Noninferiority on overall survival of every-2-weeks vs weekly schedule of cetuximab for first-line treatment of RAS wild-type metastatic colorectal cancer

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Abstract 2589

Background

Cetuximab (CET) in combination with chemotherapy is approved for a once-weekly (q1w) schedule at an initial dose of 400 mg/m², followed by weekly doses of 250 mg/m², in patients with RAS wild-type (wt) metastatic colorectal cancer (mCRC). However in clinical practice, an off-label schedule of CET 500 mg/m^2 every-2-weeks (q2w) is frequently used. This pooled analysis of patient-level data aimed to test the noninferiority of the q2w vs q1w schedule on overall survival (OS).

Methods

All post-authorization studies with patient-level data available to marketing authorization holder at time of study design, in patients with confirmed RAS wt mCRC who received a first-line treatment with CET q1w or q2w in combination with chemotherapy from 2007 to 2018 were included: 2 non-interventional cohort studies (NIS) (EREBUS, ERBITAG) and 3 clinical trials (CEBIFOX, CECOG/CORE 1.2.002, APEC). Patients were categorized into q1w or q2w groups according to the CET schedule planned at initiation. OS was calculated from first CET infusion until all-cause death and censored at the last date patients were known to be alive. The noninferiority of the q2w vs q1w schedule was tested with a hazard ratio (HR) margin of 1.25 using a Cox proportional hazards regression model. Differences in baseline characteristics were accounted for with inverse probability of treatment weighting (IPTW) based on a propensity score.

Results

763 (91% from NIS) and 554 (51% from NIS) patients were included in the q1w and q2w groups, respectively. Median (Q1-Q3) age in years was 66 (57-73) for q1w and 60 (53-69) for q2w. Liver-limited disease concerned 42.6% of patients for q1w and 37.9% for q2w. A baseline ECOG Performance Status of 0-1 was reported in 81.8% of q1w and 90.6% of q2w patients. FOLFIRI was most frequently used in combination with q1w (49.4%) and FOLFOX with q2w (59.2%). IPTW-adjusted HRs for OS were in favor of q2w: 0.83 (95% CI, 0.71-0.96) and 0.73 (95% CI, 0.61-0.88) when restricted to NIS. Other efficacy and safety results will be presented in the future.

Conclusions

This pooled analysis confirmed the noninferiority of CET q2w vs q1w. This result suggests an improved OS with the q2w schedule.

Clinical trial identification

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