Tracks 1-9

Track 1  Practical benefits of maintenance therapy compared to second-line chemotherapy

Track 2  Viewpoint on the results of the PointBreak study comparing pemetrexed/carboplatin/bevacizumab → maintenance pemetrexed/bevacizumab to the ECOG-E4599 regimen for Stage IIIIB/IV nonsquamous NSCLC

Track 3  ECOG-E5508: A Phase III study of maintenance bevacizumab, pemetrexed or the combination in advanced NSCLC

Track 4  Case discussion: A 61-year-old patient and smoker with a Stage IIIA (T2N2M0) moderately differentiated adenocarcinoma of the lung

Track 5  Management of hypomagnesemia and azotemia in patients receiving cisplatin/pemetrexed

Track 6  Case discussion: A 37-year-old patient and never smoker with a 3.9-cm adenocarcinoma of the lung and an EGFR exon 19 mutation

Track 7  Surgical resection versus neoadjuvant chemoradiation therapy for Stage III NSCLC

Track 8  Multidisciplinary management of malignant pleural effusion

Track 9  Approach to maintenance therapy for elderly patients with advanced NSCLC

Select Excerpts from the Interview

Track 1

› DR LOVE: Would you discuss the role of maintenance therapy for patients with advanced NSCLC?

› DR BELANI: Currently, approximately 45% of eligible patients with advanced NSCLC receive maintenance therapy. Although the remaining 50% are eligible, they don’t receive maintenance therapy because of physician skepticism.

Pemetrexed and erlotinib are the 2 FDA-approved agents for maintenance therapy in advanced NSCLC. Patients with nonsquamous NSCLC primarily receive maintenance pemetrexed, the indication for which it is approved. Patients who’ve received up-front platinum-based chemotherapy with or without pemetrexed are generally receiving maintenance pemetrexed, which is the most commonly administered maintenance agent based on the results of the Phase III JMEM (Ciuleanu 2009) and PARAMOUNT trials (Paz-Ares 2012, 2013), which reported that maintenance pemetrexed significantly improves overall survival and PFS.

Maintenance erlotinib is used to a lesser extent because it is primarily used as first-line therapy for patients with EGFR mutation-positive disease. Few patients with wild-type
disease receive it as maintenance therapy. They usually receive it as second- or third-line therapy instead of maintenance therapy.

**DR LOVE:** What are the most common arguments against the use of maintenance therapy?

**DR BELANI:** A key argument against maintenance therapy is that although about 60% of the patients on the placebo arm of the JMEN trial received second-line therapy, only a few received pemetrexed. However, in the Phase III study of maintenance versus second-line docetaxel, about 60% of the patients made it to second-line therapy, and almost all received maintenance docetaxel (Fidias 2009).

The overall survival was the same for patients who received maintenance and those who received second-line therapy. So some investigators believe that proper selection of patients for second-line therapy will result in survival benefits similar to those with maintenance therapy. However, those who favor second-line versus maintenance therapy discount the fact that a third of the patients on that study discontinued treatment before second-line intervention.

**Tracks 2-3**

**DR LOVE:** What is your perspective on the results of the Phase III PointBreak trial?

**DR BELANI:** The PointBreak study was not a maintenance trial per se — it was a comparison of 2 regimens. It compared the ECOG-E4599 regimen of paclitaxel/carboplatin/bevacizumab followed by maintenance bevacizumab to pemetrexed/carboplatin/bevacizumab followed by maintenance pemetrexed/bevacizumab (Patel 2012). As the trial was designed, one can’t make an argument for maintenance bevacizumab because all patients received it. Maintenance pemetrexed/bevacizumab received after the 3-drug combination was not significantly beneficial in terms of overall survival when compared to the ECOG-E4599 regimen.

Initially we thought that maintenance pemetrexed/bevacizumab increased toxicity, which in turn reduced survival, preventing the study from meeting its primary endpoint. However, a breakdown of the induction and maintenance phases of the study revealed that some benefit was observed with the 2-drug maintenance therapy, although it was associated with slightly increased toxicity. Failure to meet the primary endpoint, therefore, was not due to a reduction in survival in response to pemetrexed/bevacizumab in the maintenance phase of the trial.

The Phase III AVAPERL1 trial demonstrated that maintenance pemetrexed/bevacizumab was superior in terms of PFS versus bevacizumab alone, but no significant difference in overall survival was observed (Barlesi 2013). Though I may be biased because I have been involved in maintenance pemetrexed studies, I believe maintenance pemetrexed has a role based on the results of the JMEN and PARAMOUNT studies.

**DR LOVE:** Any comments on the ongoing Phase III ECOG-E5508 trial?

**DR BELANI:** This study is evaluating maintenance bevacizumab, pemetrexed or the combination after responsive or stable disease on carboplatin/paclitaxel/bevacizumab induction therapy for patients with advanced nonsquamous NSCLC (4.1). Enrollment is currently about half of the target accrual.
### SELECT PUBLICATIONS

**Barlesi F et al.** Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin, and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089). J Clin Oncol 2013;[Epub ahead of print].


**Patel JD et al.** A randomized, open-label, phase III, superiority study of pemetrexed (pem) + carboplatin (cb) + bevacizumab (bev) followed by maintenance pem + bev versus paclitaxel (pac) + cb + bev followed by maintenance bev in patients with stage IIIb or IV non-squamous non-small cell lung cancer (NS-NSCLC). Chicago Multidisciplinary Symposium in Thoracic Oncology 2012;Abstract LBPL1.
