Lung cancer diagnostics and treatments 2015: a renaissance of patient care

This issue of *Translational Lung Cancer Research* (*TLCR*) focuses on the rapid, changing landscape of lung cancer treatment. The topics of these reviews focus on some of the most important aspects in lung cancer patient care that we feel healthcare providers should be fully aware of. It is my pleasure to serve as guest editor and I hope you enjoy the diverse content we've included in this special *TLCR* edition.

Over the last two decades, the treatment of lung cancer has changed dramatically. In the late 1990s, treatment for late stage lung cancer consisted of platinum-based doublet chemotherapies (cisplatin/paclitaxel, cisplatin/gemcitabine, cisplatin/docetaxel, carboplatin/paclitaxel) or best supportive care. None of the regimens offered a significant improvement in overall survival over the other regimens (1). We got a clinical signal of the potential of molecularly targeted agents (e.g., gefitinib), but with no biomarkers or companion diagnostics we had no methods of identifying patients that would respond to these selected therapies.

Within the last decade, a renaissance in the treatment of lung cancer has occurred that has mirrored that of other tumor types (e.g., breast). The onset of biomarkers and companion diagnostics, with corresponding, matched treatments, has allowed precision medicine to become a reality in the treatment of lung cancer patients. In the United States, we now have Food and Drug Administration (FDA) approval for over 20 targeted agents, many of which have corresponding companion diagnostic tests (2). However, diagnostic testing for molecular abnormalities is confusing for many providers, as there are many FDA approved and laboratory developed tests available. We hope our articles in this special edition helps increase physician awareness of the available lung cancer diagnostic tests.

Approximately 20% of patients will have an actionable mutation [e.g., epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS proto-oncogene 1 (ROS1)]. Our goal is to expand the number of patients eligible to receive targeted therapies, such as afatinib, erlotinib, gefitinib, crizotinib, ceritinib, bevacizumab, and ramucirumab. The Biomarker-integrated Approaches of Targeted Therapy for Lung Cancer Elimination (BATTLE) study launched an era integrating biopsies, biomarkers, and molecular treatments into clinical assessments of patients with non-small cell lung cancer (3). Numerous international efforts, including the National Cancer Institute's Molecular Analysis for Therapy Choice Trial (NCI-MATCH) and Institute Gustave Roussy's MOlecular Screening for CAncer Treatment and Optimisation (MOSCATO), are currently working towards matching patients with tumors containing actionable mutations to targeted drug therapies. Targeted therapies are being integrated in early stage lung cancer patients in conjunction with chemotherapy and radiation therapy. The Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials (ALCHEMIST) are matching early stage lung cancer patients to targeted therapies based on tissue from surgical resection. ALCHEMIST allows drugs approved for advanced lung cancer to be used in the early stage setting. Targeted therapies have also been combined with radiation therapy in patients with non-metastatic lung cancer, as is discussed in this special edition.

Advances in immunotherapy seen across many tumor types (e.g., melanoma, kidney) are also applicable to lung cancer patients, including those with the traditionally hard to treat squamous histology. Vaccine therapy (tecemotide), checkpoint inhibition [cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed death-1/programmed death-1 ligand (PD1/PDL1)], and T-cell costimulation [4-1BB (CD-137), OX40 (CD134), and CD-27 agonists] are all novel strategies to combat lung cancer and we are excited to see how the development of these strategies progress. Immunotherapies are also being combined with radiation therapy predominantly in the metastatic setting. This treatment combination can not only provide local control, but may also increase response outside of the radiation field in some patients.

Great improvements are also being seen in the management of toxicity. As more treatments are approved, providers must be more aware of potential interactions and side effects. Safety profiles of targeted and immunotherapies are different. Clinical management requires a different awareness than in the past when cytotoxic regimens were predominant. Clinicians need to be aware of dermatologic and gastrointestinal manifestations that arise when treating patients with immunologic agents and react in an appropriate and timely manner. Targeted therapies, such as AZD9291 and rociletinib [both 3rd generation EGFR tyrosine kinase inhibitors (TKIs)], have a diverse side effect profile as well. Classical treatment side effects (e.g., rash, diarrhea, nausea) are reported with AZD9291 administration while hyperglycemia is the main dose-limiting toxicity with rociletinib (4,5). Providers must be aware of the differences in these adverse event profiles and respond appropriately.

At the Levine Cancer Institute, we have developed numerous clinical pathways to help guide physicians managing the side effects of immunotherapies. In this special edition, we've included suggestions for managing the side effects of rociletinib. Trials of these drugs targeting T790M have demonstrated high effectiveness with manageable side effect profiles and we are anticipating FDA approval of these drugs soon.

Rapid, exciting changes in lung cancer treatment are impacting patient care and outcomes. We hope the articles in this issue highlight some of the many advances in lung cancer testing, treatment, and management of toxicities that we have seen over the recent years. We also hope that we have provided a glimpse into what is on the horizon. The renaissance of lung cancer has begun and offers more hope for providers and patients.

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