TARGETED CANCER THERAPY

Treatment options for inoperable or progressive malignant pancreatic endocrine tumors (PETs) are limited, but new evidence suggests that the epidermal growth factor receptor (EGFR) and cyclo-oxygenase 2 (COX2) should be investigated as potential chemotherapeutic targets.

Resection of PETs, which account for 1–2% of all pancreatic neoplasms, is associated with 5-year survival of up to 77%, but the response rate of inoperable and progressive tumors to chemotherapy is only 10–15%.

Dr Bergmann *et al.* analyzed 110 tumor samples from 74 patients who underwent resection of PETs between 1991 and 2006. EGFR was expressed in 57% of malignant PETs and in 26% of nonmalignant (benign tumors or those with uncertain behavior) PETs. Malignant PETs were characterized by significantly higher average expression of EGFR than nonmalignant PETs. By contrast, no significant differences were observed between nonmalignant and malignant PETs regarding COX2 expression, which was uniformly high across tumor categories.

Administration of the EGFR antagonist AG1478 and of the COX2 inhibitor celecoxib to the human pancreatic carcinoid cell line BON and to the mouse pancreatic insulinoma cell line β-TC-3 resulted in significant, dose-dependent decreases of cell viability. Administered in combination, celecoxib and AG1478 displayed additive effects on cell viability in both cell lines.

Evidence suggests that EGFR and COX2 are potential chemotherapeutic targets for PETs that should be further investigated. Bergmann and colleagues are presently testing the efficacy of celecoxib and AG1478 in a xenograft mouse model. "Pending on these *in vivo* results" says Bergmann "we are optimistic to transfer the drug targets into a first clinical trial."

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Original article Bergmann, F. *et al.* Expression pattern and functional relevance of epidermal growth factor receptor and cyclooxygenase-2: novel chemotherapeutic targets in pancreatic endocrine tumors? *Am. J. Gastroenterol.* **104**, 171–181 (2009).