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

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\textbf{Background:} \textit{ROS1} receptor tyrosine kinase rearrangements define a subset of NSCLC sensitive to the small-molecule tyrosine kinase inhibitor crizotinib, approved multinational for the treatment of advanced \textit{ALK}-positive NSCLC. Updated efficacy and safety data are presented for crizotinib in patients with advanced \textit{ROS1}-rearranged NSCLC. \textbf{Methods:} \textit{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. \textbf{Results:} At the data cut-off, 33 patients with \textit{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 \textit{ROS1}-positive NSCLC is ongoing. \textbf{Conclusions:} As observed in \textit{ALK}-positive NSCLC, crizotinib had dramatic antitumor activity with a high ORR (56\%) in patients with \textit{ROS1}-positive NSCLC and a generally tolerable and manageable AE profile. These findings indicate that crizotinib is an effective therapy for advanced \textit{ROS1}-positive NSCLC. Clinical trial information: NCT00585195.