Combined treatment for locally advanced pancreatic cancer

According to new research, a high proportion of patients with locally advanced pancreatic adenocarcinoma, neoadjuvant treatment with FOLFIRINOX and anti-hypertensive drug losartan followed by chemoradiotherapy were able to achieve margin-negative (R0) resection.

Janet Murphy (Massachusetts General Hospital, Boston, MA, USA) and colleagues did a single-arm, phase 2 trial from Aug 22, 2013, to May 22, 2018, at a US academic hospital to investigate neoadjuvant FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, and irinotecan) plus losartan followed by chemoradiotherapy in patients who had previously untreated locally advanced unresectable pancreatic cancer. The primary endpoint was the proportion of patients who achieved R0 resection and the secondary endpoints included progression-free survival, overall survival, and safety.

49 patients were eligible to receive eight cycles of FOLFIRINOX and losartan, and 39 (80%) received all eight cycles of treatment. After FOLFIRINOX and losartan, seven (16%) of 45 eligible patients had short-course chemoradiotherapy, and 38 (84%) had long-course chemoradiotherapy. Surgical resection was done in 34 patients (69%; 95% CI 55–82), and R0 resection was achieved in 30 patients (61%; 46–75). Median progression-free survival was 17·5 months (95% CI 13·9–22·7) in all 49 patients, and 21·3 months (16·6-28·2) for those who underwent resection. Median overall survival was 31·4 months (95% CI 8·1–38·5) for all patients and 33·0 months (31·4 to not reached) for those who underwent resection. 25 (51%) of 49 patients had grade 3 or worse toxicity. The most common severe toxic effects included neutropaenia (n=7), thrombocytopaenia (n=7), diarrhoea (n=7), and nausea or vomiting (n=4).

Susan Bates (Columbia University Irving Medical Center, New York, NY, USA) said, "The [study] suggests that intensifying neoadjuvant therapy has the potential to substantially improve overall survival." Sunil Krishnan (MD Anderson Cancer Center, Houston, TX, USA) commented, "This team has advanced exciting preclinical findings that a readily available FDA-approved anti-hypertensive drug can be used to prune the exuberant stroma of pancreatic cancer and increase perfusion of drugs (and oxygen) to the otherwise poorly accessible hypoxic core of pancreatic cancers... This study affirms that this approach is potentially viable in a clinical setting and sets the stage for confirmatory randomised studies that the team is already embarking on."

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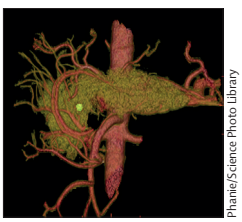

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For the **study by Murphy and colleagues** see *JAMA Oncol* 2019; published online May 30. DOI:10.1001/jamaoncol.2019.0892