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PANCREATIC CANCER

EGFR inhibition is effective against *KRAS*-wild-type disease

Patients diagnosed with pancreatic cancer have a poor prognosis and new therapeutic approaches are urgently required. Now, the findings of a randomized phase IIb study provide a potential new first-line treatment regimen for patients with *KRAS*-wild-type advanced-stage and/or metastatic pancreatic cancer.

Investigators selected the combination of gemcitabine, the current standard of care at the time trial was commenced, and the anti-EGFR antibody nimotuzumab. Beate Schultheis, lead author of the publication and Dirk Strumberg, head of the clinical trial, explain the basis for this combination: "nimotuzumab had previously shown encouraging phase II response data, as well as being approved in many countries for gliomas, nasopharyngeal cancer or head-and-neck cancer. Nimotuzumab has orphan drug status in the USA and in the European Union for diffuse intrinsic glioma and pancreatic cancer." A total of 192 patients were randomly assigned to receive either nimotuzumab plus gemcitabine, or gemcitabine alone, with 1-year overall survival rates of 34% versus 19%, and median overall survival durations of 8.6 months versus 6.0 months, respectively. In general, both approaches were well tolerated, with slightly increased risks of thrombocytopenia and leukopenia in the experimental arm.

Notably, patients with *KRAS*-wild-type disease who received nimotuzumab had significantly longer overall survival durations than those with *KRAS*-mutant disease (11.6 months versus 5.6 months). This finding emerged without preselection of patients with *KRAS* wild-type disease: Schultheis explains "at the time the clinical trial protocol was planned, no information about possible implications of *KRAS* genotype for pancreatic cancer was available. Therefore, *KRAS* analysis was conducted later on." The authors note that, at the time of study design, neither nab-paclitaxel or FOLFIRINOX were established as standards of care, and that the approach tested in this study provides similar outcomes in unselected patients. The authors also highlight the favourable adverse event profile, albeit at a phase II level of evidence, of nimotuzumab plus gemcitabine, relative to the other approaches.

When asked about future directions of this research, Schultheis adds: "based on these results, the sponsor is currently evaluating the design of a phase III trial."

Peter Sidaway

ORIGINAL ARTICLE Schultheis, B. *et al.* Gemcitabine combined with the monoclonal antibody nimotuzumab is an active first-line regimen in KRAS wildtype patients with locally advanced or metastatic pancreatic cancer: a multicenter, randomized phase IIb study. *Ann. Oncol.* http://dx.doi.org/10.1093/annonc/mdx343 (2017)