INTERVIEW

Panos Fidias, MD

Dr Fidias is Assistant Professor of Medicine at Harvard Medical School and Medical Director of the Inpatient Oncology Unit at Massachusetts General Hospital's Thoracic Oncology Service in Boston, Massachusetts.

Tracks 1-15

Select Excerpts from the Interview

Track 1

DR LOVE: Would you comment on the issue of multiplex genomic testing and the approach used in your oncology group at Mass General?

DR FIDIAS: The platform we use is called SNaPshot. It's a multiplex DNA sequencing platform that began as a research tool in an effort to identify oncogenic drivers, with EGFR being the most frequent. Several years ago we thought it should not be simply a research tool. We believed it should be integrated into clinical practice because

being applicable strictly as a research tool requires a protocol and can therefore only be utilized in 15% to 20% of the population.

We believe that every patient with lung cancer who comes into the clinic should undergo genotyping. The SNaPshot platform has now been supplemented by FISH analysis, primarily for the ALK-translocated gene and, more recently, ROS1 rearrangement. We also test everyone who comes to the clinic for MET and other less common rearrangements and mutations.

This model proved to be successful in clinical practice (Sequist 2011; [3.1]). We obtain a lot of data, many of which are unexpected — you would not have predicted these patients to have tumors with these types of mutations. The model has now spread to other disease centers, where breast cancer and colorectal cancer are screened.

3.1

Multiplex Genotyping of Non-Small Cell Lung Cancer (NSCLC) in Clinical Practice

"While widely agreed that it is important to identify patients with EGFR and ALK given the availability of effective therapeutics, it is also noteworthy that in a short time frame at a single institution, we identified over 30 patients with less common mutations like BRAF, PIK3CA and HER2, which also have relevant candidate targeted therapies.

Among the patients with advanced or recurrent NSCLC seen within these 15 months, 22% began a genotype-specific therapy in response to SNaPshot results. We anticipate that this proportion should increase further in the future, as the scope of genotype-specific clinical trial efforts is rapidly broadening.... Overall, we have demonstrated that broad clinical genotyping with SNaPshot can be tightly integrated into clinical practice and we believe it can make a real difference for patients."

Sequist LV et al. *Ann Oncol* 2011;22(12):2616-24.

Track 11

DR LOVE: Your group reported on a variation of the ECOG-E4599 regimen with carboplatin/*nab* paclitaxel and bevacizumab. What did you see, and do you have any sense of whether the regimens differ?

DR FIDIAS: In general, no overall survival benefit is evident with *nab* paclitaxel compared to paclitaxel, but we have recorded the highest response rate to date with any regimen (Heist 2011; [3.2]), although this one is more intense and causes more myelo-

3.2

Response to Carboplatin, Nanoparticle Albumin-Bound (*Nab*) Paclitaxel and Bevacizumab in Patients with Previously Untreated Advanced Nonsquamous Non-Small Cell Lung Cancer (n = 25)

Disease control rate	17/23 (74%)
Partial response	8/23 (35%)
Stable disease	9/23 (39%)

One patient is in cycle 1, and 1 dropped out without receiving any study drug. Four patients came off study prior to first restaging: 1 for painful bony disease requiring radiation therapy and 3 for toxicity (perforated diverticulitis, liver function abnormalities and nausea and vomiting).

Heist RS et al. *Proc ASCO* 2012;**Abstract e18016**.

suppression and fatigue. A motivated person can get through it, but it's too early to tell whether *nab* paclitaxel should replace regular paclitaxel.

Track 15

DR LOVE: Would you discuss the SELECT study, which you worked on with Dr Lecia Sequist? What did you report, and how do you interpret those results?

DR FIDIAS: This is an adjuvant trial for patients with EGFR mutation-positive disease, up to Stage IIIA, who can receive erlotinib either immediately if they don't receive chemotherapy or at the end of chemotherapy if the standard treatment for their tumor stage is to receive adjuvant chemotherapy after resection. It's a single-arm Phase II study, so it will not be conclusive, but the disease-free survival rate appears to be remarkably good at 94% after 2 years (Neal 2012; [3.3]).

It's still early for this population, and we have to see how the results fall along historical lines, but I would not be surprised if this regimen became a new standard. My sense is that EGFR TKI therapy will be moved earlier in the treatment algorithm. It's effective, and I can envision using TKIs in both the adjuvant and the metastatic settings. Eventually we'll need a Phase III study to find out whether we have a new standard. Until such time, I would not use this approach outside of a trial setting. ■

3.3

SELECT Study: A Multicenter Phase II Trial of Adjuvant Erlotinib for Patients with EGFR Mutation-Positive Non-Small Cell Lung Cancer

Disease-free survival	94% (95% CI: 79.5%-98.5%)*	
Select adverse events	Any (%)	Grade ≥3 (%)
Rash†	89	17
Diarrhea†	78	3
Fatigue†	61	6

* Median duration of follow-up: 2.5 years; † Toxicities leading to dose reductions

Neal JW et al. *Proc ASCO* 2012;**Abstract 7010**.

SELECT PUBLICATIONS

Heist RS et al. **Phase II trial of carboplatin, Abraxane, and bevacizumab in NSCLC.** *Proc ASCO* 2011;**Abstract e18016**.

Neal JW et al. **The SELECT study: A multicenter phase II trial of adjuvant erlotinib in resected epidermal growth factor receptor (EGFR) mutation-positive non-small cell lung cancer (NSCLC).** *Proc ASCO* 2012;**Abstract 7010**.

Oxnard GR et al. **Maintained sensitivity to EGFR tyrosine kinase inhibitors in EGFR-mutant lung cancer recurring after adjuvant erlotinib or gefitinib.** *Clin Cancer Res* 2011;17(19):6322-8.

Sequist LV et al. **Implementing multiplexed genotyping of non-small-cell lung cancers into routine clinical practice.** *Ann Oncol* 2011;22(12):2616-24.

Shao H et al. **Improved response to *nab*-paclitaxel compared with Cremophor-solubilized paclitaxel is independent of secreted protein acidic and rich in cysteine expression in non-small cell lung cancer.** *J Thorac Oncol* 2011;6(6):998-1005.

Socinski MA et al. **Weekly *nab*-paclitaxel in combination with carboplatin versus solvent-based paclitaxel plus carboplatin as first-line therapy in patients with advanced non-small-cell lung cancer: Final results of a phase III trial.** *J Clin Oncol* 2012;30(17):2055-62.

Su Z et al. **A platform for rapid detection of multiple oncogenic mutations with relevance to targeted therapy in non-small-cell lung cancer.** *J Mol Diagn* 2011;13(1):74-84.