INTERVIEW

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Tracks 1-10

Select Excerpts from the Interview

Tracks 2-4

DR LOVE: What are your thoughts on the data from the recent Canadian trial of adjuvant gefitinib for unselected patients with completely resected NSCLC?

DR PEREZ-SOLER: In the CAN-NCIC-BR19 study of adjuvant gefitinib, no advantage was evident with the use of gefitinib, and patients who received gefitinib may have experienced a disadvantage (Goss 2010; [4.1]). In patients with EGFR and K-ras mutations, the outcomes were not predictive or prognostic of survival. When we analyze data among patients with EGFR-mutated tumors, many times I question whether the assay technologies are appropriate or even correct. I believe a technical aspect exists that we need to consider.

DR LOVE: What's new in terms of the skin rash associated with the use of EGFR TKIs, both as a predictor of response and in terms of management?

4.1

Trial Schema and Outcomes in CAN-NCIC-BR19: A Phase III Study of Adjuvant Gefitinib for Patients with Completely Resected Non-Small Cell Lung Cancer (NSCLC)

Accrual: 503 (Closed)[1]

Eligibility

- Resected Stage IB, II or IIIA NSCLC
- ECOG PS 0 to 2

R

Gefitinib (n = 251)
Daily x 2 years

Placebo (n = 252)
Daily x 2 years

[1] Accrual was closed in April 2005 because of the inferiority of the gefitinib arm.

Patients were stratified by stage, histology, postoperative radiation therapy, sex and adjuvant chemotherapy.

Overall survival and disease-free survival

	Gefitinib (n = 251)	Placebo (n = 252)	Hazard ratio	*p*-value
Median overall survival	5.1 years	Not reached	1.23	0.136
Median disease-free survival	4.2 years	Not reached	1.22	0.152

Multivariate analysis

- Age ≥ 65 years and tumor size ≥ 4 cm ($p = 0.0003$) were significantly associated with shorter survival.
- Gefitinib remained not significant, but a trend suggested that it may be harmful ($p = 0.097$).

Goss GD et al. *Proc ASCO* 2010;**Abstract LBA7005**.

DR PEREZ-SOLER: Oral tetracyclines seem to reduce the incidence of severe rashes without affecting the outcome. Reducing the dose of the EGFR TKI may be another option, as such high doses may not be necessary.

Several analyses have shown that patients who develop severe rashes have better outcomes. These findings led to the thinking that dose intensity may be important or that responders have a predisposition to developing bad rashes. An interesting question that has not been addressed is whether the intensity of the rash correlates with outcome in the patients with mutations. I believe this is an area we should study further.

DR LOVE: I understand you've been involved in developing a specific cream to treat this rash.

DR PEREZ-SOLER: We developed phosphatase inhibitors. Theoretically, the alteration of balance between kinase and phosphatase by a phosphate inhibitor should rescue the skin. We selected menadione — vitamin K3 — and formulated it into a cream. The cream has been licensed to a company that is developing it and conducting the appropriate studies.

Tracks 7-8

DR LOVE: How do you approach the use of bevacizumab as first-line therapy for metastatic NSCLC?

DR PEREZ-SOLER: I administer bevacizumab regularly as front-line therapy. In general, I use bevacizumab with carboplatin/paclitaxel because the AVAiL data — bevacizumab with gemcitabine/cisplatin — were not robust (Reck 2009). With certain patients I may also discuss the possibility of using bevacizumab with pemetrexed. I believe the probability is high that the pemetrexed regimen will be the best regimen, although the data have not yet been shown.

DR LOVE: How do you approach the issue of maintenance therapy, particularly for patients who are receiving carboplatin/paclitaxel/bevacizumab or carboplatin/pemetrexed/bevacizumab?

DR PEREZ-SOLER: We normally administer bevacizumab as maintenance therapy because it makes biological sense to do so, although no study ever compared bevacizumab maintenance therapy to no maintenance therapy.

Two other agents now approved for maintenance treatment of locally advanced or advanced NSCLC are pemetrexed (Belani 2009) and erlotinib (Cappuzzo 2010). We all believe that the associated data are positive, but what do they mean? I believe the results of the maintenance trials are positive because many patients on the control arms never receive further therapy. Many patients don't receive maintenance therapy because they develop bone metastases, spinal cord compressions, et cetera.

If I see a patient who I believe is at high risk of never returning or is noncompliant or if the individual may have an EGFR mutation — for example, a former light smoker who cannot be tested for the mutation — I might administer erlotinib maintenance therapy. If the patient is a heavy smoker and I believe I will lose the patient to follow-up, I may administer pemetrexed. I believe pemetrexed is an option, but most thoracic oncologists will not administer it as a rule. It's something we consider on a case-by-case basis. ■

SELECT PUBLICATIONS

Belani CP et al. **Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care: A randomized phase III study in advanced NSCLC.** *Proc ASCO* 2009;**Abstract CRA8000**.

Cappuzzo F et al. **Erlotinib as maintenance treatment in advanced non-small-cell lung cancer: A multicentre, randomised, placebo-controlled phase 3 study.** *Lancet Oncol* 2010;11(6):521-9.

Goss GD et al. **A phase III randomized, double-blind, placebo-controlled trial of the epidermal growth factor receptor inhibitor gefitinib in completely resected stage IB-IIIA non-small cell lung cancer (NSCLC): NCIC CTG BR.19.** *Proc ASCO* 2010;**Abstract LBA7005**.

Reck M et al. **Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small-cell lung cancer: AVAil.** *J Clin Oncol* 2009;27(8):1227-34.