HER2 MAY NOT BE AN INTERESTING TARGET IN BILIARY CANCERS: RESULTS OF AN EARLY PHASE II STUDY WITH LAPATINIB

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Background: Biliary Cancers (BC) respond poorly to chemotherapy. Lapatinib is a dual inhibitor of EGFR and HER-2/neu, both thought to be implicated in cholangiocarcinogenesis. This trial was designed to determine the safety and efficacy of lapatinib in BC.

Methods: A Fleming phase II design with a single stage of 25 patients with a 90% power to exclude a true response rate of <10% and detect a true response rate of ≥30% was used. The dose of lapatinib was 1,500 mg/day administered orally in 28-day cycles. Tumor and blood specimens were analyzed for expression of HER2/neu and EGFR, as well as their respective downstream signal pathway proteins.

Results: Nine patients with BC enrolled on this study. The study was terminated early because of possible futility. Most common toxicities were nausea and fatigue (both 78%) and diarrhea (67%). No objective responses were observed. Of eight evaluable patients, only four (50%) had stable disease as their best response. Median progression-free survival was 2.6 months (95% CI, 1.6-4.4) and median overall survival was 5.1 months (95% CI, 2.0-16.5). Tissue and blood specimens were available for all patients. No somatic mutations in EGFR (exons 18-21) or HER2/neu were found. We did not find evidence of HER2 overexpression.

Conclusions: Lapatinib is well tolerated but failed to show activity as a single agent in treating patients with BC. Despite the small patient population, our study is consistent with previous findings suggesting that targeting HER2/neu does not appear to be an effective therapy for BC.