Outcomes of cetuximab in first-line therapy for metastatic colorectal cancer according to tumor RAS-BRAF mutation status from an update of EREBUS cohort

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Background: Poor efficacy has been recently reported for patients in first-line cetuximab (m) treatment with cetuximab. There are few data about cetuximab benefit in real-life according to tumor RAS/BRAF mutation status.

Methods: EREBUS is a multinational (n=585) cohort study of KRAS wild-type (wt) unresectable metastatic colorectal cancer (mCRC) patients initiating cetuximab as 1st-line treatment from 2009 to 2010, followed for 2 years (up to 5 years for vital status). Kaplan-Meier method was used to describe 2-steps PFS and OS curves. 80% of the patients were still alive at 2-year follow-up. The tested variables were all baseline variables except time-dependent variables: surgery of primary tumor, surgery of metastases, chemotherapy use, months.

Results: Among 369 included patients, 310 patients had RAS/BRAF tumor mutation status available. 186 patients were included in the RAS wt/BRAF wt arm, 60 in the RAS mt/BRAF wt arm, 64 in the RAS mt/BRAF mt arm, and 23 in the RAS wt/BRAF mt arm. Median age was 65 years (r=39-80). Median PFS of patients treated by cetuximab according to RAS/BRAF tumor mutation status was 8.0 [5.9-9.3] months in RAS wt/BRAF wt patients, and 27.6 [24.3-30.9] months in RAS mt/BRAF mt patients. Median OS was 18.4 [10.9-23.3] months in RAS wt/BRAF wt patients, and 27.5 [25.2-30.6] months in RAS mt/BRAF mt patients.

Conclusions: EREBUS confirms in real-life the difference in clinical outcomes with tumoral RAS/BRAF mutation in untreated mCRC treated with 1st-line cetuximab, showing the greatest effectiveness in double wt-type patients.