Methods: Eligible patients received cetuximab administered every 2 weeks (day 1 of each cycle, 500 mg/m²) with, based on investigator’s choice, either FOLFOX or FOLFIRI. Study treatment was continued until disease progression, the occurrence of unacceptable toxicity or withdrawal of consent. The primary endpoint was tumor response; assessed radiologically (RECIST 1.0) every 8 weeks, PFS was a secondary endpoint. EGFR expression was determined retrospectively by immunohistochemistry (IHC) using the Dako EGFR pharmDx kit with a cutoff point of ≥5% of tumor cells exhibiting a staining intensity of at least 1+. Best overall objective response and PFS were determined according to treatment in patients grouped by whether tumors were EGFR detectable or EGFR undetectable.

Results: Of the 289 patients in the intent to treat (ITT) population of the APEC study, tumor samples from 154 (53%) patients were available for EGFR IHC analysis, with the majority subsequently evaluable for EGFR expression status (147/154 [95%]). EGFR expression was detectable in 120 tumors (82%) and was undetectable in 27 tumors (18%) from the 147 evaluable patients. There were markedly more Caucasian (22/120 [18%] vs 0/27) and fewer Asian patients (97/120 [81%] vs 27/27 [100%]) in the EGFR detectable compared with the EGFR undetectable groups. Other baseline characteristics in these groups were comparable. Objective response rates (ORR, 58.8% vs 55.8%) and median PFS times (11.1 vs 11.1 months) were similar in the ITT compared with the EGFR evaluable populations, and also in the FOLFOX + cetuximab and FOLFIRI + cetuximab treatment groups in these populations (Table). In patients treated with FOLFOX + cetuximab, the ORR was 60.3% (47/78 patients) in the EGFR detectable group and 50.0% (8/16 patients) in the EGFR undetectable group. In patients treated with FOLFIRI + cetuximab, the ORR was 54.8% (23/42 patients) in the EGFR detectable group and 36.4% (4/11 patients) in the EGFR undetectable group. Median PFS times were generally comparable according to treatment in the EGFR detectable and EGFR undetectable groups (Table).

Conclusion: In this retrospective subgroup analysis of APEC study patients, there were no major differences in ORRs and median PFS times between the subgroups of patients with EGFR detectable and EGFR undetectable tumors. Because of the small numbers of patients in some subgroups, no definite conclusions could be made with regard to EGFR expression as a clinically useful biomarker for the activity of chemotherapy plus cetuximab.

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