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Supplementary appendix 1

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Supplement to: Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. *Lancet* 2023; published online Sept 11. [https://doi.org/10.1016/S0140-6736\(23\)01366-1](https://doi.org/10.1016/S0140-6736(23)01366-1).

Plain language summary

Metastatic pancreatic ductal adenocarcinoma is a type of cancer that starts in the pancreas and then spreads to other parts of the body. Patients with pancreatic ductal adenocarcinoma usually already have advanced (metastatic) disease when they are diagnosed because there are often no early warning signs. Treatments aim to shrink the cancer and slow its spread to keep patients alive, with a good quality of life, for as long as possible. However, current treatments do not work well for all patients and new therapies are needed.

The NAPOLI 3 study included 770 randomised patients with metastatic pancreatic ductal adenocarcinoma who had not been treated previously for their cancer. The study looked at whether a combination of drugs called NALIRIFOX (which includes liposomal irinotecan, oxaliplatin, leucovorin, and 5-fluorouracil) was better at improving patient survival than an existing treatment, nab-paclitaxel, and gemcitabine. The study also looked at the side effects of both treatments.

Patients treated with NALIRIFOX lived for 1·9 months longer than those who received nab-paclitaxel and gemcitabine. NALIRIFOX slowed the spread of cancer for 1·8 months longer than nab-paclitaxel and gemcitabine. More patients treated with NALIRIFOX experienced severe diarrhoea, nausea and low potassium levels compared with those treated with nab-paclitaxel and gemcitabine. However, fewer patients treated with NALIRIFOX than nab-paclitaxel and gemcitabine had severe decreases in levels of white blood cells and anaemia. Overall, these results suggest that NALIRIFOX is a new treatment option for patients with metastatic pancreatic ductal adenocarcinoma.