Patterns of Care for Stage III Non-Small cell lung cancer in Australia

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Abstract

Stage III non-small cell lung cancer (NSCLC) makes up a third of all NSCLC cases and is potentially curable. Despite this five-year survival rates remain between 15% and 20% with chemoradiation treatment alone given with curative intent. With the recent exciting breakthroughs in immunotherapy use (durvalumab) for stage III NSCLC, further improvements in patient survival can be expected.

Most patients with stage III NSCLC present initially to their General Practitioner (GP). The recommended time from GP referral to first specialist appointment is less than 14 days with treatment initiated within 42 days. Our review found that there is a shortfall in meeting these recommendations, however a number of initiatives have been established in Australia to improve timely and accurate diagnosis and treatment patterns. The lung cancer Multidisciplinary Team (MDT) is critical to consistency of evidence-based diagnosis and treatment and can improve patient survival. We aimed to review current patterns of care and clinical practice recommendations for stage III NSCLC across Australia and identify opportunities to improve practice in referral, diagnosis and treatment pathways.

Key words: **Stage III non-small cell lung cancer; patterns of care; Australia; optimal care pathways; treatment; multidisciplinary teams**

Introduction

Lung cancer is the fifth most commonly diagnosed cancer, but it is the leading cause of cancer death in Australia.[1] Most stage III NSCLC is unresectable and the survival rates are disappointing with estimates of five-year survival with chemotherapy and radiotherapy ranging from 15% to 20%.[2-5] There is no five-year survival data with the use of immunotherapy available yet, but the two-year survival data from the PACIFIC study demonstrates an additional benefit of approximately 10%.[6] Importantly, with appropriate treatment, there is the potential for cure for patients with stage III NSCLC. Timely access to consistent, safe, high quality and evidence-based care through a multidisciplinary team (MDT) results in increased survival for patients with lung cancer.[7-12] Mortality is higher in patients with poor socioeconomic status, Indigenous and Torres Strait Islander Australians, and those living in remote areas since the vast majority of these patients present late with advanced disease at the time of diagnosis.[1]

The Cancer Australia Lung Cancer Framework sets out the principles for best practice care of lung cancer in Australia.[9] These include: patient-centered care; timely access to evidence-based pathways of care; multidisciplinary care; coordination, communication and continuity of care; and data-driven improvements in lung cancer care.

The aim of this publication is to examine current patterns of care for stage III NSCLC across Australia and to identify opportunities to improve practice in referral, diagnosis and treatment pathways.

Primary Care

The role and importance of primary care in managing lung cancer is important for all stages of disease, including potentially curable stage III disease. In Australia, most referrals for NSCLC are from General Practitioners (GPs) and approximately 35% of patients are seen as acute admissions presenting to the emergency department.[13] There is currently no national lung cancer screening program in Australia due to the high rate of false positive results (particularly in the National Lung Screening Trial[14]); variability in follow-up protocols for positive tests, uncertainty regarding the target population and screening interval, uncertainty regarding cost-effectiveness and the issue of screening versus smoking cessation measures.[15 16]

A study of regional variations in referral patterns in the United Kingdom (UK) suggested that access to primary care and speed of referral to secondary care could be important in the early diagnosis of lung cancer.[17] Furthermore, increased patient awareness of early signs and symptoms could lead to earlier presentation and therefore earlier stage disease at diagnosis.[18] Patients should also be provided with support to stop smoking.[19] GPs need to be aware of the referral pathways available to them and refer patients without delay (Figure 1).

The Royal Australian College of General Practitioners (RACGP) provides recommendations for referral and patient support for investigation of lung cancer symptoms.[20] Patients presenting with persistent hemoptysis or signs of superior vena cava obstruction, those with symptoms suggestive of lung cancer following a chest X-ray or a chest computed tomography (CT) scan, those who have persistent changes on consecutive CT scans and those with clinical suspicion of

lung cancer, should be referred urgently to a specialist linked to a lung cancer MDT. Patients with large volume hemoptysis or stridor should be referred immediately to the emergency department.

The GP should also provide the patient with clear expectations for their potential diagnosis and ongoing care. Importantly, the GP plays a critical role in providing continued support for patients awaiting their specialist appointment. It is imperative that the GP and the specialist share information; advise the patient of any other healthcare professionals who will be involved in patient care; and that the GP remains closely involved in the management and follow up of the patient.[20]

Cancer Australia provide a free online lung cancer course for healthcare professionals (GPs and nurses) via the Qstream online learning platform.[21] This training may be of interest to healthcare professionals who want to know more about lung cancer signs and symptoms and the key strategies for promoting early diagnosis and referral of patients who have or may have lung cancer.

Diagnosis and Staging

Accurate staging of lung cancer is critical for optimizing treatment options and management in stage III NSCLC, for identifying candidates with potential for cure and for precision-planning of multi-modality therapy. In 2017, the TNM classification for lung cancer changed with the release of the eighth edition of the AJCC cancer staging manual.[22] This update more clearly defines the position, size and nodal involvement in stage III NSCLC to improve accuracy of staging.

The respiratory physician has the radiological, procedural and clinical expertise to make the initial decisions to decide on the modality for diagnosing the extent of disease.[23] Many patients are current or former smokers with compromised respiratory function, therefore the respiratory physician is also key to establishing the patient's fitness for treatment and identifying complications of potential treatments.[23]

In most patients a CT scan has been conducted prior to or alongside referral. The next step for diagnosis is usually tissue confirmation of lung cancer (Figure 1). Investigation with positron-emission tomography (PET)-CT can support a malignant diagnosis and establish the disease extent. A number of guidelines suggest that for patients suitable for curative therapy who have possible mediastinal involvement (PET)-CT should be considered as an early test, where findings may help to guide biopsy using endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA).[24] However, a summary of evidence and recommendations for the Australian lung cancer guidelines for the use of PET-CT showed that overall, guidance for the exact timing of PET-CT is unclear.[25] Thus, clinical judgement as part of MDT review is required to determine the sequence as well as choice of diagnostic and staging investigations.

There are a number of options for tissue confirmation of lung cancer, these range from EBUS-TBNA, transthoracic CT-scan guided biopsy, percutaneous fine needle aspiration (FNA) biopsy, percutaneous core biopsy and surgical biopsy, e.g. video-assisted thoracoscopic (VATS) pleural biopsy. While many cases are initially diagnosed by percutaneous needle biopsy, there is

increasing evidence of the utility of EBUS-TBNA as a first line investigation in lung cancer.[26-28] International guidelines recommend EBUS-TBNA (without endo-esophageal ultrasound guided biopsy) for evaluation of mediastinal and hilar lymph node involvement.[29]

The National Comprehensive Cancer Network (NCCN) recommends brain magnetic resonance imaging (MRI) for all patients with stage III NSCLC prior to treatment and the European Society of Medical Oncology (ESMO) guidelines suggest that screening for brain metastases by MRI might be useful in patients considered for curative intent.[24, 30] MRI of the brain is not routine for staging in Australia as it is not reimbursed. In most Australian centers, brain CT scans are conducted prior to treatment either routinely or in selected patients with at-risk features, such as large volume disease or unexplained symptoms. MRIs are conducted in patients where further clarification of potential brain lesions is needed to guide management decisions. Of interest, recent retrospective data shows a low detection rate of occult brain metastases using PET-CT (1.6%; n=4) in patients with stage III NSCLC (n=249)[31]

Time to Referral, Diagnosis and Treatment

The RACGP recommends that as well as rapid referral, relevant and sufficiently detailed information should be provided by the GP to the specialist.[20] As per the Optimal Care Pathways (OCPs) which define the critical steps in the patient journey, patients should be informed of any test results within one week of their initial GP consultation (Figure 1). The optimal timeframe from referral to first specialist appointment in the OCP is 14 days.[7] Although some of these benchmarks are able to be reached others are lagging behind.

As an example, a retrospective study of 1,417 patients from the Victorian Lung Cancer Registry (VLCR)[32] which collects data from six public and two private hospitals in Victoria, found that the median time from referral to diagnosis was 15 days (interquartile range (IQR), 5 to 36) between July 2011 and October 2014.[33] However, the median time from referral to initial definitive management in the VLCR study was 53 days (IQR, 25 to 106), far in excess of the OCP recommendation of less than 42 days from GP presentation to initiation of treatment.

Another survey collected data from 108 newly diagnosed patients with lung cancer in New South Wales, and found that the median time from GP presentation to first lung cancer specialist appointment was 4 days, with 83% of patients seeing the specialist within 14 days.[34] However, time to treatment within 42 days was only achieved for 52% of the surveyed patients. Notably, there did not appear to be any difference between waiting times for patients living in rural or metropolitan areas.

The Multidisciplinary Team

The role of the MDT is to establish a clear diagnosis, stage the disease, identify clinical trials or other treatment options and to establish communication between the various disciplines and the patient (Figure 1). Multidisciplinary care is the best practice approach to providing evidence-based cancer care[20, 35, 36] and is of particular relevance for the complex evaluation and decision-making processes often required for management of stage III disease. Review of patients by an MDT can improve patient survival, quality of life and improve delivery of best practice care in accordance with evidence-based guidelines, particularly in patients with stage III or IV disease.[10-12, 37, 38] In a retrospective, longitudinal study in Taiwan, 14% of 27,947

patients with stage III or IV NSCLC received care through an MDT. MDT care was found to be associated with higher survival in these patients (HR 0.87; 95% CI 0.84 to 0.90).[12]

A report published in 2011, found that approximately 50% of patients with lung cancer are reviewed by an MDT in Australia.[39] However, a single institution cohort study of 1,197 patients with NSCLC in Australia found that only 25% of patients were reviewed by an MDT.[38] This study also found that documentation of staging was higher in the MDT group compared to the non-MDT group (97% vs. 84%). Survival analyses at 1, 2 and 5 years showed greater survival in the patients reviewed by an MDT except for patients with stage IIIB NSCLC at one year. Most lung cancer MDTs in Australia include a respiratory physician, surgeon, medical oncologist, radiation oncologist, radiologist and pathologist at a minimum. When available it can be advantageous for the MDT to also include a cancer care coordinator, lung cancer nurse, nuclear medicine physician, and a palliative care physician.[7, 23]

The involvement of a lung cancer nurse can improve access and timeliness of lung cancer care and assist in patient care.[40, 41] Cancer care coordinators and lung cancer nurse coordinators are a valuable resource in some Australian centers and are involved in triaging and coordinating patient care and diagnostic procedures. The coordinator also plays a pivotal role by liaising between the patient and MDT and are able to coordinate obtaining results and treatment visits (Figure 1).[23, 36] The coordinator ensures there is continuity of care throughout the patient journey.[7]

Following diagnosis and staging of lung cancer by the respiratory physician, the results of all relevant tests and imaging are reviewed at the MDT. The care coordinator or treating clinician also presents information about the patient's concerns, preferences and social circumstances.[7] The MDT develop and document an agreed treatment plan that is circulated to relevant team members, including the GP.[7] If the patient is reviewed by the MDT prior to diagnosis and staging, the MDT can also discuss the preferred investigation modalities and identify the necessary biomarkers needed to guide treatment.

In addition to ensuring that MDT members have sufficient expertise and represent the relevant disciplines for patient care, quality of decision-making in MDTs is dependent on high quality diagnostic radiology and pathology; detailed, accurate data collection; documentation of recommendations and the decision-making process; and effective communication with the patient and community healthcare providers. Guidelines for MDTs are critical to meet these requirements and should exist for all MDTs. Such guidelines should include frequency of meetings, membership requirements, communication plan, data collection and documentation plan, and the process for care coordination. While MDT review improves coordination of care and facilitates the provision of information and support for patients, MDTs are often overburdened driving the need to prioritize patients for review.[8, 42]

Complementary to the MDT, rapid access clinics for lung cancer have been established in some Australian centers. The aims of the rapid access service are to triage and provide expedited appointments within the clinic. Rapid access clinics are designed to fit around the MDT meetings to ensure timely review and management of the patient. Best practice for rapid access clinics and MDTs involves collecting outcome data for patients seen in the clinic and the use of key performance indicators (KPIs) to measure efficiency of the process.

In addition, Integrated Cancer Services (ICS) in Victoria consist of clusters of hospitals and associated health services that deliver cancer services within a geographic area.[43] ICS aim to build relationships, implement best practice models of care, improve the effectiveness of cancer care and monitor systems and processes to improve performance. ICS include public hospitals, community-based services, GPs and other primary health organizations, private hospitals and supportive care services.

Treatment Options for Stage III NSCLC

Treatment options for stage III NSCLC include surgery, radiotherapy and chemotherapy, often in a multi-modality treatment paradigm.

Complete resection of the primary tumor and mediastinal lymph node dissection is recommended for patients with stage IIIA NSCLC.[44] The use of radiotherapy post-surgical resection (PORT) in this group of patients is not recommended routinely but may be considered in patients with pN2 disease. Neo-adjuvant or adjuvant platinum-based chemotherapy may be considered for patients with good performance status.

Guidelines for the treatment of stage III NSCLC used in Australia include ESMO Clinical Practice Guidelines,[24] NCCN,[30] American Society of Clinical Oncology (ASCO),[45] and Cancer Council Clinical Practice Guidelines[44]. NCCN is frequently updated and is the most up to date in accordance to the latest evidence and reflect on the current Australian Therapeutic Goods Administration (TGA) indications for immunotherapy treatment. NCCN is the only guideline to address treatment following chemoradiation therapy and while not evidence-based, they serve as a useful guide. NCCN also provide specific details about the chemotherapy options including drugs and doses. The remaining guidelines while robust are not updated frequently and none of them include immunotherapy options for stage III NSCLC. The Australian guidelines are non-specific providing only general principles of treatment for stage III NSCLC.

Unresectable Stage III NSCLC

For patients with good performance status and unresectable stage III NSCLC,

the concurrent administration of chemotherapy and radiotherapy is

recommended.[44] Induction chemotherapy or sequential treatment may be used for patients when up front radiotherapy may not be possible, if there are tolerability concerns or where there are long wait times for radiotherapy services. Yet, data have shown that longer wait times for radiotherapy increase the risk of local recurrence with consequent poorer outcomes.[46]

In Australia, the recommended chemotherapy regimen for stage III NSCLC is cisplatin and etoposide for patients with good performance status.[24, 30] The combination of carboplatin and paclitaxel is an appropriate option for patients who would not be expected to tolerate cisplatin therapy.[30]

The optimal radiation dose and fractionation schedule for patients with good performance status and inoperable stage III NSCLC undergoing curative intent therapy is 60-66 Gy in 30-33 fractions, given in once daily fractions to the primary and involved nodes.[47] The principles of radiotherapy are that at least 95% of the radiotherapy target volume receives 95% of the

prescribed dose (57-63 Gy) whilst meeting organs-at-risk constraints. The major limiting organs at risk in Stage III NSCLC are the lung and esophagus, and with large volumes of disease it can be extremely difficult to ensure safe coverage of the radiotherapy target volume.

Patients with stage III inoperable NSCLC who are not suitable for curative treatment with concurrent chemoradiotherapy either due to patient factors (comorbidities, poor lung function or performance status) or tumor factors (a large field of disease) may receive radiotherapy alone, chemotherapy alone or best supportive care.[44]

Skin toxicity, risk of pneumonitis and esophagitis can lead to reduction in dose intensity in patients receiving radiotherapy. New radiotherapy techniques e.g. volumetric modulated arc therapy (VMAT), intensity-modulated radiation therapy (IMRT), and stereotactic body radiation therapy (SBRT) increase the ability to treat patients radically, sparing more lung tissue.[48-50] However, this means that more patients are being treated with large volumes of nodal disease, increasing the risk of esophagitis. The use of modulated approaches also increases the low dose wash to the lung, which may increase the risk of pneumonitis.[51, 52] Hence, patient selection, choice of chemotherapy regimen, and recognition at the beginning of treatment of the risks of pneumonitis and esophagitis is important. The risk of esophagitis may be managed by providing proton pump inhibitor therapy, aggressively managing nutrition, providing enteral feeding support if needed, and by reducing the dose to the esophagus where possible.[53, 54]

Immunotherapy

Immune checkpoint inhibitors (PD-1 and PD-L1 inhibitors) are providing a new treatment option for NSCLC.[58] The basic principle of chemoradiation and immunotherapy in the treatment of NSCLC is that chemotherapy sensitizes cancer to radiation-induced DNA damage while radiation triggers antigen release from tumor damage. More specifically, chemotherapy upregulates expression of tumor antigens and may downregulate co-inhibitory molecules (including PD-L1) on the tumor cell surface to potentiate effector T cell activity. Chemotherapy may also render tumor cells more sensitive to T cell-mediated lysis.[56] Tumor cell damage from radiation exposes tumor-specific antigens to immune detection leading to priming and activation of cytotoxic T cells. Radiation may also facilitate the recruitment and infiltration of immune cells.[57] Chemoradiation therefore enhances the anti-tumor immunity benefits of PD-1/PD-L1 inhibition.[4]

While a number of immune checkpoint inhibitors (PD-1 and PD-L1 inhibitors) are available in Australia for the treatment of stage IV NSCLC, the only currently available immunotherapy option for stage III NSCLC is durvalumab. Importantly, durvalumab is indicated for the treatment of patients with locally advanced, unresectable NSCLC whose disease has not progressed following platinum-based chemoradiation therapy.[58] This indication is based on the results of phase III PACIFIC study, which included 713 patients with unresectable stage III NSCLC who did not progress after two or more cycles of platinum-based concurrent chemoradiation.[59] The study compared the anti-PD-L1 antibody, durvalumab to placebo for up to 12 months after concurrent chemoradiation.[59] Median progression-free survival (PFS) from the time of randomization improved from 5.6 months (95% CI 4.6 to 7.7) with placebo to 17.2 months (95% CI 13.1 to 23.9) with durvalumab with a hazard ratio of 0.51 (95% CI 0.41 to 0.63; p<0.001).[6] The time to distant metastasis was also prolonged in patients receiving durvalumab with a reduction in the incidence of new lesions including brain. After a median follow-up period of 25.2 months (range 0.2 to 43.1), the 24-month overall survival rate was 66.3% (95% CI 61.7 to 70.4) for patients receiving durvalumab compared to 55.6% (95% CI 48.9 to 61.8) with placebo, with a hazard ratio of 0.68 (95% CI 0.47 to 0.997; p=0.0025).[6] The benefit of durvalumab was irrespective of age, time from radiation (<14 days vs >14 days), type of chemotherapy, prior induction chemotherapy and the pre-specified PD-L1 status (<25% vs >25%).[58]

Although the rate of all grades of pneumonitis (including radiation pneumonitis) was reported to be higher in the patients who received durvalumab (33.9%) compared to those who received placebo (24.8%), the rate of grade 3 or 4 pneumonitis was similar in the two arms (3.4% vs. 2.6%).[59] Toxicities were manageable and patient reported outcome data also showed that quality of life was not compromised by adding 12 months of durvalumab after standard concurrent chemoradiation.[60]

Follow-up post curative treatment

There are no current Australian guidelines for follow-up of patients following curative treatment. In our experience, patients are commonly reviewed for assessment response and restaging approximately 8 to 12 weeks following chemoradiotherapy. However, with the emerging use of immunotherapy following radiotherapy earlier imaging may be required to plan consolidation therapy.

Discussion

Current management of unresectable stage III NSCLC is chemoradiotherapy with platinum-based chemotherapy. Treatment with chemoradiotherapy is associated with a statistically significant survival benefit compared with radiation alone.[9, 61] With the emergence of positive phase III data for immunotherapy from the PACIFIC study,[6, 59] the treatment patterns for unresectable stage III NSCLC in Australia are likely to change in the near future.

At the time of preparing this review there were an estimated 12,741 new cases of lung cancer diagnosed and an estimated 9,198 deaths due to lung cancer in Australia.[62] Approximately one in five new diagnoses were for stage III NSCLC, with five-year survival of approximately 15% to 20%.[2-5, 63, 64] Early detection through screening programs are yet to show an overall benefit and further development to address clinical and logistical challenges associated with screening is needed.[15, 65]

The optimal care pathway for patients with lung cancer in Australia recommends no more than six weeks between referral and initiation of treatment.[7] While existing data show a trend towards reducing wait times to meet the OCP recommendations, there is clearly a need for further improvements, particularly in the time to treatment. It may be helpful to consider the reasons for delays if strategies to improve service delivery are to succeed. In the VLCR study, significant reasons for delays included patients' declining or not being referred to palliative care and being treated in a public hospital.[32] Malalasekera *et al.* conducted a literature review including 128 studies of health system delays in lung cancer in Australia, the UK, Europe, the USA and Canada.[66] The most commonly reported reasons for delays were access to diagnostic procedures and obtaining results (78%), lack of rapid MDT assessment (34%), low index of suspicion by the GP (27%), waiting for multiple specialist consultations (28%), lack of clinical symptoms (21%), and presentation with early-stage disease (14%).

An Australian survey of 135 healthcare professionals involved in lung cancer care included 39 medical oncologists, 20 respiratory physicians, 7 radiation oncologists, 2 palliative care physicians, 2 cardiothoracic surgeons, 29 Lung Cancer Care Coordinators and 16 trainee physicians from across all Australian states and primarily from NSW public hospitals.[67] HCPs in the survey agreed with current guidelines for waiting times however 44% perceived delays of more than 14 days from referral to diagnosis and 4% reported the time exceeding 4 weeks. The most common reasons cited for delays included logistical difficulties for patients attending appointments (59%), waiting times to obtain tissue for diagnosis (57%), patient comorbidities (57%), lack of GP recognition of high-risk patients (51%), GP lacking in local network of

specialists (47%), GP adopting a watch and wait approach (40%) and unavailability of referral guidelines for GPs (36%).

Importantly, for a patient with stage IIIB lung cancer, a delay in treatment can lead to worsening of performance status thereby limiting treatment options. Further examination of the reasons for delays within Australian lung cancer services is therefore warranted.

Key to rapid management is ensuring that patients are seen by the appropriate specialist in the first instance for diagnosis and staging of the disease. There is a distinct lack of data for GP referral patterns in lung cancer, however HCPs in Australia perceive significant delays in primary care in identifying patients with lung cancer and a lack of awareness of referral patterns.[67] Further education of early signs and symptoms and to raise awareness of referral patterns may include tools such as the Qstream online training platform.[21] GPs may also benefit from developing and maintaining open communication with their local specialist and / or MDT.

Commonly, patients in rural or regional centers have different socioeconomic characteristics compared to metropolitan patients and present with more advanced disease, poorer performance status and more comorbidities.[68] It is important for smaller regional centers to be able to access support for patients requiring biopsies, pathology and imaging reviews from larger centers in a timely manner to ensure equity of care.[68]

While there are some minor variations in which healthcare professional is best placed for diagnosis, initial referral to a physician in the MDT is associated with improved outcomes compared to non-MDT referral and management.[10-12] MDTs are therefore critical to optimal patient-centered care; with observed benefits on patient survival.[10-12] With only half of Australian lung cancer patients seen by an MDT,[39] there is a need to improve MDT processes across Australia to bring national consistency to the quality of patient care. As rapid access clinics are established alongside the MDT with more performance data collected, we hope to show further improvements in service delivery.

Best practice for diagnosis and staging of patients for stage III NSCLC involves CT including brain and PET-CT, and tissue biopsy, and is individualized to the patient presentation, as determined by the MDT. However there remains inconsistency in the choice and timing of diagnostic techniques.

Treatment guidelines for stage III NSCLC are consistent and based on the same evidence, but NCCN is the most up to date and most specific in terms of practical management. The Australian guidelines need to be updated more frequently to stay relevant. As well as following guidelines, it is important for healthcare professionals to use clinical judgement and consider local access limitations which cannot be addressed in the guidelines. Limitations of this review include a lack of data for the proportions of patients progressing through each stage of the pathway and for wait times. Clinical data collection for lung cancer registries is common across Australia, but it is inconsistently collected between different institutions and states, usually due to lack of resources. Data collected by individual centers could be shared to create a larger, national database with consistent data collection protocols which is suitable for retrospective analysis.

Conclusions

Patients with stage III NSCLC are clinically heterogeneous and it can be difficult to fit them into a standard algorithm, thereby highlighting the value of the MDT to individualize treatment and improve survival.

GP education and awareness of referral pathways needs to be reinforced to ensure that all patients with suspected lung cancer are seen by the appropriate specialist as soon as possible.

There are gains to be had in meeting recommendations for time to treatment and further measures are required to address unnecessary delays in patient care. MDTs play a significant role in improving the efficiency of the diagnostic process and as a result lead to better clinical outcomes. The specialized lung cancer nurses and care coordinators further support the patient in their care pathway.

With the emergence of promising data for the use of immune checkpoint inhibitors, the standard of care is likely to undergo further shifts implementing the use of immunotherapy after completion of standard concurrent chemoradiation for patients with unresectable stage III NSCLC.

Disclosures

SK served on the advisory board for Pfizer, Boehringer Ingelheim, AstraZeneca, and received honoraria (paid to institution) from AstraZeneca, Roche, MSD and BMS. BH is an advisory board member for AstraZeneca, MSD, BMS, Roche, Pfizer, Eisai and Boehringer Ingelheim. SMB is an advisory board member for AstraZeneca, MSD and Roche. FH has received honoraria and trial sponsorship from Astra Zeneca and is supported by Peter MacCallum Foundation as a Clinician Researcher Fellow. RJ is an advisory board member for MSD and Pfizer. PP is an advisory board member for AstraZeneca, MSD, BMS, Roche, Pfizer and Boehringer Ingelheim. RH is an advisory board member for AstraZeneca, MSD, Roche, BMS and Novartis; and received honorarium from AstraZeneca, MSD, Roche, BMS and Novartis. IN, ES, KJ and BC have no disclosures.

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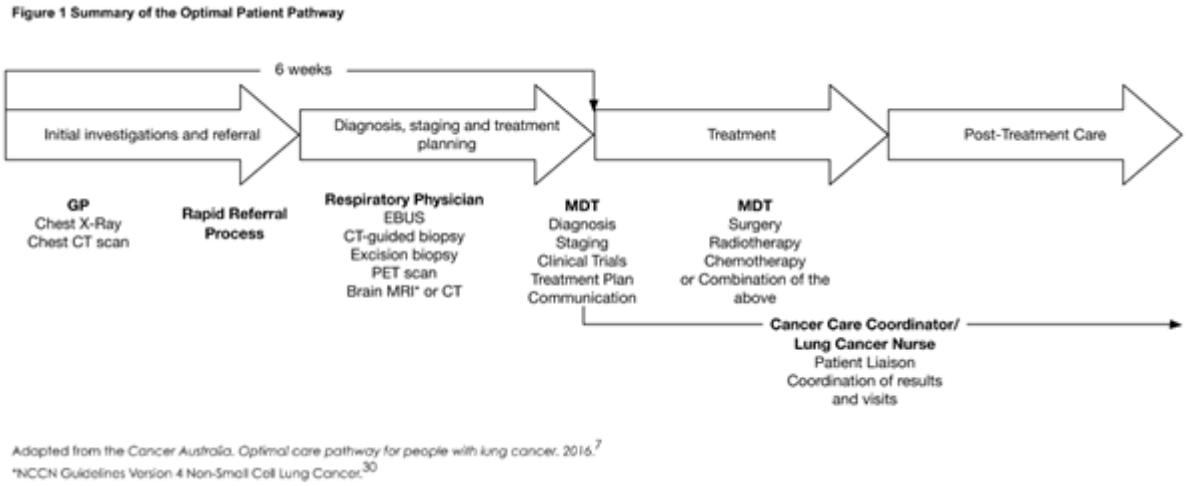
Table and Figure Legends

Figure 1 Summary of the Optimal Patient Pathway



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