INTERVIEW

Mark A Socinski, MD

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Tracks 1-17

Select Excerpts from the Interview

Tracks 7, 17

DR LOVE: How do you generally manage patients with advanced non-small cell lung cancer (NSCLC) and EGFR tumor mutations?

DR SOCINSKI: I am impressed with the IPASS trial findings (Mok 2009; [1.1]) and the recent CALGB data (Jänne 2010; [1.2]) in first-line sytemic treatment of advanced lung cancer positive for EGFR mutation, demonstrating the advantage of using an upfront EGFR TKI such as erlotinib without chemotherapy.

In IPASS, the rate of EGFR mutation was 60 percent in never or light smokers. As enthusiastic as we are about IPASS, one question that arose in the community was whether these data reflect the US population because the study population is Asian.

The CALGB-30406 data represent a mostly Caucasian population, and the incidence of EGFR mutation is close to 40 percent.

Although this is not as high as in IPASS, it is high enough that one should test for these mutations in nonsmokers, light smokers or former smokers. The incidence of the mutation is inversely related to smoking exposure.

In my practice, we evaluate EGFR mutation status in patients with advanced disease who have tumors with nonsquamous histology and a 40 pack-year or less smoking history. With this approach, we may not identify all tumors with EGFR mutations, but one must establish some criterion for testing, and that's our approach.

The ongoing RADIANT trial is evaluating erlotinib in the adjuvant setting, but it may be a long time before the results are available.

1.1

IPASS: A Phase III Randomized Trial of Gefitinib versus Carboplatin/Paclitaxel as First-Line Therapy for Clinically Selected (Asian, Nonsmokers or Former Light Smokers, Adenocarcinoma) Patients with Advanced Non-Small Cell Lung Cancer

Progression-free survival (Events)	Gefitinib	Carboplatin + paclitaxel	Hazard ratio* (95% CI)	*p*-value
Intent-to-treat population (n = 609; 608)	74.4%	81.7%	0.74 (0.65-0.85)	<0.001
EGFR mutation-positive (n = 132; 129)	73.5%	86.0%	0.48 (0.36-0.64)	<0.001
EGFR mutation-negative (n = 91; 85)	96.7%	82.4%	2.85 (2.05-3.98)	<0.001

* Hazard ratio < 1.0 favors gefitinib; CI = confidence interval

"The presence of an EGFR mutation was a robust predictor of improved progression-free survival with gefitinib, as compared with carboplatin-paclitaxel, and of the benefit of gefitinib with respect to the objective response rate, indicating that patients in whom an EGFR mutation has been identified will benefit most from first-line therapy with gefitinib.

Whenever possible, EGFR-mutation should be determined before the initial treatment of pulmonary adenocarcinoma."

Mok TS et al. *N Engl J Med* 2009;361(10):947-57.

1.2

CALGB-30406: Efficacy of Single-Agent Erlotinib (E) or Erlotinib with Carboplatin/Paclitaxel (ECP) in Never Smokers or Former Light Smokers with Advanced Lung Adenocarcinoma

Endpoint	E	ECP
Progression-free survival (n = 81, 100) EGFR mutant vs wild type*	6.7 mo 15.7 vs 2.7 mo $p < 0.0001$	6.6 mo 17.2 vs 4.8 mo $p < 0.0001$
Overall survival (n = 81, 100) EGFR mutant vs wild type*	24.3 mo 31.3 vs 18.1 mo $p = 0.0093$	19.6 mo 39.0 vs 13.7 mo $p = 0.0012$
Response rate (n = 81, 100) EGFR mutant vs wild type*	35% 67% vs 9% $p < 0.0001$	48% 73% vs 33% $p = 0.0004$

* E arm: n = 33 EGFR mutant, n = 44 EGFR wild type; ECP arm: n = 33 EGFR mutant, n = 54 EGFR wild type

"E and ECP have similar efficacy, but E is less toxic, in predominantly Caucasian never smokers with advanced NSCLC. *EGFR* mutations identify patients most likely to benefit from E and ECP."

Jänne PA et al. Presentation. ASCO 2010;**Abstract 7503**.

Tracks 12-16

DR LOVE: Can you discuss data you presented at ASCO on nanoparticle albumin-bound (*nab*) paclitaxel in the front-line treatment of NSCLC?

DR SOCINSKI: In the Phase III study comparing carboplatin/*nab* paclitaxel to carboplatin/paclitaxel, response rates in the *nab* paclitaxel arm were improved according to independent radiologic review (Socinski 2010; [1.3]). In both arms carboplatin was administered every three weeks. In the control arm paclitaxel was administered every three weeks, and in the investigational arm *nab* paclitaxel was administered weekly. Response rates by histology revealed a greater magnitude of benefit in the population with squamous cell NSCLC. Progression-free survival and overall survival results will be available later this year.

Regarding side effects, the major differences are the improved neuropathy and neutropenia on the *nab* paclitaxel arm (Socinski 2010) compared to the paclitaxel arm. I believe this difference in adverse events is real, but it would be difficult to know how much of it is a result of the formulation of *nab* paclitaxel and how much could be attributed to the weekly schedule.

Other benefits with *nab* paclitaxel include the lack of need for premedications and a much shorter infusion time — 30 minutes. In contrast, paclitaxel requires standard premedication, including steroids, and is administered over three hours. This is a real advantage in terms of convenience. I am optimistic that this is a more biologically potent way to administer a drug that has activity in breast, lung, ovarian and other types of cancer.

DR LOVE: What do we know about combining *nab* paclitaxel with bevacizumab?

DR SOCINSKI: A Phase II trial with a three-weekly schedule of carboplatin, *nab* paclitaxel and bevacizumab was published recently (Reynolds 2009; [1.4]). The response rates and other outcome measures are highly favorable. In view of these Phase II data — even in the absence of Phase III data — I personally would not hesitate to use it. ■

1.3

Efficacy of Carboplatin/*Nab* Paclitaxel versus Carboplatin/Paclitaxel as First-Line Therapy for Advanced Non-Small Cell Lung Cancer

Response by independent review	Carboplatin/ paclitaxel	Carboplatin/ *nab* paclitaxel	Response ratio*	*p*-value
Response rate — **all patients**	25% (n = 531)	33% (n = 521)	1.31	0.005
Response rate — **squamous histology**	24% (n = 221)	41% (n = 228)	1.67	<0.001
Response rate — **nonsquamous histology**	25% (n = 310)	26% (n = 292)	—	0.808

* Response ratio > 1 favors *nab* paclitaxel

Socinski MA et al. Presentation. ASCO 2010;**Abstract LBA7511**.

1.4

Efficacy of Carboplatin/*Nab* Paclitaxel/Bevacizumab in a Phase II Study in Advanced Nonsquamous Non-Small Cell Lung Cancer (N = 48)

Response rate	Stable disease	Progression-free survival	Overall survival
31%	54%	9.8 months	16.8 months

Reynolds C et al. *J Thorac Oncol* 2009;4(12):1537-43.

SELECT PUBLICATIONS

Gazdar AF. **Personalized medicine and inhibition of EGFR signaling in lung cancer.** *N Engl J Med* 2009;361(10):1018-20.

Jänne PA et al. **Randomized phase II trial of erlotinib alone or in combination with carboplatin/paclitaxel in never or light former smokers with advanced lung adenocarcinoma: CALGB 30406.** Presentation. ASCO 2010;**Abstract 7503**.

Mok TS et al. **Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma.** *N Engl J Med* 2009;361(10):947-57.

Reynolds C et al. **Phase II trial of nanoparticle albumin-bound paclitaxel, carboplatin, and bevacizumab in first-line patients with advanced non-squamous non-small cell lung cancer.** *J Thorac Oncol* 2009;4(12):1537-43.

Socinski MA et al. **Results of a randomized, phase III trial of *nab*-paclitaxel (*nab*-P) and carboplatin (C) compared with cremophor-based paclitaxel (P) and carboplatin as first-line therapy in advanced non-small cell lung cancer (NSCLC).** Presentation. ASCO 2010;**Abstract LBA7511**.