Aim: We previously reported that the addition of erlotinib to gemcitabine and oxaliplatin (GEMOX) resulted in greater antitumor activity and might be a treatment option for patients with biliary tract cancers. Molecular subgroup analysis of treatment outcomes in patients who had tumor specimens available for analysis was undertaken.

Methods: EGFR, KRAS, and PIK3CA mutations were evaluated using peptide nucleic acid–locked nucleic acid (PNA–LNA) PCR clamp reactions. Survival and response rates were analyzed according to the mutational status.

Results: 64 patients (48.1%) were available for mutational analysis in the chemotherapy alone group and 61 (45.1%) in the chemotherapy plus erlotinib group. 1.6% (2/116) harboured an EGFR mutation (2 patients; exon 20), 9.6% (12/121) harboured a KRAS mutation (12 patients; exon 2), and 9.6% (12/118) a PIK3CA mutation (10 patients; exon 9 and 2 patients; exon 20). The addition of erlotinib to GEMOX in patients with KRAS wild type disease (n = 109) resulted in significant improvements in overall response compared with GEMOX alone (30.2% vs. 12.5%, p = 0.024). In 95 patients with both wild type KRAS and PIK3CA, there was evidence of a benefit associated with the addition of erlotinib to GEMOX with respect to response rate (RR) as compared with GEMOX alone (p = 0.04).

Conclusions: This study demonstrates that KRAS mutational status might be considered a predictive biomarker for the response to erlotinib in biliary tract cancers (BTCs). Additionally, the mutation status of PIK3CA may be a determinant for adding erlotinib to chemotherapy in KRAS wild type BTCs.

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