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Neoadjuvant FOLFIRINOX Application in Borderline Resectable Pancreatic Adenocarcinoma

A Retrospective Cohort Study

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Abstract: 5-Fluorouracile, oxaliplatin, irinotecan, and leucovorin (FOLFIRINOX) has not been extensively used in the neoadjuvant setting because of concerns with safety and toxicity. We evaluated our institutional experience with neoadjuvant FOLFIRINOX in borderline resectable pancreatic adenocarcinoma (BRPAC). The primary endpoints were completion of therapy to surgery and negative resection margin (R0) rate.

Patients with BRPAC treated with neoadjuvant FOLFIRINOX were retrospectively analyzed. Between August 2011 and September 2013, 20 patients with BRPAC treated with neoadjuvant FOLFIRINOX were identified.

Most patients (88.8%) completed FOLFIRINOX therapy and underwent resection. Abutment of venous structures was identified in 13 cases (72.2%), while short segment portal vein encasement in 3 cases (16.6%) with concomitant arterial involvement in 3 cases (16.6%). Isolated superior mesenteric artery abutment was identified in 2 cases (11.2%). Patients received a median of 4 cycles of FOLFIRINOX. There was 1 case of progression. Vascular resection was performed in 9 cases (52.9%). Preoperative radiation therapy was used in 8 patients (44%). All patients underwent margin negative resection (R0). Histopathologic treatment response was evident in 10 cases (58.8%).

Neoadjuvant FOLFIRINOX was generally safe and the expected toxicity did not prevent surgery allowing for a high rate of R0 resection.

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Abbreviations: ACCORD = Actions Concertées dans les Cancers Colo-Rectaux et Digestifs, BRPAC = borderline resectable pancreatic adenocarcinoma, CAx = celiac axis, CTCAE = Common Terminology Criteria for Adverse Events, DGE = delayed gastric emptying, ECOG = Eastern Cooperative Oncology Group, FOLFIRINOX = 5-fluorouracile, oxaliplatin, irinotecan and leucovorin, HA = hepatic artery, NCCN = National Comprehensive Cancer Network, OS = overall survival, PADC = pancreatic adenocarcinoma, PFS = progression free survival, PV = portal vein, R0 = microscopic negative resection margin, R1 = microscopic positive resection margin, RECIST = Response Evaluation Criteria In Solid Tumors, SMA = superior mesenteric artery, SMV = superior mesenteric vein.

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INTRODUCTION

As the incidence of pancreatic cancer continues to increase, the mortality rate remains relatively unchanged. The American Cancer Society estimates that approximately 46,420 people will be diagnosed with pancreatic cancer in 2014 and of these, 39,590 will die from this disease.[1] This generally grim prognosis accentuates the quest to identify new treatment strategies for pancreatic adenocarcinoma (PADC).

Surgical resection with chemotherapy (usually adjuvant) remains the only potentially curative approach, offering an actuarial survival rate of about 20% at 5 years.[2,3] Unfortunately, the majority of patients present with metastatic disease, precluding any surgical intervention and leading to an estimated survival of 2% at 5 years for all comers.[4,5] Approximately, 10% of newly diagnosed pancreatic cancers present with clearly resectable localized disease and approximately 40% of patients present with locally advanced or borderline resectable disease.[6]

Negative margin status (R0 resection) is among the strongest predictors for long-term survival in pancreatic cancer and remains the goal of a curative intent resection.[7,8] Consensus statements have been developed to guide the classification of pancreatic tumors based on the likelihood of achieving a margin negative resection. The National Comprehensive Cancer Network (NCCN) consensus statement defines PADC as resectable, borderline resectable, and unresectable (Table 1).[9] Borderline resectable lesions represent a particular challenge as, although potentially resectable, they carry a high likelihood of incomplete resection because of involvement of vital structures. The rate of microscopic positive resection margins (R1) reported in the literature varies enormously between 16% and 75% of cases.[10,11] The wide range is in part secondary to inconsistencies in the pathology review of pancreatic resection specimens. Prior studies indicate that, in perhaps a third of the cases, neoadjuvant therapy could potentially improve resectability of locally advanced tumors.[12]

The enthusiasm surrounding the results of the Actions Concertées dans les Cancers Colo-Rectaux et Digestifs (ACCORD) 11 trial, showing improved survival with FOLFIRINOX (5-fluorouracile [FU], oxaliplatin, irinotecan, and

TABLE 1. Criteria Used to Determine Pancreatic Cancer Resectability

Category	Criteria
Resectable	Clear fat plane around celiac axis, hepatic artery, and SMA No radiologic evidence of SMV or PV distortion
Borderline resectable	
Venous Involvement	SMV or PV with distortion or narrowing of the vein or occlusion of the vein with suitable vessel proximal or distal, allowing for safe resection and replacement
Arterial Involvement	Encasement of short segment of hepatic artery, without evidence of tumor extension to the celiac axis and/or tumor abutment of the SMA involving $\leq 180^{\circ}$ of the artery circumference
Unresectable	
Venous Involvement	Major venous thrombosis of the PV or SMV extending for several centimeters
Arterial Involvement	Circumferential encasement of the SMA, celiac axis, or proximal hepatic artery

PV = portal vein, SMA = superior mesenteric artery, SMV = superior mesenteric vein. Adapted from the National Comprehensive Cancer Network Guidelines.

leucovorin) in metastatic PADC,[13] prompted several authors to study the effect of neoadjuvant FOLFIRINOX in locally advanced PADCs. Many of these small pilot studies were conducted on a mixed cohort of borderline resectable and locally advanced unresectable tumors. To our knowledge, Christians et al[14] were the first to report on the use of neoadjuvant FOLFIRINOX followed by chemoradiation in a cohort of patients only with borderline resectable pancreatic adenocarcinoma (BRPAC) and concluded that this was not only safe but also led to a favorable R0 resection rate. The encouraging results reported from these clinical investigations prompted our group to examine our experience with the use of neoadjuvant FOLFIRINOX in a selected population composed solely of patients with BRPAC.

Our hypothesis is that FOLFIRINOX can be used as neoadjuvant agent in borderline resectable tumor with acceptable toxicity and resection rate. The primary endpoints of this study were completion of therapy to surgery and R0 resection rates.

METHODS

A retrospective review of the University of Colorado, Aurora, CO, pancreatic database was conducted between August 2011 and September 2013. The study was approved by the Internal Review Board of the University of Colorado. Treatment-naïve patients, diagnosed with BRPAC, who received neoadjuvant FOLFIRINOX chemotherapy with or without chemoradiation, were identified. All patients were presented at a multidisciplinary tumor board and all diagnostic images were carefully reviewed by expert pancreatic surgeons and radiologists. Each patient had at least 2 multiphasic pancreatic protocol computed tomographies (CTs) available in his/her records. The CT imaging obtained at the time of PADC diagnosis was reviewed and utilized to confirm the presence of BRPAC.

Borderline resectability was defined according to the NCCN.[9] The definition includes radiologic findings of venous involvement of the superior mesenteric vein (SMV) or portal vein (PV) with distortion or narrowing of the vein or occlusion of the vein with suitable vessel proximally and distally, allowing for safe resection and reconstruction. As for arterial involvement, radiologic findings of encasement of a short segment of the hepatic artery, without evidence of tumor extension to the celiac axis and/or tumor abutment of the superior mesenteric artery involving $\leq 180^{\circ}$ of the arterial circumference were considered BRPAC. Neoadjuvant FOLFRINOX chemotherapy was generally administered following the doses and intervals described by the ACCORD 11 trial. Patients with a biopsy-proven diagnosis of PADC, with acceptable performance status as defined by an Eastern Cooperative Oncology Group (ECOG) of 0 or 1, were initially selected to undergo 4 cycles of FOLFIRNIOX. A typical cycle consists of oxaliplatin, 85 mg/m^2; irinotecan, 180 mg/m^2; leucovorin, 400 mg/m^2; and FU, 400 mg/m^2 bolus followed by 2400 mg/m^2 46-hour continuous infusion, once every 2 weeks. Adverse events during treatment were evaluated according to the Common Terminology Criteria for Adverse Events.[15] Treatment effects were evaluated by an abdominal multiphasic pancreatic protocol CT following completion of neoadjuvant chemotherapy, or in the case of excessive toxicities, soon after interruption of treatment. Patients who demonstrated tumor response proceeded to curative intent surgical resection. Patients who did not show response to neoadjuvant chemotherapeutic treatment were offered neoadjuvant chemoradiation treatment unless otherwise chosen by the treating physician or by the patient.

The treating oncologist based on patient tolerance of the therapy, adjusted the chemotherapeutic regimen accordingly. The CT imaging immediately obtained preceding definitive surgical intervention was identified in the patient record and utilized to assess disease response to treatment. In this study, the authors did not utilize the Response Evaluation Criteria in Solid Tumors (RECIST) to guide the radiographic assessment of tumor burden, as the size of the tumor was not the only determinant of disease progression or response to treatment. In addition, Katz et al[16] have shown that radiographic downstaging is rare after neoadjuvant chemotherapy and concluded that the RECIST criteria are inadequate in the evaluation of patients with BRPAC. For the purpose of this study, we focused on identifying changes in the anatomic relationship between the tumor and the surrounding vascular structures (mainly progression of vascular involvement) and evidence of new unequivocal metastatic disease.

Treatment effect was evaluated according to a categorical scale including stable disease, any subjective response to treatment, and disease progression. Stable disease was characterized

TABLE 2. Histopathological Grade of Tumor Response to Neoadjuvant Treatment

Grade	Criteria
0	No residual tumor (complete response)
1	Minimal residual cancer (marked response)
2	Moderate response
3	Poor or no response (no definitive response identified)

Adapted from the College of American Pathologists scheme.

by absence of substantial changes from diagnostic imaging or evidence of distant disease. Response to treatment was characterized by decrease in vessel involvement (artery and/or vein) or new evidence of fat plane between tumor and vital anatomic structure that was felt to improve the chances of a successful surgical resection. Disease progression was characterized by progression of vessel involvement and/or evidence of distant disease. The histologic grade of treatment response was assessed by a trained gastrointestinal pathologist on permanent sections of the surgical specimen and graded according to the College of American Pathologists scheme (Table 2).[17]

The primary endpoints for this analysis were completion of therapy to surgery, and R0 resection rate, defined as the absence of microscopic evidence of tumor within at least 1 mm from the surgical resection margins. Beginning in 2011, our institutional protocol for evaluation of surgical margins included bile duct, pancreatic duct, uncinate, retroperitoneal, and vascular groove according to the procedure performed. Patients receiving at least 1 cycle of FOLFIRINOX were included in the analysis. Progression-free survival (PFS) indicates the interval, in months, between the first cycle of neoadjuvant FOLFIRINOX and evidence of disease recurrence or progression as assessed by radiographic imaging (local or metastatic), surgical exploration, or death. Follow-up information were obtained from clinic visit records, communication with primary care physicians, or national death registry. Overall survival (OS) indicates the interval between the first cycle of chemotherapy and the occurrence of death from any cause. Patients without disease recurrence at the time of last contact were censored. The Kaplan–Meier method with a 2-sided 95% confidence interval (CI) based on Greenwood's variance was applied for the estimation of PFS and OS. The available data were summarized using descriptive statistics.

RESULTS

Between August 2011 and September 2013, a total of 336 patients with PADC were evaluated and of these, 31 (9.2%) presented with BRPAC. Neoadjuvant treatment was offered to the entire cohort of BRPAC; however, 2 patients refused treatment and elected to proceed with primary surgical resection and 9 patients were offered gemcitabine in light of poor performance status (ECOG 2). The remaining 20 chemotherapy-naïve patients diagnosed with BRPAC were treated with neoadjuvant FOLFIRINOX. Two patients established care in a different state during treatment and were eventually lost to follow-up and therefore excluded from the analysis (Figure 1). A total of 18 patients remained available for final data analysis (Table 3). One patient experienced a significant adverse event (5-FU-associated coronary vasospasm with elevated troponin level) during the administration of the first cycle of FOLFIRINOX. The patient required treatment interruption and was eventually transitioned to gemcitabine. Median age at diagnosis was 65 years (range: 58–68 years) with 10 males (55.6%) and 8 females (44.4%). Pancreatic head adenocarcinoma was

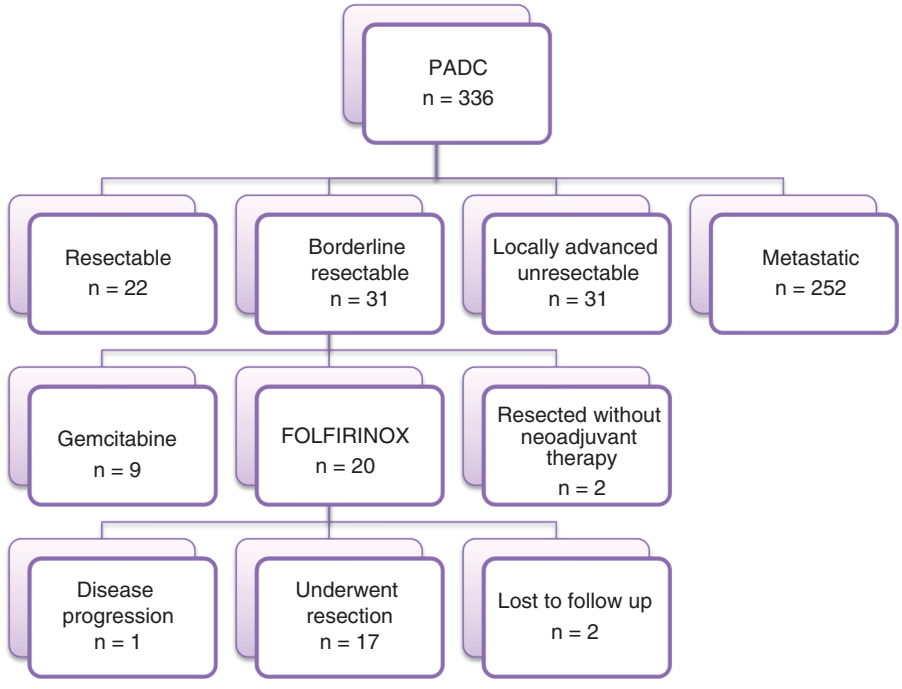

FIGURE 1. Distribution of PADC between July 2011 and August 2013 based on resectability and treatment allocation. PADC = pancreatic adenocarcinoma.

TABLE 3. Patients and Surgical Characteristics, n = 18

Characteristics	N (%)
Age, y	
Median	65
Range	58–68
Gender	
Male	10 (55.6)
Female	8 (44.4)
ECOG	
0	9 (50)
1	9 (50)
Tumor location	
Head	11 (61.1)
Uncinate	1 (5.6)
Body	4 (22.1)
Tail	1 (5.6)
Head and tail	1 (5.6)
Surgical procedure	
Whipple	12 (70.6)
Distal pancreatectomy	4 (23.5)
Total pancreatectomy	1 (5.9)
Vein resection	
Performed	9 (52.9)
Not Performed	8 (47.1)
Surgical margins	
Negative (R0)	17 (100)
Lymph nodes removed	
Median	19
Range	16–25
Lymph nodes status	
Negative	7 (41.2)
Positive	10 (58.8)
Lymphovascular invasion	7 (41.2)
Perineural invasion	12 (70.6)
Hospital LOS, d	
Median	9
Range	8–10
Postoperative complications	
DGE	4 (23.5)
SSI	3 (17.6)
Chyle leak	2 (11.8)

Surgical characteristics and postoperative complications refer to n = 17 patients. DGE = delayed gastric emptying, ECOG = Eastern Cooperative Oncology Group, LOS = length of hospital stay, SSI = surgical site infection.

TABLE 4. Characteristics of Borderline Resectable Tumor by Vessel Involvement Preneoadjuvant and Postneoadjuvant Treatment, Assessed by CT Imaging, n = 18

Characteristics	Pretreatment, N (%)	Posttreatment, N (%)
Isolated venous involvement		
PV abutment	5 (27.8)	5 (27.8)
SMV abutment	3 (16.6)	1 (5.6)
PV/SMV abutment	3 (16.6)	2 (11)
PV encased (short segment)	1 (5.6)	0
PV/SMV encased	1 (5.6)	1 (5.6)
Isolated arterial involvement		
SMA abutment	2 (11)	2 (11)
Synchronous arterial and venous involvement		
HA and PV abutment	1 (5.6)	1 (5.6)
CAx and PV abutment	1 (5.6)	1 (5.6)
SMA and PV encased (short segment)	1 (5.6)	1 (5.6)
Disease progression		
Liver metastasis	0	1 (5.6)

CAx = celiac axis, HA = hepatic artery, PV = portal vein, SMA = superior mesenteric artery, SMV = superior mesenteric vein.

identified in 10 patients (61.1%) representing the most common anatomic tumor location. Abutment of venous vessels (PV/SMV) was present in 13 patients (72.2%) and represented the leading determinant for borderline resectability followed by short segment encasement of venous vessels in 3 patients (16.8%). Determinants for borderline resectability are summarized in Table 4. Overall, a total of 74 cycles of chemotherapy were administered with a median of 4 cycles of FOLFIRINOX per patient (range: 3–5 cycles). Three patients (16.7%) received only 2 cycles prior to operative intervention and 3 patients (16.7%) received >6 cycles prior to definitive surgical intervention. A total of 10 patients (55.6%) experienced grade 3 or 4 toxicities during treatment; the most common adverse events were anorexia (n = 3; 16.7%), nausea/vomiting (n = 2; 11.1%), and peripheral neuropathy (n = 4; 22.2%). Adverse events during treatment required hospitalization in 3 patients (16.7%), including 1 patient who developed neutropenic fever. Neoadjuvant chemoradiation was offered to 8 patients (44.4%) of whom 5 eventually had radiographic response (Table 5). Two patients, with no evidence of response to neoadjuvant chemotherapy, proceeded straight to surgery without chemoradiation treatment. In one case, this was dictated by patient preference to avoid chemoradiation treatment and intention to proceed directly to surgical intervention. In the second case, the treating surgeon decided to directly proceed to surgical intervention. Median interval from the date of first FOLFIRINOX cycle to definitive surgical treatment was 4 months (range: 2–4 months). One patient experienced disease progression (biopsy proven liver metastasis) 7 months after the first dose of chemotherapy. At that time, he had received 6 doses of neoadjuvant FOLFIRNOX and completed neoadjuvant chemoradiation. Treatment response via multiphasic pancreatic protocol CT was carefully evaluated in all patients prior to surgical intervention at a median of 2.5 months (range: 1–4 months) from first administered dose of FOLFIRINOX. We observed some evidence of radiographic disease response in 7 patients (41.2%) and stable disease in the remaining 10 patients (55.6%). In particular, 4 patients (22.1%) experienced complete resolution of venous involvement (Table 4). A Whipple procedure was performed in 12 cases (70.6%), distal pancreatectomy in 4 cases (23.5%), and 1 case (5.9%) required total pancreatectomy. Vascular resection with reconstruction was performed in 9 cases (52.9%) with tumor involvement of PV/SMV; primary vascular anastomosis was performed in all cases. None of the patients in our cohort required arterial resection/reconstruction. All patients underwent a margin negative (R0) resection (Table 3). Histopathologic analysis of tumor

TABLE 5. Neoadjuvant Treatment Characteristics and Histopathological Tumor Response of Patients that Underwent Surgical Resection

Characteristics	n (%)
FOLFIRINOX cycles	
≤2	3 (16.7)
3–5	12 (66.6)
≥6	3 (16.7)
Grade 3/4 toxicities	10 (55.6)
Neutropenia	1 (5.6)
Neutropenic fever	1 (5.6)
Anemia	1 (5.6)
Thrombocytopenia	2 (11.1)
Fatigue	2 (11.1)
Mucositis	1 (5.6)
Anorexia	3 (16.7)
Nausea/vomiting	2 (11.1)
Diarrhea	3 (16.7)
Neuropathy	4 (22.2)
Venous thrombosis	1 (5.6)
Coronary vasospasm	1 (5.6)
Hospitalization	3 (16.7)
Neoadjuvant chemoradiation	
Not administered	10 (55.6)
Administered	8 (44.4)
Histophatological tumor response	
No residual tumor	1 (5.6)
Minimal residual tumor	4 (23.5)
Moderate response	5 (29.4)
Poor/no response	7 (41.2)

specimens revealed complete tumor response in 1 patient (5.9%), evidence of partial response in 9 patients (52.9%), and poor or no response in 7 patients (41.2%) (Table 5). The median length of hospital stay was 9 days (range 8–10). There were no perioperative or in-hospital deaths attributable to the surgical procedure. The main postoperative complications were delayed gastric emptying in 4 patients (23.5%), surgical site infections in 3 patients (17.6%), and chyle leak in 2 patients (11.8%). None of the patients required hospital admission following surgical intervention and their complications were managed in our surgery clinic. The median follow-up from the date of first administered dose of FOLFIRINOX was 14.5 months (range: 10–17 months). The Kaplan–Meier estimated median PFS and OS were not reached because of the limited follow-up. For the entire cohort (n = 18), the 1-year PFS from first administered dose of FOLFIRINOX was 73.1% (95% CI: 43.1%–89.0%). We observed 4 (22.1%) local recurrences and 5 (27.8%) distant recurrences including the patient who experienced metastatic liver disease during the treatment (Figure 2). The estimated 12-month PFS was not significantly different for the patients who achieved Grade 3 response (83%; 95% CI: 27%–97%) compared to those who demonstrated Grade 1 or 2 response (87%; 95% CI: 39%–98%, $P = 0.74$) (Figure 3). At a median of 17.5 months from the date of first administered dose of FOLFIRINOX, we observed 4 deaths with the earliest death occurring at 13 months and the latest at 25 months. The longest surviving patient is living 26 months from the first dose of chemotherapy without evidence of disease recurrence (Figure 4). Of the 18 patients treated with neoadjuvant

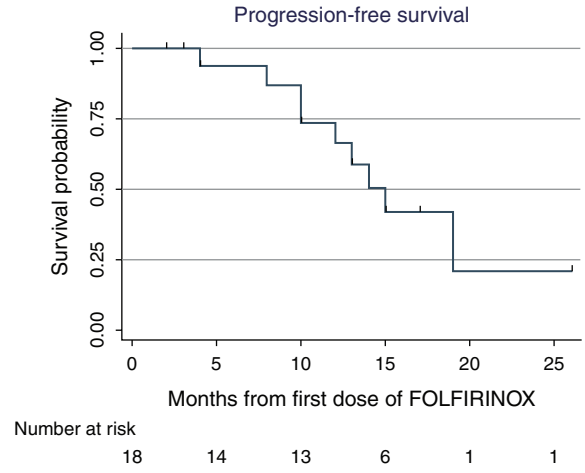

FIGURE 2. Progression-free survival from first dose of chemotherapy administration.

FOLFIRINOX, 16 patients (88.9%) went on to receive adjuvant chemotherapy following resection. One patient refused adjuvant chemotherapy and 1 patient was still recovering from surgery at the time of this study. The only patient, who required treatment interruption and transition to neoadjuvant gemcitabine because of severe toxicity, eventually received 4 cycles of gemcitabine and underwent negative margin surgical resection. The patient is currently alive without evidence of disease recurrence. One patient who experienced complete histopathologic response to neoadjuvant treatment (including neoadjuvant FOLFIRINOX and neoadjuvant chemoradiation), eventually recurred with liver metastasis 4 months following surgical resection.

DISCUSSION

At the time the ACCORD 11 trial was reported, FOLFIRINOX represented the most significant improvement in OS for patients with metastatic pancreatic cancer and was associated with an overall 32% tumor response rate.[13] However, its use as

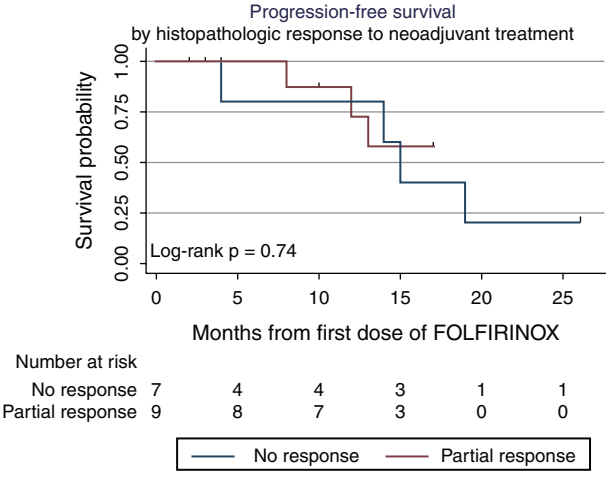

FIGURE 3. Progression-free survival stratified by histopathologic response to neoadjuvant treatment. Grade 3: no response; Grades 1 and 2: partial response.

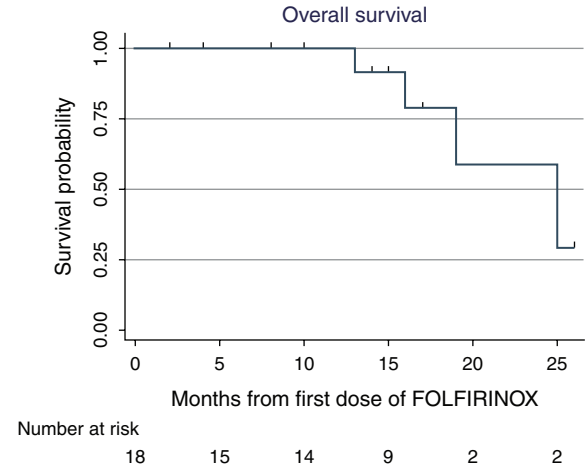

FIGURE 4. Overall survival from first dose of neoadjuvant treatment for all patients.

neoadjuvant treatment remains under investigation.[18–21] In our experience with borderline resectable pancreatic cancer, neoadjuvant FOLFIRINOX treatment allowed surgical resection in 17 of the 18 patients (94.4%) initially selected for neoadjuvant treatment allowing margin negative (R0) resection. The rationale for considering an aggressive neoadjuvant approach in BRPAC is based on the premise that the neoadjuvant period acts as a biologic selector for the identification of patients most likely to benefit from surgical intervention. Furthermore, it holds the potential to enhance the chances of an R0 resection, which has been associated with improved long-term survival.[22] Prior case series documented the efficacy of FOLFIRINOX as neoadjuvant treatment in the setting of locally advanced pancreatic cancer; however, such studies grouped both borderline resectable and locally advanced unresectable tumors together. Hosein et al[20] reported on a total of 18 patients of which only 4 were diagnosed with BRPAC. In their series, the authors observed that 3 of the original 4 patients met imaging criteria for resectability after neoadjuvant FOLFIRINOX treatment and eventually underwent a R0 resection. Faris et al[18] described a cohort composed of locally advanced unresectable PADC. In their study, none of the patients had progression of disease during treatment; partial response was observed in 27.3% of the cases and stable disease in the remaining 72.7% of the cases. The authors reported a R0 resection rate of 23% (5 of 22 patients). Christians et al[14] described their single-institutional experience with neoadjuvant FOLFIRINOX in a cohort of 18 patients diagnosed with BRPAC. The authors reported a therapy completion rate of 83% (15 of 18 patients) and a resection rate of 67% (12 of 18 cases), all with negative (R0) surgical resection margins. It is worth noting that following the initial administration of neoadjuvant FOLFIRINOX (mean 4.3 [±1.6] cycles/patient), none of the patients in their series were found to have disease progression. Furthermore, as part of their treatment protocol, an additional 5.6 weeks of chemoradiation were administered to all patients. Remarkably, at the time of post-chemoradiation preoperative restaging, 16.7% (3 of 18 cases) showed local disease progression and an additional 16.7% (3 of 18 cases) were found to have distant disease at the time of surgical exploration, leading to an overall progression rate of 33 % (6 of 18 cases).[14]

Similar to the study by Christians et al,[14] our patient population was solely composed of BRPAC as defined by the NCCN criteria. In addition, we experienced a comparable high rate of negative (R0) surgical resection margins and a slightly inferior rate of disease progression. The latter could have been influenced by a shorter interval from initiation of neoadjuvant therapy to definitive surgical resection, as 64% of our patients directly preceded to pancreatic resection following completion of neoadjuvant FOLFIRINOX. The higher rate of R0 resection in this study compared to prior studies could be explained by our selected cohort as we did not include patients with locally advanced unresectable tumor. Although FOLFIRINOX has been associated with considerable side effects, especially grade 3 or 4 neutropenia, febrile neutropenia, thrombocytopenia, diarrhea, and sensory neuropathy,[13] side effects did not prevent surgical resections in our experience. It is possible that the limited number of cycles administered in our study compared to the ACCORD 11 trial could have partially limited the onset of severe side effects that would have prevented or significantly delayed surgical interventions. Our criteria for response to treatment was different to the one defined in the ACCORD 11 trial as our intent was to select patients for surgical resection based on evidence of resolution/regression of tumor involvement of vascular structure or lack of evidence of disease progression. This study analyzes a small subgroup of all locally advanced (borderline resectable) patients with PADC and therefore has a number of limitations. First, the design of the study is subject to the inherent flaws of retrospective data collection. Second, the definition of borderline resectability is SUBJECT to imaging interpretation by the reading physicians. Although we employed thorough tumor board review with experienced pancreatic surgeons and radiologists, it is possible that tumors considered borderline resectable could have been interpreted as locally advanced and vice versa, by other readers. Third, the heterogeneous use of neoadjuvant chemoradiation limits our ability to discern whether radiation can be omitted in patients with localized pancreas cancer, if it should still be used in borderline resectable disease, and if FOLFIRINOX changes the need to use radiation at all in a neoadjuvant approach. Finally, the short follow-up period does not allow us to make any definitive description of local, systemic recurrence rates, and OS in the setting of a R0 resection following neoadjuvant FOLFIRINOX therapy. Despite achieving a R0 resection in all study participants that underwent surgery, these patients experienced a disease recurrence rate of 50% at a median of 15 months from first dose of chemotherapy. This observation supports the common concept that most PADCs represent systemic disease at the time of diagnosis and that chemotherapy may delay but not prevent recurrences.

CONCLUSION

This limited study of patients treated with neoadjuvant FOLFIRINOX for BRPAC suggests that the majority of patients tolerated the therapy with expected toxicities and were able to undergo an R0 resection.

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