First- and Second-Line Palliative Systemic Treatment Outcomes in a Real-World Metastatic Pancreatic Cancer Cohort

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ABSTRACT

Background: Metastatic pancreatic ductal adenocarcinoma (PDAC) is characterized by a poor survival rate, which can be improved by systemic treatment. Consensus on the most optimal first- and second-line palliative systemic treatment is lacking. The aim of this study was to describe the use of first- and second-line systemic treatment, overall survival (OS), and time to failure (TTF) of first- and second-line treatment in metastatic PDAC in a real-world setting. **Patients and Methods:** Patients with synchronous metastatic PDAC diagnosed between 2015 and 2018 who received systemic treatment were selected from the nationwide Netherlands Cancer Registry. OS and TTF were evaluated using Kaplan-Meier curves with log-rank test and multivariable Cox proportional hazard analyses. **Results:** The majority of 1,586 included patients received FOLFIRINOX (65%), followed by gemcitabine (18%), and gemcitabine + nab-paclitaxel (13%) in the first line. Median OS for first-line FOLFIRINOX, gemcitabine + nab-paclitaxel, and gemcitabine monotherapy was 6.6, 4.7, and 2.9 months, respectively. Compared to FOLFIRINOX, gemcitabine + nab-paclitaxel showed significantly inferior OS after adjustment for confounders (hazard ratio [HR], 1.20; 95% CI, 1.02–1.41), and gemcitabine monotherapy was independently associated with a shorter OS and TTF (HR, 1.98; 95% CI, 1.71–2.30 and HR, 2.31; 95% CI, 1.88–2.83, respectively). Of the 121 patients who received second-line systemic treatment, 33% received gemcitabine + nab-paclitaxel, followed by gemcitabine (31%) and FOLFIRINOX (10%). **Conclusions:** Based on population-based data in patients with metastatic PDAC, treatment predominantly consists of FOLFIRINOX in the first line and gemcitabine with or without nab-paclitaxel in the second line. FOLFIRINOX in the first line shows superior OS compared with gemcitabine with or without nab-paclitaxel.

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Background

Despite recent therapeutic advances, the prognosis of patients with metastatic pancreatic ductal adenocarcinoma (PDAC) remains poor.[1,2] Because >80% of patients with pancreatic cancer are diagnosed at an advanced stage, chemotherapy is the cornerstone of treatment.[3–5] However, international consensus on the most optimal first- and second-line palliative systemic treatment regimen is lacking.

Since 1997, single-agent gemcitabine has been the standard first-line palliative treatment,[3–7] and progress in the development of new agents has been slow. Many cytotoxic agents in combination with gemcitabine did not show improvement in overall survival (OS) or quality of life (QoL).[3–5,8–12] In 2011, irinotecan/oxaliplatin/5-FU (FOLFIRINOX) was the first treatment regimen that showed a significant advancement (OS of 11.1 months) over gemcitabine but its use is generally restricted to patients with a good WHO performance status (PS).[13] Another chemotherapy combination that demonstrated a survival improvement compared with gemcitabine monotherapy was gemcitabine in combination with nab-paclitaxel, with a median OS of 8.5 months versus 6.7 months for gemcitabine alone.[5,14] Currently FOLFIRINOX and gemcitabine with or without nab-paclitaxel are widely used first-line regimes,[15] but there is limited evidence supporting use as second-line treatment of metastatic PDAC, especially after FOLFIRINOX.[16,17] In 2016, the NAPOLI-1 trial showed that nanoliposomal irinotecan in combination with 5-FU and folinic acid prolonged survival for patients previously treated with gemcitabine-based therapy in the first line, with a median OS of 6.1 months.[18]

Current practice is based on the results of randomized controlled trials (RCTs).[9,14] However, these trials do not sufficiently reflect the patient population as seen in


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daily clinical practice.[19] For instance, elderly and fragile patients are not included in most clinical trials. Therefore, the aim of this real-world data study was to describe first- and second-line systemic treatment in patients with metastatic PDAC and analyze the association between first- and second-line treatment regimens on OS and time to failure (TTF) of first- and second-line treatment.

Patients and Methods

Data Collection

All patients diagnosed with synchronous metastatic PDAC in the Netherlands between 2015 and 2018 were identified in the Netherlands Cancer Registry (NCR) (supplemental eTable 1, available with this article at JNCCN.org). The NCR is a population-based registry that covers the total Dutch population of >17 million people and is directly linked to the pathologic archive that comprises all histologically confirmed cancer diagnoses and is in combination with the National Hospital Discharge Register a suitable representation of the metastatic PDAC patient population nationwide (microscopically verified and nonverified PDAC).

Information about the patient (sex, age, PS, previous cancer diagnosis, comorbidities), tumor (TNM stage, tumor histology, location of metastases), treatment (systemic treatment, radiotherapy, other palliative interventions such as stents/bypasses), and follow-up were recorded from the hospital's electronic health record system or medical records by trained registrars of the NCR.

Patients who received first-line systemic treatment outside the Netherlands were excluded (n=4). This study was designed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[20]

Systemic Therapy

First-line systemic treatment was defined as the first chemotherapeutic agent(s) given until discontinuation. A combination regimen was defined as all systemic agents starting within 3 days after the start of the first systemic agent. If the same therapy was restarted after a treatment break, this was still regarded first-line treatment. If one agent of a combination therapy was discontinued but the other agents continued, this was considered as continuation of first-line therapy (eg, irinotecan + 5-FU combination after FOLFIRINOX). Treatment was considered as next line if an agent of a new drug group was started that was not applied in the previous systemic treatment regimen.

Systemic therapy strategies, first- and second-line, were classified into the following regimens: FOLFIRINOX, gemcitabine monotherapy, gemcitabine + nab-paclitaxel, and other. FOLFIRINOX was assumed if only oxaliplatin and irinotecan were registered (n=6). Targeted therapy in addition to FOLFIRINOX or in combination with gemcitabine + nab-paclitaxel was ignored (n=5). If the start date of first-line palliative systemic therapy was missing (n=6), we used the date of diagnosis to calculate the survival rates. If the start date of second-line palliative systemic therapy was missing (n=3), we used the stop date of first-line treatment as start date of second-line treatment to calculate the survival rates.

Second-line systemic treatment was described in patients in whom follow-up was completed (ie, diagnosed between 2015 and 2016). The follow-up of sequential treatment lines of patients diagnosed from 2017 to 2018 was not completed entirely by the NCR, and therefore these years were not included.

OS and TTF of First-Line Treatment

OS was defined as the interval from start of first- or second-line treatment until the end of follow-up or death and was updated on February 1, 2020. If the start date of first systemic treatment was missing, and in patients who received best supportive care (BSC) only, OS was calculated since the day of diagnosis. Because progression in the NCR is not registered according to formal RECIST criteria, we calculated TTF from start of treatment to end of follow-up or first termination of treatment, as representation of the progression-free survival. Data on TTF were only available for patients with complete follow-up (diagnosis in 2015–2016).

Statistical Analysis

Data in this study were analyzed using SAS 9.4 (SAS Institute Inc). Baseline characteristics were described using means with standard deviations or medians with interquartile ranges (IQRs) for continuous variables, and absolute numbers with percentages for categorical variables. Chi-square tests were used to analyze differences between groups (with and without systemic treatment) in combination with Fisher exact tests where appropriate. A Kaplan-Meier analysis described the median OS between the different treatment groups, including log-rank test. To identify independently associated systemic treatment strategies for OS, multivariable Cox proportional hazard regression analyses were used with adjustments for sex, age, number of comorbidities, PS, year of diagnosis, and number of metastatic organ sites. The probability of a type I error was set at 0.05.

Results

Patient Characteristics

A total of 5,892 patients with metastatic PDAC were included in this study (Figure 1). Patients were predominantly male (52%) with a median age of 71 years (IQR, 63–78 years) (Table 1). Most patients had pancreatic

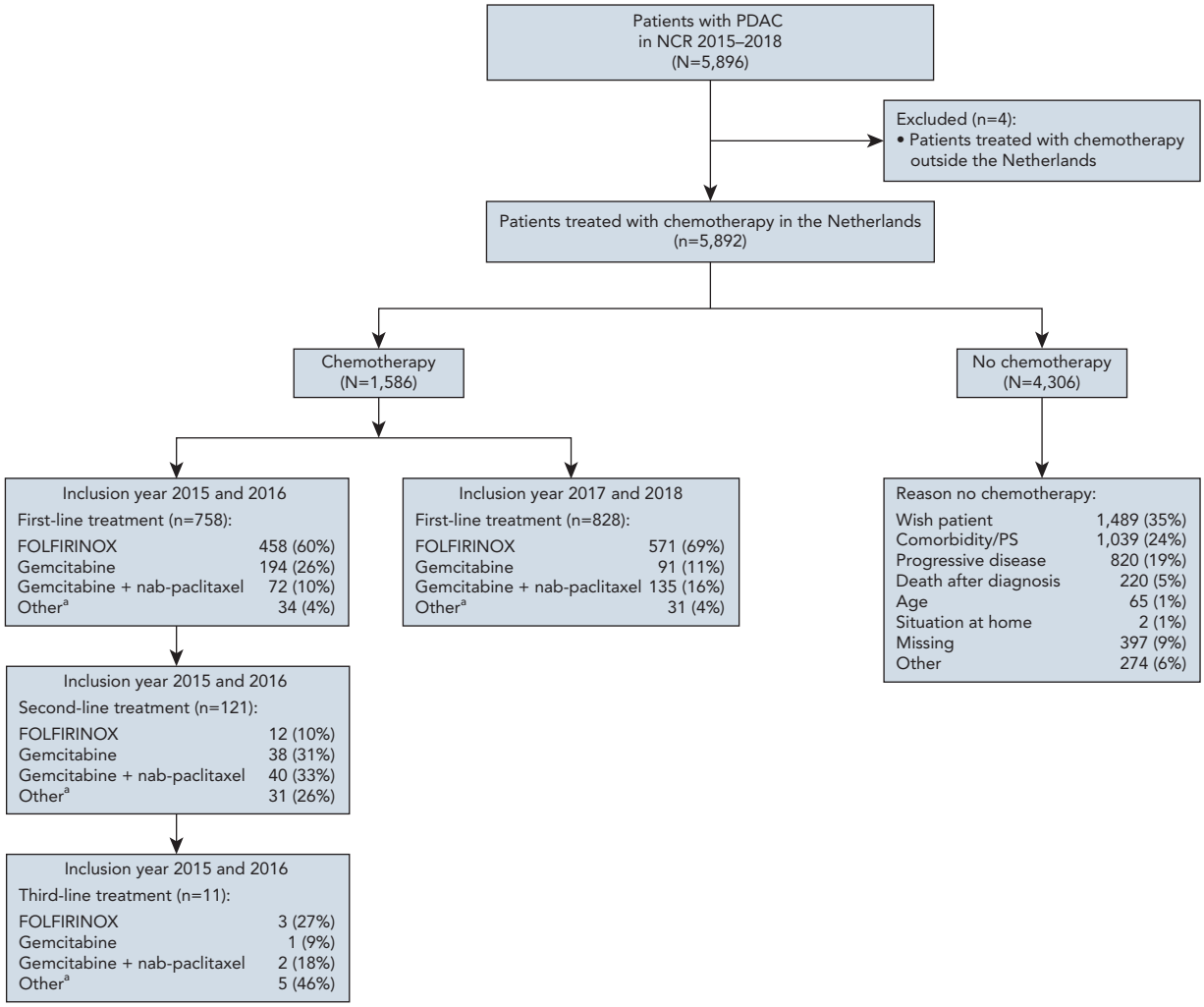

Figure 1. Study flow diagram.
Abbreviations: FOLFIRINOX, irinotecan/oxaliplatin/5-FU; NCR, Netherlands Cancer Registry; PDAC, pancreatic ductal adenocarcinoma PS, performance status.
[a]Consists of 14 different first-line regimens.

head tumors (42%), no comorbidities (40%), and one metastatic location at diagnosis (61%). PS was 0 to 1 in 36% of patients and was unknown in 46%.

Of all patients, 1,586 (27%) were treated with palliative systemic treatment. Patients treated with systemic therapy were significantly younger, had fewer comorbidities, and had a better PS than those who did not receive systemic treatment (Table 1).

First- and Second-Line Systemic Treatment Regimens and Strategies

We found 17 different first-line regimens, of which FOLFIRINOX (65%) was administered most often, followed by gemcitabine (18%), gemcitabine + nab-paclitaxel (13%), and other regimens (4%). The percentage of patients receiving treatment with FOLFIRINOX was comparable in the inclusion years 2015–2016 and 2017–2018. Compared with inclusion year 2015–2016, treatment with gemcitabine + nab-paclitaxel was given more often and fewer patients received gemcitabine monotherapy in 2017–2018.

In general, of the 1,586 patients who received first-line systemic therapy, 419 died and 339 did not die within 90 days of stopping treatment. Of the patients who died within 90 days, only 4% received second-line chemotherapy, and of the patients who did not die within 90 days, 31% received second-line chemotherapy (supplemental eFigure 1).

Of the 758 patients treated with first-line systemic therapy in 2015–2016, 121 (8%) received second-line treatment consisting of gemcitabine + nab-paclitaxel (33%), gemcitabine (31%), FOLFIRINOX (10%), and other regimens (26%) (Figure 2). The proportion of patients who received second-line treatment after first-line

Table 1. Baseline Patient Characteristics

Variable	Total	Patients Treated With Chemotherapy	Patients Treated Without Chemotherapy	*P* Value
Total, n	5,892	1,586	4,306	
Sex				.0660
Male	3,049 (52%)	852 (54%)	2,197 (51%)	
Female	2,843 (48%)	734 (46%)	2,109 (49%)	
Age				<.0001
Median (IQR), y	71 (63–78)	65 (58–70)	73 (66–80)	
<55 y	449 (8%)	264 (17%)	185 (4%)	
55–64 y	1,200 (20%)	512 (32%)	688 (16%)	
65–74 y	2,168 (37%)	639 (40%)	1,529 (36%)	
≥75 y	2,075 (35%)	171 (11%)	1,904 (44%)	
Tumor location				.0001
Head	2,465 (42%)	616 (39%)	1,849 (43%)	
Body	993 (17%)	318 (20%)	675 (16%)	
Tail	1,436 (24%)	400 (25%)	1,036 (24%)	
Overlapping sites	610 (10%)	166 (11%)	444 (10%)	
Pancreas NOS	388 (7%)	86 (5%)	302 (7%)	
Comorbidities				<.0001
0	2,384 (40%)	827 (52%)	1,557 (36%)	
1	1,988 (34%)	502 (32%)	1,486 (34%)	
2	1,064 (18%)	169 (11%)	895 (21%)	
Missing	456 (8%)	88 (5%)	368 (9%)	
WHO PS				<.0001
0–1	2,077 (36%)	996 (63%)	1,081 (25%)	
2	607 (10%)	166 (10%)	441 (10%)	
3–4	476 (8%)	25 (2%)	451 (11%)	
Unknown	2,732 (46%)	399 (25%)	2,333 (54%)	
Year of diagnosis				.0039
2015	1,378 (24%)	385 (24%)	993 (23%)	
2016	1,531 (26%)	373 (24%)	1,158 (27%)	
2017	1,481 (25%)	442 (28%)	1,039 (24%)	
2018	1,502 (25%)	386 (24%)	1,116 (26%)	
Metastatic sites				.3900
1	3,569 (61%)	975 (61%)	2,594 (60%)	
≥2	2,323 (39%)	611 (39%)	1,712 (40%)	

Abbreviations: IQR, interquartile range; NOS, not otherwise specified; PS, performance status.

treatment with gemcitabine was significantly lower compared with first-line treatment with FOLFIRINOX and gemcitabine + nab-paclitaxel (*P*=.0003). Patients who received second-line treatment were predominantly male (54%), had a median age of 62 years (IQR, 56–69 years), had a PS of 0–1 in most cases (59%), and largely had no comorbidities (75%). Cancer was diagnosed in the head (44%), body (20%), tail (20%), overlapping sites (12%), or a location not otherwise specified (4%) (data not shown).

Survival

Median OS (n=1,586) and median TTF (in patients diagnosed in 2015–2016, n=758) were 5.4 months (IQR, 2.5–10.4 months) and 3.4 months (IQR, 1.6–7.5 months), respectively, for patients who received first-line palliative systemic treatment (Figures 3 and 4). For patients receiving FOLFIRINOX, median OS and TTF were 6.6 and 4.8 months, respectively, and the median OS for those with a PS of 0–1 and 2 was 7.4 and 5.1 months, respectively (*P*=.043). For patients receiving gemcitabine + nab-

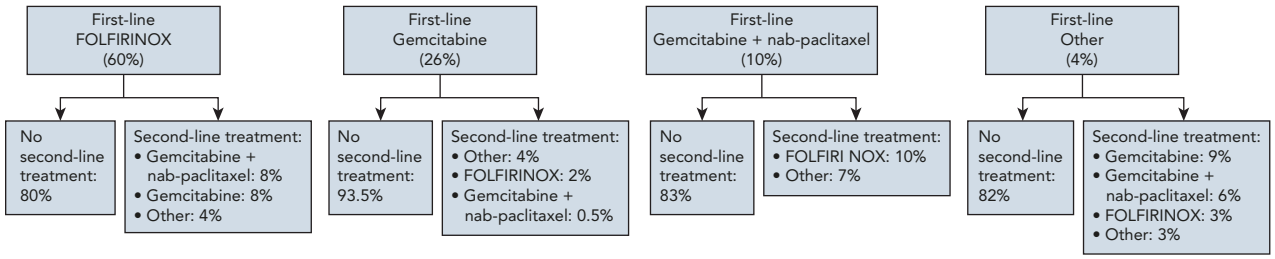

Figure 2. First- and second-line treatment administration in patients with metastatic PDAC diagnosed in 2015 and 2016.
Abbreviation: FOLFIRINOX, irinotecan/oxaliplatin/5-FU.

paclitaxel, median OS and TTF were 4.7 and 4.1 months, respectively, and the median OS for those with a PS of 0–1 and 2 was 4.3 and 5.2 months, respectively (P=.575). For gemcitabine monotherapy, the median OS and TTF were 2.9 and 1.9 months, respectively, and the median OS for those with a PS of 0–1 and 2 was 3.9 and 2.4 months, respectively (P=.116) (Figures 3 and 4). When we restricted our analyses to patients with PS 0–1, those treated with gemcitabine + nab-paclitaxel and gemcitabine monotherapy had an OS of 4.3 and 3.9 months respectively. Compared with FOLFIRINOX, gemcitabine + nab-paclitaxel showed significantly inferior OS after adjustment for confounders (adjusted HR, 1.20; 95% CI, 1.02–1.41) but no significant inferior TTF (HR, 1.22; 95% CI, 0.92–1.62), whereas gemcitabine monotherapy was independently associated with a shorter OS and TTF (HR, 1.98; 95% CI, 1.71–2.30 and HR, 2.31; 95% CI, 1.88–2.83, respectively) (eTables 2 and 3).

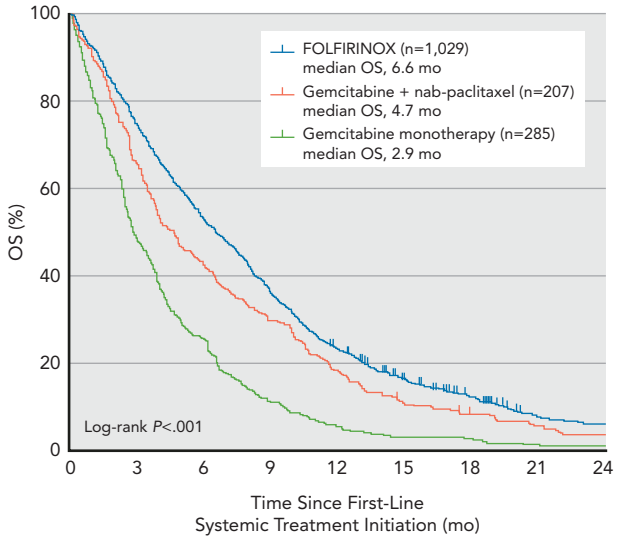

Figure 3. Kaplan-Meier curve displaying OS in patients who received first-line systemic therapy. OS is displayed for the treatment regimens that were administered in at least 100 patients.
Patients who received "other" treatment (n=65) are not depicted.
Abbreviations: FOLFIRINOX, irinotecan/oxaliplatin/5-FU; OS, overall survival.

In patients diagnosed in 2015–2016 who received second-line systemic treatment (n=121), the median OS since start of second-line treatment was 4.6 months (IQR, 2.5–8.3 months). Numbers were too small to analyze various treatment sequences.

Median OS for patients who received first-line treatment followed by BSC was 4.1 months (n=637) and was 11.2 months for those who received first- and second-line treatment (n=121) (eFigure 2). Median OS since day of diagnosis in patients who received BSC only (n=4,306) was 1.5 months (IQR, 0.8–3.0 months).

Discussion

This nationwide study included 5,892 patients with synchronous metastatic PDAC diagnosed between 2015 and 2018, of whom 1,586 (27%) received palliative systemic treatment. FOLFIRINOX was the most frequently applied first-line treatment, with a superior OS compared with gemcitabine + nab-paclitaxel and gemcitabine monotherapy in multivariable analyses. A minority of patients

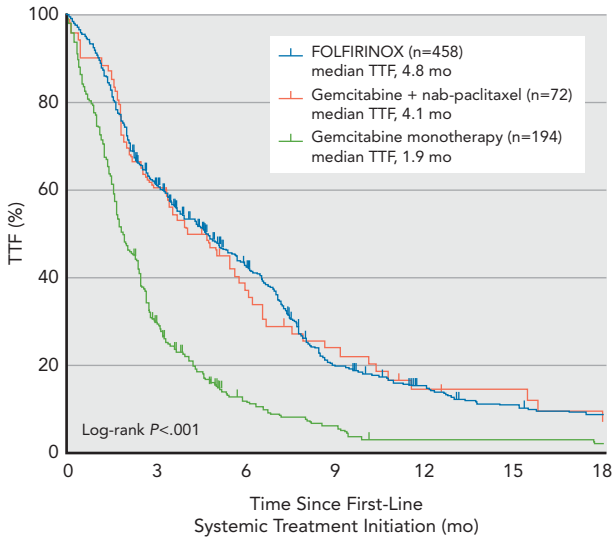

Figure 4. Kaplan-Meier curves displaying TTF in patients diagnosed in 2015–2016 who received first-line systemic therapy.
Patients who received "other" treatment (n=34) are not depicted.
Abbreviations: FOLFIRINOX, irinotecan/oxaliplatin/5-FU; TTF, time to failure.

received second-line treatment (8% of patients treated in the first line), with a favorable survival compared with patients who received BSC (OS, 11.2 vs 4.1 months; $P<.001$).

For both first- and second-line systemic treatment, the OS on a population-based level is disappointing compared with the OS results of RCTs. The OS of patients who received first-line treatment with FOLFIRINOX in our study was 6.6 months compared with 11.1 months in the landmark RCT.[13] The same applies for gemcitabine + nab-paclitaxel and gemcitabine monotherapy (OS, 4.7 and 2.9 months, respectively, in our study compared with 8.5 and 6.7 months, respectively, in the RCT[14]). This difference in OS might be explained by the different inclusion criteria in RCTs compared with population-based studies. Patients in RCTs must meet strict inclusion and exclusion criteria before entering a clinical trial and tend to have, for example, better PS and fewer comorbidities than patients treated outside a clinical trial. PS is one of the strongest predictors of OS in this setting[19,21]; however, even when we restricted our analyses to patients with PS 0–1, the OS was still unsatisfactory compared with RCTs. It should be mentioned that PS was not found in 25% of patients. Therefore, real-world data are a valuable addition to trial results because they deepen the understanding of the outcome of therapies in patients encountered on a day-to-day basis.

OS of patients receiving first-line systemic treatment in our study was also lower compared with other real-world studies. In our study, the OS of patients receiving FOLFIRINOX, gemcitabine + nab-paclitaxel, and gemcitabine monotherapy in first-line treatment was 6.6, 4.7, and 2.9 months, respectively. Other real-world studies found OS of 14.1 and 9.0 months for FOLFIRINOX, 10.5 and 6.6 months for gemcitabine + nab-paclitaxel, and 4.2 months for gemcitabine monotherapy.[22–25] This survival difference might be partly explained by differences in definition of OS. In our study, OS was defined as time from start of systemic treatment to death or the date of last follow-up, whereas OS in most other studies is defined as time from diagnosis to death.[22,24,25] The median time between diagnosis and start treatment in our study was 27 days (supplemental eTable 4). This could be specifically important to patients with pancreatic head tumors, because patients with non–pancreatic head tumors tend to start chemotherapy sooner after diagnosis.[26] Another explanation might be that in our study the median age at diagnosis was higher compared with other population-based studies, and that these studies included patients with locally advanced disease, who are known to have a better prognosis.[22–25]

As first-line treatment, most patients received FOLFIRINOX, which was also the dominant regimen in nearly all Dutch hospitals.[15] Compared with other real-world studies, our study shows a higher rate of first-line treatment with FOLFIRINOX.[22–24] Although OS has significantly improved compared with gemcitabine monotherapy, in current practice FOLFIRINOX is often reserved for patients with a PS of 0 or 1, because of the FOLFIRINOX-associated incidence of grade 3/4 toxicities (eg, neutropenia, thrombocytopenia, fatigue, vomiting).[13,27,28] Because the OS of patients receiving FOLFIRINOX in our study was higher among both those with PS 0–1 and those with PS 2 compared with those receiving gemcitabine + nab-paclitaxel (7.4 and 5.1 months vs 4.7 months, respectively; $P=.043$), one could question whether FOLFIRINOX should be administered only to patients with the most favorable PS, when our study showed that patients with less optimal PS also benefited from FOLFIRINOX treatment in terms of OS. However, this finding should be balanced with data on toxicity/adverse events and QoL, which are not yet available.

Although we observed inferior OS associated with first-line systemic gemcitabine + nab-paclitaxel compared with FOLFIRINOX, preferably OS of both regimens would be compared directly, also taking into account QoL, toxicity and exposure to second-line therapy, to identify the most preferable first-line treatment regimen. Alternative first- and second-line sequences may be, for example, gemcitabine + nab-paclitaxel followed by FOLFIRINOX or the NAPOLI regimen.[29]

In our study, gemcitabine monotherapy had a significantly lower OS and TTF (2.9 and 1.9 months, respectively) compared with the other regimens. Patients receiving BSC in our study (n=4,306) had a median OS of 1.5 months. Therefore, one could argue that the marginal survival benefit of treatment with monotherapy gemcitabine does not outweigh the possible adverse effects of gemcitabine, and that instead these patients should receive BSC only.[30,31]

Only 8% of patients in our study who started first-line treatment received second-line treatment, of which gemcitabine with or without nab-paclitaxel were the most frequently administered regimens. This is a reasonable choice of regimens because most patients received first-line treatment with FOLFIRINOX. However, the number of patients treated with second-line chemotherapy in our study is lower compared with other real-world studies.[22,23] This might be explained by the fact that in other real-world studies, patients were predominantly treated with gemcitabine with or without nab-paclitaxel in the first line, which provides more opportunities for treatment in the second line compared with our study in which FOLFIRINOX was the predominant regimen in first-line treatment (eg, FOLFOX).[22,23,32] It may be hypothesized that clinicians find FOLFIRINOX after a gemcitabine-containing regimen in first-line therapy less optimal given the superiority of FOLFIRINOX over gemcitabine with or without nab-paclitaxel. Moreover, there

is little randomized evidence for second-line therapy in patients with metastatic PDAC, and the fact that treatment administration in the last months before death is generally considered undesirable.[16,17,33,34]

Although this is the largest population-based study describing the use of first- and second-line systemic treatment in metastatic PDAC, our study has several limitations. First, there is likely an underestimation of pancreatic cancer in the NCR due to insufficient notification sources for older patients without pathologic confirmation of PDAC and no hospital admission related to PDAC.[35] With the inclusion of these patients, median OS for patients treated with BSC could be even shorter than described here. Second, the PS was unknown in nearly half of the patients before the start of first-line systemic treatment, resulting in less optimal adjustment for PS in multivariable analyses. In addition, toxicity information was missing for most patients and could not be reported in our study. Third, we did not have data on follow-up and beyond first-line treatment in patients who were diagnosed in 2017–2018, which resulted in a limited number of patients. Therefore, future research should include complete follow-up data after implementation of nanoliposomal irinotecan and 5-FU to be able to make statements about the best sequence strategy for first- and second-line treatment in patients with metastatic PDAC.

Conclusions

This nationwide study including real-world data on systemic treatment in patients with synchronous metastatic PDAC in the Netherlands shows that in an era before implementation of nanoliposomal irinotecan and 5-FU in second-line therapy, treatment predominantly consists of FOLFIRINOX in the first-line and gemcitabine with or without nab-paclitaxel in the second-line therapy.

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Supplemental online content for:

First- and Second-Line Palliative Systemic Treatment Outcomes in a Real-World Metastatic Pancreatic Cancer Cohort

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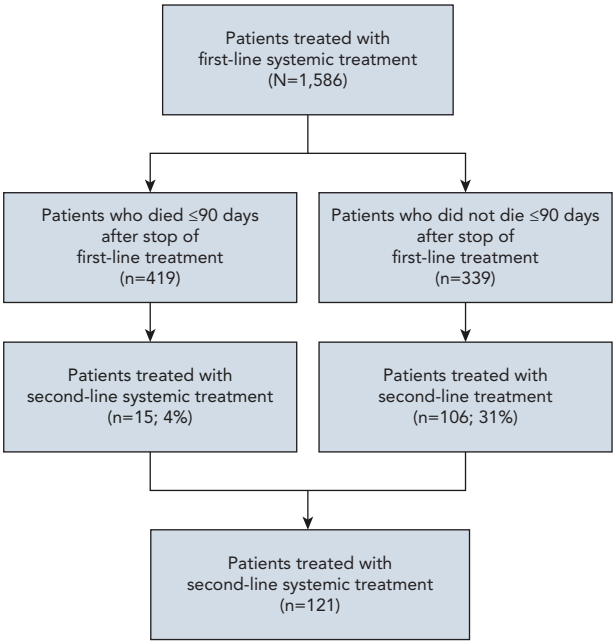
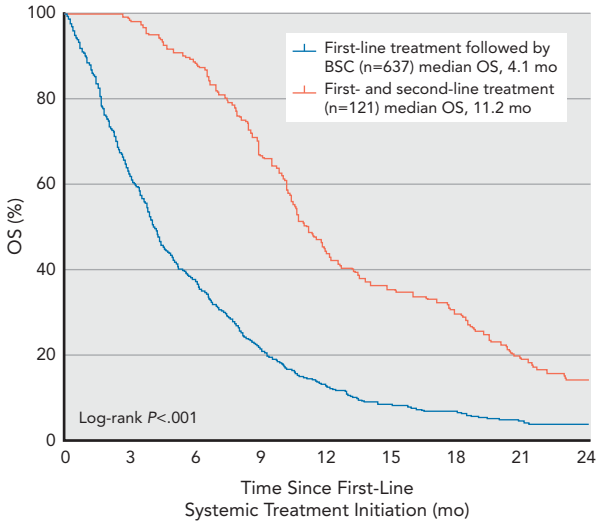


eFigure 1. Flow diagram of first- and second-line systemic treatment.



eFigure 2. Kaplan-Meier curve displaying OS in patients who received first-line treatment followed by BSC and first- and second-line treatment.
Abbreviations: BSC, best supportive care; OS, overall survival.

eTable 1. ICD-10 Morphology Codes Included in Analyses

Morphology Codes Included in Analyses
8000, 8001, 8010, 8011, 8012, 8020, 8021, 8022, 8031, 8032, 8033, 8035, 8046, 8070, 8071, 8072, 8140, 8141, 8143, 8144, 8145, 8154, 8163, 8201, 8211, 8255, 8260, 8263, 8310, 8440, 8480, 8481, 8490, 8500, 8510, 8521, 8523, 8560, 8570, 8572, 8575, 8576

eTable 2. Multivariable Cox Regression Analyses of First-Line Systemic Therapy

Parameter	HR (95% CI)	*P* Value
FOLFIRINOX (n=1,029)	Ref	
Gemcitabine (n=285)	1.983 (1.707–2.304)	<.0001
Gemcitabine + nab-paclitaxel (n=207)	1.200 (1.024–1.407)	.0244
Other (n=65)	1.042 (0.800–1.357)	.7594

Adjusted for sex, age, number of comorbidities, performance status, year of diagnosis, and number of metastases locations.
Abbreviations: FOLFIRINOX, irinotecan/oxaliplatin/5-FU; HR, hazard ratio.

eTable 3. Multivariable Cox Regression Analyses of Time to Failure of First-Line Systemic Therapy

Parameter	HR (95% CI)	*P* Value
FOLFIRINOX (n=458)	Ref	
Gemcitabine (n=194)	2.307 (1.882–2.828)	<.0001
Gemcitabine + nab-paclitaxel (n=72)	1.224 (0.922–1.624)	.1627
Other (n=34)	1.318 (0.855–2.032)	.2117

Adjusted for sex, age, number of comorbidities, performance status, year of diagnosis, and number of metastases locations.
Abbreviations: FOLFIRINOX, irinotecan/oxaliplatin/5-FU; HR, hazard ratio.

eTable 4. Baseline Characteristics in Patients Who Received First-Line Treatment

Variable	FOLFIRINOX	Gemcitabine + Nab-Paclitaxel	Gemcitabine	Other
Total, n	1,029	207	285	65
Sex				
Male	556 (54%)	104 (50%)	152 (53%)	40 (61%)
Female	473 (46%)	103 (50%)	133 (47%)	25 (39%)
Age				
Median (IQR), y	62 (56–68)	69 (62–74)	70 (65–74)	66 (57–72)
<55 y	225 (22%)	14 (7%)	14 (5%)	11 (18%)
55–64 y	391 (38%)	47 (23%)	57 (20%)	17 (27%)
65–74 y	371 (36%)	98 (47%)	144 (51%)	26 (39%)
≥75 y	42 (4%)	48 (23%)	70 (25%)	11 (15%)
Tumor location				
Head	393 (38%)	80 (39%)	115 (40%)	28 (42%)
Body	212 (21%)	46 (22%)	51 (18%)	9 (15%)
Tail	270 (26%)	49 (24%)	66 (23%)	15 (24%)
Overlapping sites	100 (10%)	24 (12%)	39 (14%)	3 (4%)
Pancreas NOS	54 (5%)	8 (4%)	14 (5%)	10 (14%)
Comorbidities				
0	597 (58%)	83 (40%)	113 (40%)	34 (52%)
1	299 (29%)	75 (36%)	107 (38%)	21 (34%)
2	73 (7%)	34 (16%)	57 (20%)	5 (7%)
Missing	60 (6%)	15 (7%)	8 (3%)	5 (7%)
WHO PS				
0–1	711 (69%)	134 (65%)	120 (42%)	31 (48%)
2	69 (7%)	32 (15%)	57 (20%)	8 (11%)
3–4	11 (1%)	0 (0%)	12 (4%)	2 (3%)
Unknown	238 (23%)	41 (20%)	96 (34%)	24 (38%)
Year of diagnosis				
2015	217 (21%)	33 (16%)	119 (42%)	16 (24%)
2016	243 (24%)	39 (19%)	75 (26%)	16 (24%)
2017	294 (29%)	74 (36%)	61 (21%)	13 (21%)
2018	275 (27%)	61 (29%)	30 (11%)	20 (31%)
Metastatic sites				
1	639 (62%)	128 (62%)	172 (60%)	36 (55%)
≥2	390 (38%)	79 (38%)	113 (40%)	29 (45%)
Median days between date of diagnosis and start of first-line treatment (IQR)	26 (17–38)	24 (15–36)	34 (20–56)	28 (17–55)

Abbreviations: FOLFIRINOX, irinotecan/oxaliplatin/5-FU; IQR, interquartile range; NOS, not otherwise specified; PS, performance status.