INTERVIEW

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Tracks 1-11

Select Excerpts from the Interview

Tracks 3-4

DR LOVE: The Phase III ECOG-E4599 study previously demonstrated a significant survival advantage with the addition of bevacizumab to carboplatin/paclitaxel versus chemotherapy alone for patients with untreated advanced NSCLC (Sandler 2006). Would you talk about your recent paper on the clinical outcomes with maintenance bevacizumab for patients on that study (Lopez-Chavez 2012)?

DR SANDLER: After the ECOG-E4599 study, a question arose about the contribution of the induction regimen versus maintenance bevacizumab to the survival advantage. This was a retrospective analysis to address the role of maintenance bevacizumab in the ECOG-E4599 study.

A landmark analysis was conducted for patients in both groups who were progression free after completing 6 cycles of induction therapy. The survival of patients who received bevacizumab maintenance after induction with carboplatin/paclitaxel/

bevacizumab was compared to that of those patients who received induction with carboplatin/paclitaxel alone. The results indicated that patients who received bevacizumab maintenance had significantly better progression-free and overall survival (Lopez-Chavez 2012; [4.1]).

4.1

Bevacizumab (Bev) Maintenance Therapy for Patients with Advanced Non-Small Cell Lung Cancer in the ECOG-E4599 Study: Results of an Exploratory Analysis

Survival	CP + bev induction followed by bev maintenance (n = 217)	CP induction + no maintenance (n = 134)
Progression-free survival	4.4 mo	2.8 mo
	HR = 0.64, $p < 0.001$	
Overall survival	12.8 mo	11.4 mo
	HR = 0.75, $p = 0.03$	

C = carboplatin; P = paclitaxel; HR = hazard ratio

Lopez-Chavez A et al. *J Thorac Oncol* 2012;7(11):1707.

4.2

PointBreak: A Phase III Trial of Pemetrexed (Pem)/Carboplatin (Cb)/Bevacizumab (B) Followed by Maintenance Pem + B versus Paclitaxel (Pac)/Cb/B Followed by Maintenance B for Patients with Advanced Nonsquamous Non-Small Cell Lung Cancer

All patients	Pem/Cb/B (n = 472)	Pac/Cb/B (n = 467)	HR	*p*-value
Median PFS	6.0 mo	5.6 mo	0.83	0.012
Median OS	12.6 mo	13.4 mo	1.00	0.949
Overall response rate	34.1%	33.0%	NR	NR
Maintenance phase	(n = 292)	(n = 298)		
Median PFS	8.6 mo	6.9 mo	NR	NR
Median OS	17.7 mo	15.7 mo	NR	NR
	Pem/Cb/B (n = 442)		**Pac/Cb/B** (n = 443)	
Adverse events	Grade 1 or 2	Grade 3 or 4	Grade 1 or 2	Grade 3 or 4
Anemia*	31.0%	14.5%	24.4%	2.7%
Thrombocytopenia*	17.9%	23.3%	17.2%	5.6%
Neutropenia*	14.7%	25.8%	8.4%	40.6%
Hemorrhage – GI/pulmonary†	3.6%	1.8%	3.8%	0.5%
Thromboembolic event	0.5%	3.2%	0.2%	2.0%
Neuropathy/sensory*	11.8%	0%	35.7%	4.1%
Alopecia‡	6.6%	—	36.8%	—

HR = hazard ratio; PFS = progression-free survival; OS = overall survival; NR = not reported
* Significant difference between arms for Grade 3 and 4 toxicities
† Grade 5 events: Pac/Cb/B = 0.7%; Pem/Cb/B = 0.5%
‡ Maximum grade is Grade 2

Conclusion: The primary endpoint of superior OS was not met in this trial, although Pem/Cb/B improved PFS. Toxicity profiles differed and both regimens demonstrated tolerability.

Patel J et al. Chicago Multidisciplinary Symposium in Thoracic Oncology 2012;**Abstract LBPL1**.

DR LOVE: Would you also discuss the results from the PointBreak trial for patients with advanced NSCLC?

DR SANDLER: The PointBreak study evaluated pemetrexed, carboplatin and bevacizumab followed by maintenance pemetrexed/bevacizumab versus the ECOG-E4599 regimen of paclitaxel, carboplatin and bevacizumab followed by bevacizumab maintenance (Patel 2012; [4.2]). The study reported no difference between the 2 arms with respect to overall survival, the primary endpoint.

The toxicities between the 2 arms were different, and overall both regimens were well tolerated. The taxane arm had a higher incidence of neurologic toxicity and alopecia, whereas the pemetrexed group experienced more hematologic toxicity.

The taxane regimen uses fewer drugs and is less expensive, so one could argue that it is superior. However, the pemetrexed regimen has a role for patients who don't want a taxane because of the side effects, such as hair loss and neuropathy.

Of course, in the maintenance phase you do have 2 agents versus 1, the latter of which is obviously less expensive. Both were well tolerated. These are both still reasonable options. And I don't necessarily look at the cost as much as my role as a physician to administer the best therapy for the patient.

Track 5

DR LOVE: You recently published a review of the incidence of CNS bleeding with anti-VEGF therapy in patients with NSCLC and brain metastases (Sandler 2012; [4.3]). What are your thoughts on the use of bevacizumab for patients with brain metastases?

DR SANDLER: Patients with brain metastases were previously considered ineligible for bevacizumab because of the concern about cerebral and pulmonary hemorrhage. Subsequently, studies have clearly shown that patients with treated brain metastases are eligible for treatment with bevacizumab (4.3). However, we have less evidence to support its use for patients with untreated brain metastases.

DR LOVE: Do you delay starting bevacizumab for patients who are receiving radiation therapy?

4.3

An Evidence-Based Review of the Incidence of CNS Bleeding with Anti-VEGF Therapy in Patients with Non-Small Cell Lung Cancer and Brain Metastases

- Recently, the prospective, randomized Phase III ATLAS trial, the open-label Phase II PASSPORT trial, the single-arm Phase IV SAiL study and the observational cohort study ARIES in NSCLC have provided data on the incidence of CNS hemorrhage in large patient populations, reflective of community practice.
- This literature review of patients with NSCLC and brain metastases receiving anti-VEGF therapy **showed no significantly increased risk of CNS hemorrhage for patients** with emerging (previously untreated) or pretreated CNS metastases.
- Clinical trial data indicate that anti-VEGF therapy can be considered for patients with NSCLC with emerging or pretreated CNS metastases.

Sandler A et al. *Lung Cancer* 2012;78(1):1-7.

DR SANDLER: For patients with an isolated lesion who are receiving stereotactic radiation therapy and have not had any problems with bleeding, I would start bevacizumab relatively soon after the radiation therapy. With patients who have multiple lesions or if there is a concern that would require a follow-up scan, I would consider waiting until the second cycle of chemotherapy before adding bevacizumab.

Tracks 7-8

DR LOVE: Nanoparticle albumin-bound (*nab*) paclitaxel was recently approved in combination with carboplatin for the first-line treatment of locally advanced or metastatic NSCLC in patients who are not eligible for curative surgery or radiation therapy. What is your take on the role of this agent in lung cancer?

DR SANDLER: *Nab* paclitaxel is a reformulation of paclitaxel without the Cremophor® vehicle. With *nab* paclitaxel, hypersensitivity reactions are less of a concern. Additionally, it does not have to be administered with steroids and is thought to penetrate the tumor better.

Higher response rates were achieved with *nab* paclitaxel versus solvent-based paclitaxel, particularly for patients with squamous cell histology. No difference was observed in terms of progression-free and overall survival (Socinski 2012, 2013; [4.4]).

For elderly patients, those with diabetes who want to avoid steroids or those who may not be eligible for pemetrexed based on poor renal function, *nab* paclitaxel has a role. It would also be a consideration for patients with squamous cell carcinoma. ■

4.4

Phase III Trial of *Nab* Paclitaxel/Carboplatin (*Nab*-PC) versus Solvent-Based Paclitaxel/Carboplatin (sb-PC) as First-Line Therapy for Patients with Advanced Non-Small Cell Lung Cancer

	Nab-PC	sb-PC	*p*-value
Overall response rate			
All patients (n = 521, 531)	33%	25%	0.005
Squamous (n = 229, 221)	41%	24%	<0.001
Nonsquamous (n = 292, 310)	26%	25%	0.808
Median progression-free survival			
All patients (n = 521, 531)	6.3 mo	5.8 mo	0.214
Patients aged ≥70 y (n = 74, 82)	8.0 mo	6.8 mo	0.134
Median overall survival			
All patients (n = 521, 531)	12.1 mo	11.2 mo	0.271
Patients aged ≥70 y (n = 74, 82)	19.9 mo	10.4 mo	0.009

Socinski MA et al. *Ann Oncol* 2013;24(2):314-21; Socinski MA et al. *J Clin Oncol* 2012;30(17):2055-62.

SELECT PUBLICATIONS

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. **Safety and efficacy of weekly *nab*®-paclitaxel in combination with carboplatin as first-line therapy in elderly patients with advanced non-small-cell lung cancer.** *Ann Oncol* 2013;24(2):314-21.

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.