INTERVIEW

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Tracks 1-7

Track 1 Erlotinib as first-line treatment for advanced EGFR-mutant NSCLC

Track 2 Forecasting future opportunities and challenges in the development of new therapeutic targets

Track 3 Potential use of the fibroblast growth factor receptor as a therapeutic target in patients with squamous cell carcinoma of the lung

Track 4 **Case discussion:** A 40-year-old woman and light smoker with EGFR-mutant adenocarcinoma of the lung with liver and multiple bone metastases rapidly develops acquired resistance to gefitinib

Track 5 Activity of afatinib/cetuximab in patients with NSCLC and acquired resistance to EGFR TKIs

Track 6 **Case discussion:** A 29-year-old woman and light smoker with EGFR wild-type, K-ras wild-type, ALK-negative metastatic adenocarcinoma of the lung is found to have ALK-positive disease upon tumor rebiopsy with IHC

Track 7 Perspective on the role of maintenance therapy in advanced NSCLC

Select Excerpts from the Interview

Track 1

DR LOVE: At ASCO 2011, you presented the findings of the EURTAC trial conducted in Europe, which compared the EGFR TKI erlotinib to chemotherapy as first-line treatment for EGFR mutation-positive disease. Would you discuss those findings?

DR ROSELL: The primary endpoint of the EURTAC trial was to demonstrate the superiority of EGFR TKI therapy with erlotinib compared to chemotherapy for PFS in patients who were screened for EGFR mutations.

The trial was positive, and I believe this could be of great relevance at the administrative level for health authorities to recognize that the new approach to first-line therapy for patients with EGFR-mutant NSCLC should be EGFR TKIs (Rosell 2011a; [3.1]).

3.1

EURTAC: A Phase III Trial of Erlotinib versus Chemotherapy for Patients with Advanced Non-Small Cell Lung Cancer with EGFR Activating Mutations

	Erlotinib (n = 86)	Chemotherapy (n = 87)	Hazard ratio	*p*-value
Median progression-free survival	9.7 mo	5.2 mo	0.37	<0.0001
Median overall survival	22.9 mo	18.8 mo	0.80	0.42
Best overall response rate	58%	15%	—	—
Complete response rate	2%	0%	—	—
Partial response rate	56%	15%	—	—
Disease control rate	79%	66%	—	—

Rosell R et al. *Proc ASCO* 2011a;**Abstract 7503**.

Track 5

DR LOVE: Some interesting data were also presented at ASCO 2011 on the irreversible TKI afatinib combined with cetuximab for patients with NSCLC and acquired resistance to erlotinib or gefitinib. What is your take on the biology of this combination?

DR ROSELL: That's an important question. Afatinib is a potent second-generation TKI that also targets HER2 and EGFR. We do not yet have enough information on the degree of efficacy of afatinib in patients with acquired resistance to erlotinib or gefitinib, nor do we have enough data on the benefit of afatinib in the presence of the T790M mutation. Other clinical trials with afatinib should be presented within the next year.

3.2

Activity of Afatinib and Cetuximab in Patients with Non-Small Cell Lung Cancer with Acquired Resistance to Erlotinib or Gefitinib

Best response	T790M-positive (n = 26)	T790M-negative (n = 14)	T790M unknown (n = 3)	No EGFR mutation (n = 2)
Any partial response (PR)	50%	57%	67%	—
Confirmed PR	35%	50%	67%	—
Stable disease (SD)	42%	36%	33%	—
Clinical response (any PR + SD)	92%	93%	100%	100%

Select adverse events (n = 47)	All grades	Grade ≥3
Rash	89%	6%
Diarrhea	74%	6%

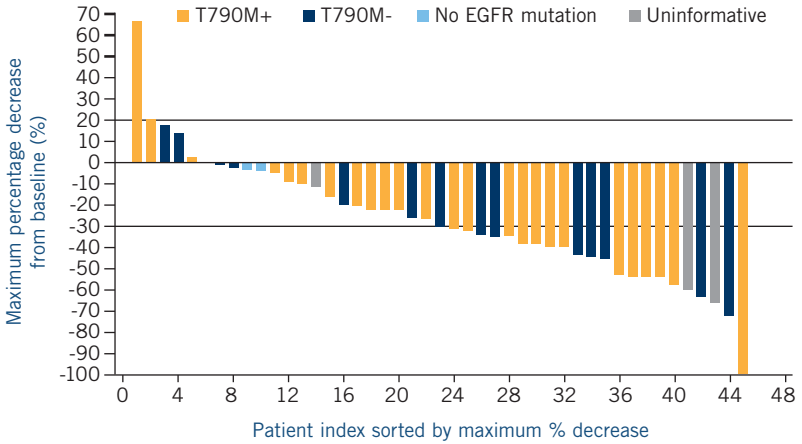
Janjigian YY et al. *Proc ASCO* 2011;**Abstract 7525**.

In this study of afatinib with cetuximab for patients in this setting, the authors were able to demonstrate an approximate 50% response rate. Interestingly, these responses were reported equally in patients with T790M acquired resistance mutations at the time of disease progression and those with clinical progression and no evidence of T790M mutations (Janjigian 2011; [3.2, 3.3]).

We have to keep in mind that other mechanisms of resistance to erlotinib or gefitinib are in the process of being identified, and we hope they will provide useful information regarding appropriate new forms of treatment. ■

3.3

Best Response at Maximum Tolerated Dose to Afatinib/Cetuximab for Patients with Advanced Non-Small Cell Lung Cancer and Resistance to an EGFR Tyrosine Kinase Inhibitor



With permission from Janjigian YY et al. *Proc ASCO* 2011;**Abstract 7525**.

SELECT PUBLICATIONS

Janjigian YY et al. **Activity and tolerability of afatinib (BIBW 2992) and cetuximab in NSCLC patients with acquired resistance to erlotinib or gefitinib.** *Proc ASCO* 2011;**Abstract 7525**.

Metro G, Crinò L. **The LUX-Lung clinical trial program of afatinib for non-small-cell lung cancer.** *Expert Rev Anticancer Ther* 2011;11(5):673-82.

Murakami H et al. **Phase I study of continuous afatinib (BIBW 2992) in patients with advanced non-small cell lung cancer after prior chemotherapy/erlotinib/gefitinib (LUX-Lung 4).** *Cancer Chemother Pharmacol* 2011;[Epub ahead of print].

Rosell R et al. **Erlotinib versus chemotherapy (CT) in advanced non-small cell lung cancer (NSCLC) patients (p) with epidermal growth factor receptor (EGFR) mutations: Interim results of the European erlotinib versus chemotherapy (EURTAC) phase III randomized trial.** *Proc ASCO* 2011a;**Abstract 7503**.

Rosell R et al. **Pretreatment EGFR T790M mutation and BRCA1 mRNA expression in erlotinib-treated advanced non-small-cell lung cancer patients with EGFR mutations.** *Clin Cancer Res* 2011b;17(5):1160-8.