INTERVIEW

Alice Shaw, MD, PhD

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Tracks 1-14

Select Excerpts from the Interview

Track 6

DR LOVE: What is known now about the clinical features of patients with NSCLC who harbor the EML4-ALK fusion gene, which is one of the newest molecular targets in lung cancer?

DR SHAW: They share certain features with patients who have EGFR mutations, in particular never smoker or light smoker status, and almost all have adenocarcinoma histology (Shaw 2009; [2.1]). A slight enrichment of

ALK translocations probably exists in Asians, although it is not as significant as with EGFR mutations.

In evaluating our study along with data from several studies published in other countries, overall the frequency of ALK in NSCLC is roughly three to four percent of all patients (Shaw 2009). When we evaluated the patient population at Massachusetts General Hospital and studied the patients who were never smokers or light smokers, we found the frequency of ALK translocations to be higher — roughly 10 to 15 percent (Shaw 2009).

You can enrich further if you isolate the patients who are never smokers or light smokers and are known not to harbor EGFR mutations. In that subset, we see ALK translocations in approximately 30 percent of patients.

2.1

Demographic Features of Patients by EML4-ALK and EGFR Mutation

Characteristic	ALK+ (n = 19)	EGFR+ (n = 31)	ALK WT/WT*
Mutation-positive†	13%†	22%†	65%†
Age (median)	52 y	66 y	64 y
Male gender	58%	26%	32%
Never smoker	74%	68%	26%
Light smoker	26%	19%	16%
Smoker	0%	13%	57%

* ALK wild type/EGFR wild type
† ALK-mutant tumors were nonoverlapping with EGFR-mutant tumors.

The majority of tumors were **adenocarcinomas**, with ALK but not EGFR-mutant tumors strongly associated with **signet-ring cell subtype**.

Shaw AT et al. *J Clin Oncol* 2009;27(26):4247-53.

Tracks 7, 11

DR LOVE: Would you discuss the data on the clinical activity observed with PF-02341066, the small-molecule c-MET inhibitor that targets the EML4-ALK fusion gene, that your group recently reported?

DR SHAW: The first data on the safety/toxicity and efficacy were reported by Dr Eunice Kwak at ASCO 2009. The vast majority of patients had stable disease or a response, although a handful of patients did not respond to PF-02341066 despite having the ALK translocation.

The waterfall plot of the initial 18 patients or so was impressive. The response rate was close to 60 percent, and the disease control rate — which is equivalent to the number of complete responses, partial responses (PR) and stable disease — was approximately 80 percent (Kwak 2009).

At the recent AACR-IASLC joint meeting, Dr Camidge presented the most up-to-date results on efficacy. We have now enrolled more than 70 patients with metastatic NSCLC harboring the ALK translocation.

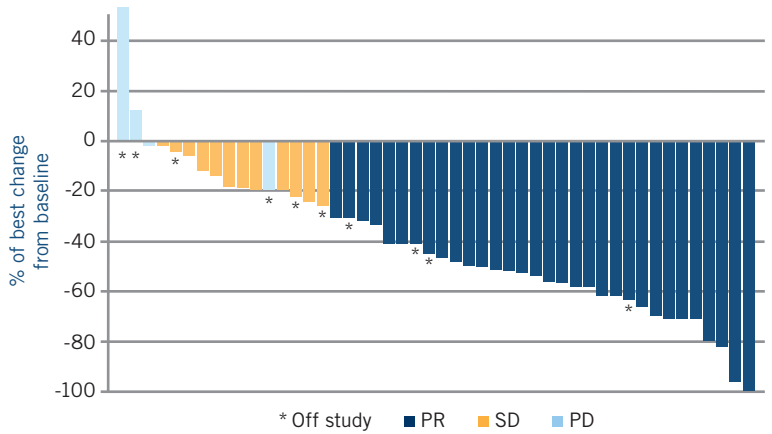
The objective response rate among these patients is now 64 percent, and the disease control rate is close to 90 percent (Camidge 2010; [2.2]). The median duration of treatment to date has been about 28 weeks, but most of the patients who have achieved a PR are still on the trial and are faring well. One patient is now approaching 15 months of PF-02341066 treatment.

DR LOVE: What is the current status of clinical research with this agent?

DR SHAW: We have now moved into a second-line Phase III trial for patients with metastatic NSCLC and proven ALK translocations. Patients will be randomly assigned to receive either PF-02341066 or standard chemotherapy, which on this trial will be pemetrexed or docetaxel. ■

2.2

Tumor Response to PF-02341066 in Patients with Pretreated NSCLC and ALK Fusion Oncogenes



Objective response rate = 64% CR + PR + SD = 95%

Median progression-free survival not yet reached

With permission from Camidge DR et al. *Proc AACR-IASLC* 2010. No abstract available

SELECT PUBLICATIONS

Camidge DR et al. **Addressing right drug-right target-right patients in phase I studies to accelerate bench to clinical benefit time: ALK gene rearrangements and the development of PF-02341066 in NSCLC.** *Proc AACR-IASLC* 2010. No abstract available

Kwak EL et al. **Clinical activity observed in a phase I dose escalation trial of an oral c-Met and ALK inhibitor, PF-02341066.** *Proc ASCO* 2009;**Abstract 3509**.

Shaw AT et al. **Clinical features and outcomes of patients with non-small-cell lung cancer who harbor EML4-ALK.** *J Clin Oncol* 2009;27(26):4247-53.