Tracks 1-12

Track 1  The Cancer Genome Atlas consortium’s identification of mutations in squamous cell lung cancer

Track 2  Potential role of nab paclitaxel as treatment for advanced squamous cell lung cancer

Track 3  Perspective on targeting MET in NSCLC

Track 4  MetLung: A Phase III study of onartuzumab (MetMAb)/erlotinib versus erlotinib/placebo in advanced MET diagnostic-positive NSCLC after failure of 1 to 2 platinum-based regimens

Track 5  Use of erlotinib in EGFR wild-type, squamous cell lung cancer

Track 6  Targeting angiogenesis in NSCLC

Track 7  Case discussion: A 66-year-old patient and never smoker with resected Stage IB NSCLC and 2 uncommon EGFR mutations (E709A, G719C)

Track 8  Adjuvant chemotherapy options for Stage IB NSCLC

Track 9  TREAT: Results of a Phase II trial on the refinement of early-stage NSCLC adjuvant chemotherapy with cisplatin/pemetrexed versus cisplatin/vinorelbine

Track 10  Case discussion: A 50-year-old patient and never smoker with EGFR wild-type, ALK-negative, HER2-positive Stage IV adenocarcinoma of the lung

Track 11  Incidence of HER2 mutations in NSCLC

Track 12  Perspective on the PointBreak trial results: Pemetrexed, carboplatin and bevacizumab followed by maintenance pemetrexed/bevacizumab versus the ECOG-E4599 regimen for Stage IIIB/IV nonsquamous NSCLC

Select Excerpts from the Interview

Track 2

DR LOVE: Nanoparticle albumin-bound (nab) paclitaxel was recently approved by the FDA in combination with carboplatin for the first-line treatment of locally advanced or metastatic NSCLC in patients who are not eligible for curative surgery or RT. What role does it play in patients with squamous cell lung cancer?

DR HEYMACH: According to some preclinical suggestions, nab paclitaxel may be more active in squamous cell lung cancer than it is in nonsquamous histology because the receptor that nab paclitaxel binds to seems to be more highly expressed in squamous cell carcinoma. Mark Socinski confirmed this in a Phase III trial in which the response rate was significantly higher with nab paclitaxel/carboplatin compared to solvent–based paclitaxel/carboplatin in patients with squamous cell carcinoma (Socinski 2012; [3.1]). Although overall survival — which wasn’t the primary endpoint of the study — wasn’t significantly longer, nab paclitaxel did appear to be more active. We also know that this agent may be better tolerated than conventional paclitaxel.
Often I’ll administer nab paclitaxel when I’m concerned about neuropathy or other toxicity in patients with squamous cell carcinoma. Additional research is now under way evaluating the receptors that bind nab paclitaxel as well as other proteins involved in that cascade that seem to be more prevalent in squamous cell carcinoma. It is possible that this agent could be combined with targeted therapies, and we are currently trying to ascertain whether we can combine nab paclitaxel on an every 3-week basis with targeted agents and whether that works as well as combining it with other drugs.

We know nab paclitaxel combined with platinum alone won’t dramatically change outcomes in lung cancer as compared to standard chemotherapy, but it has advantages. And if it becomes a platform for combining targeted agents, it’s possible that it will become more widely used.

Dr. Love: What are your thoughts on the strategy of targeting MET in NSCLC?

Dr. Heymach: MET is an interesting target for lung cancer for a number of reasons. MET is often amplified in tumors that have become resistant to EGFR inhibitors. Also, after you radiate a tumor, it can upregulate MET even if the tumor didn’t express MET initially. MET is a protein that not only drives resistance to EGFR inhibitors and other pathways, but it also drives metastases — that’s how it was initially characterized in different types of cancer.

Onartuzumab (MetMAb) is one of the advanced MET-targeted agents in terms of investigations on clinical trials. In a Phase II study, it appeared as though the combination of onartuzumab and erlotinib provided a significant benefit in the subgroup of patients who expressed MET by either FISH or immunohistochemistry compared to those who didn’t express MET (Spigel 2011; [3.2]).

Those results prompted a large Phase III trial, which is ongoing (3.3). We’re eagerly awaiting results from this study because it’s clear that MET is a key player in resistance to EGFR inhibitors. We believe it may also be a mediator of resistance to angiogenesis inhibitors and other agents. In my mind I see no question that targeting MET will be part of future therapeutic strategies.
Track 6

DR LOVE: Bevacizumab is very much a part of clinical practice, but what other anti-angiogenic agents are on the horizon in NSCLC?

DR HEYMACH: One is ramucirumab, a monoclonal antibody that targets VEGF receptor 2 instead of targeting the VEGF ligand as bevacizumab does. We’ve also discovered recently that not only is VEGF receptor 2 a key driver of angiogenesis, but it also is often on tumor cells themselves so it may be a tumor-derived target in lung cancer.

You may ask why you would want to target the receptor instead of the ligand. A couple of different ligands can bind to VEGF receptor 2. So it may be the case that if you block VEGF, these other VEGF ligands may become upregulated and still activate VEGF receptor 2 even though VEGF is blocked, whereas if you block the receptor itself it may not matter which ligands are upregulated. Phase III studies evaluating ramucirumab are ongoing in lung cancer (3.4), and we’re eagerly awaiting those results to ascertain if this adds something different than targeting VEGF by itself.
Nintedanib (BIBF 1120) is another agent undergoing Phase III testing in combination with pemetrexed (NCT00806819) and docetaxel (NCT00805194). (Editor’s note: Subsequent to this interview the initial results of these studies were presented [3.5].) The exciting aspect about this agent is that it not only blocks the VEGF receptor pathways, but it also blocks multiple FGF receptors and a couple of other targets such as the PDGF receptor and RET. So we have reason to be hopeful that, either by targeting the VEGF pathway more effectively or by targeting the VEGF pathway and some of these other pathways, we may make anti-angiogenic therapy more effective.

### Select Publications


**Spigel DR et al.** The MetLUNG study: A randomized, double-blind, phase III study of onartuzumab (MetMAb) plus erlotinib versus placebo plus erlotinib in patients with advanced, MET-positive non-small cell lung cancer (NSCLC). *Proc ASCO* 2012;Abstract TPS7616.

**Spigel DR et al.** Final efficacy results from OAM4558g, a randomized phase II study evaluating MetMAb or placebo in combination with erlotinib in advanced NSCLC. *Proc ASCO* 2011;Abstract 7505.