



INTERVIEW

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Tracks 1-13

- Track 1** Maintenance therapy with pemetrexed (JMEN and PARAMOUNT) or erlotinib (SATURN) in advanced NSCLC
- Track 2** PointBreak study: Pemetrexed/carboplatin/bevacizumab → maintenance pemetrexed/bevacizumab versus paclitaxel/carboplatin/bevacizumab → maintenance bevacizumab in Stage IIIB or IV nonsquamous NSCLC
- Track 3** ECOG-E5508 trial: Maintenance pemetrexed, bevacizumab or the combination after first-line carboplatin/paclitaxel/bevacizumab in advanced nonsquamous NSCLC
- Track 4** Approach to maintenance therapy for bevacizumab-eligible patients in clinical practice
- Track 5** **Case discussion:** A 72-year-old patient with EGFR/ALK wild-type, KRAS-mutant advanced NSCLC who receives an anti-PD-1 antibody on a clinical trial after disease progression on carboplatin/pemetrexed → maintenance pemetrexed
- Track 6** Efficacy and side effects of the PD-1 and PD-L1 checkpoint inhibitors in lung cancer
- Track 7** **Case discussion:** A 50-year-old patient and never smoker with EGFR/KRAS/ALK/ROS1 wild-type advanced NSCLC receives multiple lines of systemic treatment followed by dabrafenib after identification of a BRAF mutation on retesting
- Track 8** **Case discussion:** A 48-year-old Vietnamese patient with EGFR-mutant advanced NSCLC receives systemic and local therapies to manage multiple metastatic sites
- Track 9** Studies of the multikinase inhibitor cabozantinib in lung cancer
- Track 10** Afatinib/cetuximab in patients with EGFR-mutant advanced NSCLC progressing on erlotinib
- Track 11** Treatment for patients with EGFR-mutant, advanced NSCLC who are experiencing slow disease progression on erlotinib
- Track 12** **Case discussion:** A 74-year-old patient with symptomatic, p63-positive, advanced squamous cell carcinoma (SCC) of the lung receives 2 lines of chemotherapy and stereotactic body radiation therapy for localized brain metastases prior to hospice referral
- Track 13** Role of nanoparticle albumin-bound (*nab*) paclitaxel in the treatment of advanced SCC of the lung

Select Excerpts from the Interview

Tracks 1-2, 4

▶ **DR LOVE:** You recently authored an editorial in *Lancet Oncology* about maintenance therapy for NSCLC (Reckamp 2012). Can you talk about some key points of the paper?

► **DR RECKAMP:** The issue of maintenance therapy in lung cancer has exploded in the past few years, and in some ways we are more confused than we are clear. The first study that brought the issue of maintenance therapy to us was the JMEN trial, in which carboplatin with a nonpemetrexed-containing platinum-based doublet was administered for 4 cycles and patients who did not experience disease progression went on to receive either maintenance pemetrexed or placebo. That study demonstrated an improvement in progression-free survival (Ciuleanu 2009; [4.1]), which you would expect with an active agent in lung cancer, and an overall survival benefit was also observed among the patients who received pemetrexed maintenance.

Then the PARAMOUNT study evaluated a platinum-based doublet with pemetrexed for 4 cycles followed by continuation pemetrexed maintenance versus nonpemetrexed maintenance, or “switch maintenance.” Here we also observed an improvement in progression-free survival (Paz-Ares 2012; [4.1]), and recently published data indicated an improvement in overall survival for patients who received pemetrexed maintenance after a platinum-based doublet with pemetrexed (Paz-Ares 2013). These results clearly indicate that pemetrexed has a role as maintenance therapy in NSCLC as switch maintenance or continuation maintenance.

For another cohort of patients one can use erlotinib maintenance, as in the SATURN trial (4.1). That study was similar to the JMEN trial in that patients received a platinum-based doublet for 4 cycles, and the patients who did not experience disease progression went on to receive erlotinib or placebo. In this study a small but statistically significant improvement in both progression-free survival and overall survival was observed across all subgroups. However, the subgroup that benefitted most was that of the patients with EGFR mutations. So erlotinib does potentially have a role, especially if patients can't receive chemotherapy.

► **DR LOVE:** Would you discuss the design of the PointBreak trial and how that relates to your approach to maintenance therapy?

► **DR RECKAMP:** In the PointBreak trial patients received either carboplatin, paclitaxel and bevacizumab, as in the ECOG-E4599 trial (Sandler 2006), followed by bevacizumab maintenance, or carboplatin/pemetrexed/bevacizumab followed by pemetrexed/bevacizumab maintenance. The results showed no overall survival differ-

4.1

Key Phase III Trials of Maintenance Therapy in Advanced Non-Small Cell Lung Cancer

PARAMOUNT ^{1,2}	Pem + BSC	Placebo + BSC	Hazard ratio	p-value
Median PFS*	4.1 months	2.8 months	0.62	<0.0001
Median OS	13.9 months	11.0 months	0.78	0.0195
JMEN ³	Pem + BSC	Placebo + BSC	Hazard ratio	p-value
Median PFS	4.3 months	2.6 months	0.50	<0.0001
SATURN ⁴	Erlotinib	Placebo	Hazard ratio	p-value
Median PFS	12.3 weeks	11.1 weeks	0.71	<0.0001

* By independent review

Pem = pemetrexed; BSC = best supportive care; PFS = progression-free survival; OS = overall survival

¹Paz-Ares L et al. *Lancet Oncol* 2012;13(3):247-55. ²Paz-Ares LG et al. *J Clin Oncol* 2013;31(23):2895-902.

³Ciuleanu T et al. *Lancet* 2009;374(9699):1432-40. ⁴Cappuzzo F et al. *Lancet Oncol* 2010;11(6):521-9.

ence between the 2 arms. A slight benefit was suggested among patients who received pemetrexed/bevacizumab maintenance, but it was a prespecified exploratory analysis (Patel 2012; [4.2]).

I believe you can interpret the data in almost any way you want. Because no difference in efficacy was apparent, I consider the side effects, and that usually favors pemetrexed. If you consider the cost, however, pemetrexed/bevacizumab doesn't make sense.

- ▶ **DR LOVE:** What's your usual approach in terms of maintenance therapy for the average bevacizumab-eligible patient presenting with metastatic adenocarcinoma of the lung?
- ▶ **DR RECKAMP:** For patients who are bevacizumab eligible and age 75 or younger I tend to use carboplatin/pemetrexed/bevacizumab. Peripheral neuropathy is much less of an issue than it is with paclitaxel. As far as maintenance, if I use bevacizumab up front I tend to continue it in the absence of specific bevacizumab-related toxicities because we don't have any data on discontinuation. ■

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

HR = hazard ratio; PFS = progression-free survival; OS = overall survival; NR = not reported

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

SELECT PUBLICATIONS

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.

Ciuleanu T et al. **Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for non-small-cell lung cancer: A randomised, double-blind, phase 3 study.** *Lancet* 2009;374(9699):1432-40.

Paz-Ares LG et al. **PARAMOUNT: Final overall survival results of the phase III study of maintenance pemetrexed versus placebo immediately after induction treatment with pemetrexed plus cisplatin for advanced nonsquamous non-small-cell lung cancer.** *J Clin Oncol* 2013;31(23):2895-902.

Paz-Ares L et al. **Maintenance therapy with pemetrexed plus best supportive care versus placebo plus best supportive care after induction therapy with pemetrexed plus cisplatin for advanced non-squamous non-small-cell lung cancer (PARAMOUNT): A double-blind, phase 3, randomised controlled trial.** *Lancet Oncol* 2012;13(3):247-55.

Reckamp KL. **Is benefit of maintenance therapy for NSCLC best defined by progression-free survival?** *Lancet Oncol* 2012;13(5):435-6.

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.