INTERVIEW

Everett E Vokes, MD

Dr Vokes is John E Ultmann Professor of Medicine and Radiation and Cellular Oncology and Chairman of The University of Chicago's Department of Medicine in Chicago, Illinois.

Tracks 1-10

Select Excerpts from the Interview

Track 1

DR LOVE: Would you discuss the recent evolution of tissue biomarkers in the management of NSCLC?

DR VOKES: For approximately five years we've known that EGFR biomarkers matter, but we were debating which ones. The IPASS trial was the first instance in which we could say, "This means that a patient who does not have this biomarker should not receive the targeted agent in the first line and vice versa" (Mok 2009; [4.1]).

That has been solidified in the past year with the ALK fusion oncogene, for which a second targeted agent has become available — crizotinib. Crizotinib is associated with high response rates and seemingly good disease progression rates and perhaps overall survival as well, although that is somewhat premature.

4.1

IPASS: A Phase III Study of Up-Front Gefitinib versus Carboplatin/Paclitaxel in a Population of Asian Patients with Non-Small Cell Lung Cancer Phenotypically Enriched for EGFR Mutation

	Gefitinib	Carboplatin/ paclitaxel	Hazard ratio	*p*-value
PFS events (intent-to-treat population, N = 609; 608)	74.4%	81.7%	0.74	<0.001
PFS events (EGFR mutation-positive population, N = 132; 129)	73.5%	86.0%	0.48	<0.001
Response rates (EGFR mutation-positive population, N = 132; 129)	71.2%	47.3%	—	<0.001

PFS = progression-free survival

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

Dave Spigel presented data at ESMO on erlotinib with or without a c-MET inhibitor in the second- and third-line settings. Overall, no significant difference was observed in progression-free or overall survival, but a benefit was seen among c-MET overexpressors, although for those who had no or weak c-MET expression, addition of the agent was detrimental (Spigel 2010).

DR LOVE: What exactly is c-MET, and what's the epidemiology? How often do you see it, and where do you see it?

DR VOKES: c-MET is another receptor that has been shown to be overexpressed in tumors. It can also be mutated, but it's not mutated frequently and we're not sure yet, functionally, what the mutations mean. However, overexpression is observed commonly, and it can be inhibited. Inhibition can be achieved either by targeting an antibody to the ligand or by inhibiting the receptor directly. Two agents have been tested, including the receptor inhibitor ARQ 197 (Sandler 2011; [4.2, 4.3]), which showed a slight benefit as second-line treatment for c-MET overexpressors. Subset analysis of a second agent under development suggests that if you add it to erlotinib for overexpressors they will experience benefit.

4.2

Phase II Trial of the Oral c-MET Inhibitor ARQ 197 (A) in Combination with Erlotinib (E) for Patients with Previously Treated, EGFR Inhibitor-Naïve Advanced Non-Small Cell Lung Cancer

	E + A (n = 84)	E + placebo (n = 83)	Hazard ratio	*p*-value
Median progression-free survival	3.7 months	2.2 months	0.68	<0.05
Median overall survival	8.4 months	6.8 months	0.88	<0.52

Sandler A et al. *Proc ASCO* 2011;**Abstract TPS217**.

4.3

MARQUEE: A Phase III Trial of Erlotinib with ARQ 197 versus Erlotinib with Placebo for Patients with Previously Treated, Locally Advanced or Metastatic Nonsquamous Non-Small Cell Lung Cancer (NSCLC)

Protocol ID: NCT01244191 **Target Accrual:** 988 (Open)

Eligibility

- Nonsquamous NSCLC
- Disease progression on 1 to 2 lines of chemotherapy (one of which must be a platinum doublet)

R

- Erlotinib PO qd + ARQ 197 PO BID
- Erlotinib PO qd + placebo PO BID

Sandler A et al. *Proc ASCO* 2011;**Abstract TPS217**; **www.clinicaltrials.gov**, July 2011.

Track 5

DR LOVE: What are your thoughts on the selection of first-line therapy for squamous cell and nonsquamous cell metastatic NSCLC?

DR VOKES: I believe that it has become difficult for us to point to progress in squamous cell NSCLC in recent years. We don't have a good target in that population. Cetuximab may be of benefit, but the data aren't clear yet. We do know that pemetrexed is not the best agent for these patients, so we're left with carboplatin/paclitaxel or docetaxel and, based on Giorgio Scagliotti's trial evaluating cisplatin/gemcitabine versus cisplatin/pemetrexed, cisplatin and gemcitabine for patients with squamous cell NSCLC (Scagliotti 2008).

Also based on the Scagliotti study, I believe pemetrexed is the preferred agent for patients with adenocarcinoma (Scagliotti 2008). Bevacizumab is also a candidate for these patients.

DR LOVE: How do you make the decision about whether to use bevacizumab?

DR VOKES: It's a difficult decision. If you have a clear-cut bevacizumab case — adenocarcinoma, no EGFR mutation — administering carboplatin/paclitaxel/bevacizumab is perfectly reasonable. The alternative is carboplatin or cisplatin/pemetrexed. We have Phase II data supporting the use of carboplatin/pemetrexed/bevacizumab, but the data with that regimen compared to carboplatin/paclitaxel/bevacizumab are pending. Until then, these are equally valid options. I prefer cisplatin or carboplatin and pemetrexed. ■

SELECT PUBLICATIONS

Scagliotti GV et al. **Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naïve patients with advanced-stage non-small-cell lung cancer.** *J Clin Oncol* 2008;26(21):3543-51.

Spigel D et al. **Randomized multicenter double-blind placebo-controlled Phase III study evaluating METMAB, an antibody to MET receptor, in combination with erlotinib, in patients with advanced non-small-cell lung cancer.** *Proc ESMO* 2010;**Abstract LBA15**.