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ORIGINAL ARTICLE – PANCREATIC TUMORS

First-Line Gemcitabine and Nab-Paclitaxel Chemotherapy for Localized Pancreatic Ductal Adenocarcinoma

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ABSTRACT

Background. Preoperative chemotherapy provides early treatment of micro-metastases and guaranteed delivery of all components of multimodality therapy for localized pancreatic ductal adenocarcinoma (PDAC). For locally advanced (LA) PDAC, induction chemotherapy is the standard of care. This study evaluated the use of gemcitabine and nab-paclitaxel (Gem/nab-P) as first-line therapy for localized PDAC.

Methods. Clinicopathologic features, treatment, and outcomes were evaluated for 99 patients with localized PDAC. The patients were staged using previously published criteria as follows: potentially resectable (PR), borderline type A (BR-A) (anatomy amenable to vascular resection), BR-B (biology suspicious for metastatic disease including high CA19-9), BR–C (comorbidities requiring medical optimization), and LA.

Results. The 99 patients (PR/BR/LA: 45/14/40) were treated with Gem/nab-P. Clinical staging showed that 20 patients had PR or BR-A disease, whereas 39 patients had BR-B or BR-C disease. The BR-B+C cases included one or more of the following: age of 80 years or older (13%), Eastern Cooperative Oncology Group performance status (ECOG PS) of 2 or more (13%), moderate to severe comorbidities (55%), CA19-9 of 1000 or higher (28%), and suspicion for metastases (21%). The majority of the patients received biweekly Gem/nab-P dosing, which was well tolerated. Pancreatectomy was performed for 12 (60%) of 20 patients with PR+BR-A, 2 (5%) of 39 patients with BR-B+C, and 1 (3%) of 40 patients with LA disease. During a median follow-up period of 26 months, the median overall survival (OS) period was 18 months (95% confidence interval [CI], 15.6–20.5 months) for all the patients, 17 months (95% CI, 14.6–19.5 months) for the unresected patients, and not reached for the resected patients ($p = 0.028$ for resected vs unresected patients).

Conclusions. A significant number of patients with radiographically resectable PDAC albeit aggressive biology (BR-B), medically inoperable conditions (BR-C), or

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both received biweekly first-line Gem/nab-P. The resection rates were lower for the BR-B/BR-C patients than for the PR/BR-A patients (hazard ratio [HR], 0.43; 95% CI, 0.19–1.00; $p = 0.05$).

Pancreatic ductal adenocarcinoma (PDAC) is among the most lethal cancers, with an estimated 55,440 new cases in 2018 and a 5-year overall survival (OS) rate of 7%.[1] The incidence of PDAC is rising steadily and on track to become the second leading cause of cancer deaths by 2030.[2] Surgical resection currently offers the only potential cure for PDAC. However, only 10–20% of patients have anatomically resectable disease at presentation.[3]

Localized PDAC can be classified into the three following categories based on vascular involvement by the tumor assessed on cross-sectional imaging: potentially resectable (PR; absence of vascular involvement), borderline resectable (BR; minor/moderate vascular involvement), and locally advanced (LA; unreconstructable venous occlusion or significant arterial involvement).[3] We have previously further classified BR PDAC into the three following subtypes reflecting derangements in the tumor's anticipated behavior and the patient's physiologic profile in addition to tumor anatomy: type A (anatomic variant), type B (biologic variant with suspicion for extra-pancreatic/metastatic disease including high CA19-9), and type C (conditional variant with comorbidities requiring medical optimization).[4]

Besides BR and LA PDAC, for which induction chemotherapy is the standard of care, chemotherapy use for PR PDAC lacks high-level evidence. Although no prospective randomized trials have evaluated the benefit of chemotherapy as first-line treatment for patients with PR PDAC, many institutions use a multimodality treatment approach including chemotherapy with or without radiotherapy followed by surgery.[5] Preoperative chemotherapy for PR/BR PDAC provides early treatment of occult micrometastases, guaranteed delivery of all components of multimodality therapy, and selection of a physiologically robust population of patients with biologically favorable tumors who are likely to benefit from a potentially morbid operation.[5]

Two standard regimens are FDA-approved for the treatment of metastatic PDAC patients: FOLFIRINOX and gemcitabine/nab-paclitaxel (Gem/nab-P).[3] The MPACT trial demonstrated the superiority of the combined Gem/nab-P over gemcitabine, with an overall survival (OS) improvement of 1.8 months in the combination arm (8.5 vs 6.7 months; hazard ratio [HR], 0.72; 95% confidence interval [CI], 0.62–0.83; $p < 0.001$) for patients with metastatic PDAC.[6] Several smaller studies have evaluated the use of first-line chemotherapy with Gem/nab-P for localized PDAC (Table S1).[7–17] Our study aimed to evaluate the characteristics and outcomes of a large cohort of patients with localized PDAC who received Gem/nab-P as first-line therapy at a single institution.

PATIENTS AND METHODS

Patients

The Institutional Review Board at the University of Texas MD Anderson Cancer Center approved the data collection and analysis for this retrospective study (PA17-0037). We used our institutional multidisciplinary pancreatic cancer database[18] to identify all patients with localized PDAC who initiated first-line chemotherapy with Gem/nab-P between 2013 and 2015. Patients who were recommended for treatment using this regimen without subsequent verification or follow-up evaluation were excluded from further analysis.

Baseline Evaluation

Multi-detector computed tomography (CT) using a 16- or 64-detector row scanner (General Electric Medical Systems, Milwaukee, WI, USA) was performed using standard protocol optimized for imaging pancreatic tumors for staging at baseline.[19] Patients were classified by radiographic staging as potentially resectable (PR), borderline resectable (BR), or locally advanced (LA). Clinical staging was performed using previously published criteria as follows: borderline type A (BR-A: vascular involvement amenable to resection), BR- B (clinical findings suspicious for extrapancreatic disease including high CA19-9), and BR-C (comorbidities requiring extensive evaluation or optimization).[4]

Performance status was assessed using European Cooperative Oncology Group (ECOG) criteria,[20] and comorbidity was prospectively measured using the Adult Comorbidity Evaluation (ACE) 27 index,[21] which quantifies the extent of comorbidity on the basis of 27 ailments in 12 different systems. The severity of each patient's comorbidity profile was graded as 0 (none), 1 (mild), 2 (moderate), or 3 (severe).

Treatment

Chemotherapy and radiation dosing, subsequent therapies received, and outcomes were evaluated for each patient. With regard to choice of chemotherapy, our first choice is always a clinical trial, and we have both mFOLFIRINOX-based and Gem/nab-P-based preoperative studies incorporating additional novel agents or Stereotactic Body Radiation Therapy in combination. Patients

with a germline BRCA mutation or germline/somatic mutations in a homologous recombination repair pathway or a strong family history also are given the benefit of a platinum agent. Furthermore, the choice of neoadjuvant chemotherapy regimen is based on the overall functional status, comorbidity profile, biliary stent-related issues, and lab results including hematologic/renal/hepatic function.

Chemotherapy dosing was described as standard (Gem/nab-P given on days 1, 8, and 15 of each 28-day cycle), alternate (Gem/nab-P given every 14 days), or modified (Gem/nab-P given on days 1 and 8 of each 21-day cycle) based on previously published studies.[6,22] After preoperative chemotherapy with or without radiation, patients without evidence of disease progression and with adequate physiologic status were considered as candidates for surgical resection by pancreatectomy. The decision to operate was made primarily on the basis of a critical assessment of the relationship between the primary tumor and the major mesenteric vasculature in cross-sectional imaging studies. Anatomic stage was assigned before the administration of preoperative therapy, and in the absence of radiographic progression to locally advanced or metastatic disease or a decline in performance status, patients were brought to the operating room after completion of planned treatment. Rare intraoperative findings that precluded resection included identification of occult metastatic disease in the peritoneum, liver, or second echelon lymph nodes and poor quality of the distal vein target that precluded safe reconstruction.

Pathologic evaluation of the specimen was performed using a standardized system previously described by the College of American Pathologists, and the pathologic stage was designated in accordance with the criteria of the American Joint Committee on Cancer (AJCC) staging manual, seventh edition.[23] For subsequent therapies, a change in the line of therapy was defined as 1 (a change to 5-fluorouracil [5-FU]-based therapy) or 2 (a switch back to gemcitabine-based therapy after intolerance/progression with 5-FU-based chemotherapy).

Objectives

The primary objective was to assess the difference in OS and metastatic disease-free survival (MDFS) by resection status, radiographic stage, and clinical stage. We also evaluated the association of OS and MDFS with patient characteristics such as age, comorbidity, and CA19-9.

Statistical Analysis

Patient characteristics were summarized using frequency (%) for categorical variables and median (range) for continuous variables. In this study, OS was calculated from the time of diagnosis to death or the date at which the patient was last known to be alive if death had not been reported, and MDFS was calculated from the date of diagnosis to the date of recurrence or was censored at the date of the last follow-up evaluation with no evidence of disease if recurrence or death was not reported. Probabilities of OS and MDFS were estimated using the Kaplan–Meier method.[24] Cox proportional hazards regression models were fitted to assess the association between OS and patient characteristics.[25] Resection status (yes vs no) was included in the Cox model as a time-dependent covariate. Statistical analysis was performed using SAS (SAS Institute, Cary, NC, USA) and Splus (Tibco Software, Palo Alto, CA, USA) with significance established at a p value lower than 0.05.

RESULTS

Between January 2013 and December 2015, 99 patients with localized PDAC were treated with first-line Gem/nab-P chemotherapy. The demographic and clinical characteristics of the study population are listed in Table 1. The median age of the study population was 70 years (range, 30–85 years). Of the 99 patients, 75 (76%) had primary tumors in the head of the pancreas, whereas 24 (24%) had body/tail tumors. On the basis of radiographic criteria, 45 patients (45%) had PR disease, 14 patients (14%) had BR disease, and 40 patients (41%) had LA disease at the time of diagnosis.

We further evaluated the 59 patients with PR and BR disease using previously published clinical staging criteria and found that 20 patients had PR or BR-A disease, whereas 39 patients had BR-B or BR–C disease.[4] Of the patients with BR-B or BR–C disease, we found that 55% had moderate/severe comorbidities using the ACE 27 scoring system, 13% were 80 years old or older, 13% had a ECOG PS of 2 or more, 28% had a CA19-9 of 1000 or higher, and 21% had suspicion for extra-pancreatic/metastatic disease.

The treatment summary for all the patients classified by radiographic staging is shown in Fig. 1. Of the 45 patients (45%) who received chemoradiation after completion of first-line Gem/nab-P chemotherapy, 33% received hypofractionated radiation (30 Gy/10 fractions), whereas 67% received standard fractionation radiation (50.4 Gy/28 fractions) (Fig. 2a). No chemoradiation was administered to 54 patients (55%). Of 15 patients (15%) who underwent curative resection, 14 (93%) underwent pancreaticoduodenectomy, whereas the remaining patient (7%) underwent distal pancreatectomy (Table 2).

Resection was performed for 12 (60%) of 20 patients with PR/BR-A disease, 2 (5%) of 39 patients with BR-B or C disease, and 1 (3%) of 40 patients with LA disease

TABLE 1 Demographic and clinical characteristics of patients with localized pancreatic ductal adenocarcinoma (PDAC) who received first-line gemcitabine and nab-paclitaxel chemotherapy (n = 99)

Variable	*N*
Median age: years (range)	70 (30–85)
Sex	
Male	50
Female	49
Race	
White	70
Black	16
Asian	3
Hispanic	8
Other	2
Location	
Head	75
Body/tail	24
Radiographic staging	
PR	45
BR[a]	14
Locally advanced	40
Clinical staging (for PR and BR)	
PR	14
BR-A	6
BR-B	13
BR-C	7
BR-A and B	6
BR-A and C	2
BR-B and C	11
Tobacco use	
Active	9
Never smoker	48
Former smoker	38
Recent quitter	4
Comorbidities[b]	
None	11
Mild	36
Moderate	33
Severe	19
Median CA19-9: U/mL (range)	
All	240 (< 1–12,350)
PR	278 (< 1–3509)
BR	236 (11–3701)
Locally advanced	191 (< 1–12,350)
Radiation regimen	
Hypofractionated (30 Gy/10 fx)	15
Standard fractionated (50.4 Gy/28 fx)	30
Radiation chemosensitizer	
5-FU/capecitabine	40
Gemcitabine	3
None	2

PR potentially resectable, *BR* borderline resectable, *5-FU* 5-fluorouracil

[a]Using MD Anderson definition

[b]Using adult comorbidity evaluation 27 scoring system

(Fig. 1). The resection rates were significantly lower for the patients with BR-B or BR–C disease than for the patients with PR/BR-A disease (HR, 0.43; 95% CI, 0.19–1.00; p = 0.05). An R0 resection was performed for 10 patients (67%), and an R1 resection was performed for 5 patients (33%) (Table 2). Adjuvant chemotherapy was performed for 13 patients (87%) and not performed for 2 patients (13%) (Table 2).

With regard to the use of Gem/nab-P chemotherapy in the first-line setting, we found that the number of patients receiving this regimen has been increasing every year from 2013 to 2015 (Fig. 2b). The majority of the patients (81%) received biweekly (alternate) Gem/nab-P dosing, whereas fewer patients (19%) received standard or modified dosing (Fig. 2c). The regimen was safe, with minimal grade 3 or 4 toxicity, and no treatment-related deaths occurred. Based on the available data, the most common grade 3 or 4 toxicities associated with biweekly gemcitabine/nab-paclitaxel chemotherapy in our cohort were neutropenia (12.4%), fatigue (4.5%), neutropenic fever (3.3%), neuropathy (1.1%), and anemia (1.1%).

During a median follow-up period of 26 months (95% CI, 24.0–27.9 months), the median OS was 18 months (95% CI, 15.6–20.5 months) for all the treated patients, 17 months (95% CI, 14.6–19.5 months) for the unresected patients, and not reached for the resected patients (p = 0.028) (Table 3, Fig. 3). During a median follow-up period of 17 months (95% CI, 11.4–22.6 months), the median MDFS was 11 months (95% CI, 5.0–17.0 months) for all the patients, 9 months (95% CI, 4.1–13.9 months) for the unresected patients, and not reached for the resected patients (p = 0.011) (Table 3, Fig. 3).

In the univariate analysis, surgical resection was associated with a significantly higher median OS (HR, 0.32; 95% CI, 0.12–0.89; p = 0.03; Table S2) and MDFS (HR, 0.33; 95% CI, 0.13–0.82; p = 0.02; Table S3). For the subgroup of patients with PR and BR disease, the median OS was 15 months (95% CI, 12.9–17.1 months) for all the patients, 15 months (95% CI, 14.1–16.0 months) for the unresected patients, and not reached for the resected patients (p = 0.054) (Table S4, Fig. S1). Meanwhile, for the subgroup of patients with PR and BR disease, the median MDFS was 10 months (95% CI, 7.6–12.5 months) for all the patients, 9 months (95% CI, 7.6–10.4 months) for the unresected patients, and not reached for the resected patients (p = 0.007) (Table S4, Fig. S1). The number of lines of chemotherapy received did not differ significantly between the patients with PR or BR disease and the patients with LA disease (Table S5).

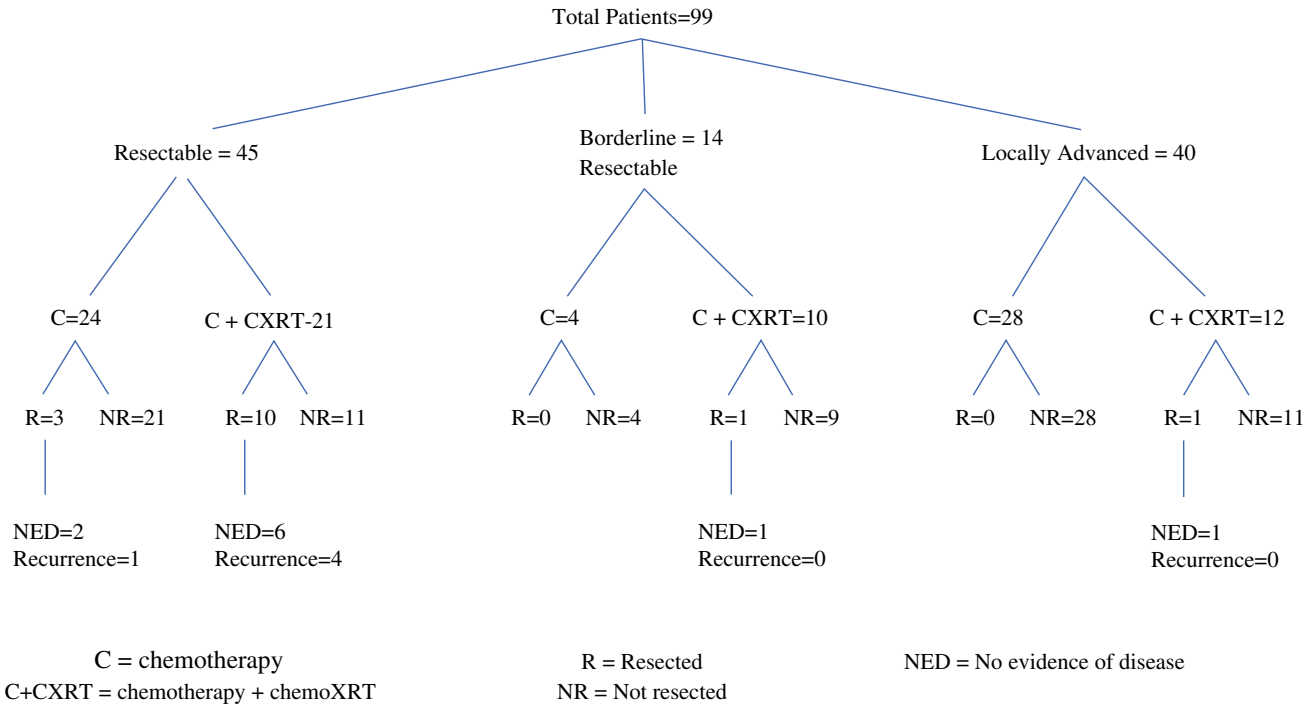

FIG. 1 Consort diagram summarizing treatment for patients with localized pancreatic ductal adenocarcinoma (PDAC) who received first-line gemcitabine and nab-paclitaxel chemotherapy

DISCUSSION

This study demonstrated that patients with radiographically resectable PDAC who are marginal candidates for surgical resection have survival outcomes similar to those for patients with locally advanced PDAC after front-line Gem/nab-P chemotherapy (approximately 17 months). Given the median age of 72 years for patients with PDAC, this is not an uncommon presentation (for the elderly frail patient with comorbidities), and we believe the outcomes data can help multidisciplinary teams to have survival discussions with patients who present with inoperable localized PDAC.

Although commonly used in clinical practice, outcomes data on the use of Gem/nab-P for localized PDAC have not been reported to the extent that data on the use of FOLFIRINOX has been reported. Additionally the data are sparse on patients who fall into the category of never operable albeit radiographically resectable PDAC. Given the median age of patients with PDAC, the associated comorbidities and frailty among patients (BR-C status), and the patients at high risk (BR-B status), this is a large population of patients with no reasonable option for surgery.

The A021101 trial was a prospective, multicenter, single-arm trial of preoperative FOLFIRINOX followed by Xeloda-based chemoradiation before pancreatectomy for borderline-resectable PDAC.[26] The median age of the study population (n = 22) was 64 years, and no patients older than 80 years were enrolled on this study. None of the enrolled patients had a CA19-9 of 1000 or higher or an ECOG PS greater than 1. Of 22 patients, 15 (68%; 95% CI, 49–88%) completed their preoperative treatment and underwent pancreatectomy. By contrast, in our study population, 59 patients had PR or BR disease. Of these patients, 20 (34%) had PR or BR-A disease, whereas 39 (66%) had BR-B or BR-C disease. The BR-B+C group included one or more of the following factors: age of 80 years or older (13%), an ECOG PS of 2 or higher (13%), moderate to severe comorbidities (55%), a CA19-9 of 1000 or higher (28%), and suspicion for metastatic disease (21%). A significantly lower number of patients (14/59, 24%) with PR or BR disease who received first-line Gem/nab-P subsequently underwent pancreatectomy. These findings suggest that due to the frailty and high-risk features of these patients, Gem/nab-P was the chemotherapy of choice due to better tolerance compared with FOLFIRINOX. Moreover, the majority of patients receiving Gem/nab-P who do undergo pancreatectomy have PR or BR-A disease (12/20, 60%), whereas fewer patients with BR-B, BR-C, or LA disease undergo pancreatectomy (3/79; 4%).

Hammel et al.[7] recently reported the Locally Advanced Pancreatic Cancer (LAPACT) trial with 107 treatment-naïve patients who had unresectable LA PDAC. This trial included patients with BR and LA PDAC and a PS of 1 or

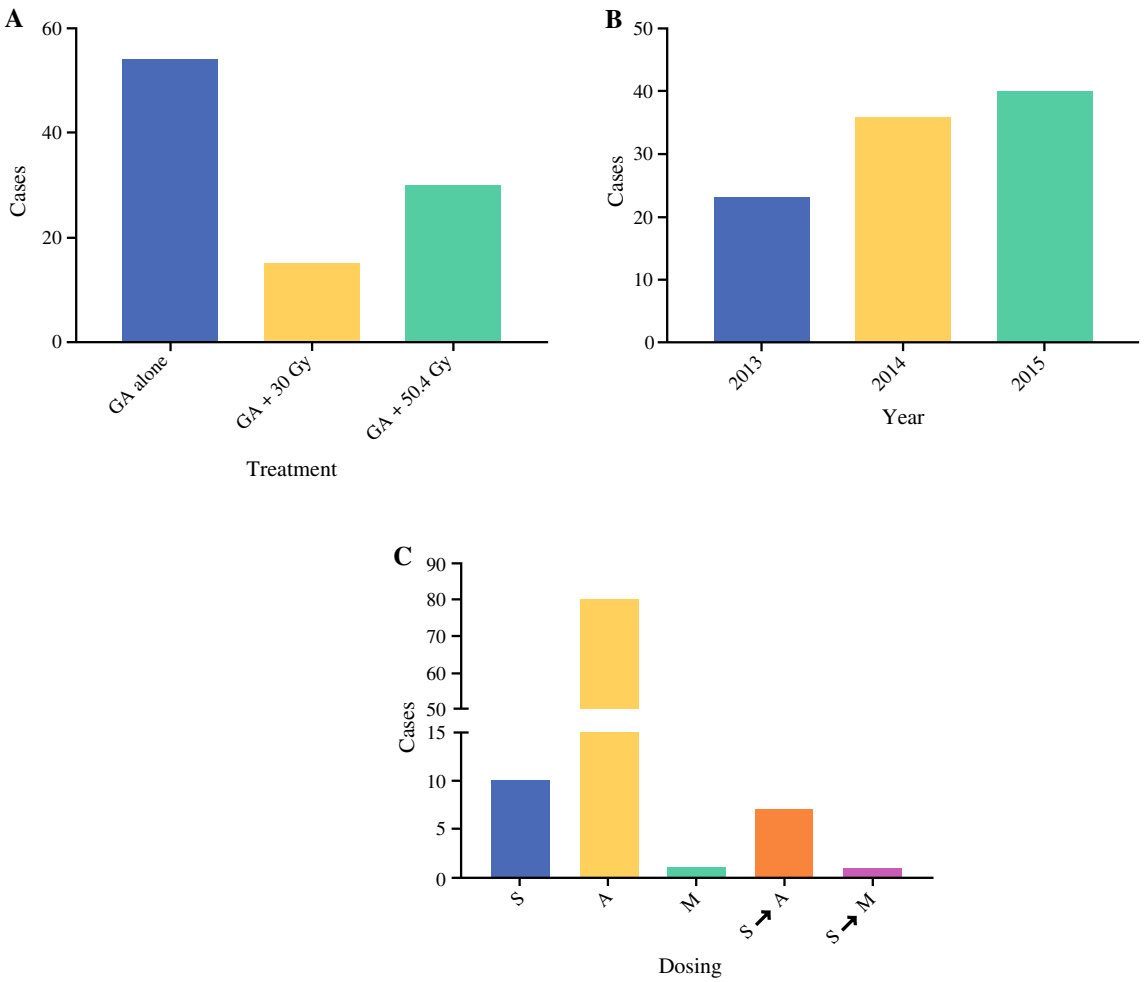

FIG. 2 **a** Number of patients with localized pancreatic ductal adenocarcinoma (PDAC) who received first-line gemcitabine and nab-paclitaxel chemotherapy alone versus number of patients who received gemcitabine and nab-paclitaxel chemotherapy followed by chemoradiation (standard fractionation [50.4 Gy/28 fx] or hypofractionated [30 Gy/10 fx]). GA, gemcitabine and nanoparticle albumin-bound paclitaxel. **b** Number of patients per year with localized pancreatic ductal adenocarcinoma (PDAC) who received first-line gemcitabine and nab-paclitaxel chemotherapy. **c** Number of patients with localized pancreatic ductal adenocarcinoma (PDAC) who received first-line gemcitabine and nab-paclitaxel chemotherapy, standard dosing (S) versus alternate dosing (A) versus modified dosing (M) and number of patients who started treatment with standard dosing and subsequently were changed to alternate (S → A) or modified (S → M) dosing

higher. The induction phase was six cycles of Gem/nab-P (given on days 1, 8, and 15 of each 28-day cycle). After induction, the patients without progressive disease or unacceptable adverse events were eligible for continued treatment with Gem/nab-P, chemoradiation, or surgery as per the physician's choice. After induction, 13 (12%) continued Gem/nab-P chemotherapy, 17 (16%) received chemoradiation, and 16 (15%) underwent surgical resection ($R0 = 7$, $R1 = 9$). During induction, the disease control rate was 78%, and the overall response rate was 32%. The median time to treatment failure was 8.6 months. The median PFS was 10.8 months, and the 12-month estimated OS was 72%.

Combination therapy with Gem/nab-P (gemcitabine dosed at 1000 mg/m^2, nab-paclitaxel dosed at 125 mg/m^2 each given on days 1, 8, and 15 of each 28-day cycle) is associated with high rates of neutropenia, fatigue, diarrhea, and neuropathy.[6,22] An alternate dosing of this regimen (gemcitabine dosed at 1000 mg/m^2, nab-paclitaxel dosed at 125 mg/m^2 every 14 days) was found to be associated with a higher median OS (11.1 months) and less severe neutropenia and peripheral neuropathy than with the standard dosing of this regimen,[22] with retrospective reported studies suggesting no loss of efficacy and confirming decreased toxicity. We found that biweekly (alternate) dosing is being used to treat the majority of localized PDAC patients (80/99; 81%) and appears to be well tolerated with minimal grade 3 or 4 toxicity and no treatment-

TABLE 2 Surgical, pathologic, and adjuvant treatment summary for patients with localized pancreatic ductal adenocarcinoma (PDAC) who underwent pancreatectomy after first-line gemcitabine and nab-paclitaxel chemotherapy (n = 15)

Variable	n
Type of surgery	
Pancreatoduodenectomy	14
Distal pancreatectomy	1
Microscopic perineural invasion	
Positive	13
Negative	2
Microscopic lymphovascular invasion	
Positive	8
Negative	7
Degree of differentiation	
Moderate	10
Poor	5
AJCC pN[a]	
N0	4
N1	11
Margin status	
R0	10
R1	5[b]
AJCC stage[a]	
IA	1
IIA	3
IIB	11
Viable tumor (%)	
< 5	0
5–50	5
50–90	10
Adjuvant chemotherapy	
Yes	13
No	2
Adjuvant chemotherapy regimen	
Gemcitabine	5
Gemcitabine/nab-paclitaxel	2
Gemcitabine/cisplatin	2
Gemcitabine/capecitabine	1
Gemcitabine/nab-paclitaxel/cisplatin	1
Gemcitabine/nab-paclitaxel/capecitabine	1
FOLFIRINOX	1

AJCC American Joint Committee on Cancer

[a]AJCC version 7

[b]Pancreatic margin (n = 4); SMA margin (n = 1)

related deaths. Notably, although many groups are using days 1/8 or days 1/15 Gem/nab-P dosing, noninferiority to standard dosing has not been demonstrated in prospective trials, and our reported data reflect our institutional practice.

After primary surgical resection for localized PDAC, the administration of adjuvant chemotherapy for PDAC is associated with improved oncologic outcomes compared with surgery alone.[3] Three large trials have demonstrated the benefit of adjuvant chemotherapy with gemcitabine (CONKO-1),[27] gemcitabine or 5-FU (ESPAC-3),[28] and gemcitabine with capecitabine (ESPAC-4).[29] However, no large trials have evaluated the benefit of adjuvant chemotherapy for localized PDAC patients who have undergone preoperative chemotherapy, chemoradiation, or both before pancreatectomy.

We have previously demonstrated that addition of adjuvant chemotherapy is associated with a better median OS for patients with PR/BR/LA disease than for those who received preoperative chemotherapy without adjuvant chemotherapy after resection, specifically those with a low lymph node ratio (73 vs 36 months; p = 0.02).[30] Although the type of adjuvant chemotherapy administered did not vary significantly, the majority of patients received gemcitabine-based regimens. Similarly, Shubert et al.[31] found that postoperative adjuvant chemotherapy was associated with improved OS (31.6 vs 22.6 months; p = 0.03) compared with adjuvant chemotherapy for stage 3 PDAC patients. Our findings in this study are consistent with previous findings as the majority of the patients (13/15; 87%) received adjuvant chemotherapy, with most of the patients (12/13; 92%) receiving gemcitabine-based regimens.

Our study limitations included the retrospective nature of the data in a single institution and the inclusion of only patients who received all their treatment at our institution. Also, we considered evaluating radiographic response rates of Gem/nab-P, but the change in tumor size was not available for all the patients. We believe this does not affect the conclusion, especially because this parameter is not very useful in localized PDAC and is subject to inter-observer variability in retrospective studies.

In summary, our data demonstrate that Gem/nab-P can be administered safely and in a well-tolerated manner to patients with significant comorbidities that may preclude pancreatectomy, although they may be radiographically PR or BR. In particular, the alternate (bi-weekly) dosing regimen showed low rates of grades 3 and 4 toxicities and no treatment-related deaths. Our real-world data, outside the context of a clinical trial, suggest that the survival rate for these patients with inoperable PDAC and front line Gem/nab-P is similar to that for patients with LA PDAC (16 vs 17 months, respectively). To our knowledge, this is the first study to evaluate outcomes for a large cohort of patients treated with first-line Gem/nab-P chemotherapy for localized PDAC.

TABLE 3 Summary of overall survival and metastatic disease-free survival end points for all patients with localized pancreatic ductal adenocarcinoma (PDAC) who received first-line gemcitabine and nab-paclitaxel chemotherapy

End point	Median	95% CI	Log-rank (Mantel-Cox)	
			Chi square	*p* value
Overall survival				
All patients	18.00	15.55–20.46	4.808	0.02
Resected patients	NR	NR		
Unresected patients	17.00	14.55–19.45		
Metastatic disease-free survival				
All patients	11.00	5.00–16.99	6.501	0.008
Resected patients	NR	NR		
Unresected patients	9.00	4.14–13.86		

CI confidence interval, *NR* not reached

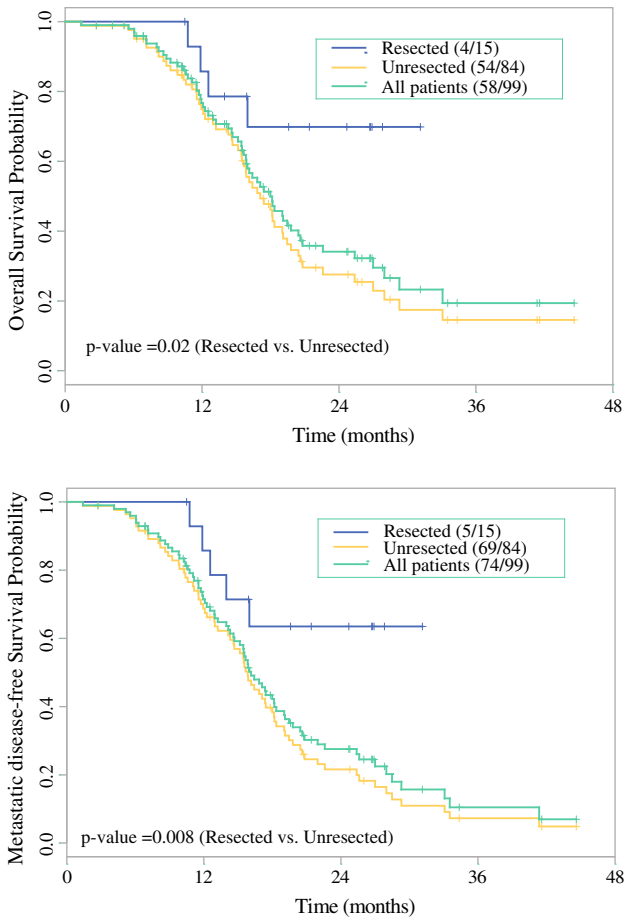

FIG. 3 Overall survival (upper panel) and metastatic disease-free survival (lower panel) for all patients (black) with localized pancreatic ductal adenocarcinoma (PDAC) who received first-line gemcitabine and nab-paclitaxel chemotherapy and subsequently underwent resection (red) versus no resection (blue)

DISCLOSURE Gauri R. Varadhachary serves on the strategic council and scientific advisory board and received an honorarium from Celgene. The remaining authors have no conflicts of interest.

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