INTERVIEW

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Tracks 1-16

Select Excerpts from the Interview

Track 3

DR LOVE: Would you discuss the IPASS trial, which evaluated first-line gefitinib versus carboplatin/paclitaxel as treatment for metastatic NSCLC?

DR RAMALINGAM: The IPASS study evaluated more than 1,000 patients with adenocarcinomas who had no smoking history or less than a 10 pack-year smoking history. Patients were randomly assigned to treatment with a standard doublet of carboplatin/paclitaxel versus gefitinib.

The primary endpoint was PFS, and for the overall patient population, the PFS was superior, with gefitinib compared to chemotherapy with a hazard ratio of 0.74. When the data were evaluated by EGFR mutation status in the patients for whom they had tumor tissue — approximately 500 patients — PFS was far superior in favor of gefitinib for the patients with EGFR mutations, with a trend toward a survival benefit compared to chemotherapy (Mok 2009; [3.1]).

On the flip side of this analysis, chemotherapy resulted in much better outcomes for patients without EGFR mutations (3.1). As a result, we might conclude that if you know that the patient's EGFR mutation status is positive, gefitinib or EGFR TKIs are optimal as front-line therapy. However, if you don't know the mutation status or the patient does not have the mutation, then administering chemotherapy might be the better approach.

3.1

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 NSCLC

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

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

Tracks 4-5, 12

DR LOVE: Where are we with maintenance erlotinib for NSCLC?

DR RAMALINGAM: In the SATURN trial — which compared maintenance erlotinib to placebo in patients who had received four cycles of front-line chemotherapy — the improvement in the primary PFS endpoint was significant, and for patients with EGFR mutations, the improvement in PFS in favor of erlotinib was dramatic — the hazard ratio was 0.1. So for patients with EGFR mutations, it is a fairly straightforward decision. If the patient has not received front-line erlotinib, then after four to six cycles of chemotherapy I switch to an EGFR inhibitor. A PFS benefit was also noted in patients with

EGFR wild-type disease. So erlotinib is a reasonable option to consider even for patients without EGFR mutations, although the benefit may not be quite as large as reported with EGFR-mutated tumors (Cappuzzo 2009; [3.2]).

DR LOVE: What about erlotinib and bevacizumab as maintenance?

DR RAMALINGAM: That approach was evaluated in the ATLAS trial in which patients who initially received four cycles of chemotherapy with bevacizumab were then randomly assigned to bevacizumab with erlotinib versus continuation on bevacizumab alone.

The PFS was 4.8 months for the combination versus 3.7 months for bevacizumab, which was a significant improvement that met the primary endpoint of the trial. The survival data have not yet been formally presented (Miller 2009). Considering the survival benefits reported in the pemetrexed trial (Ciuleanu 2009) and the erlotinib trial, we need to see the survival data from this study before we can use this approach. ■

3.2

SATURN: Efficacy of Maintenance Erlotinib versus Placebo After Nonprogression with First-Line Platinum-Based Chemotherapy for Patients with Advanced NSCLC

Progression-free survival	Erlotinib vs placebo HR (95% CI)	*p*-value
ITT population (n = 437; 447)	0.71 (0.62-0.82)	<0.0001
EGFR IHC-positive (n = 307; 311)	0.69 (0.58-0.82)	<0.0001
EGFR mutation-positive (n = 22; 27)	0.10 (0.04-0.25)	<0.0001
EGFR wild type (n = 199; 189)	0.78 (0.63-0.96)	0.0185
Adenocarcinoma (n = 204; 197)	0.60 (0.48-0.75)	<0.0001
Squamous cell (n = 166; 193)	0.76 (0.60-0.95)	0.0148

HR = hazard ratio; CI = confidence interval; ITT = intent-to-treat; IHC = immunohistochemistry

Cappuzzo F et al. *Proc ASCO* 2009;**Abstract 8001**.

SELECT PUBLICATIONS

Cappuzzo F et al. **SATURN: A double-blind, randomized, phase III study of maintenance erlotinib versus placebo following nonprogression with first-line platinum-based chemotherapy in patients with advanced NSCLC.** *Proc ASCO* 2009;**Abstract 8001**.

Ciuleanu T et al. **Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for non-small-cell lung cancer: A randomised, double-blind, phase 3 study.** *Lancet* 2009;374(9699):1432-40.

Miller VA et al. **A randomized, double-blind, placebo-controlled, phase IIIb trial (ATLAS) comparing bevacizumab (B) therapy with or without erlotinib (E) after completion of chemotherapy with B for first-line treatment of locally advanced, recurrent, or metastatic non-small cell lung cancer (NSCLC).** *Proc ASCO* 2009;**Abstract LBA8002**.

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