

**Gabriel Carabulea, M.D.**

665 Camino de los Mares, Suite 208  
San Clemente, Ca 92673

26800 Crown Valley Pkwy, Suite 475  
Mission Viejo, Ca 92691  
(949) 218-2800



**OCEAN VIEW HEMATOLOGY/ ONCOLOGY MEDICAL  
GROUP NEWSLETTER**

**Lung Cancer News**

**NEW STRATEGIES/THERAPIES-NEW HOPE IN THE WAR AGAINST LUNG  
CANCER**

**NIVOLUMAB (Opdivo) approved in NSCLC.**

The FDA has approved the anti-PD-1 agent for the treatment of patients with advanced squamous non-small cell cancer (NSCLC) who have progressed on or after platinum-based chemotherapy. Opdivo introduces an entirely new treatment modality for the previously treated metastatic squamous NSCLC, with the potential to replace chemotherapy for these patients. The approval was based on data from the phase III CheckMate-017 trial in which nivolumab improved overall survival (OS) by 3.2 months versus docetaxel. The study involved 272 previously treated patients who were randomized to the fully human IgG4 monoclonal antibody nivolumab at 3 mg/kg IV every 2 weeks or docetaxel at 75 mg/m<sup>2</sup> IV every 3 weeks. Treatment with nivolumab improved OS by 41% versus docetaxel (9.2 vs 6.0 months). Data from the phase II trial of nivolumab in NSCLC showed at 11 months' follow-up ORR of 15%, with a median duration of response that was not yet reached. The durability of response is one of the most promising aspects of this type of immunotherapy.

**ISSUES IN SCREENING AND PREVENTION**

**LUNG CANCER screening can save lives, and is covered by insurance now. USPSTF/ACS is now recommending annual screening with LDCT in adults 55 to 80 years who have a 30 pack-year smoking history- or 20 pack-year + one additional risk factor-, and currently smoke or have quit within the past 15 years=high risk category). Beginning in early 2015, more than eight million Americans at high risk for lung cancer became eligible for annual**

screening with LDCT through new private-insurer and Medicare coverage requirements.

It is important to discuss the potential benefits and harms, including non-definitive findings, which can be associated with increased anxiety, with the patient. Also important is for testing to take place in settings with multidisciplinary expertise in diagnostic workup and treatment.

### **NEW TECHNOLOGIES-NEW HOPE**

**STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR)** achieves better overall survival than invasive surgery – the current standard of care - for early lung cancer, according to the findings of a phase III randomized international study published in *The Lancet Oncology*. In the 58 patients analyzed, the estimated three-year survival rates were 79 percent in the surgery group and 95 percent in the SABR group, while recurrence-free survival rates at three years were 80 percent and 86 percent, respectively. Stereotactic radiation treatment is a relatively new approach for operable early stage lung cancer. This study can give physicians confidence to consider a non-invasive alternative, especially for elderly patients and for those with significant comorbidities.

**PERCEPTA BRONCHIAL GENOMIC CLASSIFIER.** Veracyte, Inc., a molecular diagnostic company, has announced the launch of its Percepta, a new genomic test to resolve ambiguity in lung cancer diagnosis. The Percepta test is designed to reduce the number of invasive biopsies and other procedures that can follow when suspicious lung nodules are found on computerized tomography (CT) scans. Veracyte's test comprises a 23-gene molecular classifier that uses proprietary "field of injury" technology to detect molecular changes that occur in the epithelial cells lining the lung's respiratory tract in response to smoking – the cause of 85-90 percent of lung cancers. These changes can be detected in cells obtained from standard cytology brushings taken during bronchoscopy from the proximal airway, and indicate the presence of malignancy or disease processes from distant sites in the lung. Percepta test has the ability to identify patients whose lung nodules are at low risk of malignancy so that they can be monitored with CT scans in lieu of invasive diagnostic procedures.

### **ADVANCES IN PERSONALIZED THERAPY**

Activating mutations in epidermal growth factor receptor (*EGFR*) exon 19 are among the most commonly observed mutations in patients with non-small cell lung cancer (NSCLC). Abundant evidence points to a role for

therapy with tyrosine kinase inhibitors (TKIs) in these patients, although it is not yet clear whether all TKIs will perform equally well in this setting, or whether one TKI could be recommended over another.

#### **EGFR Mutations in NSCLC: Key Findings**

- **Most patients with NSCLC who have *EGFR* mutations have sensitizing exon19 deletions, or substitutions in exon 21 (eg, *L858R*).**
- **Studies have shown that patients with *EGFR* exon 19 mutations have significantly longer survival and higher response rates to TKIs than those with other mutations, such as exon 21 *L858R*. For example, in one retrospective study, patients with *EGFR* exon 19 mutations treated with gefitinib or erlotinib, had significantly longer survival versus those with exon 21 *L858R* mutation (34 months vs 8 months;  $P = .01$ ).**
- **Subanalysis from the LUX-Lung 3 and LUX-Lung 6 trials has shown a benefit in overall survival with afatinib over chemotherapy in the subgroup of patients with exon 19 deletions.**
- **The addition of an antiangiogenesis agent (bevacizumab) to erlotinib therapy in patients with activating *EGFR* mutations improved progression-free survival (PFS) over erlotinib alone in a study from Japan; further confirmation of this combination therapy is warranted in a larger NSCLC population.**
- **Third-generation TKIs (AZD9291; rociletinib) are becoming available for patients with *T790M* mutations and may be useful for patients with exon 19 deletions whose disease progresses with first-line TKIs.**

In addition to antiangiogenic strategies, there are ongoing efforts evaluating the addition of checkpoint inhibitors (anti-programmed cell death-1 [PD-1] and its ligand, anti-PD-L1, drugs) in combination with TKI therapy, because preclinical work suggests that EGFR signaling upregulates PD-L1 expression. Results of these studies will hopefully be reported soon.

#### **Services provided by OVHOMG:**

Cancer screening and prevention  
Second opinions  
Genetic testing and counseling  
Chemotherapy  
Immunotherapy  
Infusion Therapy  
Palliative care  
DVT prevention/management

