8032 Poster Discussion Session (Board #21), Sun, 8:00 AM-12:00 PM and 11:30 AM-12:30 PM

Efficacy and safety of crizotinib in patients with advanced *ROS1*-rearranged non-small cell lung cancer (NSCLC).

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Background: *ROS1* receptor tyrosine kinase rearrangements define a subset of NSCLC sensitive to the small-molecule tyrosine kinase inhibitor crizotinib, approved multinationally for the treatment of advanced *ALK*-positive NSCLC. Updated efficacy and safety data are presented for crizotinib in patients with advanced *ROS1*-rearranged NSCLC. **Methods:** *ROS1* status was determined by break-apart FISH assays, and patients were enrolled into an expansion cohort of an ongoing phase 1 crizotinib study (NCT00585195). Patients received crizotinib 250 mg BID. Responses were assessed using RECIST v1.0. The disease control rate (DCR; % stable disease [SD] + partial response [PR] + complete response [CR]) was evaluated at weeks 8 and 16. **Results:** At the data cut-off, 33 patients with *ROS1*-positive NSCLC had enrolled, and 31 had received crizotinib, with 25 evaluable for response. Median age was 51 years (range 31–72), 79% of patients were never-smokers and 97% had adenocarcinoma histology. The median number of prior treatments for advanced disease was 1 (range 0–7). The objective response rate (ORR) was 56% (95% CI: 24.4–65.1), with 2 CRs, 12 PRs and 8 SDs. 8-week and 16-week DCRs were 76% and 60%, respectively. Median PFS has not been reached, with ~60% of patients still in follow-up for PFS; 6-month PFS probability was 71% (95% CI: 45.6–86.0). Median treatment duration was 24 weeks (range 2.3–112), and 24 patients were on treatment at the data cut-off; 5 patients died (all disease-related). 91% of patients had treatment-related adverse events (AEs): most commonly visual impairment (82%), nausea (36%) and diarrhea (33%). Most AEs were grade 1 in severity. Peripheral edema and elevated transaminases were also reported, similar to the previous experience of crizotinib. There were no treatment-related serious AEs or treatment-related permanent discontinuations. Accrual of patients with *ROS1*-positive NSCLC is ongoing. **Conclusions:** As observed in *ALK*-positive NSCLC, crizotinib had dramatic antitumor activity with a high ORR (56%) in patients with *ROS1*-positive NSCLC and a generally tolerable and manageable AE profile. These findings indicate that crizotinib is an effective therapy for advanced *ROS1*-positive NSCLC. Clinical trial information: NCT00585195.