THERAPEUTIC ADVANCES in
Medical Oncology

Original Research

Retrospective analysis of capecitabine maintenance therapy in pancreatic ductal adenocarcinoma

Ther Adv Med Oncol

2025, Vol. 17: 1–9

DOI: 10.1177/17588359251321894

Jordan Powell, Alexa F. Viniotis, Chase Irwin, Gayle S. Jameson, Lana Caldwell and Erkut H. Borazanci

Abstract

Background: Pancreatic ductal adenocarcinoma (PC) is an aggressive form of cancer treated with chemotherapy regimens such as leucovorin, 5-fluorouracil (5-FU), irinotecan, oxaliplatin (FOLFIRINOX), and gemcitabine plus albumin-bound paclitaxel (nab-Paclitaxel). Maintenance chemotherapy is increasingly being studied as an option for patients with a prior response to chemotherapy, prolonged stable disease, and those unable to tolerate the toxicities of traditional chemotherapy.

Objective: Our retrospective analysis aims to evaluate the effectiveness and tolerability of capecitabine as maintenance therapy in patients with PC.

Design: Thirty-three patients treated for PC with capecitabine (an oral formulation of 5-FU) maintenance therapy at our single institution between 8/01/2013 and 9/02/2021 were identified on chart review via the electronic medical record (EMR).

Methods: Kaplan–Meier curves were fit to evaluate patient progression-free survival (PFS) and overall survival (OS).

Results: Thirty-three individuals were identified: 21 males and 12 females, with a median age of 69 years. Fifteen of 33 had stage IV PC. Nineteen had progression of disease; 8 completed therapy and transitioned to observation or other treatments; 2 did not tolerate treatment; and 4 were still undergoing treatment. The median PFS was 13.01 months (396.0 days), and the median OS was 28.42 months (865.0 days).

Conclusion: Maintenance with capecitabine seems safe and may represent a valuable option in patients with advanced PC controlled using FOLFIRINOX or gemcitabine/nab-Paclitaxel induction treatment.

Keywords: maintenance therapy, metastasis, oral chemotherapy, pancreatic cancer, survivorship

Received: 2 September 2024; revised manuscript accepted: 28 January 2025.

Correspondence to:
Alexa F. Viniotis
HonorHealth Thompson Peak Internal Medicine Residency, 7400 E Thompson Peak Parkway, Scottsdale, AZ 85255, USA
aviniotis@honorhealth.com

Jordan Powell
Chase Irwin
The University of Arizona College of Medicine, Phoenix, AZ, USA

Gayle S. Jameson
Lana Caldwell
Erkut H. Borazanci
HonorHealth Research and Innovation Institute, Scottsdale, AZ, USA

Introduction

Pancreatic ductal adenocarcinoma (PC) is an aggressive cancer that generally carries a poor prognosis and is diagnosed late in the disease process due to the lack of screening tests. Despite advances in surgical and medical therapies, PC is expected to become the second leading cause of cancer deaths in the United States in the next decade.[1] Five-year survival was estimated to be 11% for all stages and 3% for those with metastatic disease.[2,3] The evolution of therapies has modestly improved survival but does not usually result in complete remission, so pancreatic cancer remains a treatment challenge. Much effort is needed to find new targets for novel therapies.[1]

Gemcitabine is one chemotherapy agent that became accepted as the standard of care due to its effectiveness for advanced-stage pancreatic

cancer.[4] Many combination chemotherapy regimens have been tested in comparison to gemcitabine and several have shown improvement in efficacy and tumor response.[5] In recent years, leucovorin (LV), 5-fluorouracil (5-FU), irinotecan, and oxaliplatin (FOLFIRINOX) combination chemotherapy regimen and gemcitabine plus albumin-bound paclitaxel (nab-Paclitaxel) have emerged as common first-line chemotherapy options for PC.[6]

Although effective, tolerability remains a concern with these combination regimens as harmful side effects often result in dose reductions and premature termination of treatment.[5,7] As outcomes have improved for patients with advanced PC, long-term maintenance therapies following initial chemotherapy have emerged with the hopes of enhancing patient survival while limiting toxicity.

Capecitabine, an oral chemotherapy agent, could be a good option for maintenance therapy. Capecitabine generates 5-FU when metabolized and works by inhibiting DNA and RNA synthesis.[8] However, data investigating capecitabine for long-term maintenance therapy in patients with metastatic PC remain limited. We conducted a retrospective analysis of PC patients treated with capecitabine maintenance therapy at HonorHealth from 8/01/2013 to 9/02/2021.

Materials and methods

We conducted a retrospective chart review for patients with a diagnosis of PC who were treated at HonorHealth in Scottsdale, AZ between 08/01/2013 and 09/02/2021 with oral daily capecitabine maintenance chemotherapy at 1000 mg twice daily. The inclusion criteria included any adult with a diagnosis of pancreatic cancer who received capecitabine maintenance therapy at HonorHealth and all other subjects were excluded. A thorough electronic medical record (EMR) review was completed to retrieve demographic information, clinical stage of disease, date of capecitabine initiation, date of capecitabine termination, reason for termination of therapy, date of progression of disease (POD), date of death, and the presence of any pathogenic germline mutations. The project received approval from the local institutional review board (IRB), and all patients found were included in the study.

The primary outcome examined progression-free survival (PFS) in patients with PC who received capecitabine as maintenance therapy. There were four reasons for termination of therapy in this cohort: POD, did not tolerate (DNT), ongoing, and therapy complete. POD was determined by clinical notes in the EMR by the oncologist describing new findings that met the criteria for termination of therapy. Patients were tracked from the date of capecitabine initiation to the date of POD or the date of data collection (9/02/2021) in which case they were right-censored. The secondary outcome assessed the overall survival (OS) in PC patients who received capecitabine as maintenance therapy. Patients were tracked from the date of capecitabine initiation to the date of death or the date of data collection (9/02/2021) in which case they were right-censored.

Patient age, sex, stage at the start of capecitabine as maintenance therapy, and outcome of treatments were calculated as medians and interquartile ranges or frequencies and proportions (Table 1). PFS and OS of patients receiving oral daily capecitabine maintenance chemotherapy were evaluated with Kaplan–Meier curves (Figures 1 and 2). We also reported the median survival time and its corresponding 95% confidence interval (CI) for both outcomes. All analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC, USA). The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement[9] (Supplemental Table 1).

Results

In all, 33 patients were included in the analysis. The population had a median age of 69 years and the majority were men (63.6%), shown in Table 1. At the date of assessment (9/02/2021), nine patients (27.3%) had passed away (Table 1). There were four reasons for the termination of capecitabine. The primary reason for the termination of capecitabine was due to POD ($n = 19$; 57.6%; Table 1). Two (6.1%) stopped because they DNT therapy, citing abdominal cramps, and fatigue. Eight (24.2%) patients completed therapy as it was part of their post-adjuvant treatment plan and transitioned to observation due to a lack of visible disease (Table 1). Four (12.1%) patients were still undergoing treatment with capecitabine at the date of data collection (Table 1). There were no patients with clinical stage IA disease, and 15 (45.5%) had stage IV disease at the time of capecitabine

Table 1. Demographics of pancreatic cancer patients.

Covariate	Study sample ($n = 33$)
Age in years, median (IQR)	69.0 (62.0–73.0)
Sex, *n* (%)	
Male	21 (63.6)
Female	12 (36.4)
Deceased, *n* (%)	9 (27.3)
Result of treatment, *n* (%)	
POD	19 (57.6)
DNT	2 (6.1)
Therapy complete	8 (24.2)
Ongoing	4 (12.1)
Stage at start of capecitabine, *n* (%)	
IA	0 (0.0)
IB	4 (12.1)
IIA	3 (9.1)
IIB	3 (9.1)
III	8 (24.2)
IV	15 (45.5)

DNT, did not tolerate; IQR, interquartile range; POD, progression of disease.

initiation (Table 1). Of those patients who did not have metastatic disease, they had locally advanced PC or were ineligible for surgery. These individuals had maximized or had difficulty tolerating prior systemic chemotherapy with or without radiation as listed in Table 2. Patient 30 trialed capecitabine due to concerns for recurrence following surgery.

Kaplan–Meier curves were constructed to visually represent both progression-free and OS. Figure 1 shows the PFS. Censored events are indicated in the curve. Based on the censored survival analysis, the estimated median PFS in this population was 396.0 (95% CI: 206.0–553) days or 13.01 months (Figure 1). Figure 2 represents OS in the study. The median estimated OS for all patients who received capecitabine for PC was 865.0 (95% CI: 808.0–infinity) days or 28.42 months (Figure 2).

Five patients had a pathogenic germline mutation among which only one was targetable (BReast CAncer 2—BRCA2). This patient did not benefit from capecitabine administration after the failure of olaparib as maintenance therapy, but it is possible that the reintroduction of platinum could have been more efficacious. Table 3 summarizes the demographics of these patients, the clinical stage of the disease, specific mutation information, individual OS, and individual PFS.

Discussion

Treatment for pancreatic cancer is challenging due to diagnosis in more advanced stages and the need to balance the therapeutic benefit and toxicity of the many agents. As chemotherapy combinations have improved survival, maintenance therapy has found its way to the forefront as a strategy to maximize time on therapy and minimize disease progression.

The PANOPTIMOX prospective randomized trial was essential in studying maintenance therapy in PC.[10] The traditional standard of care group or arm A received 6 months (12 cycles or less) of FOLFIRINOX; the maintenance group or arm B received 4 months (8 cycles) of induction FOLFIRINOX followed by leucovorin plus fluorouracil until disease progression; and arm C received sequential treatment alternating irinotecan, leucovorin, and fluorouracil for 2 months (FOLFIRI.3) with 2 cycles of gemcitabine (FIRGEM).[10] The median OS in the maintenance treatment arm B was superior to the median OS in arm A and arm C. However, patients on maintenance therapy over time received a higher total cumulative dose of oxaliplatin resulting in grade 3 and 4 neurotoxicity, but this side effect was reached later than before.[10] Ultimately, maintenance therapy with leucovorin and fluorouracil after induction chemotherapy with FOLFIRINOX was shown to offer an effective treatment option aimed at preserving functional status for patients with metastatic PC.[10] The study suggested other maintenance agents like capecitabine may be even more beneficial with better ease of administration and fewer medical visits.[10]

Another randomized trial evaluating maintenance therapy for metastatic PC investigated sunitinib versus best supportive care following first-line chemotherapy treatment.[11] It illustrated improvement both in PFS and OS in patients.[11] A phase Ib randomized trial of metformin with and

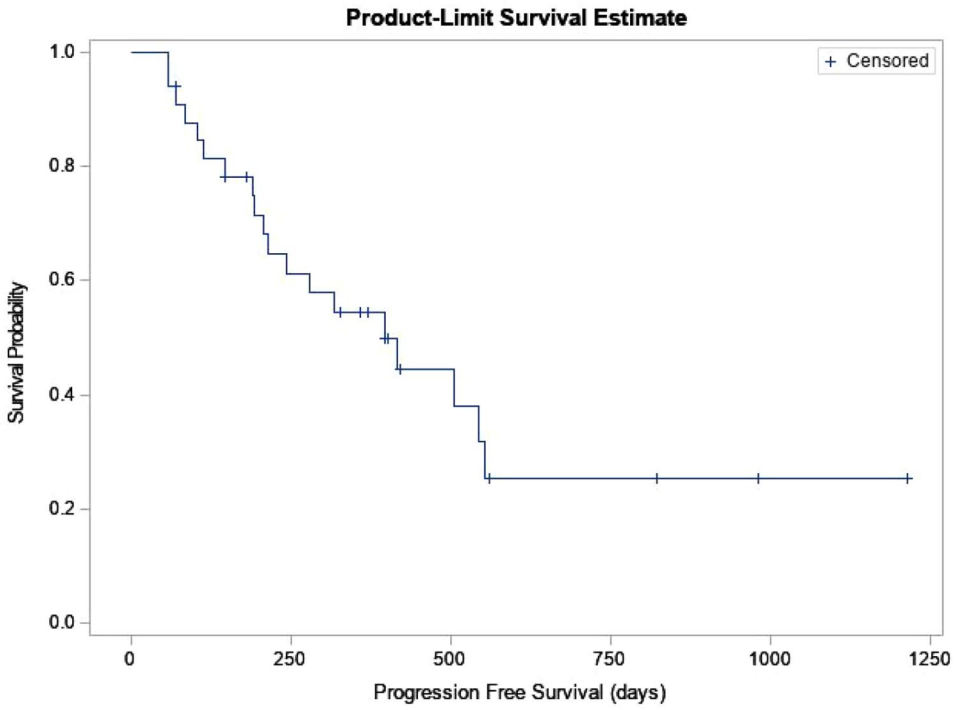

Figure 1. PFS of patients with pancreatic cancer receiving capecitabine.
PFS probability. Median PFS of 396.0 days (95% CI: 206.0–553 days) for PC patients on capecitabine.
CI, confidence interval; PC, pancreatic ductal adenocarcinoma; PFS, progression-free survival.

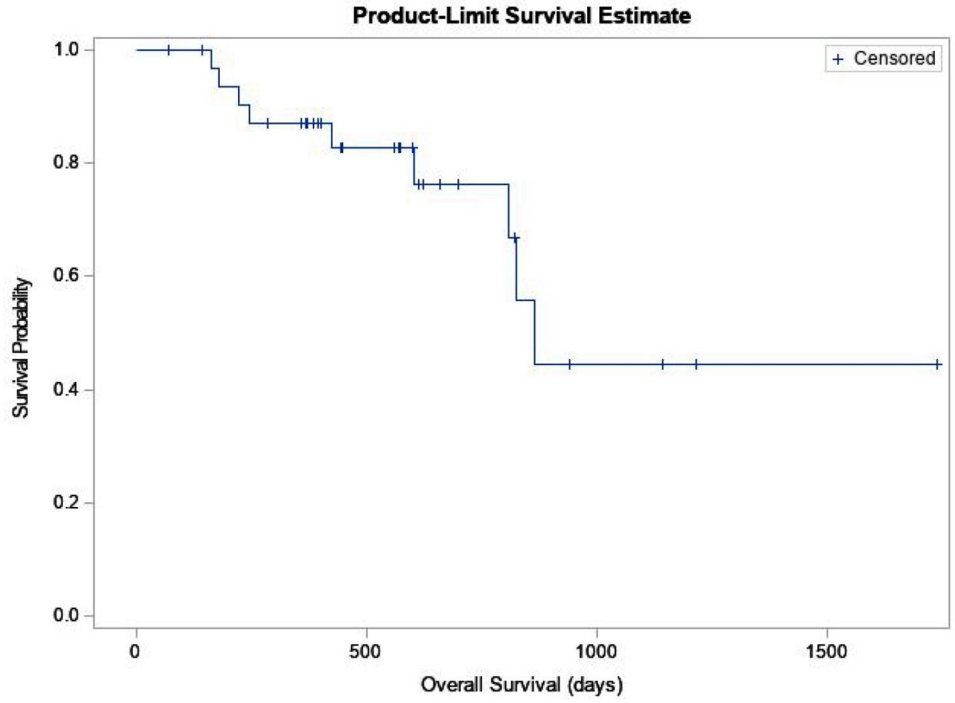

Figure 2. OS of patients with pancreatic cancer receiving capecitabine.
OS probability. Median OS of 865.0 days (95% CI: 808.0–infinity days) for PC patients on capecitabine.
CI, confidence interval; OS, overall survival; PC, pancreatic ductal adenocarcinoma.

Table 2. Prior treatments before capecitabine.

Patient number	Pancreatic cancer stage at the time of capecitabine	First-line treatment	Second-line treatment	Third-line treatment	Fourth-line treatment	Fifth-line treatment
1	III	GAP + paricalcitol	IMRT/Xeloda			
2	IIA	GAP + paricalcitol	IMRT/Xeloda			
3	IV	Gemcitabine/ paricalcitol				
4	III	GAP	IMRT/Xeloda			
5	IIA	GAP + paricalcitol	IMRT/Xeloda			
6	IB	GAP + paricalcitol				
7	IV	GAP	FOLFIRINOX			
8	IIB	Gemcitabine/nab-paclitaxel	SBRT			
9	IB	GAP + paricalcitol				
10	IIB	FOLFIRINOX				
11	IB	GAP	SBRT			
12	IV	FOLFIRINOX	5-FU/LV			
13	IB	GAP + paricalcitol				
14	IV	Gemcitabine	5-FU/IMRT	FOLFIRINOX		
15	IV	GAP + paricalcitol	FOLFIRINOX			
16	IV	Gemcitabine/Xeloda	GAP			
17	III	GAP	Capecitabine/IMRT			
18	IV	GAP	Metformin ± Rapamycin maintenance	GAP		
19	III	GAP + paricalcitol	Capecitabine/IMRT			
20	IV	GAP				
21	IV	GAP + paricalcitol				
22	IV	GAP				
23	III	Gemcitabine/nab-paclitaxel	IMRT/Xeloda	mFOLFIRINOX		
24	IV	Gemcitabine/nab-paclitaxel	Clinical Trial			
25	IV	GAP + AA				
26	IV	GAP + AA				

(Continued)

Table 2. (Continued)

Patient number	Pancreatic cancer stage at the time of capecitabine	First-line treatment	Second-line treatment	Third-line treatment	Fourth-line treatment	Fifth-line treatment
27	IV	GAP + paricalcitol/ nivolumab				
28	III	GAP	IMRT/Xeloda			
29	IIB	GAP + paricalcitol	SBRT			
30	IIA	Gemcitabine/ nab-paclitaxel/ paricalcitol	Whipple procedure	Gemcitabine/ nab-paclitaxel/ paricalcitol		
31	III	FOLFIRINOX	Gemcitabine/abraxane	GAP	IMRT/ Xeloda	5-FU/LV
32	IV	GAP + paricalcitol/ nivolumab	Olaparib	GAP		
33	III	GAP + paricalcitol	SBRT			

5-FU, 5-fluoruracil; AA, ascorbic acid; FOLFIRINOX, 5-fluoruracil/leucovorin/irinotecan/oxaliplatin; GAP, gemcitabine/nab-paclitaxel/cisplatin; IMRT, intensity modulated radiation therapy; LV, leucovorin; nab-paclitaxel, albumin-bound paclitaxel; SBRT, stereotactic body radiation therapy.

Table 3. OS and PFS in patients with germline mutations.

Patient number	Age (years)	Sex	Stage	Germline mutations	OS[a]	PFS[a]
1	62	Male	III	CFTR: (TG) 12-5T	164	57
7	68	Male	IV	APC: pathogenic mutation, MSS	699[b]	193
12	74	Female	IV	CFTR: pathogenic mutation	575[b]	396
14	69	Female	IV	APC: c3920>A	827	544
32	73	Male	IV	BRCA2: pVal2908Gly; pASP2913_Ala2915del PTEN: pGln298Glu	143[b]	71

[a]Reported in days.
[b]Indicates censored data.
Ala, alanine; APC, adenomatous polyposis coli; BRCA2, BReast CAncer 2; CFTR, cystic fibrosis transmembrane conductance regulator; del, deletion; Gln, glutamine; Glu, glutamic acid; Gly, Glycine; MSS, microsatellite stable; OS, overall survival; PFS, progression-free survival; PTEN, phosphatase tensin homolog; Val, valine.

without rapamycin for maintenance therapy in patients with stable metastatic PC following initial treatment also demonstrated encouraging activity.[12] Metformin/rapamycin was well tolerated and demonstrated a 24-month survival rate of 37% in the 22 patients.[12]

Capecitabine has been investigated as a maintenance regimen for other gastrointestinal malignancies. One specific study investigated the use of FOLFIRINOX induction and 5-FU/leucovorin maintenance with reinduction when necessary.[13] Their results suggested that alternating with maintenance therapy may increase PFS and combat cumulative toxicity.[13] Capecitabine was also evaluated as maintenance therapy in patients with metastatic PC following initial treatment with FOLFIRINOX chemotherapy.[14] The study

observed that patients were able to extend the amount of time receiving chemotherapy by implementing maintenance therapy until disease progression was observed, and then FOLFIRINOX was reintroduced for further treatment.[14] Median OS from the time of capecitabine initiation was 17 months.[14]

In this study, capecitabine 1000 mg twice daily, Monday through Friday, appears to be a promising maintenance strategy for advanced PC based on the survival analysis. Greater than 80% of patients were alive at 1 year, and greater than 65% were alive at 2 years, with a median estimated OS of greater than 2 years. Comparatively, a prior study of capecitabine in the post-adjuvant setting estimated a median OS as high as 48 months, but it included only patients with stage I or II localized disease and those without disease recurrence on adjuvant chemotherapy.[15] Conversely, approximately 46% of our patients had stage IV disease and 24% had locally advanced/stage III PC at the time of capecitabine initiation. The OS and PFS seen in our study are promising given that individuals diagnosed with stage IV pancreatic cancer usually have a relative survival rate of 22% at 1 year.[16] Very little data have been reported on the effectiveness of capecitabine maintenance therapy in a population with advanced pancreatic disease. Further research is needed to examine the benefits of capecitabine as maintenance therapy versus other agents.

In general, capecitabine was well tolerated, even in some who received therapy for several years. However, some patients required dose reductions or interruptions due to an expected adverse event of palmar-plantar erythrodysesthesia (PPE or hand–foot syndrome). Patients with PPE were able to continue capecitabine with dose modifications and aggressive topical lubrication. Two of the 33 patients had to end treatment with capecitabine, one due to persistent abdominal cramps and the other due to fatigue and diffuse shoulder pain.

As survival has slowly improved in patients with PC, research has been aiming to find biological targets for potential therapies. It is estimated that approximately 5%–7% of patients with pancreatic cancer have a DNA repair mutation in a BRCA gene.[17] Approximately 17% of individuals have a pathogenic mutation in a DNA double-stranded break repair gene.[17] In our study, five patients were found to have pathogenic germline mutations, represented in Table 3. Due to the limited sample size, it is difficult to ascertain any statistical comparison to patients without these mutations. The BRCA2 patient had the poorest OS in days when compared to other mutations. It is also important to note that the use of the poly ADP ribose polymerase inhibitor olaparib for individuals with metastatic PC with a germline BRCA mutation was approved in 2019 based upon improved PFS of olaparib of 7.4 months compared to 3.8 months with placebo.[18]

There were several limitations to our study. Foremost, this was a retrospective analysis rather than a prospective analysis. Clinical trials with control groups will be necessary to determine the true efficacy and dosing of capecitabine as monotherapy. Another limitation was the small sample size of 33 patients. Enrolling more subjects in the future would be more reflective and applicable to the larger population. Currently, there is an ongoing phase II maintenance study of the histone deacetylase inhibitor ivaltinostat with capecitabine compared to capecitabine alone in metastatic PC in those who have not progressed on front-line fluoropyrimidine-based chemotherapy (NCT05249101).

Our findings lend evidence that capecitabine is generally well tolerated as maintenance chemotherapy, even in a population with mostly advanced disease. As a monotherapy, it offers an appropriate palliative approach aimed at prolonging life and helping to minimize recurrence. In addition, it may be more cost-effective and helps to promote compliance. Future larger prospective studies are needed to evaluate capecitabine as maintenance therapy.

Conclusion

Pancreatic cancer remains difficult to treat due to its aggressive nature. Chemotherapy with FOLFIRINOX and gemcitabine/nab-Paclitaxel has prolonged survival in this patient population but is associated with many side effects such as fatigue, neuropathy, and pancytopenia that cause dose reduction or early termination of therapy. In our retrospective cohort, capecitabine represents a convenient maintenance option with the suspension of systemic chemotherapy in a subset of patients who have prolonged tumor control after administering FOLFIRINOX or gemcitabine/nab-Paclitaxel induction chemotherapy.

Declarations

Ethics approval and consent to participate

This retrospective chart review study involving human participants was in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments. It was approved by the HonorHealth Institutional Review Board as exempt on September 3, 2021, given the retrospective nature and as all the procedures were performed as part of routine care (protocol number 1768816-1). The HonorHealth Institutional Review Board committee waived the need for informed consent given that it is a retrospective analysis.

Consent for publication

Not applicable.

Author contributions

Jordan Powell: Conceptualization; Investigation; Methodology; Visualization; Writing – original draft; Writing – review & editing.

Alexa F. Viniotis: Conceptualization; Visualization; Writing – original draft; Writing – review & editing.

Chase Irwin: Formal analysis; Software; Writing – review & editing.

Gayle S. Jameson: Investigation; Project administration; Resources; Supervision; Writing – review & editing.

Lana Caldwell: Investigation; Project administration; Resources; Supervision; Writing – review & editing.

Erkut H. Borazanci: Conceptualization; Investigation; Methodology; Project administration; Resources; Supervision; Visualization; Writing – original draft; Writing – review & editing.

Acknowledgements

None.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Competing interests

Financial interests: E.H.B.: BPG, Conjupro, Vivacitas Oncology, Nanology. G.S.J.: Celgene. Non-financial interests: E.H.B.: Bristol-Myers Squibb, Merck, Biontech, Corcept, Bioline, Minneamrita Therapeutics, Helix Biopharma, Biosplice, Fujifilm, Ideaya, TGen Foundation, HonorHealth Foundation, Seena Magowitz Foundation. G.S.J.: Bristol-Myers Squibb. The other authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of data and materials

Data are provided within the manuscript file. The data presented in this study are available by written request from the corresponding author.

ORCID iDs

Alexa F. Viniotis https://orcid.org/0000-0002-8990-4684

Erkut H. Borazanci https://orcid.org/0000-0001-5136-5462

Supplemental material

Supplemental material for this article is available online.

References

1. Nishimoto A. Effective combinations of anticancer and targeted drugs for pancreatic cancer treatment. *World J Gastroenterol* 2022; 28: 3637–3643.
2. Wilbur HC, Durham JN, Lim SJ, et al. Gemcitabine, docetaxel, capecitabine, cisplatin, irinotecan as first-line treatment for metastatic pancreatic cancer. *Cancer Res Commun* 2023; 3: 1672–1677.
3. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. *CA Cancer J Clin* 2022; 72: 7–33.
4. Burris HA, Moore MJ, Andersen J, et al. Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. *J Clin Oncol* 1997; 15: 2403–2413.
5. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med* 2011; 364: 1817–1825.
6. NCCN.org National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. NCCN Evidence Blocks—Pancreatic Adenocarcinoma, www.nccn.org/guidelines/guidelines-with-evidence-blocks (2024, accessed 25 August 2024).

7. Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med* 2013; 369: 1691–1703.
8. Miwa M, Ura M, Nishida M, et al. Design of a novel oral fluoropyrimidine carbamate, capecitabine, which generates 5-fluorouracil selectively in tumours by enzymes concentrated in human liver and cancer tissue. *Eur J Cancer* 1998; 34: 1274–1281.
9. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg* 2014; 12: 1495–1499.
10. Dahan L, Williet N, Malicot KL, et al. Randomized phase II trial evaluating two sequential treatments in first line of metastatic pancreatic cancer: results of the PANOPTIMOX-PRODIGE 35 trial. *J Clin Oncol* 2021; 39: 3242–3250.
11. Reni M, Cereda S, Milella M, et al. Maintenance sunitinib or observation in metastatic pancreatic adenocarcinoma: a phase II randomised trial. *Eur J Cancer* 2013; 49: 3609–3615.
12. Bever KM, Borazanci EH, Thompson EA, et al. An exploratory study of metformin with or without rapamycin as maintenance therapy after induction chemotherapy in patients with metastatic pancreatic adenocarcinoma. *Oncotarget* 2020; 11: 1929–1941.
13. Hann A, Bohle W, Egger J, et al. Feasibility of alternating induction and maintenance chemotherapy in pancreatic cancer. *Sci Rep* 2017; 7: 1–7.
14. Reure J, Follana P, Gal J, et al. Effectiveness and tolerability of maintenance capecitabine administrated to patients with metastatic pancreatic cancer treated with first-line FOLFIRINOX. *Oncology* 2016; 90: 261–266.
15. Weinberg BA, Wang H, Yang X, et al. Maintenance therapy with capecitabine in patients with resected pancreatic adenocarcinoma after adjuvant therapy: a retrospective cohort study. *Gastrointest Cancer Res* 2014; 7: 91–97.
16. SEER*Explorer. An interactive website for SEER cancer statistics. Surveillance Research Program, National Cancer Institute, https://seer.cancer.gov/statistics-network/explorer/ (2024, accessed 25 August 2024).
17. Hammel P, Vitellius C, Boisteau É, et al. Maintenance therapies in metastatic pancreatic cancer: present and future with a focus on PARP inhibitors. *Ther Adv Med Oncol* 2020; 12: 1–9.
18. Golan T, Hammel P, Reni M, et al. Maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer. *N Engl J Med* 2019; 381: 317–327.