For myself I am an optimist – it does not seem to be much use being anything else.
Sir Winston Churchill

Perpetual optimism is a force multiplier.
Colin Powell

All of us in thoracic oncology are the ironic perpetual “glass half full” optimists who care for patients who are less than optimistic, given their diagnosis of lung cancer. We have to be the optimists who fight on behalf of our patients in their ongoing battle against all the negative facts about lung cancer, including the statistics on the epidemic-like incidence and the disheartening relative survival rates of lung cancer. So what if statistics estimate that 228,190 new lung cancer cases (13.7% of all new cancer cases) were diagnosed in 2013 or that 159,480 lung cancer deaths (27.5% of all cancer deaths) occurred in 2013? The pessimists say that the overall lung cancer relative survival rate over the past 4 decades has remained below 18%, while we optimists proclaim that the overall lung cancer relative survival rate in the United States has almost doubled, from 11% in 1975 to 17% in 2005. Based on patients diagnosed in 2003–2005, we at Moffitt Cancer Center are even more encouraged by our own lung cancer patients’ comparatively better overall survival rate of 32%, almost twice the national overall survival rate.

To gain insight into some of the contributing factors to these encouraging results, we need only peruse the various articles in this issue of Cancer Control. Among these pages, we will find articles from our colleagues at Moffitt as well as across the United States that review the advancements in lung cancer screening, minimally invasive mediastinal nodal staging, systemic and targeted therapies, genomic and proteomic profiling, and survivorship issues in patients with or suspected of having non–small-cell lung cancer (NSCLC).

In addition to always advising our patients who smoke to cease smoking in attempts to prevent lung cancer, detecting lung cancer at its earliest stages would contribute toward increasing overall lung cancer survival rates. Dr Nanavaty and colleagues start off this issue by reviewing the advantages, controversies, and applications of lung cancer screening. Their article reviews various randomized lung cancer screening clinical trials, focusing on the National Lung Screening Trial (NLST). The authors also examine the outcomes and costs related to lung cancer screening. Once lung cancer is diagnosed, then accurate staging of lung cancer is paramount to optimize treatment decision-making for our NSCLC patients. In the second article, Dr Harris and colleagues review non-invasive and minimally invasive techniques available to stage the mediastinum in patients with NSCLC as alternatives to cervical mediastinoscopy. They briefly review computed tomography and positron-emission tomography and the accuracy of these techniques at mediastinal lymph node staging in NSCLC patients. The authors then review in more detail endobronchial ultrasound, endoscopic ultrasound, and fine-needle aspiration of mediastinal lymph nodes.

In an effort to increase cure rates and improve survival in patients with resectable NSCLC, numerous clinical trials have been conducted to evaluate neoadjuvant and adjuvant chemotherapy. In the third article, Drs Byron and Pinder-Schenck review the results of the prospective randomized clinical trials that have established adjuvant chemotherapy as the standard of care for patients with surgically resected NSCLC. In addition, the authors summarize data on predictive and prognostic markers for patients with early-stage NSCLC and discuss novel therapies and clinical trials currently underway in early-stage NSCLC.

These predictive and prognostic markers and the novel therapies that target these tumor markers would not have been discovered without the ability to detect the genetic and protein differences between survivors of NSCLC and patients who succumbed to NSCLC. Dr Tanvetyanon and colleagues, in the fourth article, review the applications of genomic and proteomic profiling in NSCLC. They discuss the literature on important genomic and proteomic applications already adopted as standard care and those still under investigation in the fight against NSCLC.

With improved survival among our NSCLC patients, survivorship concerns for these patients include quality of life and physical and psychological issues. Dr Pratt and colleagues review the literature on lung cancer survivorship and the late- and long-term effects of treatment, which can impair the quality of life of a lung cancer survivor. The authors point out that high levels of physical and psychological distress are common among lung cancer survivors and that recognizing the potential late- and long-term effects
of treatment may help health care professionals intervene early to minimize negative implications.

These five invited articles on early-stage NSCLC are followed by a series of special reports on other topics that contribute to improving the diagnosis, treatment, and survival of lung cancer patients in all stages of NSCLC. In the first of these special reports, Dr Schabath and colleagues discuss the changes in demographics and overall survival of NSCLC patients who were seen at Moffitt Cancer Center over a span of 22 years. Their analysis included almost 5,000 NSCLC patients grouped within five 2-year periods spread over these 22 years and assessed changes in percentages of patients over 70 years of age, women, never-smokers and former smokers, and patients with stage I tumors and the corresponding changes in survival rates over the five time periods.

The treatment of stage IIIA NSCLC differs from that for stage I and II NSCLC in that the former usually comprises two or all three treatment modalities: chemotherapy and radiation therapy, with or without surgery. In the randomized intergroup trial (INT 0139), which initially concluded that the addition of surgery to chemoradiation did not improve overall survival for stage IIIA patients, subset analyses of that clinical trial suggested that trimodality treatment incorporating lobectomy may be superior to bimodality therapy with chemoradiation alone. In this issue's second special report, Dr Aggarwal and colleagues analyzed the outcomes of almost 250 stage IIIA NSCLC patients treated at Fox Chase Cancer Center from 2000 to 2008 and report similar results to those of the INT 0139 clinical trial.

With rates of obesity on the rise, the impact of excessive body weight on medical treatment outcomes comprises an important concern for administering health care. In the third special report included in this issue, Dr Jatoi and colleagues point out that the American Society of Clinical Oncology (ASCO) in 2012 issued a guideline that urged health care professionals to “routinely use an obese patient’s actual body weight, rather than an ideal body weight or other estimate, to calculate the appropriate dose of nearly all chemotherapy drugs.” However, the ASCO guidelines did not address dosages for morbidly obese patients (body mass index [BMI] ≥ 40) and who are receiving concomitant chemotherapy and radiation. The authors describe their experience at Mayo Clinic (Rochester, Minnesota) with 16 patients who had a BMI of ≥ 40 within 2 weeks of starting concomitant chemotherapy and curative-intent radiation among almost 1,900 total patients with lung cancer or esophageal cancer treated over a 14-year span. Their findings suggest chemotherapy dose reductions may be appropriate in specific instances due to severe toxicity noted in this cohort of morbidly obese cancer patients.

A majority of NSCLC patients present with advanced or metastatic disease and have poor survival rates, with little impact on these outcomes by conventional chemotherapy. Drs Kuykendall and Chiappori point out that targeted and/or biologic cancer therapies composed of small molecules or monoclonal antibodies have jumped to the forefront of the oncologist’s therapeutic armamentarium and clinical research. Among these targeted therapies are treatments against the epidermal growth factor receptor (EGFR) gene and gene products. The authors present a case report and review the literature to provide guidelines to the approach and management of advanced EGFR mutation-positive NSCLC.

In the subsequent special report, Dr Mahipal and colleagues discuss the clinical evidence supporting the benefits of targeted agents directed against EGFR. These authors review both monoclonal antibodies that block ligand binding to the EGFR extracellular domain and the small-molecule tyrosine kinase inhibitors that exert their effects at the intracellular portion of the receptor to prevent tyrosine kinase phosphorylation and activation of signal transduction pathways. They also specifically discuss the survival end points used in the pivotal clinical trials, current applications, and future research directions.

While EGFR and ALK molecular targets are often found in lung adenocarcinomas, pulmonary squamous cell carcinomas have been historically found not to contain exploitable molecular aberrations for targeted therapy. In the subsequent special report, Dr Creelan notes that the immune checkpoint proteins, including the B7/CD28 receptor superfamily, have become important targets for pharmacologic blockade by new monoclonal antibodies against this novel target. He reports that tumor PD-L1 expression may be usable as a predictive biomarker for antitumor response, especially when dual checkpoint blockade strategies may increase the proportion and durability of tumor responses.

In the final special report in this issue, Dr Hirsch and colleagues note that adherence to national quality measures and guideline recommendations may be less than ideal despite physicians having the necessary framework for patient care. The authors designed a performance improvement initiative that met national continuing medical education standards. Focusing on NSCLC patient care, they subjected oncologists to a three-step process, including a self-assessment of predetermined performance measures, the development and implementation of an actionable plan for improvement, and a second round of assessment to measure practice change. The authors conclude that their data support the value of performance improvement initiatives to help increase physician delivery of evidence-based care to patients.
The mission of Moffitt Cancer Center is to contribute to the prevention and cure of cancer. This issue of *Cancer Control* is dedicated to the efforts of our colleagues both at Moffitt Cancer Center and throughout the United States to contribute to the prevention and cure of NSCLC. The invited articles and the special reports contained within this issue, as well as the *Ten Best Readings* feature, provide evidence of such tireless efforts on behalf of our NSCLC patients. With continued effort, our perpetual optimism will surely enjoy watching our glass become more than half full.

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**References**