

Session 4: NSCLC symposium (Lilly)

OCPS 21: New developments in the management of NSCLC

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Platinum-based regimens - For years, platinum based regimens has been the cornerstone of most combination regimens in advanced NSCLC and guidelines recommend that first-line treatment for NSCLC should include a platinum combination, cisplatin in younger patients, with a good performance status, carboplatin in older patients or those with significant comorbidities. Several randomized controlled trials failed to show a clear superiority of one platinum-containing combination over another, all doublets had similar median survival (7.9 mo) and 1- and 2-year overall survival at 33% and 11%, respectively. A preplanned subset analysis of a phase III trial comparing upfront cisplatin-pemetrexed with cisplatin-gemcitabine in stage III and IV NSCLC showed that median survival in patients with nonsquamous histology was significantly better with cisplatin-pemetrexed than with cisplatin-gemcitabine: 12.6 versus 10.9 mo for patients with adenocarcinoma and 10.4 versus 6.7 mo for those with large cell histology. In contrast, the patients with squamous cell histology did better with the cisplatin-gemcitabine combination: 10.8 versus 9.4 mo. Cisplatin-pemetrexed is now the preferred combination for adenocarcinoma. In a 2012 systematic review and meta-analysis of randomized phase II/III trials, adding bevacizumab to platinum-based chemotherapy as first-line treatment in patients with advanced NSCLC significantly prolonged overall and progression-free survival. The effects of bevacizumab on overall survival were significantly greater in patients with adenocarcinoma versus other histologies. No unexpected toxicity was observed. With standard doublet chemotherapy for NSCLC several recent studies demonstrated survival benefits for patients treated beyond induction chemotherapy. Chemotherapeutic compounds successfully investigated in the maintenance setting are Gemcitabine, Docetaxel and Pemetrexed. Patients with stable disease or response after four cycles, immediate treatment with an alternative, single-agent chemotherapy such as pemetrexed in patients with nonsquamous histology, docetaxel in unselected patients, or erlotinib in unselected patients may be considered. Selected patients with good responses to first-line chemotherapy, good performance status, and a long disease-free period between initial chemotherapy and relapse may be candidates for second-line chemotherapy. Docetaxel and pemetrexed and erlotinib are approved in this indication. There is no guidelines for third line

and more. EGFR mutations can be found in 10 to 15% patients with advanced NSCLC more frequently in women, never smoker and those with adenocarcinomas. Gefitinib, Erlotinib and afatinib are approved as first line treatment in these patients. No benefit was seen when these target therapies were combined with chemotherapy. Crizotinib is approved for the treatment of locally advanced or metastatic NSCLC that is anaplastic lymphoma kinase (ALK) positive (5% of the patients, more frequently young and no smoker). Ceritinib an another ALK inhibitor, was approved in April 2014 by the FDA. Immunotherapy in lung cancer will be the next challenge. Nivolumab, a monoclonal antibody inhibitor of programmed death protein-1 (PD-1) in phase I trial, in heavily pre-treated group of patients showed a response rate was 17%, a median overall survival was 14.9 months with durables responses (24% alive at 24 months) and acceptable toxicity.

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