir	ng				
(Select highest sta	age from above	data; for synch	nronous prin	naries, use protoco	l above;	
use prefix 'y' for re	esection during of	or following tre	atment and	'r' for recurrence a	fter treatment)	
pTpN	pM					
Complete resection at all margins Yes □ No □						
SNOMED code:						
Commonto						
Comments						



NHS Foundation Trust

Thoracic Surgery Referral Form

NHS No: Consultant: Hosp, No Key Worker (Local Nurse Specialist) DOB: Name: 62 day Cancer Treatment Target Date: Address: MDT Date Accepted/Referred Surgeon in MDT Mr. Bittar/ Mr. Duncan/Mr. Purohit/ Mr. Zacharias/NONE Patient Tel No: **Presenting Symptoms:** SOB Hemoptysis Cough Bone Pain Wt. Loss Other..... **Performance Status** (Tick as appropriate): 0 \square 1 🔲 3 🗌 2 🗌 Exercise Tolerance.....Limited by..... CT Scan: □ STAGING T Site of Nodule/Tumour (Circle as appropriate) Right – RUL Left- LUL Other Important Findings..... RML IIIIRLL PET CT Scan: □ STAGING T Date: CT Scan **Head** (Large central Tumours,T4 tumours,N2 diseases, Possible pneumonectomy): Histological Diagnosis: If Histology available report must be attached State method used for tissue sample: Date: **Previous Medical History** Y N Previous Malignancy1 IHD **CVA** Y 🗆 N 🗆 Asbestos exposure Y N N PVD $Y \square N \square$ % .RATIO Lung Function Test:FEV1-FEV1/FVC TLCO All patients for lung resection must have Full Lung Function Tests included with referral. **Smoking history** Current smoker: Ex-smoker: Never smoked: Year Stopped: Number per day: Pack year: Antiplatelet/Anticoagulation Medication: Other Medication Has the patient been informed of this referral? YES □ ΝО □ Other relevant information:(e.g., Specific MDT discussion, i.e., assessment only/wedge only/biopsy/Lymph nodes etc)

Authors: Mr M Purohit, Consultant Cardiothoracic Surgeon / Bernie McAlea, Thoracic Specialist Nurse V2.31/01/2017



High Risk Lung Cancer Surgical MDT Referral for 2nd opinion at BVH

Please email to Cardiac.Referral@bfwhospitals.nhs.uk

NHS NO	Consultant
H No DOB	Lung Ca Nurse specialist
Name	Surgeon Present in MDT AD/MP/MNB/JZ
Address	Date of MDT
Pt Tel no	
	CT/PET/MRI/Bone Scan
Site Right U,M,L Left U,L	Date of Breach
Final Staging T N M	Important Bronchoscopy finding
Any Important Invasion-	
Histology	Cardiac History
Tilstology	Cardiac Flistory
Obtained by	
•	
Lung Function	Other Comorbidities
FEV1 L (%) DLCO	1
	2
FEV1/FVC KCO	3
	4
Performance Status 0 1 2 3 4	Smoking History:- Current Ex Never
The Question for the High Risk MDT	Cirioking History. Current Ex 146461
(Reason for referral)	
1.	
2.	
Alta mantina Tanatana art	
Alternative Treatment 1.	
1.	
2.	

Authors: Mr M Purohit, Consultant Cardiothoracic Surgeon / Bernie McAlea, Thoracic Specialist Nurse V1.23/02/2016

Optimisation



National Optimal Lung Cancer Pathway Medical and Fitness Optimisation Checklist

Please action this checklist as soon as a decision has been made that the patient may be suitable for surgery.

Condition	Action	Checked
Anaemia	IV Iron	
Active cardiac condition	Refer to Cardiologist	
Stroke/TIA/CVA	Waiting time of 4-6 weeks before surgery	
Atrial Fibrillation	Needs to be controlled	
Hypertension	Needs to be controlled	
Active Haematological or coagulation issues	To be reviewed by Haematologist	
Diabetes	Needs to be reviewed and controlled	
Smoking Cessation	Needs to be actioned	
Excess Alcohol Consumption	Needs to be reviewed and controlled	
Incidental finding on scans	Requires clarification	
Medications		
Cytotoxic/Chemotherapy	Wait 4-6 weeks before surgery	
Antiplatelet	Do not stop without date and surgical input	
Anticoagulation	Inform team but no further action	

This checklist is for internal use only. It is not an exhaustive list and should be based upon clinical judgement.

Appendix 10

Staging Cards

Please click on the below PDF document to access:



Staging cards.pdf

https://thorax.bmj.com/content/thoraxjnl/56/2/89.full.pdf



"Routine post-Surgery Follow-up"

Authors: J Thekkudan, M Purohit

Consensus Follow-up plan for Lancashire and South Cumbria region:

Time since surgery	Investigation
1 st year	
~ 4 weeks	CXR
3 months	CXR
6 months	CT scan ¹
9 months	CXR
12 months	CT scan ¹
2 nd year	
18 months	CT scan ¹
24 months	CT scan ¹
3 rd year	CT scan ¹
4 th year	CT scan ¹
5 th year	CT scan ¹

CT scan¹ = contrast CT chest/upper abdomen (including adrenals)

Discharge if no signs of recurrence at 5 years

Patient advice to contact if signs/symptoms of recurrence

V1.0 January 2022



Appendix 12

