

The changing landscape of thoracic malignancies

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Friends and Colleagues,

We welcome you to this supplemental issue in *Current Oncology*: “Advances in Breast and Lung Cancers for the Community Oncologist.” During the last decade, treatment for non-small-cell lung carcinoma (NSCLC) has changed dramatically. The days of classifying lung cancer into only small-cell or non-small-cell are over. As well, treatment planning using only histology is no longer acceptable. The science has evolved, and many lung cancers can be molecularly profiled for directed treatment. Treatment is now personalized for multiple biomarkers, leading to marked improvements in survival and quality of life.

The use of small-molecule tyrosine kinase inhibitors (TKIs) in patients with advanced disease started before the importance of mutation in the epidermal growth factor receptor (EGFR) was understood. A retrospective exploratory biomarker analysis of the IPASS trial showed that the EGFR mutation selected for the patients best able to benefit from a first-generation EGFR TKI: gefitinib. A decade has passed, and second-generation EGFR TKIs are now in use. The benefits of using second-generation EGFR TKIs in treatment-naïve patients, refractory disease, and squamous histology are reviewed by Drs. Morin-Ben Abdallah and Hirsh, illustrating a benefit of irreversibly inhibiting all members of the ErbB family. Unfortunately, all patients become resistant to first- and second-generation TKIs in that setting. The efficacy and safety of third-generation inhibitors for acquired resistance mutation T790 mean that those inhibitors have now become a standard of care (Dr. O’Kane *et al.*). Using circulating tumour DNA to find that biomarker of resistance, T790, in both tissue and plasma is fascinating and has changed the treatment paradigm (Drs. Cabanero and Tsao). Targeting angiogenesis is recognized as an effective approach in many malignancies, including lung cancer. Adding angiogenesis inhibitors to EGFR inhibitors has produced promising results. As well, preclinical research suggests an immunosuppressive effect of proangiogenic factors. That observation leads to a rationale for adding antiangiogenic agents to immune checkpoint inhibitors (Dr. Alshangiti *et al.*).

Although the incidence of ALK rearrangements in NSCLC is low, the prevalence of patients with that subset of disease is much higher because of their prolonged survival. Second- and next-generation ALK inhibitors have transformed the standard of care in those patients (Drs. Rothenstein and Chooback).

Next-generation sequencing is now identifying rare oncogenic drivers, and successful drug development has occurred. Algorithms are presented, separated by histology, because many of the rare mutations are exclusive to the nonsquamous histology subtype (Dr. Melosky). Squamous histology deserves its own consideration, and potential molecular targets and innovative agents are explored (Dr. Daaboul *et al.*). The rare carcinoid and atypical carcinoid tumours of lung origin are important to understand, because new treatment options exist. With proper care and treatment, affected patients experience extended survival (Dr. Melosky).

The impact of immunotherapy in NSCLC is huge, and the story is amazing. Survival plateaus continue to increase and impress the practitioner community. The new label “immuno-oncology,” which reflects the activation a patient’s own immune system, has changed thoracic malignancies. Trials combining PD-1 or PD-L1 inhibitors with chemotherapy, other immuno-oncology agents, or targeted therapy are reviewed, because those strategies aim to improve the percentage of patients achieving benefit (Drs. Pabani and Butts).

Finally, quality of life for the patient is a major goal of lung oncologists. Brain metastases affect lifespan, and optimal treatment options must be found. As patients with lung cancer live longer, the short- and long-term effects of brain metastases and toxicities of treatment will require important decision-making from oncologists and patients alike (Drs. Morin-Ben Abdallah and Wong).

We still have to strive for improvement in patients with advanced NSCLC. Standardized national molecular testing is needed so that all patients receive excellent care. Molecular testing should include EGFR, ALK, ROS1, and BRAF in patients with nonsquamous histology. Rare mutations of RET, HER2, NTRK, and c-Met exon 14 skip could be added, because therapy options are available. Squamous histology patients should also be tested for molecular drivers, because c-Met exon 14 splice is just one example of a driver that might be found. Attempts to inhibit and understand the KRAS mutation in NSCLC should continue, because that driver is the one most commonly identified. Testing for PD-L1 should be reflexive, because that biomarker can still help to direct treatment and predict efficacy.

Treatment for NSCLC has never been more complex. The ultimate goal is prevention, but in the meantime, our

care should ensure that patients live longer and in dignity. Major advances have been made in lung cancer, and with this important issue of *Current Oncology*, we welcome you to share in them.

CONFLICT OF INTEREST DISCLOSURES

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