

NAPOLI 3, a phase 3 study of NALIRIFOX in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC): Final overall survival (OS) analysis and characteristics of the long-term survivors.

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Background: Metastatic pancreatic ductal adenocarcinoma (mPDAC) is an aggressive malignancy with a median overall survival (mOS) of between 8 and 11 months. With the use of modern chemotherapy regimens, some patients with mPDAC have been shown to achieve long-term survival of 18 months or longer (Rochefort *et al. Oncol.* 2019;24:1543–8). The aim of this analysis was to describe long-term survivors among the North American population treated with liposomal irinotecan plus 5-fluorouracil/leucovorin and oxaliplatin (NALIRIFOX) in the NAPOLI 3 trial and to explore clinical and pathological factors that might be associated with prolonged survival. **Methods:** Patients with confirmed untreated mPDAC randomized to receive NALIRIFOX in NAPOLI 3 were treatment on days 1 and 15 of a 28-day cycle. In this *post hoc* analysis of patients enrolled from centers in North America ($n = 120$), baseline characteristics and NALIRIFOX dosing patterns were evaluated for individuals who survived for 18 months of longer (long-term survivors; $n = 15$). The analysis was descriptive; no statistical tests were performed. Kaplan–Meier methods were used to estimate mOS (interquartile range [IQR]). **Results:** Among the long-term survivors, the mOS was 19.5 (IQR: 18.8–22.6) months and 53.3% were male. At baseline, long-term survivors had a median age of 61.0 (IQR: 49.0–70.5) years, had a median CA 19–9 level of 166.8 U/ml (IQR: 32.7–1728.4), 53.3% had Eastern Cooperative Oncology Group Performance Score (ECOG PS) 0, 53.3% had the main pancreatic tumor located in the body of the pancreas, 66.7% had liver metastasis, and 53.3% had ≥ 3 metastatic sites. Liposomal irinotecan and oxaliplatin dose reductions were experienced by 66.7% and 80.0% of long-term survivors, respectively, and dose delays by 86.7% and 80.0%, respectively. Median cumulative dose of liposomal irinotecan was 1229.4 (IQR: 821.9–1513.9) mg/m² for long-term survivors and median cumulative dose of oxaliplatin was 962.3 (655.0–1470.3) mg/ml. Median duration of exposure was 65.1 (IQR: 40.1–89.0) weeks for liposomal irinotecan and 39.9 (26.6–76.4) weeks for oxaliplatin. **Conclusions:** This *post hoc* analysis investigated characteristics and dosing patterns of long-term survivors from NAPOLI 3 treated with NALIRIFOX in North America. Patients with prolonged OS were generally younger (vs typical mPDAC diagnosis), few had tumors in the head or tail of the pancreas and, overall, CA19–9 levels and ECOG PS were low. A large proportion of long-term survivors experienced liposomal irinotecan and/or oxaliplatin dose reductions or treatment delays, but had prolonged exposure and high cumulative doses of both drugs. Despite liver metastasis and ≥ 3 metastatic sites in a substantial proportion of long-term survivors, dose modifications and an otherwise good clinical profile enabled attainment of a long mOS. Small sample size limits the generalizability of these results. Clinical trial information: NCT04083235. Research Sponsor: Ipsen.