Diagnosis and management of patients with stage III non-small cell lung cancer: A joint statement by the Lebanese Society of Medical Oncology and the Lebanese Pulmonary Society (Review)

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Abstract. Proper management of stage III non-small cell lung cancer (NSCLC) might result in a cure or patient long-term survival. Management should therefore be preceded by adequate and accurate diagnosis and staging, which will inform therapeutic decisions. A panel of oncologists, surgeons and pulmonologists in Lebanon convened to establish a set of recommendations to guide and unify clinical practice, in alignment with international standards of care. Whilst chest computerized tomography (CT) scanning remains a cornerstone in the discovery of a lung lesion, a positron-emission tomography (PET)/CT scan and a tumor biopsy allows for staging of the cancer and defining the resectability of the tumor(s). A multidisciplinary discussion meeting is currently widely advised for evaluating patients on a case-by-case basis, and should include at least the treating oncologist, a thoracic surgeon, a radiation oncologist and a pulmonologist, in addition to physicians from other specialties as needed. The standard of care for unresectable stage III NSCLC is concurrent chemotherapy and radiation therapy, followed by consolidation therapy with durvalumab, which should be initiated within 42 days of the last radiation dose; for resectable tumors, neoadjuvant therapy followed by surgical resection is recommended. This joint statement is based on the expertise of the physician panel, available literature and evidence governing the treatment, management and follow-up of patients with stage III NSCLC.

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1. Context

Available therapeutic modalities have the potential to cure patients with locally advanced non-small cell lung cancer (NSCLC). However, given the aggressive nature of current treatments, proper staging remains the cornerstone for designing the optimal management strategy. More accurate, easy to perform staging procedures and the diversity of treatment modalities have made medical decisions more challenging. The advancement of clinical and pathological descriptions of the disease, coupled with the multitude of targeted, precision and personalized medication strategies, have raised the patients' (and the treating oncologists') hopes for prolonged survival time. The medical professionals involved in the management of these patients are under increased pressure to provide accurate diagnosis to inform clinical management and best possible patient care. This obligation is further accentuated in the case of locally advanced (non-metastatic) disease, in which medical decisions are quite literally a matter of life and death. Members of the Lebanese Society of Medical Oncology and the Lebanese Pulmonary Society have convened to discuss and lay down a set of recommendations that govern NSCLC screening, staging, clinical management and follow-up, in an attempt to share their collective experience and unify medical care for patients with locally advanced NSCLC.

2. Screening and diagnosis

NSCLC is a heterogeneous disease that might remain asymptomatic while invading the lung and adjacent tissues, eventually progressing and spreading to distant sites, thus compromising response to treatment and prognosis. Whilst chances for a complete remission or a cure are highest in early-stage cancers, survival rates decrease when the cancer is locally advanced, or even further when it has metastasized (1). Therefore, the earlier a lung lesion is discovered, the better the medical outcome. In addition, survival rate among patients with NSCLC is also enhanced by individual factors, such as young age, stage IIIA versus stage IIIB or IIIC, and concurrent chemoradiation, as well as other conventional prognostic factors, such as metabolic activity of the tumor and biomarkers of cell cycle regulation and apoptosis (2,3). Glucose avidity (high uptake) on the positron-emission tomography (PET) scan is indicative of metabolic activity and is associated with a 2.18-fold lower chance for patient survival from the disease (3). Biomarkers of interest in stage III NSCLC with unfavorable prognostic value include KRAS, p53, EGFR, VEGF, c-erbB-2 (or HER-2), Bcl-2, Ki-67, microvessel density and aneuploidy (3).

Lung cancer screening can be performed on specific population strata at higher risk for developing malignant pulmonary lesions, including those with a family history of lung cancer, workers in chemical plants and older adults with previous exposure to carcinogens or with respiratory disease history, in addition to active personal or second-hand smokers (1,4,5).

Lung cancer risk prediction tools can be used to identify individuals at high-risk for lung cancer and select them for screening (6). In particular, recently updated lung cancer guidelines recommend using risk models to refer ever-smokers for screening (7). The different risk prediction models are all based on the risk stratification approach, and were shown to yield comparable results (8). In addition to age and smoking status (pack years and quit time), the Prostate, Lung, Colorectal and Ovarian 2012 risk model ($PLCO_{m2012}$) addresses other risk factors, such as the presence of chronic pulmonary diseases, family history of cancer (in general and lung cancer in particular) and socioeconomic status (1,6). Other tools can also be used depending on the physician's preference and on the regulations laid down by governmental agencies, such as the Ministry of Public Health. These models include the Bach model (9), the Lung Cancer Death Risk Assessment Tool (10,11), and the Liverpool Lung Project (12), which together with the $PLCO_{m2012}$ have proven accurate in predicting lung cancer risk in ever-smokers (8,13). NSCLC, specifically lung adenocarcinoma, can affect never-smokers; however, tobacco smoking remains the major contributor to lung cancer (14), given the malignant genomic landscape that characterizes smokers (15,16). These mutations shape the tumor microenvironment and are more abundant in metastases than in primary tumors (14). Advanced lung cancer is associated with poor prognosis.

Based on the available evidence, the European Society of Radiology and the European Respiratory Society recommend systematic lung cancer screening where possible and when supported by the local healthcare system and infrastructure (17).

3. Diagnosing and staging lung cancer

According to international recommendations, a low-dose chest computerized tomography (CT) scan is the preferred tool for lung tumor detection (1,18). For lung nodules, a CT scan or PET/CT scan of the chest and abdomen using the glucose analogue ^{18}fluorodeoxyglucose (^{18}F-FDG) with intravenous contrast will confirm the diagnosis of a lung tumor, inform on the number of masses, the size of the primary tumor, the degree of invasion of the mediastinum and chest wall, as well as on the presence of abdominal lesions (19). The patient should then undergo pathological analyses to determine the exact type of lung cancer, followed by clinical staging.

Staging procedures include non- or minimally invasive methods, as well as invasive non-surgical and surgical methods. Minimally or non-invasive staging methods include CT or PET/CT scan with the glucose analogue ^{18}F-FDG, and magnetic resonance imaging (MRI), which is mostly for brain evaluation. The PET/CT scan is superior to the simple chest CT scan owing to its high sensitivity for the detection of pathological lymph nodes (especially those >1 cm in their shortest dimension) and distant metastases. For pathological and molecular profiling purposes, a tumor biopsy can be obtained using minimally invasive techniques, such as bronchoscopy-guided, endoscopic ultrasound (EUS)-guided or endobronchial ultrasound (EBUS)-guided fine-needle aspiration (FNA) or core-needle biopsy (CNB), transthoracic CT-guided FNA or CNB and transbronchial FNA or CNB (20-22). Although minimally or non-invasive staging methods are preferred, they might present some pitfalls, which warrant careful interpretation of imaging results for accurate staging. For instance,

while conventional MRI and CT scanning might have similar accuracies in detecting chest wall invasion, bone destruction is best assessed by CT scan, whereas lymphangitic carcinomatosis and pleural invasion are best assessed by MRI (23), particularly by respiratory functional MRI (24). In fact, the CT scan technology might not allow evaluating the exact depth of pleural invasion, but functional MRI is laborious and expensive with relatively poor spatial resolution (24).

In the absence of pathological lymph nodes showing on the PET/CT scan, but in cases in which the disease presents as a central tumor or a peripheral tumor with a diameter >3 cm, occult N2 lymph nodes might be present, thus warranting exploration of the mediastinum and lymph node dissection (25). Mediastinal lymph node involvement is important for prognosis of stage III disease; therefore, preoperative mediastinal staging is necessary (25,26). In NSCLC, not all N2 cases are the same (26). In particular, mono-station versus multi-station lymph node involvement, bulky versus non-bulky disease, and adherence to central airways, all entail very different implications in terms of treatment (resectable versus unresectable) and prognosis (26). Needle techniques allow the confirmation of mediastinal involvement in accessible lymph node stations, including paratracheal, posterior tracheal, sub-carinal, hilar, interlobar and lobar lymph nodes (26). EBUS-guided puncture can be supplemented by EUS to assess paratracheal, sub-carinal, paraesophageal and pulmonary ligament lymph nodes (26). When sampled lymph nodes are sent to the pathology laboratory, it is important to indicate the number of sampled lymph nodes and their site of origin, as fragmenting them will make quantification obsolete (27).

If the patient's status motivates pleural exploration, a thoracentesis with or without needle pleural biopsy (commonly referred to as pleural tap) is usually the first procedure performed to diagnose exudative pleural effusion and determine its etiology (malignant or not) by differential and cytopathological analysis (28). More advanced techniques (such as pleuroscopy) or newer techniques (such as narrow band imaging, infrared or auto-fluorescence thoracoscopy, and video-assisted thoracic surgery) are also available (29). These techniques are used when more extensive sampling of tissue or advanced procedures are needed, such as stapled lung biopsy, resection of pulmonary nodules, lobectomy, pericardial window and lower nodal stations examination (30). However, exploratory thoracoscopy should not exceed 1% of procedures (31).

Tumor staging encompasses three descriptors: Tumor size (T), involved lymph nodes (N) and presence of metastatic lesions (M), known as the TNM classification. Stage III NSCLC is a locally advanced lung cancer, with no evidence of distant metastatic lesions (M0). Tumor size is one of the most important tumor parameters (32,33), it is reported based on the CT scan in the projection that gives the greatest dimension. Fig. 1A presents the classification of NSCLC tumors, according to their size. When establishing nodal involvement, a PET/CT scan has the highest sensitivity in detecting enlarged lymph nodes and determining their dimensions (32), compared with either imaging technique alone (34). N1 disease refers to the involvement of one ipsilateral hilar nodal station; N2 disease refers to the involvement of one or multiple ipsilateral mediastinal nodal stations, with or without N1 (35); and N3 indicates contralateral lymph node malignancy (Fig. 1B). Lymph nodes have been mapped into zones and stations according to the TNM classification seventh edition (36,37), which has been maintained in the TNM classification eighth edition (38). Fig. 1C associates the T and N components of TNM classification to determine if the cancer is stage IIIA, IIIB or IIIC, according to the currently applicable TNM classification.

4. Cardiopulmonary assessment

The patient should be clinically evaluated by a cardiologist and a pulmonologist to determine their surgical risk (39). Cardiologic assessment starts with a checkup of the cardiac function and a revision of any chronically prescribed medications. The Cardiac Risk Index is an algorithm developed in 1999 and revised in 2013, which can help calculate a cardiac risk score in patients considered for thoracic surgery (39,40). The Revised Cardiac Risk Index tailored for patients undergoing thoracic surgery is free and is available online and may help identify patients at risk of cardiac complications following lung tumor resection. Patients who score <1.5 points are considered low-risk and additional assessments may not be necessary 40).

Pulmonary function assessment helps predict tolerance to general anesthesia and post-operative pulmonary function (41,42). The maximum expiratory volume in the first second of forced expiration (FEV1) and the diffusion capacity of the lung for carbon monoxide (DLCO) can be calculated (43). Post-operative FEV1 and DLCO levels can be estimated by quantitative perfusion scintigraphy. If both values are >60% of their planned post-operative level, then the patient can safely proceed to surgery (43). However, if either FEV1 or DLCO is <30% of the planned post-operative value, then cardiopulmonary exercise testing (CPET) should be performed (39,43). Fig. 2 visually illustrates the proposed pre-operative lung assessment flow.

5. Tools to evaluate clinical profiles and performance of patients

The Karnofsky Performance Status (KPS) measures the ability of patients with cancer to perform ordinary tasks, and scores range from 0 (unable) to 100 (very able) (44). The Eastern Cooperative Oncology Group (ECOG) score helps quantify a patients' performance status (45), and ranges from 0 (full functionality) to 5 (death). Either the KPS or the ECOG score can be used for assessing performance and to inform treatment decisions (46). Response Evaluation Criteria In Solid Tumors is a set of published guidelines to help evaluate the patient's response to treatment, using imaging techniques (47-49). The Patient-Reported Outcomes Measurement Information System® is another tool that allows the evaluation of clinical profile and performance from the patient's standpoint (50). This set of person-centered questions relies on technology, psychometrics, and qualitative and cognitive health-related outcomes to describe the medical, mental and social health of individuals.

6. Treatment and management of stage III NSCLC

Trimodal therapy. A trimodal therapy combining radiotherapy and chemotherapy followed by surgery is currently

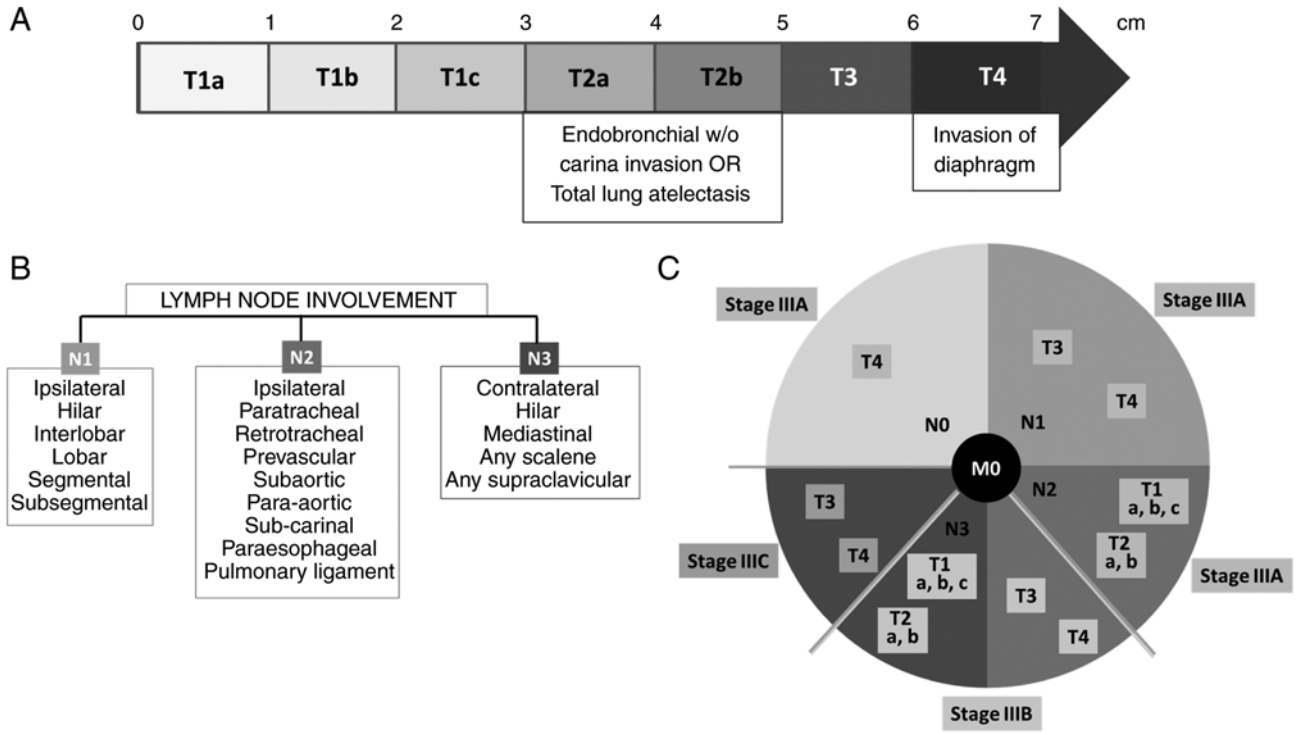

Figure 1. TNM classification of NSCLC. The TNM eighth edition (32) for lung cancer defines four major levels (T1 to T4) depending on (A) tumor size and (B) three nodal stations. (C) Stage III NSCLC can be classified as Stage IIIA, IIIB or IIIC. NSCLC, non-small cell lung cancer; TNM, tumor-node-metastasis; w/o, without.

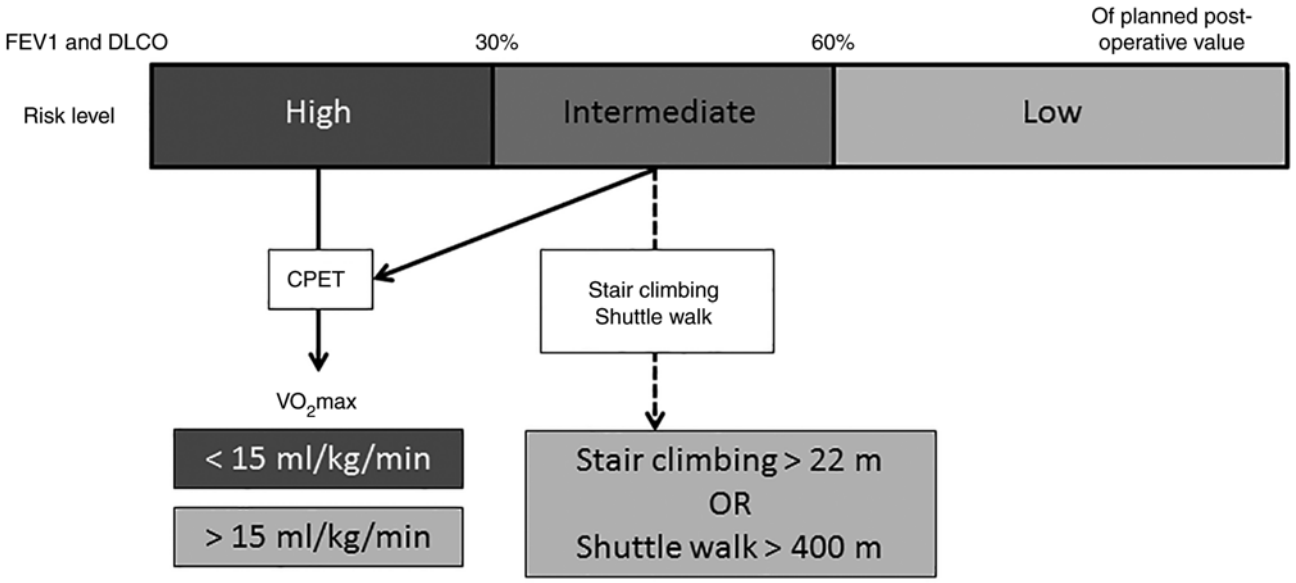

Figure 2. Functional assessment of the lungs. For patients with high- or intermediate-risk level, CPET must be performed. Stair climbing and shuttle walk tests can also be performed in intermediate-risk patients (33,35). CPET, cardiopulmonary exercise testing; DLCO, diffusion capacity of the lung for carbon monoxide; FEV1, maximum expiratory volume in the first second of forced expiration; VO_2max, maximum oxygen consumption.

a widely accepted approach for the management of stage III NSCLC (51), even in the case of surgically challenging tumors such as superior sulcus or Pancoast's tumors (52). It is strongly recommended to hold a multidisciplinary board meeting to evaluate tumor resectability according to size, location, lymph node involvement and prognosis, as well as the patient's general status and cardiopulmonary function (37). A multidisciplinary team approach to lung cancer management has been widely recognized to improve patient outcomes (53,54), and has been endorsed by the International Association for the Study of Lung Cancer, the American Thoracic Society and the European Respiratory Society (55).

Adjuvant chemotherapy was shown to offer substantial improvement in the management of resectable stage IIIA NSCLC (56). If the tumor presents an EGFR mutation, targeted adjuvant therapy with EGFR tyrosine kinase inhibitors (TKIs)

might improve disease-free survival (57). The Food and Drug Administration has recently approved the EGFR-TKI osimertinib for adjuvant therapy in patients with exon 19 deletions or exon 21 L858R mutations (58). In patients with unresectable stage IIIA or with stage IIIB or IIIC NSCLC, the current standard treatment is definitive or palliative concurrent chemoradiotherapy (59,60), especially for larger tumors (>7 cm) (61,62). In patients for whom concomitant chemoradiotherapy is not recommended (e.g., unacceptable weight loss, large irradiation surface), sequential chemotherapy followed by radiation therapy can be used (63). Treatment should be followed by CT scan within 3 weeks (preferably 2 weeks) of the last radiation dose.

If none of these options (surgery or chemoradiotherapy) is medically acceptable, other therapeutic modalities might be available. For instance, in 2019, after being exclusively indicated for metastatic stage IV NSCLC, the use of pembrolizumab was extended to cover first-line treatment for patients with stage III NSCLC ineligible for surgical resection or definitive chemoradiation (64). Immunotherapy with the programmed death-ligand 1 inhibitor, durvalumab, is used as maintenance treatment for 12 months when the disease is stable following chemoradiotherapy, as it was reported to prolong progression-free and overall survival (65,66). Indeed, a previous review presented evidence on promising potential of durvalumab as consolidation therapy for patients with unresectable stage III NSCLC who have completed two cycles of platinum-based chemotherapy with concurrent radiotherapy (67).

Surgical resection. A locally advanced lung tumor is resectable if surgery is sufficient to achieve complete tumor removal and if the patient can tolerate the surgery (e.g., absence of severe cardiac problems, adequate pulmonary reserve). Usually, patients with single-station N2 disease or multi-station N1 disease are considered candidates for surgery, which offers a potential cure, whereas multi-station N2 disease confers a worse prognosis and surgical resection should be discouraged (68). A pneumonectomy is indicated when the tumor crosses the major fissure, extending to more than one lobe or to the hilum (69). Tumors that have invaded vital mediastinal structures are unresectable, with the following exceptions: i) Invasion of the carina and 3-4 cm of the trachea; ii) minimal left atrial invasion; iii) extension into the intrapericardial portions of the pulmonary arteries; iv) invasion of the aortic adventitia or the superior vena cava; and v) those limited to the vertebral body and amenable to *en bloc* resection (69). Invasion of the chest wall, in addition to mediastinal involvement, indicates poor prognosis and surgical resection of the primary lung nodule(s) becomes obsolete. The integrated PET/CT scan is the best available imaging technique to evaluate mediastinum or chest wall involvement, despite a 20-25% possibility of false-positive or false-negative results (37).

Intraoperative staging is also important to determine the benefits of surgical resection and to describe previously undetected lesions (70). A thoracotomy will help determine whether the tumor is peripheral or central, which lymph node stations are affected and whether the tumor has crossed the fissure (37). If a lobectomy is likely to provide complete removal of the lung lesion(s), it should be performed in addition to hilar and mediastinal lymph node dissection (51,71).

Table I. Radiation doses for patients with stage III non-small cell lung cancer.

Radiation therapy	Total radiation dose, Gy	Dose per daily fraction[a], Gy/fraction
Radical	60-66	2
Sequential (accelerated)	60-66	3
Pre-operative (induction)	45-54	1.8-2.0
Post-operative	50-54	1.8-2.0

[a]Radiation therapy is usually given 5 days (or 5 fractions) per week, for 6 weeks. Gy, gray.

Radiation therapy. Radiation therapy is rarely prescribed as monotherapy, given its limited benefit in terms of prognosis (51). However, patients with stage III NSCLC who are unsuitable for chemoradiotherapy are offered radiation therapy alone (72). Pre-operative radiotherapy in addition to induction chemotherapy might not improve the overall outcome of the surgery and should be decided on a case-by-case basis (73). Patients who are likely to undergo radiation therapy should be assessed for the risk of lung toxicity secondary to radiation (e.g., radiation-induced lung injury or radiation pneumonitis). The mean lung dose and the volume of healthy lungs receiving ≥20 Gy radiation doses are good indicators of the risk of radiation-induced lung injury, mainly grade 2 radiation pneumonitis (43,74,75).

Radiation doses. A meta-analysis and systematic review published in 2019 described radiation therapy protocols given to patients concomitantly with or following chemotherapy (62). Table I proposes radiation dosage for patients with stage III NSCLC. Palliative radiation therapy is given at a dose of 10 Gy in a single fraction or 16 Gy in two fractions at 1-week intervals.

Radiation volumes. The radiation oncology team should define the following radiation volumes for each patient: i) Gross tumor volume for primary tumors and affected lymph nodes; ii) clinical target volume (CTV) for three-dimensional margins of the disease (post-operative CTV should include the bronchial stump, the subcarinal, ipsilateral and contralateral hilar, and paratracheal nodal stations); and iii) planning target volume, which is a CTV that takes into account tumor movement and patient positioning. Image-guided radiation therapy, or more advanced technologies, should be used whenever available (76,77).

Chemotherapy. Chemotherapy can be used as neoadjuvant or adjuvant therapy, or as the main treatment for patients ineligible for surgery; it is generally given with radiotherapy. The most commonly used chemotherapeutic agents in NSCLC are: i) Platinum-based cisplatin and carboplatin, which induce DNA damage and inhibit its replication, leading to cell death; ii) paclitaxel and docetaxel, which stabilize microtubules, blocking mitosis; iii) vinorelbine, which prevents the formation of mitotic spindle; and iv) gemcitabine, etoposide and pemetrexed, which interfere with DNA synthesis. These agents are most commonly used in combination. The gold

Table II. Summary of recommendations for the diagnosis and management of stage III non-small cell lung cancer.

Clinical activity	Recommendations
Diagnosis and staging	Screen individuals at risk of lung cancer with a low-dose CT scan and if lung cancer is suspected, perform a chest and abdomen CT scan with contrast. Start with non-invasive techniques: PET/CT scan and/or MRI.If needed, recur to more invasive EBUS and EUS-guided, transthoracic or transbronchial FNA or CNB to obtain a biopsy. If lung cancer is confirmed, assess mediastinal involvement and lymphadenopathy. Use the currently applicable TNM classification to precisely define the lung cancer stage that will inform treatment. For patients who might be treated for curative purposes, perform a brain MRI to rule out brain lesions.
Management of stage III NSCLC	Eligible patients should undergo trimodal therapy: Chemotherapy, radiation therapy and surgical excision of the tumor. Unresectable tumors [stages IIIA (N2), IIIB and IIIC] should be treated by concurrent or sequential chemoradiation. Patients with non-progressive stage IIIA (N2), IIIB or IIIC cancer should be given durvalumab for 12 months (consolidation therapy). Durvalumab is best initiated within 42 days of the last radiation dose. Targeted therapies might be prescribed, according to cytopathology results and the patient's general status and prognosis. While anti-neoplastic treatment should be defined and prescribed by a clinical oncologist with experience in lung cancer, decisions about tumor resectability should involve the surgeon and functional assessment of the lungs should be performed by a pulmonologist. The decision on the management of stage III NSCLC should be performed at the level of the multidisciplinary team. Immune-related adverse events should be managed by a multidisciplinary team; in particular, patients who develop radiation-related pneumonitis should be quickly referred to an expert pulmonologist. When a patient is considered cured or in remission, clinical evaluation and follow-up CT scans should be performed every 6 months during the first 2 years after the cancer is cleared, and then once a year for up to 5 years, with a PET/CT scan at the 1-year milestone.

CNB, core needle biopsy; EBUS, endobronchial ultrasound; EUS, endoscopic ultrasound; FNA, fine needle aspiration; NSCLC, non-small cell lung cancer; PET, positron-emission tomography.

standard for chemotherapy in unresectable stage III NSCLC is doublet chemotherapy: Cisplatin with vinorelbine/etoposide, or carboplatin with paclitaxel (78,79). Patients with potentially resectable tumors might benefit from pre-operative induction therapy, which aims at destroying metastatic and nodal lesions undetected by imaging and at reducing the extent of the surgery (43). Surgical resection aims to achieve complete tumor removal, which includes microscopically confirmed clear resection margins, mediastinal lymph node removal, absence of extracapsular invasion of lymph nodes and absence of tumor cells in the most distal lymph node resected (72,80).

Rescue or salvage surgery refers to surgical resection following chemotherapy and/or radiotherapy, and it can be performed in patients who have responded exceptionally well to therapy and for whom surgery might pose a potential cure (72). This mainly occurs when the tumor was judged unresectable at diagnosis (81). A previous meta-analysis presented evidence that neoadjuvant chemotherapy or chemoradiotherapy would improve prognosis compared with definitive treatment alone (82). Fig. 3 presents a treatment algorithm for stage III NSCLC, which can serve as a visual guide for physicians and patients. Adverse events should be closely monitored by a multidisciplinary team and, in particular, radiation-related pneumonitis should be followed-up by an expert pulmonologist.

7. Post-treatment management

Restaging. Video-assisted mediastinoscopy allows for a highly specific, sensitive and accurate staging and restaging of NSCLC (83). A PET/CT scan can be useful to determine a positive response to treatment (leading to disease down-staging) or disease recurrence (leading to disease up-staging) (84). Taking into account patient safety and risk minimization without

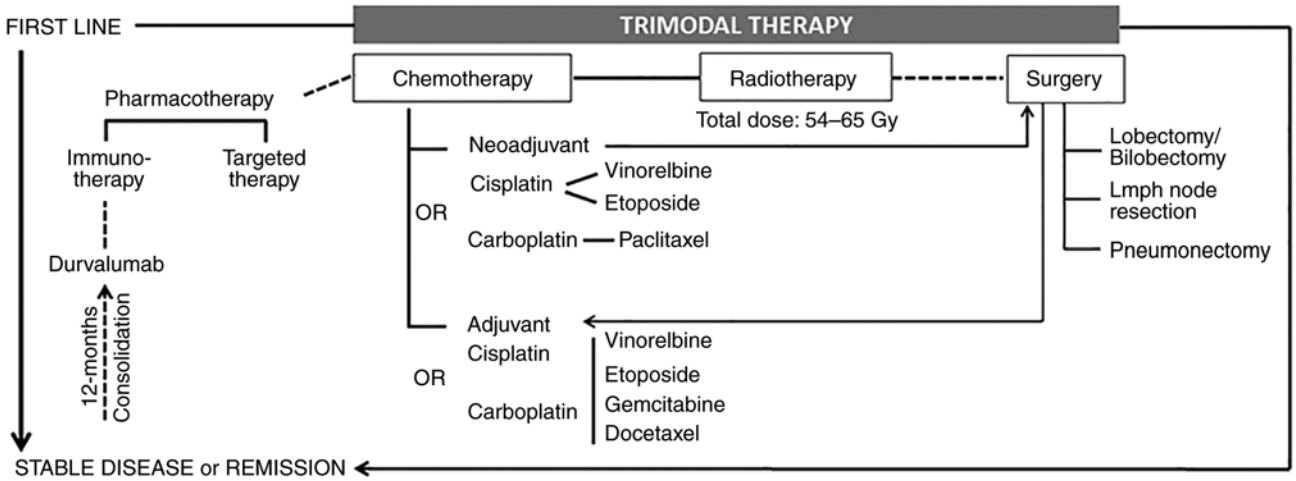

Figure 3. Stage III NSCLC treatment algorithm. Trimodal therapy is recommended for patients whose clinical status can sustain concurrent chemoradiation and surgery. Immunotherapy and targeted therapy can be prescribed for eligible patients according to cytopathology. Durvalumab is a PD-L1 inhibitor given as consolidation immunotherapy. Terms in bold font indicate the medically preferred option. Dashed lines indicate interventions prescribed in case the patient is eligible. Gy, gray; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1.

compromising clinical accuracy, optimal restaging would combine a PET/CT scan with cytopathological analysis of biopsies obtained by EBUS or EUS-guided needle aspiration.

Functional assessment. Pulmonary function should be assessed after surgical resection to determine FEV1 and DLCO. Some patients may require post-operative pulmonary rehabilitation, which should be decided on a case-by-case basis; cardiac assessment might also be required for some patients. For patients prescribed adjuvant chemotherapy, liver and kidney function should also be evaluated before starting treatment, with kidney function (i.e. serum creatinine levels) checked before each chemotherapeutic cycle.

Follow-up of patients with stage III NSCLC. Patients whose pharmacological treatment and/or surgical resection are considered to have achieved complete remission and are 'cancer-free' should undergo a CT scan every 6 months in the first 2 years after treatment, and then yearly afterwards for 5 years, with a PET/CT prescribed at the 1-year milestone (85).

Signs of relapse or disease progression. Some patients with stage III NSCLC who are in remission might show early signs of relapse, such as a slightly enlarged lymph node (>1 cm), fatigue or bone pain. According to the organ preference of metastasis, lung tumors tend to metastasize to bone, brain and adrenal tissues (75). Recent-onset fatigue should prompt an evaluation of the patient's cardiopulmonary function to check for malignant pleural or pericardial effusion. Onset of bone pain should prompt evaluation of skeletal lesions and the initiation of treatment to prevent further damage or bone embrittlement and fracture. Patients who relapse or show signs of disease progression might benefit from immunotherapy or a course of chemotherapy with or without radiation.

Table II provides a summary of recommendations by the Lebanese panel of experts, for the diagnosis and management of stage III non-small cell lung cancer.

8. Conclusion

Diagnosis and management of stage III NSCLC have evolved in the past decade, presenting patients and physicians with several tools for staging and several therapeutic options. While this joint statement aims at providing guidance and closing some gaps in the management of locally advanced lung cancer in Lebanon, we underscore the importance of designing the therapeutic approach on a patient-by-patient basis, considering the clinical, demographic and socioeconomic profiles. A multidisciplinary team meeting is recommended in the management of lung cancer to decide on the best possible treatment. It should therefore be an obligation to stay updated on novel therapies and treatment modalities, which are continuously being refined and fine-tuned, to keep up with the highest level of evidence-based medicine.

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Authors' contribution

ZAB and NB were involved in manuscript outline, writing and editing. WAS, HA, JB, PB, HC, GD, FEK, FF, HG, MG, GJ, FN, RN, MR, GT, AT, MW and PY critically contributed to the

drafting of sections falling within their expertise, reviewed and corrected the manuscript. Data authentication is not applicable. All authors approved the current version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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