INTERVIEW

Gregory J Riely, MD, PhD

Dr Riely is Assistant Attending at Memorial Sloan-Kettering Cancer Center in New York, New York.

Tracks 1-17

Track 1 **Case discussion:** A 70-year-old woman and never smoker with metastatic EGFR-mutant NSCLC receives afatinib on a clinical trial and remains progression free two years later

Track 2 Mutual exclusivity of K-ras, EGFR and ALK mutations in NSCLC

Track 3 Biomarker evaluation in lieu of smoking status

Track 4 Duration of disease control with reversible and irreversible EGFR TKIs in advanced, EGFR-mutant NSCLC

Track 5 Tolerability and side effects of afatinib

Track 6 Activity of afatinib in patients with advanced NSCLC after chemotherapy and an EGFR TKI in the LUX-Lung 1 study

Track 7 **Case discussion:** A 55-year-old woman and oligosmoker with EGFR and K-ras wild-type, Stage IV adenocarcinoma of the lung involving pleura and bone receives carboplatin/paclitaxel/bevacizumab followed by maintenance bevacizumab for two years

Track 8 Crizotinib for ALK-positive advanced NSCLC

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Track 10 Zoledronic acid, bevacizumab and osteonecrosis of the jaw

Track 11 Choice of first-line therapy and continuation or switch maintenance therapy for advanced NSCLC in the current era

Track 12 Potential role of *nab* paclitaxel as treatment for advanced squamous cell NSCLC

Track 13 Lack of concordance among pathologists in identification of adenocarcinoma, squamous cell and mixed histology NSCLC

Track 14 Treatment decision-making for adjuvant chemotherapy doublets in NSCLC

Track 15 Evaluating targeted agents as adjuvant therapy for EGFR-mutant and ALK-mutant NSCLC

Track 16 Ongoing neoadjuvant and adjuvant strategies evaluating the role of bevacizumab in early-stage NSCLC

Track 17 **Case discussion:** A 55-year-old woman and smoker with a Stage IIIA, EGFR wild-type adenocarcinoma of the lung receives neoadjuvant cisplatin/docetaxel, refuses surgery and remains disease free two years after definitive radiation therapy

Select Excerpts from the Interview

Tracks 2-3

DR LOVE: What is the approach to biomarker evaluation at your institution? Do you await results on EGFR mutation status before testing for ALK translocation?

DR RIELY: We use a staged evaluation system in which we initially evaluate patients for EGFR and K-ras mutations in parallel. If a patient has either an EGFR mutation or a K-ras mutation, we stop there because we know that those are driver mutations, which are unlikely to occur in tandem with an ALK translocation. If both of those results are negative, then we perform ALK FISH analysis, testing for a variety of rearrangements that can lead to activation of ALK, with EML4-ALK being the most common rearrangement.

DR LOVE: Does smoking history alter your approach to workup?

DR RIELY: No, we don't assume bias based on smoking history. We realize that even patients with significant smoking histories can have EGFR mutations or ALK rearrangements. Because patients with heavy smoking histories represent such a large proportion of our patients, we'd be missing a large number of patients if we didn't test them.

Track 9

DR LOVE: What are your thoughts on re-treatment with erlotinib? What do we know about repeat responses in patients who've previously received an EGFR TKI?

DR RIELY: For patients with EGFR mutation-positive disease who respond well to erlotinib and then develop progressive disease, our first-line management would be enrollment on a clinical trial, but even at a large center like ours, a clinical trial is not always available. You have to come up with treatment decisions off protocol. For patients with EGFR mutations who experience a clear response to erlotinib, I continue erlotinib and add chemotherapy.

3.1

Changes in Tumor After EGFR TKI Discontinuation and Reinitiation in Patients with Non-Small Cell Lung Cancer Previously Responding to Erlotinib or Gefitinib

Median/mean change in:	After stopping EGFR TKI	After restarting EGFR TKI
Tumor diameter	+9%/+9%	-1%/1%
Tumor volume	+50%/+61%	-1%/-4%
Tumor SUV(max)	+18%/+23%	-4%/-11%

Riely GJ et al. *Clin Cancer Res* 2007;13(17):5150-5.

In the absence of a randomized trial, I rely on results from a small study performed at our institution in which we selected patients with EGFR mutations who were developing resistance to EGFR TKI therapy. When we stopped treatment, we saw a relatively clear flare in tumor size. Their tumors grew and became more FDG avid on PET scans.

When we restarted erlotinib or gefitinib, the tumors either shrank or stabilized, and a number of patients again experienced some improvement in symptoms (Riely 2007; [3.1]).

Track 12

DR LOVE: What role do you envision for nanoparticle albumin-bound (*nab*) paclitaxel in advanced NSCLC?

DR RIELY: *Nab* paclitaxel is as efficacious as paclitaxel in NSCLC, and reported data are beginning to suggest that *nab* paclitaxel may work a little better for patients with squamous cell lung cancer (Socinski 2010; [3.2]). As we move forward, we need some prospective trials for patients with squamous cell lung cancer only.

Many of the big advancements in lung cancer — EGFR mutations, ALK, pemetrexed, bevacizumab — are for the most part restricted to patients with adenocarcinoma. Although the number of patients with squamous cell carcinoma is small, they still make up a significant proportion of patients with NSCLC, and an agent like *nab* paclitaxel may be a good option in that setting.

DR LOVE: What tends to be your initial systemic therapy for metastatic squamous cell carcinoma? Do you currently use *nab* paclitaxel in this setting?

DR RIELY: I typically administer gemcitabine/cisplatin if possible, but gemcitabine/carboplatin is also a reasonable option. I prefer that approach to carboplatin/paclitaxel. Our institution is somewhat restrictive in allowing us to use albumin-bound paclitaxel. The setting in which I've used it a number of times is for patients who have a hypersensitivity reaction to paclitaxel or docetaxel. Then I make the switch to *nab* paclitaxel.

3.2

Efficacy of Carboplatin/*Nab* Paclitaxel versus Carboplatin/Paclitaxel as First-Line Therapy for Advanced Non-Small Cell Lung Cancer

Response rate by histological subtype	Carboplatin/ paclitaxel	Carboplatin/ *nab* paclitaxel	Response ratio*	*p*-value
All patients (n = 531; 521)	25%	33%	1.31	0.005
Squamous (n = 221; 228)	24%	41%	—	<0.001
Nonsquamous (n = 310; 292)	25%	26%	—	0.808

* Response ratio >1 favors *nab* paclitaxel

Socinski MA et al. *Proc ASCO* 2010;**Abstract LBA7511**.

Track 16

DR LOVE: What are your thoughts on ongoing research strategies evaluating the role of bevacizumab in early-stage NSCLC?

DR RIELY: The ECOG-E1505 trial is evaluating whether the addition of bevacizumab in the adjuvant setting provides a benefit. The study randomly assigns patients with resected lung cancer to chemotherapy alone or chemotherapy and bevacizumab. That's certainly the biggest trial ongoing in the adjuvant arena and certainly one with the most anticipated results.

At our institution, we've considered incorporating bevacizumab into induction chemotherapy. We know from the ECOG-E4599 study data that the addition of bevacizumab to carboplatin/paclitaxel significantly increases response rate, progression-free survival and overall survival (Sandler 2006).

We are evaluating bevacizumab with cisplatin/docetaxel (BEACON, NCT00130780). One interesting aspect of this trial is that we administer the first dose of bevacizumab a few weeks before the first dose of chemotherapy to study what effect bevacizumab has on its own. Tumor shrinkage with single-agent bevacizumab has been reported (Price 2009).

These are not partial responses by any measure for most patients, although the occasional patient has a tumor that cavitates as a result of that dose of bevacizumab.

After that single dose of bevacizumab, patients receive four cycles of neoadjuvant cisplatin/docetaxel and bevacizumab, followed by surgery and adjuvant bevacizumab alone. Not many significant toxicities have been associated with preoperative bevacizumab. ■

SELECT PUBLICATIONS

Miller VA et al. **Phase IIB/III double-blind randomized trial of afatinib (BIBW 2992, an irreversible inhibitor of EGFR/HER1 and HER2) + best supportive care (BSC) versus placebo + BSC in patients with NSCLC failing 1–2 lines of chemotherapy and erlotinib or gefitinib (LUX-Lung 1).** *Proc ESMO* 2010;**Abstract LBA1**.

Price K et al. **Phase II study of induction and adjuvant bevacizumab in patients with stage IB-IIIA non-small cell lung cancer (NSCLC) receiving induction docetaxel and cisplatin.** *Proc ASCO* 2009;**Abstract 7531**.

Riely GJ et al. **Prospective assessment of discontinuation and reinitiation of erlotinib or gefitinib in patients with acquired resistance to erlotinib or gefitinib followed by the addition of everolimus.** *Clin Cancer Res* 2007;13(17):5150-5.

Sandler A et al. **Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer.** *N Engl J Med* 2006;355(24):2542-50.

Socinski MA et al. **Results of a randomized, phase III trial of *nab*-paclitaxel (*nab*-P) and carboplatin (C) compared with Cremophor-based paclitaxel (P) and carboplatin as first-line therapy in advanced non-small cell lung cancer (NSCLC).** *Proc ASCO* 2010;**Abstract LBA7511**.