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Comparison of two standard first-line treatments in metastatic pancreatic cancer

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Abstract

FOLFIRINOX or modified FOLFIRINOX (mFFX) and nab-paclitaxel plus gemcitabine (Nab-G) are both standard first-line treatment options in metastatic pancreatic cancer (mPC). This study aimed to analyze the efficacy and safety of mFFX and Nab-G as first-line treatments in real-life situations. mPC patients treated with either mFFX or Nab-G as first-line were retrospectively analyzed. The Kaplan-Meier method was used to estimate progression-free survival (PFS) and overall survival (OS), and the log-rank test was used to compare groups. There were 54 and 17 patients in the mFFX and Nab-G groups respectively. Baseline characteristics were comparable. The disease control rate (DCR) was 64.8% in the mFFX group and 29.4% in the Nab-G group ($p = 0.01$). The median PFS (mFFX: 6.3 months vs Nab-G: 3.6 months; $p = 0.021$) and the median OS (mFFX: 11.5 months vs Nab-G: 7.6 months; $p = 0.013$) were statistically higher in the mFFX group. The median OS was prolonged in patients who received second-line treatment (14 vs 8.6 months; $p = 0.007$). There was no significant difference between the two groups in terms of grade 3–4 toxicity. Our study demonstrated better DCR and increased survival outcomes with mFFX vs Nab-G with comparable toxicity profiles.

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Introduction

Pancreatic cancer has an extremely poor prognosis with a five-year survival rate of only 12%[1]. It is predicted to overtake breast cancer in Europe as the third leading cause of cancer death by 2025[2]. Surgery remains the only curative treatment option but unfortunately, almost half of the patients have metastatic disease at diagnosis. Metastatic pancreatic cancer (mPC) is generally considered incurable and is treated palliatively with chemotherapy (ChT)[3]. Although the survival advantage was modest, single-agent gemcitabine has demonstrated mainly clinical benefit over 5-fluorouracil (5-FU) and was considered the standard-of-care first-line approach for over a decade[4]. Subsequently, in pivotal phase III trials, FOLFIRINOX (the combination of 5-FU, oxaliplatin, and irinotecan) and nab-paclitaxel plus gemcitabine (Nab-G) showed markedly better clinical outcomes than gemcitabine monotherapy for first-line treatment[5,6]. Because of concerns about toxicity with the FOLFIRINOX (FFX) dosage schedule, a modified form of FFX (mFFX) with a reduced dose of irinotecan and omission of bolus 5-FU is commonly used in daily practice[7]. More recently, the NAPOLI-3 trial compared NALIRIFOX (the combination of 5-FU, leucovorin, liposomal irinotecan, and oxaliplatin) with Nab-G in the first-line setting and demonstrated a survival benefit, making it a candidate for a new treatment strategy[8]. While these regimens are recommended treatment alternatives in the first-line setting; randomized, head-to-head comparison studies are limited. Treatment is chosen based on the patient's performance status (PS), comorbidities, and toxicities[9].

The real-world practice is often different from the context in which the clinical trial was studied. Clinical trials often select fit patients but is not representative of the real world. In addition, preferences for first-line treatment differ among countries, depending on reimbursement and drug accessibility[10]. Therefore, retrospective data representing the real-world experience are crucial in evaluating the efficacy and safety of treatment strategies. In this study, we aimed to analyze the efficacy and safety of mFFX and Nab-G as first-line treatments in mPC patients treated in real-life settings.

Materials and methods

Patients and study design

This was a retrospective, cohort study conducted in Antalya Training and Research Hospital (Türkiye). The medical records of patients with histologically proven pancreatic cancer who were treated and followed up between September 2015 and September 2022 were reviewed. Patients with inadequate archive records, a pathological diagnosis other than adenocarcinoma, nonmetastatic disease, ineligible for treatment after diagnosis for certain reasons (poor PS, treatment refusal, etc.), or receiving ChT other than mFFX or Nab-G as first-line treatments were excluded. Finally, a total of 71 patients aged ≥18 years old who had received at least one cycle of mFFX or Nab-G as first-line treatment for mPC were included in the study.

Treatment and response assessment

mFFX consisted of a 2-h intravenous infusion of oxaliplatin 85 mg/m^2, a 90-min intravenous infusion of irinotecan 150 mg/m^2, a 2-h infusion of leucovorin 400 mg/m^2, and a 46-h continuous infusion of 5-FU 2,400 mg/m^2, administered every two weeks. Nab-G consisted of a 30-min intravenous infusion of nab-paclitaxel at a dose of 125 mg/m^2 followed by gemcitabine at a dose of 1,000 mg/m^2 on days 1, 8, and 15, every four weeks. Tumor response was assessed every 8–12 weeks using computed tomography or positron emission tomography. Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 was used for grading the best response as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). Patients with PD received second-line treatment or were followed with the best supportive care according to their first-line therapy, PS, toxicity profile, and physician preference. Toxicity was evaluated by Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

Study endpoints

Progression-free survival (PFS) was defined as the time from the initiation of first-line ChT until the progression date or death from any cause whichever occurred first. Overall survival (OS) was defined as the time from the mPC diagnosis until death or the last follow-up time.

Statistical analysis

SPSS version 25.0 (IBM Corp, Armonk, NY, USA) was used for statistical analyses. Descriptive statistics were presented as numbers (n) and percentages (%) for categorical variables and median (IQR or min-max) for continuous variables. The Mann-Whitney U test was used to compare data that were not normally distributed. The Chi-square test or Fisher's exact test, as appropriate, was performed to compare categorical variables. The Kaplan-Meier method was used to estimate OS and PFS, and the log-rank test was used to compare groups. Univariate analyses were performed separately for each prognostic variable using the Cox-regression test. As no statistically significant variables were identified in the univariate analysis, multivariate Cox regression analysis could not be performed. A *p*-value less than 0.05 was considered to be statistically significant.

Results

Baseline characteristics

Of the 71 patients included in the study, 54 were treated with mFFX, and 17 were treated with Nab-G as the first-line treatment. The median cycle number of mFFX was 8.5 and the median cycle number of Nab-G was 3 ($p < 0.001$). The male gender was approximately twice that of females, but there was no statistical difference between the two treatment groups ($p = 0.241$). The median tumor diameter was 4.5 cm in both groups and there was no difference between the groups according to median diameter ($p = 0.839$). Overall, baseline characteristics were comparable between the two groups (Table 1).

Efficacy and prognostic factors

First-line treatment response and efficacy data are shown in Table 2. Regarding the best response, the disease control rate (DCR) in the mFFX group was significantly higher than in the Nab-G group (64.8% vs 29.4%, respectively) ($p = 0.01$). Five patients (9.3%) experienced CR with mFFX. There was no CR in the Nab-G group and 70.6% of patients developed PD.

The median follow-up time was 10 months (range, 2–55). At the last follow-up date, eight patients in the mFFX group and three patients in the Nab-G group were still alive. The median PFS was 5.7 months (95% CI, 4.2–7.3) and the 12-months PFS was 13.7% in all patients. According to first-line ChT groups median PFS was significantly higher in the mFFX group than in the Nab-G group (6.3 months [95% CI, 5.5–7] vs 3.6 months [95% CI, 3–4.1]) ($p = 0.021$) (Fig. 1). The median OS was 11.2 months (95% CI, 9.3–13.1), and the 12-months OS was 40% in all patients. The median OS was statistically higher in the mFFX group (11.5 months [95% CI, 10–12.9]) than in the Nab-G group (7.6 months [95% CI, 4.4–10.8]) ($p = 0.013$) (Fig. 2).

Regarding Eastern Cooperative Oncology Group (ECOG) PS, Kaplan-Meier analysis estimated that the OS decreased from PS 0 to 2 (12.1, 11.2, and 8.6 months for PS 0, 1, and 2, respectively), but this decrease was not statistically significant (0 vs 1; $p = 0.625$), (0 vs 2; $p = 0.053$), and (1 vs 2; $p = 0.070$). Estimated PFS was decreased from PS 0 to 2 (5.9, 5.5, and 4.3 months for PS 0, 1, and 2, respectively), but this decrease was also not statistically significant (0 vs 1; $p = 0.858$), (0 vs 2; $p = 0.142$), and (1 vs 2; $p = 0.126$).

Table 1. Baseline demographic and clinicopathologic characteristics of the patients.

Variables	Total (n = 71)	mFFX (n = 54)	Nab-G (n = 17)	*p*-value
Age, median (min-max)	63.0 (37–82)	63.0 (37–82)	63.0 (42–77)	0.762
Gender, n (%)				
Female	25 (35.2)	17 (31.5)	8 (47.1)	0.241
Male	46 (64.8)	37 (68.5)	9 (52.9)	
ECOG PS, n (%)				
0	14 (19.7)	13 (24.1)	1 (5.9)	0.197
1	40 (56.3)	30 (55.6)	10 (58.8)	
2	17 (23.9)	11 (20.4)	6 (35.3)	
T stage, n (%)				
T2	19 (26.8)	17 (31.5)	2 (11.8)	0.207
T3	35 (49.3)	26 (48.1)	9 (52.9)	
T4	17 (23.9)	11 (20.4)	6 (35.3)	
Median tumor diameter, cm (IQR)	4.5 (2.7)	4.5 (2.9)	4.5 (1.8)	0.267
Tumor diameter, cm, n (%)*				
≤ 4.50	38 (53.5)	29 (53.7)	9 (52.9)	0.839
> 4.50	31 (43.6)	23 (42.6)	8 (47.1)	
Primary tumor location, n (%)				
Head	35 (49.3)	24 (44.4)	11 (64.7)	0.443
Corpus	18 (25.4)	15 (27.8)	3 (17.6)	
Tail	18 (25.4)	15 (27.8)	3 (17.6)	
CA 19.9 (U/ml), median (IQR)	1,361 (4,882.6)	1,506.6 (4,956.8)	698.8 (6,364.1)	0.370
Liver metastasis, n (%)				
No	21 (29.6)	18 (33.3)	3 (17.6)	0.055
Yes	50 (70.4)	36 (66.7)	14 (82.4)	
Lung metastasis, n (%)				
No	57 (80.3)	42 (77.8)	15 (88.2)	0.493
Yes	14 (19.7)	12 (22.2)	2 (11.8)	
Bone metastasis, n (%)				
No	65 (91.5)	50 (92.6)	15 (88.2)	0.625
Yes	6 (8.5)	4 (7.4)	2 (11.8)	
Lymph node metastasis, n (%)				
No	23 (32.4)	16 (29.6)	7 (41.2)	0.375
Yes	48 (67.6)	38 (70.4)	10 (58.8)	
Other metastasis sites, n (%)				
No	60 (84.5)	43 (79.6)	17 (100)	0.055
Yes**	11 (15.5)	11 (20.4)	0 (0)	

mFFX, modified FOLFIRINOX; Nab G, Nab-paclitaxel + Gemcitabine; ECOG PS, Eastern Cooperative Oncology Group Performance Status. * The maximum tumor diameter of two patients on imaging was not specified, ** Periton or surrenal gland metastasis.

Table 2. Efficacy of first-line treatments.

Best response, n (%)	First-line treatment		*p*-value
	mFFX	Nab-G	
Objective response rate (CR + PR)	22 (40.7)	4 (23.5)	0.199
Disease control rate (CR + PR + SD)	35 (64.8)	5 (29.4)	**0.010**
SD	13 (24.1)	1 (5.9)	0.068
PR	17 (31.5)	4 (23.5)	
CR	5 (9.3)	0 (0)	
PD	19 (35.2)	12 (70.6)	

mFFX, modified FOLFIRINOX; Nab-G, nab-paclitaxel + Gemcitabine; SD, stable disease; PR, partial response; CR, complete response; PD, progressive disease; the number in bold indicates statistical significance.

Univariate Cox regression analysis to evaluate the effect of clinicopathologic factors on survival showed that none of the factors had a statistically significant impact on PFS and OS ($p > 0.05$) (Table 3).

Second-line treatment

Three patients did not develop progression after first-line treatment. Among the patients who progressed, 47% in the mFFX group and 88.2% in the Nab-G group failed to receive second-line treatment. Second-line treatments are listed in Table 4. Patients with any grade of anemia in the first-line had a significantly higher rate of failure to receive second-line treatment (p = 0.038). There was no statistically significant difference in terms of failure to receive second-line treatment in patients experiencing any degree of neutropenia or thrombocytopenia during first-line treatment (p = 0.914 and p = 0.168, respectively). The OS was significantly longer in the patients who received second-line therapy compared to those who did not (median OS 14 vs 8.6 months, respectively) (p = 0.007) (Fig. 3).

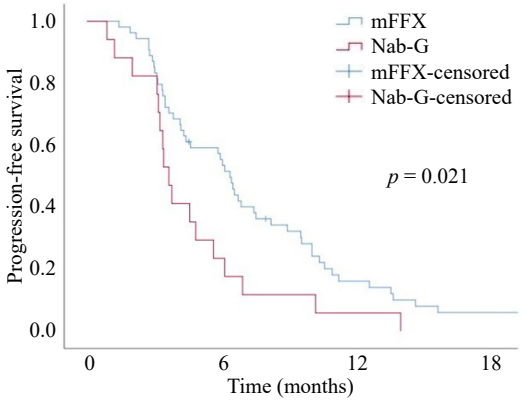

Fig. 1 Progression-free survival with modified FOLFIRINOX (mFFX) and Nab-paclitaxel + Gemcitabine (Nab-G).

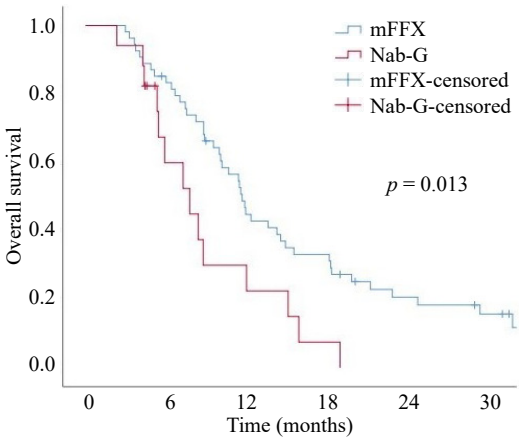

Fig. 2 Overall survival with modified FOLFIRINOX (mFFX) and Nab-paclitaxel + Gemcitabine (Nab-G).

Safety profile

Toxicities are presented in Table 5. Grade 3–4 hematologic toxicities were statistically similar in both groups. There was not any case of febrile neutropenia in patients treated with Nab-G. The fatigue rate was higher in the Nab-G group than mFFX group (82% vs 52%, respectively). Although the safety profile was comparable between treatment groups, dose reduction was significantly higher in the mFFX group (57% vs 18%, p = 0.004).

Discussion

Our study demonstrated that mFFX is a better first-line option than Nab-G in terms of disease control and survival in patients with mPC. Furthermore, an improvement in survival rates was also noted among patients who could receive second-line treatment.

The Dutch pancreatic cancer group presented their large patient database, demonstrating a median OS of approximately six months, which was much worse than our results[11,12]. However, all patients in their studies received treatment before 2018, and approximately one-fifth of the patients received single-agent gemcitabine. Patients who received FFX or Nab-G had more unfavorable baseline demographic and clinicopathologic characteristics compared to our study. Furthermore, 80% of patients who received FFX and 83% of patients who received Nab-G failed to receive second-line treatment[12]. Although our cohort had a higher proportion of patients with ECOG PS 2, survival was not as poor as expected. Most PS 2 patients treated with mFFX were able to receive six or more cycles of treatment. Possibly due to the rapid tumor response and shrinkage, these patients were able to continue treatment without complications. Another possible cause is that the physician evaluating the

Table 3. Univariate Cox regression analysis for progression-free survival and overall survival.

Variables	Univariate analysis (PFS)		Univariate analysis (OS)	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Gender (ref: male)	1.20 (0.73–1.98)	0.472	1.41 (0.82–2.41)	0.210
Age	1.01 (0.98–1.03)	0.731	1.02 (0.99–1.04)	0.129
ECOG PS (ref: 0)		0.244		0.101
1	0.94 (0.50–1.76)	0.852	0.85 (0.44–1.61)	0.621
2	1.55 (0.75–3.18)	0.230	1.70 (0.81–3.56)	0.157
T stage (ref: T2)		0.934		0.622
T3	0.95 (0.54–1.72)	0.887	0.79 (0.42–1.47)	0.465
T4	1.07 (0.51–2.11)	0.845	1.06 (0.51–2.22)	0.879
Tumor diameter, cm (ref: ≤ 4.50)	0.77 (0.47–1.26)	0.308	1.02 (0.60–1.72)	0.930
Primary tumor location (ref: head)		0.352		0.339
Corpus	0.68 (0.37–1.23)	0.207	0.87 (0.46–1.65)	0.678
Tail	0.72 (0.40–1.30)	0.278	0.62 (0.33–1.17)	0.142
CA 19.9 level (ref: < 1361 U/ml)	0.85 (0.51–1.42)	0.547	0.77 (0.44–1.34)	0.364
Liver metastasis (ref: no)	0.94 (0.56–1.58)	0.836	0.80 (0.46–1.39)	0.433
Lung metastasis (ref: no)	1.20 (0.66–2.19)	0.540	1.51 (0.80–2.85)	0.198
Bone metastasis (ref: no)	1.05 (0.45–2.46)	0.904	1.47 (0.62–3.44)	0.376
Lymph node metastasis (ref: no)	1.26 (0.75–2.13)	0.370	1.13 (0.65–1.98)	0.657

PFS, progression–free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; ref, reference; ECOG PS, Eastern Cooperative Oncology Group Performance Status. As no statistically significant variables were identified in the univariate analysis, multivariate analysis was not performed.

Table 4. Second-line treatments.

First-line treatment	Second-line treatment	n (%)
mFFX	None	24 (47)
	Nab-G	18 (35.3)
	Gemcitabine	6 (11.8)
	Cisplatin + Gemcitabine	3 (5.9)
Nab-G	None	15 (88.2)
	mFFX	1 (5.9)
	mFOLFOX6	1 (5.9)

mFFX, modified FOLFIRINOX; Nab-G, nab-paclitaxel + Gemcitabine.

patient before first-line treatment may have underestimated the PS due to the mPC tumor burden and/or recorded it as PS 2 due to higher subjective complaints. As mentioned above, the rapid tumor response may have helped the patients stay on treatment and resulted in better survival than expected.

Results of retrospective studies comparing the two treatment regimens were conflicting. Some studies have shown that FFX has better survival results[13,14], while others have reported comparable PFS and OS[15–17]. In a study by Williet et al. using the propensity score matching (PSM) method to minimize the bias; after adjusting the groups for characteristics such as age, PS, metastasis sites, and liver metastasis, the FFX was associated with improved OS[18]. Another retrospective study using the PSM method also found

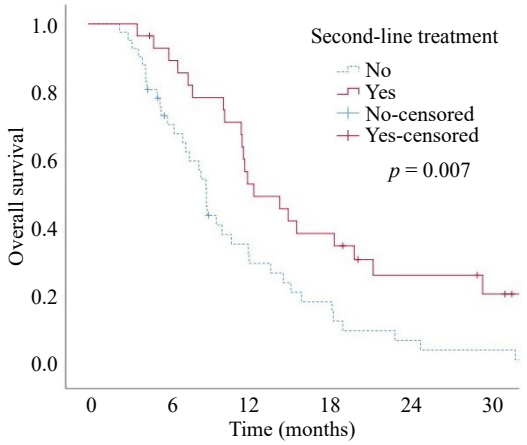

Fig. 3 Overall survival according to second-line treatment.

Table 5. Safety profile of first-line treatment options.

Adverse event, n (%)	mFFX (n = 54)		Nab-G (n = 17)		*p*-value
	Grade 1–2	Grade 3–4	Grade 1–2	Grade 3–4	
Hematologic					
Neutropenia	9 (17)	18 (33)	2 (12)	5 (29)	0.596
Anemia	14 (26)	6 (11)	7 (41)	3 (18)	0.669
Thrombocytopenia	16 (29)	7 (13)	3 (18)	5 (29)	0.206
Non-hematologic					
Fatigue	27 (50)	1 (2)	12 (70)	2 (12)	0.254
Nausea	15 (28)	7 (13)	8 (47)	1 (6)	0.379
Vomiting	17 (31)	3 (5)	6 (35)	1 (6)	1.000
Diarrhea	5 (9)	0	0	0	N/A
Stomatitis/mucositis	8 (15)	1 (2)	3 (18)	1 (6)	1.000
	mFFX		Nab-G		*p*-value
Febrile neutropenia	2 (4)		0		0.631
Dose reduction	31 (57)		3 (18)		**0.004**
Dose delay	32 (59)		12 (70)		0.401
Hospitalization	14 (26)		6 (35)		0.540

mFFX, modified FOLFIRINOX; Nab-G, nab-paclitaxel + Gemcitabine; N/A, not applicable. Fisher's Exact test; numbers in bold indicate statistical significance.

longer PFS and OS with FFX[19]. These results were also obtained with mFFX in our study. For patients with mPC, maintaining effective treatment for as long as possible is critical to prolonging survival. Approximately half of patients with mPC could receive second-line treatment[20]. For patients treated with a 5-FU-based regimen in the first-line setting, Nab-G may be an effective second-line option. Conversely, patients receiving gemcitabine-based regimens in the first-line setting have more toxic and difficult-to-adhere-to second-line 5-FU-based treatment options[12,21]. In our study, Nab-G could be used in the second-line setting in 35% of patients who received mFFX in the first line, but the access rate to effective second-line treatment after first-line Nab-G remained extremely low. This may explain the survival results favoring first line mFFX. Moreover, the survival results of mFFX in our study (median PFS 6.3 months and median OS 11.5 months) were in line with the results of the phase III PRODIGE4/ACCORD11 trial (median PFS 6.4 months and median OS 11.1 months).

The mFFX group showed a higher DCR than the Nab-G group in our study, consistent with the findings of a retrospective study conducted on Turkish patients[22]. The superior DCR observed with mFFX was primarily because there were five CR patients and a higher proportion of patients with SD in the mFFX group, as well as a higher proportion of patients with PD in the Nab-G group. Among factors that may be prognostic and lead to poor treatment compliance, the proportion of PS 2 patients and patients with liver metastases was higher in the Nab-G group, although not statistically significant. Dose modification was higher in the mFFX group, which may have allowed more patients to adhere to the treatment schedule and receive effective treatment for a longer period of time than in the Nab-G group. Although it was not statistically significant, the Nab-G group had a higher rate of hospitalizations and ChT dose delays. This may have meant that patients on Nab-G were treated for a shorter period of time and had difficulty adhering to their treatment plans, which could have led to progression. A similar trend was observed, although it did not reach statistical significance, with grade 3 or 4 fatigue being proportionally more common in the Nab-G group. By potentially affecting adherence, this could also be a potential factor leading to reduced efficacy of Nab-G.

The treatment duration is an important determinant of its efficacy. In our study, patients received a median of 8.5 cycles of mFFX and 3 cycles of Nab-G. We observed that early progression or toxicity led to early treatment discontinuation, especially in the Nab-G group. However, comparable median treatment cycles have been published in the literature[19,23–25].

With improved survival of mPC in recent decades, treatment sequencing has become an important concern. There is no established standard of care for second-line ChT, as no randomized trials are evaluating subsequent treatment after failure of first-line mFFX or Nab-G. Similar to the retrospective data[10,26], we observed that patients who received mFFX in the first-line setting were treated with gemcitabine-based regimens in the second-line. In our study, 88% of the Nab-G group failed to receive second-line treatment either because they died during or immediately after progression on first-line treatment, because of poor performance after first-line treatment, or due to their refusal to receive therapy. Consistent with data showing that effective subsequent treatment after progression on first-line therapy can provide relatively prolonged survival[27], the OS was significantly longer in patients receiving second-line therapy in our study.

According to results of pivotal studies, triplet ChT showed higher toxicity rates, with increased high-grade neutropenia (45.7% vs 38%), fatigue (23.6% vs 17%), and diarrhea (12.7% vs 6%) when

compared to gemcitabine monotherapy[5,6]. Meta-analyses and retrospective studies generally concluded an increase in hematologic toxicity with mFFX and neuropathy with Nab-G[28,29]. While others reported a similar safety profile[22,30,31]. In our study, we found no statistical difference between mFFX and Nab-G treatment regimens, especially in terms of grade 3–4 toxicities; but due to lack of data on neuropathy questioning and recording, neuropathy could not be reported. Although febrile neutropenia is expected to be high with mFFX[29,30], our results did not show a marked difference in the incidence of febrile neutropenia. This could be related to the effective use of prophylactic G-CSF in the mFFX group.

Current guidelines recommend both FFX or mFFX and Nab-G regimens in first-line treatment, considering patient characteristics[9,32]. The prospective GENERATE trial was the first to aim to compare mFFX, Nab-G, and S-IROX (a regimen most commonly used in Asia that replaces continuous intravenous 5-FU with oral administered fluoropyrimidine of S-1) in a head-to-head analysis. This trial suggested that Nab-G should be considered as a superior first-line treatment in terms of OS[33]. It is crucial to highlight that, in contrast to other pivotal studies, this was a single-nation, Asian study. Additionally, the response rates in the mFFX arm were in line with previous data, but the high ORR observed with Nab-G is difficult to interpret.

Our study had some limitations. It was a single-center, retrospective, nonrandomized study with a relatively small sample size. A notable limitation is the relatively small number of patients in the Nab-G arm, which can be attributed to the challenges in accessing nab-paclitaxel across our country. In addition, safety profiles in our analysis may have missing data due to a lack of recording of adverse events as a result of the retrospective nature of the analysis.

Conclusions

The findings of our study indicated that the first-line administration of mFFX in the treatment of mPC was associated with superior DCR and prolonged survival in eligible patients compared to the Nab-G regimen, with a comparable side effect profile. Furthermore, we observed that survival was significantly improved in patients who were able to receive second-line treatment. However, prospective, multinational randomized studies are required to confirm these findings.

Ethical statements

All procedures were reviewed and preapproved by the Ethics Committee of Antalya Training and Research Hospital (Identification No. 1/7, approval date: 12/01/2023). Because of the retrospective nature of the study written informed consent was waived by the committee.

Author contributions

The authors confirm contribution to the paper as follows: study conception and design: Kivrak Salim D, Arici MO; data collection: Arici MO; analysis and interpretation of results: Kivrak Salim D; draft manuscript preparation: Kivrak Salim D, Arici MO. Both authors reviewed the results and approved the final version of the manuscript.

Data availability

The datasets generated during and/or analyzed during the current study are not publicly available due to their containing information that could compromise the privacy of research participants and ethical restrictions.

Conflict of interest

The authors declare that they have no conflict of interest.

Dates

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References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. 2023. Cancer statistics, 2023. *CA: A Cancer Journal for Clinician* 73:17–48
2. Ferlay J, Partensky C, Bray F. 2016. More deaths from pancreatic cancer than breast cancer in the EU by 2017. *Acta Oncologica* 55:1158–60
3. Kolbeinsson HM, Chandana S, Wright GP, Chung M. 2023. Pancreatic cancer: a review of current treatment and novel therapies. *Journal of Investigative Surgery* 36:2129884
4. Burris HA, 3rd, Moore MJ, Andersen J, Green MR, Rothenberg ML, et al. 1997. Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. *Journal of Clinical Oncology* 15:2403–13
5. Conroy T, Desseigne F, Ychou M, Bouché O, Guimbaud R, et al. 2011. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *New England Journal of Medicine* 364:1817–25
6. Von Hoff DD, Ervin T, Arena FP, Gabriela Chiorean E, Infante J, et al. 2013. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *New England Journal of Medicine* 369:1691–703
7. Mahaseth H, Brutcher E, Kauh J, Hawk N, Kim S, et al. 2013. Modified FOLFIRINOX Regimen With Improved Safety and Maintained Efficacy in Pancreatic Adenocarcinoma. *Pancreas* 42:1311–15
8. Wainberg ZA, Melisi D, Macarulla T, Pazo Cid R, Chandana SR, et al. 2023. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. *The Lancet* 402:1272–81
9. Sohal DPS, Kennedy EB, Cinar P, Conroy T, Copur MS, et al. 2020. Metastatic pancreatic cancer: ASCO guideline update. *Journal of Clinical Oncology* 38:3217–30
10. Taieb J, Prager GW, Melisi D, Westphalen CB, D'Esquermes N, et al. 2020. First-line and second-line treatment of patients with metastatic pancreatic adenocarcinoma in routine clinical practice across Europe: a retrospective, observational chart review study. *ESMO Open* 5:e000587
11. Latenstein AEJ, van der Geest LGM, Bonsing BA, Groot Koerkamp B, Haj Mohammad N, et al. 2020. Nationwide trends in incidence, treatment and survival of pancreatic ductal adenocarcinoma. *European Journal of Cancer* 125:83–93
12. Pijnappel EN, Dijksterhuis WPM, van der Geest LG, de Vos-Geelen J, de Groot JWB, et al. 2021. First- and second-line palliative systemic treatment outcomes in a real-world metastatic pancreatic cancer cohort. *Journal of the National Comprehensive Cancer Network* 20:443–450.e3
13. Boyne DJ, Brenner DR, Gupta A, MacKay E, Arora P, et al. 2023. Head-to-head comparison of FOLFIRINOX versus gemcitabine plus nab-paclitaxel in advanced pancreatic cancer: a target trial emulation using real-world data. *Annals of Epidemiology* 78:28–34
14. Klein-Brill A, Amar-Farkash S, Lawrence G, Collisson EA, Aran D. 2022. Comparison of FOLFIRINOX vs Gemcitabine Plus Nab-Paclitaxel as First-Line Chemotherapy for Metastatic Pancreatic Ductal Adenocarcinoma. *JAMA Network Open* 5:e2216199
15. Cartwright TH, Parisi M, Espirito JL, Wilson TW, Pelletier C, et al. 2018. Clinical Outcomes with First-Line Chemotherapy in a Large Retrospective Study of Patients with Metastatic Pancreatic Cancer Treated in a US Community Oncology Setting. *Drugs - Real World Outcomes* 5:149–59
16. Kang J, Hwang I, Yoo C, Kim KP, Jeong JH, et al. 2018. Nab-paclitaxel plus gemcitabine versus FOLFIRINOX as the first-line chemotherapy for

patients with metastatic pancreatic cancer: retrospective analysis. *Investigational New Drugs* 36:732–41
17. Kim S, Signorovitch JE, Yang H, Patterson-Lomba O, Xiang CQ, et al. 2018. Comparative effectiveness of nab-paclitaxel plus gemcitabine vs FOLFIRINOX in metastatic pancreatic cancer: a retrospective nationwide chart review in the United States. *Advances in Therapy* 35:1564–77
18. Williet N, Saint A, Pointet AL, Tougeron D, Pernot S, et al. 2019. Folfirinox versus gemcitabine/nab-paclitaxel as first-line therapy in patients with metastatic pancreatic cancer: a comparative propensity score study. *Therapeutic Advances in Gastroenterology* 12:1–14
19. Chun JW, Lee SH, Kim JS, Park N, Huh G, et al. 2021. Comparison between FOLFIRINOX and gemcitabine plus nab-paclitaxel including sequential treatment for metastatic pancreatic cancer: a propensity score matching approach. *BMC Cancer* 21:537
20. Martín AM, Hidalgo M, Alvarez R, Arrazubi V, Martínez-Galán J, et al. 2018. From first line to sequential treatment in the management of metastatic pancreatic cancer. *Journal of Cancerr* 9:1978–88
21. Liu Y, Guo X, Xu P, Song Y, Huang J, et al. 2024. Clinical outcomes of second-line chemotherapy in patients with advanced pancreatic adenocarcinoma: a real-world study. *Cancer Biology & Medicine* 21:799–812
22. Ay S, Atcı MM, Arıkan R, Dülgar Ö, Özyükseler DT, et al. 2022. FOLFIRINOX versus gemcitabine plus nab-paclitaxel as the first-line chemotherapy in metastatic pancreatic cancer. *Journal of Chemotherapy* 34:465–71
23. Cho IR, Kang H, Jo JH, Lee HS, Chung MJ, et al. 2020. FOLFIRINOX vs gemcitabine/nab-paclitaxel for treatment of metastatic pancreatic cancer: Single-center cohort study. *World Journal of Gastrointestinal Oncology* 12:182–94
24. Franco F, Camara JC, Martín-Valadés JI, López-Alfonso A, Marrupe D, et al. 2021. Clinical outcomes of FOLFIRINOX and gemcitabine–nab paclitaxel for metastatic pancreatic cancer in the real world setting. *Clinical and Translational Oncology* 23:812–19
25. Park CS, Park BK, Han JH, Lee KJ, Son KJ. 2024. Real-world outcomes of first-line chemotherapy in metastatic pancreatic cancer: a nationwide population-based study in Korea. *Cancers* 16:3173
26. Mie T, Sasaki T, Takeda T, Okamoto T, Hamada T, et al. 2023. Treatment outcomes and prognostic factors of gemcitabine plus nab-paclitaxel as second-line chemotherapy after modified FOLFIRINOX in unresectable pancreatic cancer. *Cancers* 15:358
27. Chae H, Jeong H, Cheon J, Chon HJ, Ryu H, et al. 2020. Efficacy and safety of second-line nab-paclitaxel plus gemcitabine after progression on FOLFIRINOX for unresectable or metastatic pancreatic ductal adenocarcinoma: multicenter retrospective analysis. *Therapeutic Advances in Medical Oncology* 12:1–8
28. Chiorean EG, Cheung WY, Giordano G, Kim G, Al-Batran SE. 2019. Real-world comparative effectiveness of nab-paclitaxel plus gemcitabine versus FOLFIRINOX in advanced pancreatic cancer: a systematic review. *Therapeutic Advances in Medical Oncology* 11:1–17
29. Pusceddu S, Ghidini M, Torchio M, Corti F, Tomasello G, et al. 2019. Comparative effectiveness of gemcitabine plus nab-paclitaxel and FOLFIRINOX in the first-line setting of metastatic pancreatic cancer: a systematic review and meta-analysis. *Cancers* 11:484
30. Chen J, Hua Q, Wang H, Zhang D, Zhao L, et al. 2021. Meta-analysis and indirect treatment comparison of modified FOLFIRINOX and gemcitabine plus nab-paclitaxel as first-line chemotherapy in advanced pancreatic cancer. *BMC Cancer* 21:853
31. Han SY, Kim DU, Seol YM, Kim S, Lee NK, et al. 2020. Comparison of gemcitabine plus nab-paclitaxel and FOLFIRINOX in metastatic pancreatic cancer. *World Journal of Clinical Casess* 8:3718–29
32. Ducreux M, Cuhna AS, Caramella C, Hollebecque A, Burtin P, et al. 2015. Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology* 26:v56–v68
33. Ohba A, Ozaka M, Ogawa G, Okusaka T, Kobayashi S, et al. 2023. 1616O: Nab-paclitaxel plus gemcitabine versus modified FOLFIRINOX or S-IROX in metastatic or recurrent pancreatic cancer (JCOG1611, GENERATE): a multicentred, randomized, open-label, three-arm, phase II/III trial. *Annals of Oncology* 34:S894