cause dose reductions and a significant impact on activities of daily living (ADL's). Identification, prevention, and management are important tasks for oncology nurses to master to allow patients to remain on therapy. Figure 2. Other classes of TKI toxicities include the Anaplastic Leukemia Kinase (ALK) inhibitors, where there are currently 3 drugs approved for use, alectinib, ceritinib, and crizotinib. Each of the ALK inhibitors carries different yet important toxicities, ranging from nausea/vomiting, diarrhea, edema, bradycardia, pneumonitis, myalgias with elevated CPK levels, and hepatotoxicity. Several other TKI's are in development for potential use in lung cancer, such as HER2 inhibitors, BRAF inhibitors, and drugs targeting pathways dealing with RET, MET and KRAS (see table 1).[5-7]

***BRAF* mutations**	• 4% NSCLC • Most common is *V600E* • Drugs in trials: dabrafenib, vemurafenib, dasatinib,
***RET* rearrangements**	• 1-2% NSCLC • Highly associated with young, never-smokers • Drugs in trials: vandetanib, cabozantinib, sunitinib, ponatinib
***MET* amplification**	• Drugs in trials: crizotinib, tivantinib, onartuzumab, MET inhibitors
***HER2* mutations**	• Drugs in trials: trastuzumab, afatinib, dacomitinib, neratinib
***KRAS* mutations**	• 25-30% NSCLC, most common mutation • MEK, PI3K, FAK inhibitors

It is important for thoracic oncology nurses to have a firm understanding of these drugs and their toxicities. Management strategies must be tailored to the patient's symptoms and side effects, as well as to the specific drug and dosage.

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Keywords: TKI toxicities, EGFR rash

NU05.01
Use of Inspiratory Muscle Training in Managing Dyspnoea in Lung Cancer Patients

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Lung cancer, the most common cause of cancer-related death in men and women, is responsible for 1.3 million deaths worldwide annually. Lung cancer (LC) patients face many symptoms throughout the cancer trajectory and these often co-occur. Among the most prevalent (ranging from 21—90%), burdening and depilating symptoms that patients face is dyspnea. Although this symptom tends to become more frequent and persistent towards end-of-life, evidence show that even in early stage NSCLC patients who are most likely to be cured may also be faced with debilitating dyspnea that results in poor QOL during survivorship (Sarna et al 2008). Dyspnea in the setting of lung cancer has a complex aetiology that includes: direct involvement of lung tissue by cancer, indirect respiratory complications related to the cancer, treatment related complications (fibrosis secondary to chemotherapy or radiation), respiratory co-morbidities (pulmonary embolism) and other co-morbid conditions (i.e. COPD)(Kvale et al 2007). Due to its complex aetiology, dyspnea also has a multimodal management strategy including both pharmacological

and non-pharmacological interventions (Kloke & Cherny 2015). Pharmacological management options include bronchodilators, corticosteroids, anxiolytics, antidepressants, opiods and oxygen (Ferrell et al 2011; Kloke & Cherny 2015). The non-pharmacological interventions include patient's education on measures for ameliorating the symptom, such as opening windows, using small ventilators, adequate positioning, respiratory training and relaxation techniques (Galbraith et al 2010; Molassiotis et al 2015). A non-pharmacological intervention that has been widely used for the management of respiratory symptoms in asthma and COPD but not lung cancer is Inspiratory Muscle Training (IMT). This method can reduce dyspnea mainly through two distinct ways. Firstly, by strengthening the inspiratory muscles therefore lessening the effort during a given task (dyspnea) and secondly by providing a means for controlled breathing. An improved inspiratory muscle strength and endurance can lead to the better management of dyspnea and therefore facilitate the increase in the level of activity and improving the quality of life for patients. Despite the wealth of data on the effect of IMT on inspiratory muscle strength and endurance, exercise capacity, dyspnea and quality of life for adults with COPD, there are no available data for lung cancer patients. Whilst the literature shows that COPD and lung cancer are correlated (Sekine et al 2012), this is not sufficient to advocate towards the use of IMT in lung cancer patients experiencing dyspnea. Despite the scarcity of evidence, the fact that both COPD and lung cancer patients face many common problems such as increased resistance to airflow, air trapping and hyperventilation of the lung, increases the likelihood that IMT can also have a positive effect on lung cancer patients' dyspnea.

Aim: This randomized study aimed to assess the feasibility and effectiveness of inspiratory muscle training in patients with lung cancer regarding their dyspnea, psychological distress and quality of life.

Design: The trial is a two-arm, non-blinded, randomized controlled, proof-of-principle study. Patients were randomly assigned to IMT or a control group. The IMT group received standard care and additionally included the intervention with home follow-up every month for 3 months. Patients were recruited from the outpatients' clinics of two large cancer centers in the UK and one in Cyprus. Participants were eligible if they a) were adults with histological diagnosis of primary LC or mesothelioma; b) had refractory dyspnea not responding to current treatment for the past 2 weeks (breathlessness daily for 3 months at rest or on minimal exertion where contributing causes have been treated maximally); c) expected prognosis of >3 months as judged by the clinicians and d) had oxygen saturation above 85 % at rest. Patients were excluded if: they suffered from unstable COPD with frequent or acute exacerbations, had rapidly worsening dyspnea requiring urgent medical intervention, they received palliative radiotherapy to the chest received within 4 weeks or chemotherapy within 2 weeks, they were experiencing intractable cough, and those having unstable angina or clinically significant pleural effusion needing drainage.

Intervention: A pressure threshold device was used to deliver IMT, which controls a constant inspiratory pressure training load that is maintained unless the patient drastically alters his/her breathing pattern. Based on the literature on COPD patients, the intervention protocol included five sessions weekly for 12 weeks for 30 mins/day, divided over two sessions (the actual intervention had duration of 3-5 min for each session and progressively the time was increased to 30mins/day). The IMT resistance level was set to a low level (baseline) that allowed the patient to inhale comfortably. Progressively, the resistance level was increased according to the patient's performance.

Outcome measures: Outcome measures were completed at baseline and monthly for 3 months, and included: physiological parameters (FEV1,FVC); perceived severity of breathlessness using six 10-point NRS; modified Borg Scale; quality of life using the short form Chronic Respiratory Disease Questionnaire; Hospital Anxiety and Depression Scale, and safety.

Results: The final sample included 46 patients (M=37, F=9) at a mean age of 69.5 years old and a mean of 16 months post-diagnosis mainly with NSCLC and advanced disease (70%). Statistical and clinically important differences were seen with regard to distress from breathlessness ($p=0.03$), ability to cope with breathlessness ($p=0.01$), satisfaction with breathlessness management ($p=0.001$), fatigue ($p=0.005$), emotional function ($p=0.011$), breathlessness mastery ($p=0.015$) and depression ($p=0.028$). Changes were more evident in the 3-month assessment where the effect of the intervention came to its peak.

Discussion: This trial showed that the IMT is feasible and potentially effective in patients with lung cancer. A larger trial will provide more concrete conclusions on the usefulness of IMT in the management of dyspnoea in lung cancer patients with relatively stable disease, relatively higher performance status and life expectancy of >3 months. However, those patients with acute or severe dyspnoea should be treated according to established protocols rather than IMT.

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Keywords: Inspiratory muscle training, Integrative medicine, lung cancer, dyspnoea