Predictors of overall survival and time to next treatment in real-world patients with metastatic pancreatic ductal adenocarcinoma who received FOLFIRINOX or gemcitabine plus nab-paclitaxel in the first line

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Background

- The prognosis of patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) is poor. Even with the most common treatments of standard combination chemotherapy, median overall survival (OS) is less than one year.[1]
- FOLFIRINOX (FFX) and gemcitabine + nab-paclitaxel (GnP) are the two most common first-line (1L) treatments for mPDAC. Each regimen is associated with a different toxicity profile that impacts patient quality of life.
- The two regimens have not been directly compared in a clinical trial. In the real world, FFX tends to be used among younger and healthier patients than GnP, complicating assessment of which regimen has better outcomes.
- In addition, both FFX and GnP are often modified in the real world, using lower doses and less frequent administration than clinical trials.
- Studies to date have found mixed evidence on which regimen should be preferred.[2,3]
- Understanding how patient characteristics affect treatment response can guide clinician recommendations and improve patient outcomes.

Objective

Using real-world data, we evaluated differences in overall survival (OS) and time to next treatment (TTNT) between 1L FFX and GnP and assessed factors associated with these outcomes.

Methods

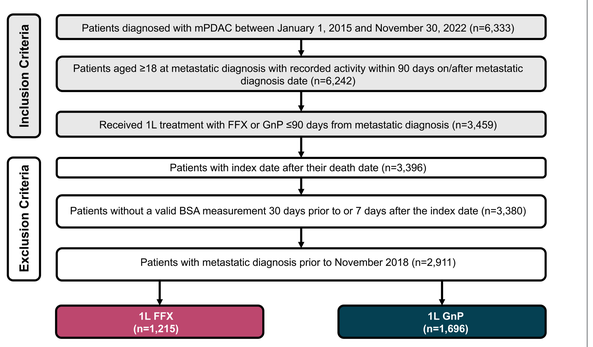
- This retrospective observational study utilized the Ontada Clinical Data View: Pancreatic Cancer database.
- The study included adult mPDAC patients diagnosed November 2018–November 2022 treated with 1L FFX or GnP ≤90 days after metastatic diagnosis.
- Kaplan-Meier (KM) analyses assessed unadjusted OS and TTNT, while Cox proportional hazards models adjusted these outcomes for patient age, race, sex, treatment year, baseline body surface area (BSA) and ECOG, and baseline lab values [serum albumin (SA), bilirubin, AST/ALT, ALP, CA 19-9, and white blood cell (WBC) count].
- Baseline lab values were categorized into normal, abnormal, and not documented, with normal serving as the reference level in the Cox model.

Results

Patient selection criteria

- From 6,333 patients diagnosed with mPDAC, 2,911 patients met the inclusion criteria for the study: 1,215 (42%) were treated with 1L FFX and 1,696 (58%) with 1L GnP. (**Figure 1**)

Figure 1. Patient selection criteria



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Results

Patient demographics and clinical characteristics

- Patients treated with 1L FFX vs 1L GnP were more likely to be younger (65 years vs 71 years, p<.01), male (57% vs. 52%, p = .013), diagnosed in stage IV (79% vs 63%, p<.01), and have an ECOG performance score (PS) <2 (55% vs 50%, p<0.01). (**Table 1**)
- Differences in race, ethnicity, and practice region were small and not statistically significant.

Table 1. Patient demographics and clinical characteristics

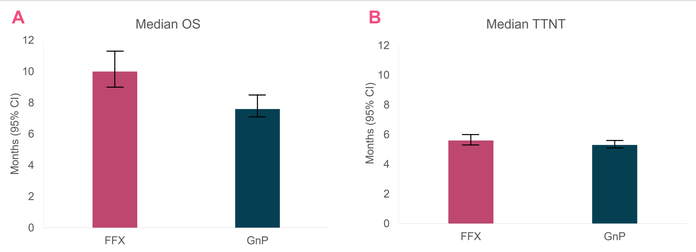
Characteristic	FFX (n=1,215)	GnP (n=1,696)
Age at 1L treatment initiation, median years (Q1, Q3)	65 (58, 71)	71 (64, 76)
Year of 1L start, n (%)		
2018	19 (1.6)	46 (2.7)
2019	295 (24.3)	406 (23.9)
2020	304 (25.0)	408 (24.1)
2021	322 (26.5)	444 (26.2)
2022	275 (22.6)	392 (23.1)
Sex, n (%)		
Female	526 (43.3)	813 (47.9)
Male	689 (56.7)	883 (52.1)
Race, n (%)		
African American	100 (8.2)	128 (7.5)
American Indian or Alaska Native	4 (0.3)	9 (0.5)
Asian	23 (1.9)	31 (1.8)
Other	5 (0.4)	7 (0.4)
Unknown	253 (20.8)	415 (24.5)
White	830 (68.3)	1106 (65.2)
Ethnicity, n (%)		
Hispanic or Latino	59 (4.9)	85 (5.0)
Not Hispanic of Latino	860 (70.8)	1141 (67.3)
Unknown	296 (24.4)	470 (27.7)
Practice Region, n (%)		
Midwest	334 (27.5)	486 (28.7)
Northeast	91 (7.5)	129 (7.6)
South	464 (38.2)	582 (34.3)
West	326 (26.8)	499 (29.4)
Stage at initial diagnosis, n (%)		
IV	964 (79.3)	1065 (62.8)
Not documented	68 (5.6)	122 (7.2)
Other	183 (15.1)	509 (30.0)
BSA (m^2)*, median (Q1, Q3)	1.89 (1.72, 2.07)	1.81 (1.65, 1.99)
ECOG score*, n (%)		
0	188 (15.5)	165 (9.7)
1	477 (39.3)	675 (39.8)
2	77 (6.3)	172 (10.1)
3	5 (0.4)	17 (1.0)
Not documented	468 (38.5)	667 (39.3)

Abbreviations: BSA, body surface area; ECOG, Eastern Cooperative Oncology Group.
*Measurements recorded -30days ±7 days of 1L start.

Median OS and TTNT (Unadjusted Analyses)

- Unadjusted median OS for FFX vs. GnP via Kaplan-Meier (KM) analysis was 10.0 (95% CI:9.0–11.3) vs. 7.6 months (95% CI:7.1–8.5) (p<.001). (**Figure 2A**)
- Unadjusted median TTNT for FFX vs. GnP was 5.6 (95% CI:5.3–6.0) vs. 5.3 months (95% CI:5.1–5.6) (p=.175). (**Figure 2B**)

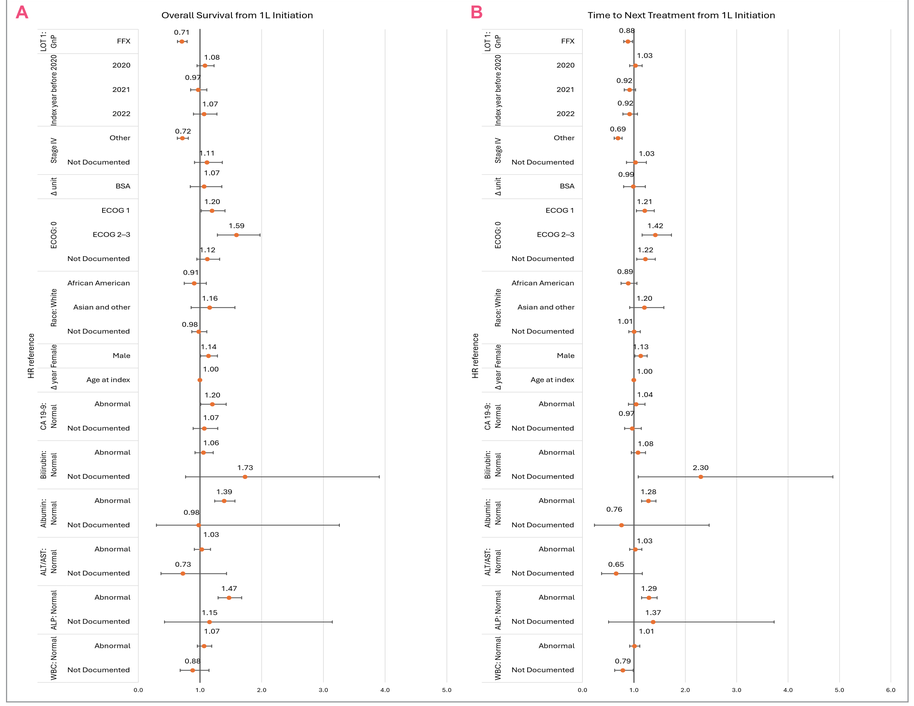
Figure 2. Median OS and TTNT (Unadjusted)



Hazard Ratios (HRs) for OS and TTNT (Adjusted Analyses)

- HRs of OS and TTNT were lower for FFX vs. GnP (HR:0.71, 95% CI:0.63–0.79; HR:0.88, 95% CI:0.80–0.98, respectively). (**Figure 3**)
- Significant predictors of lower OS were abnormal SA (HR:1.39, 95% CI:1.24–1.57), ALP (HR:1.47, 95% CI:1.29–1.68), and CA 19-9 (HR:1.20, 95% CI:1.01–1.42). (**Figure 3A**)
- Compared to a baseline ECOG=0, OS was lower for ECOG=1 (HR:1.20, 95% CI:1.02–1.40) and 2–3 (HR:1.59, 95% CI:1.28–1.97). (**Figure 3A**)
- Significant predictors of lower TTNT were male sex (HR:1.13; 95% CI:1.02–1.26), and abnormal SA (HR:1.28, 95% CI:1.15–1.43) and ALP (HR:1.29, 95% CI:1.15–1.45). (**Figure 3B**)
- Compared to baseline ECOG=0, TTNT was lower for ECOG=1 (HR:1.21; 95% CI:1.05–1.40) and 2–3 (HR:1.42; 95% CI:1.16–1.73). (**Figure 3B**)

Figure 3. HRs for OS and TTNT (Adjusted Analyses)



Limitations

- The data was collected from community oncology centers in the Ontada network only, and results may not be generalizable to other populations.
- Data was collected from electronic health records that were not designed for research purposes. It may be subject to missingness and data entry errors.
- ECOG score is an approximate measure of health status and was unobserved in nearly 40% of patients. Unobserved health status or other patient characteristics that were correlated with treatment selection and outcomes may confound results.

Conclusions

- In a real-world sample of 2,911 mPDAC patients receiving treatment at community oncology practices in the US, 1L GnP was associated with lower OS and marginally lower TTNT relative to 1L FFX.
- Abnormal SA, ALP, and higher ECOG score predicted inferior outcomes. This is consistent with previous research on real-world prognostic factors in mPDAC.[4]
- Future research should seek to further understand the factors driving differences in real-world outcomes as well as to assess the tradeoff between regimen toxicity and survival benefit.

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