

Effect of dose adjustments on overall survival (OS) in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) treated with NALIRIFOX: A post hoc analysis of NAPOLI 3.

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Background: NALIRIFOX is approved by the US Food & Drug Administration and European Medicines Agency for the first-line treatment of adults (no upper age limit) with mPDAC. Approval was based on the results of NAPOLI 3 (NCT04083235), in which NALIRIFOX demonstrated significant improvements in OS (primary outcome) and progression-free survival compared with nab-paclitaxel plus gemcitabine. In this exploratory post-hoc analysis of NAPOLI 3, we examined the impact of NALIRIFOX dose adjustments on OS in patients treated in North America. **Methods:** Patients (N = 770) with confirmed untreated mPDAC were randomized (1:1) to receive liposomal irinotecan 50 mg/m² + oxaliplatin 60 mg/m² + leucovorin 400 mg/m² + 5-fluorouracil 2400 mg/m² (NALIRIFOX) on days 1 and 15 of a 28-day cycle or nab-paclitaxel 125 mg/m² and gemcitabine 1000 mg/m² on days 1, 8 and 15 of a 28-day cycle. In this analysis, liposomal irinotecan dose reductions, delays, and exposure were examined descriptively in patients who received NALIRIFOX at centers in North America. OS was evaluated using Kaplan–Meier methods; no statistical tests were performed. **Results:** Overall, 120 patients were randomized to receive NALIRIFOX at centers in North America (intention-to-treat [ITT] population) and 112 received treatment (safety population). Dose adjustments (dose reductions and dose delays) occurred in a higher proportion of patients presenting with longer OS. Patients with the longest duration of liposomal irinotecan exposure and highest cumulative dose had the longest OS. **Conclusions:** This finding suggests that tolerability-guided dose modification of liposomal irinotecan does not adversely affect efficacy outcomes and suggests a path forward to further optimize the OS of patients with mPDAC receiving NALIRIFOX. Clinical trial information: NCT04083235. Research Sponsor: Ipsen.