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ORIGINAL RESEARCH

Effectiveness of Palliative Chemotherapy and Associated Prognostic Factors in Advanced Small Bowel Adenocarcinoma: A Propensity Score-Matched Analysis

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Purpose: Small bowel adenocarcinoma (SBA) is a rare gastrointestinal malignancy with limited evidence guiding systemic treatment in the advanced stages. This study evaluated the effectiveness of palliative chemotherapy and revealed the prognostic factors associated with survival in patients with metastatic or unresectable SBA.

Patients and Methods: We conducted a retrospective cohort study of patients diagnosed with advanced SBA at a single tertiary center in Thailand between 2005 and 2024. The patients were treated with palliative systemic chemotherapy or best supportive care (BSC). Survival outcomes were assessed using Kaplan–Meier estimates and Cox regression analyses. Propensity score-matching (PSM) was performed to adjust for baseline imbalances.

Results: This study included 106 patients; of these, 39 (36.8%) received palliative chemotherapy. After 1:1 PSM, 39 matched pairs were analyzed. Chemotherapy significantly improved overall survival (OS) compared with that of the BSC, with a median OS of 10.4 vs 2.6 months (hazard ratio 0.36; 95% confidence intervals 0.22–0.59; P <0.001). Among chemotherapy-treated patients, the median progression-free survival was 5.95 months, and the objective response rate was 10.3% overall, increasing to 21.1% among evaluable patients receiving doublet regimens. Multivariate analysis revealed that poor Eastern Cooperative Oncology Group performance status (≥2), poorly differentiated histology, and duodenal tumor location independently predicted worse OS.

Conclusion: Palliative chemotherapy significantly prolongs survival in patients with advanced SBA compared with that of BSC, particularly in those with a good performance status. Doublet fluoropyrimidine-based regimens offered superior outcomes. These findings support the use of systemic chemotherapy for this rare malignancy, highlighting the significance of patient selection and performance status in guiding treatment decisions.

Keywords: small bowel cancer, metastasis, survival, efficacy, best supportive care, prognosis

Introduction

Small bowel adenocarcinoma (SBA) is a rare malignancy that accounts for <5% of gastrointestinal cancers, despite the small intestine's extensive length and surface area in the gastrointestinal tract.[1] The global incidence of SBA is estimated to be approximately 1 case per 100,000 people annually, with increasing trends observed in recent decades.[2,3] Owing to its rarity and nonspecific clinical presentation, SBA is usually diagnosed at an advanced stage, when curative resection is no longer feasible.[4,5]

While surgery remains the gold standard treatment for localized disease,[6,7] the optimal management of metastatic or unresectable SBA remains poorly defined.[8] In contrast to colorectal cancer, for which systemic therapy options are well-established based on robust evidence, treatment strategies for advanced SBA have historically been extrapolated from colorectal cancer regimens, such as fluoropyrimidine- and oxaliplatin-based combinations.[9–11] However, these

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recommendations are largely based on small retrospective series and limited Phase II single-arm studies with no randomized controlled trials specifically dedicated to this population.[10,12–15]

Real-world data on the effectiveness of systemic chemotherapy in advanced SBA are scarce. Furthermore, the survival benefits of systemic therapy compared with those of best supportive care (BSC) have not been systematically assessed. In addition to evaluating treatment efficacy, identifying the clinicopathological factors that influence outcomes is essential for refining prognosis and guiding personalized treatment strategies.

This study addressed these gaps in knowledge by evaluating the real-world effectiveness of systemic chemotherapy in patients with metastatic or unresectable SBA. Specifically, we assessed overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) and examined the prognostic significance of baseline clinical and pathological features. A comparative analysis of patients who received chemotherapy and those treated with BSC was performed to provide further insights into the impact of active treatment on this rare and understudied malignancy.

Materials and Methods

Study Participants and Procedures

This retrospective cohort study included patients diagnosed with advanced-stage SBA at Songklanagarind Hospital, a tertiary referral center in Southern Thailand, over 20 years (between January 2005 and December 2024). Patients were eligible for inclusion if they: 1) were aged ≥18 years; 2) had histologically confirmed adenocarcinoma originating from the duodenum, jejunum, or ileum; 3) were diagnosed with metastatic or unresectable disease; and 4) had received palliative systemic chemotherapy or BSC as initial management. Individuals were excluded if 1) the histology was not adenocarcinoma; 2) small bowel involvement was secondary to primary cancers of other organs; or 3) they had undergone curative-intent surgery.

Relevant clinical and demographic data were extracted from the electronic medical records. The dataset included information on age at diagnosis, sex, body mass index (BMI), Eastern Cooperative Oncology Group (ECOG) performance status, primary tumor site, histological grade, extent and distribution of metastasis, serum tumor marker levels, treatment regimens, and clinical follow-up.

This study was reviewed and approved by the Human Research Ethics Committee of the Faculty of Medicine at the Prince of Songkla University (REC.68305141). Owing to the retrospective nature of the study and use of anonymized data, the requirement for informed consent was waived following the institutional and ethical guidelines.

Outcome Measures

The primary endpoint of this study was OS, which was assessed by comparing patients who received palliative chemotherapy with those who received BSC. Secondary endpoints included PFS, ORR, and identification of prognostic factors influencing OS. The OS was calculated from the date of diagnosis of advanced-stage disease to the date of death from any cause. PFS was defined as the interval between the initiation of systemic chemotherapy and earliest documentation of disease progression, based on radiological evidence or death from any cause, whichever occurred first. Radiological assessments, including chest and abdominal computed tomography scans, were performed every 2–3 months as part of routine clinical follow-up. Tumor response was evaluated using the Response Evaluation Criteria in Solid Tumors, version 1.1.

Statistical Analysis

OS and PFS were estimated using the Kaplan–Meier method, and survival distributions between groups were compared using the Log rank test. To mitigate potential confounding owing to baseline characteristic imbalances in retrospective studies, we used a 1:1 propensity score-matching (PSM) approach. Matching was conducted using a nearest-neighbor algorithm without replacement, incorporating the following covariates: age, sex, ECOG performance status, BMI, primary tumor site, histologic differentiation, disease extent (metastatic vs unresectable), number of metastatic organs, and presence of liver or peritoneal metastases. Following matching, the balance of the baseline characteristics between the chemotherapy and BSC groups was reassessed to confirm adequacy. Cox proportional hazard models were used to evaluate prognostic factors for OS. Variables with

a *P*-value <0.20 in univariate analysis were subsequently included in the multivariate model. Statistical analyses were conducted using the R software version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was defined as a two-sided *P*-value <0.05.

Results

Baseline Characteristics

This study included 106 patients with advanced SBA. Of these, 39 patients (36.8%) received palliative chemotherapy, and the remaining 67 (63.2%) were managed with BSC. The overall median age was 64.8 years, with approximately half of the cohort aged >65 years. Notably, 50% had an ECOG performance status of ≥2 and metastatic involvement of two or more organs. Based on the BMI criteria, 41.5% of patients were classified as underweight. The duodenum was the most frequent primary tumor location (85.8%), and most patients had metastatic disease (88.7%).

The baseline characteristics stratified using treatment group are summarized in Table 1. Compared with those who received BSC, patients in the chemotherapy group tended to be <65 years, have an ECOG performance status of 1, and have tumors with well- or moderately-differentiated histology. Peritoneal metastasis was also more prevalent in the chemotherapy group. The distribution of metastatic sites is detailed in Table S1.

Treatment Information

Of the 39 patients who received palliative chemotherapy, 69.2% were treated with combination regimens, and the remaining 30.8% received single-agent chemotherapy (Table 2). Approximately one-third of these patients discontinued

Table 1 Baseline Characteristics

	Palliative Chemotherapy (n = 39)	**Best Supportive Care (n = 67)**	**Total (n = 106)**	***P*-value**
Age, years (IQR)	60.1 (54.5,65.5)	68.6 (55.0,73.9)	64.8 (54.3.72.8)	0.023
Age ≥65 years, n (%)	13 (33.3)	40 (59.7)	53 (50.0)	0.016
Sex, n (%)				0.718
Female	17 (43.6)	33 (49.3)	50 (47.2)	
Male	22 (56.4)	34 (56.4)	56 (52.8)	
BMI, n (%)				0.150
<18.5 kg/m^2	15 (38.5)	29 (43.3)	44 (41.5)	
18.5–22.9 kg/m^2	10 (25.6)	25 (37.3)	35 (33.0)	
≥23.0 kg/m^2	14 (35.9)	13 (19.4)	27 (25.5)	
ECOG PS, n (%)				<0.001
1	33 (84.6)	19 (28.4)	52 (49.1)	
2	6 (15.4)	38 (56.7)	44 (41.5)	
3	0 (0)	10 (14.9)	10 (9.4)	
Tumor location, n (%)				0.085
Duodenum	30 (76.9)	61 (91.0)	91 (85.8)	
Non-duodenum	9 (23.1)	6 (9.0)	15 (14.2)	
Jejunum	8 (20.5)	1 (1.5)	9 (8.5)	
Ileum	1 (2.6)	5 (7.5)	6 (5.7)	
Histology differentiation, n (%)				0.040
Well	14 (35.9)	20 (29.9)	34 (32.1)	
Moderately	15 (38.5)	14 (20.9)	29 (27.4)	
Poorly	10 (25.6)	33 (49.2)	43 (40.5)	

(*Continued*)

Table 1 (Continued).

	Palliative Chemotherapy (n = 39)	Best Supportive Care (n = 67)	Total (n = 106)	*P*-value
Type of advanced stage, n (%) Metastatic disease Unresectable disease	 37 (94.9) 2 (5.1)	 57 (85.1) 10 (14.9)	 94 (88.7) 12 (11.3)	0.203
Number of organ metastasis, n (%) 1 ≥2	 21 (53.8) 18 (46.2)	 33 (49.3) 34 (50.7)	 54 (50.9) 52 (49.1)	0.799
Liver metastasis, n (%)	14 (35.9)	19 (28.4)	33 (31.1)	0.555
Peritoneal metastasis, n (%)	21 (53.8)	20 (29.9)	41 (38.7)	0.025
CEA level, n (%) <5 ng/mL ≥5 ng/mL	(n = 23) 11 (47.8) 12 (52.2)	(n = 36) 18 (50.0) 18 (50.0)	(n = 59) 29 (49.2) 30 (50.8)	1.000
CA19-9 level, n (%) <37 U/mL ≥37 U/mL	(n = 15) 6 (50.0) 9 (60.0)	(n = 28) 15 (53.6) 13 (46.4)	(n = 43) 21 (48.8) 22 (51.2)	0.597

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; PS, performance status; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19–9; IQR, interquartile range.

Table 2 Treatment Information

Treatment Information	N (%)
Regimen	
Combination regimen	27 (69.2)
FOLFOX	9 (23.1)
CAPOX	6 (15.4)
FOLFIRI	5 (12.8)
Cisplatin plus 5-FU	4 (10.3)
Carboplatin plus 5-FU	1 (2.6)
Cisplatin plus gemcitabine	1 (2.6)
Docetaxel plus cisplatin and 5-FU	1 (2.6)
Single-agent regimen	12 (30.8)
5-FU	9 (23.1)
Gemcitabine	3 (7.7)
Discontinuation	
Disease progression	15 (38.5)
Death	11 (28.2)
Complete	4 (10.3)
Patients' preference	4 (10.3)
Intolerance to side effects	1 (2.6)
Referral to another hospital	2 (5.1)
Subsequent treatment	
Metastasectomy	2 (5.1)
Second-line chemotherapy	8 (20.5)
Third-line chemotherapy	1 (2.6)

Abbreviations: 5-FU, 5-fluorouracil; FOLFOX, folinic acid, 5-fluorouracil, and oxaliplatin; CAPOX, capecitabine and oxaliplatin; FOLFIRI, folinic acid, 5-fluorouracil, and irinotecan.

treatment because of disease progression, and death-related discontinuation occurred in 28.5% of patients. Only 20.5% of patients proceeded to second-line chemotherapy.

Two patients underwent metastasectomy after first-line chemotherapy. One patient underwent liver resection, and the other underwent total hysterectomy with bilateral oophorectomy and omentectomy. The reasons for selecting the BSC among the patients in the BSC group are summarized in Table S2.

OS

The median follow-up duration for the entire cohort was 4.02 months (range: 0.16–71.35 months). The overall median OS was 4.02 months (95% confidence interval [CI]: 3.02–6.37). Patients who received palliative chemotherapy had significantly longer survival than those treated with BSC, with a median OS of 10.38 months vs 2.37 months (hazard ratio [HR]: 0.31; 95% CI: 0.19–0.48; P <0.001; Figure 1). After adjusting for potential confounders, including age, sex, ECOG performance status, BMI, tumor location, histologic differentiation, disease stage (metastatic vs unresectable), number of metastatic organs, and presence of liver or peritoneal metastasis, multivariate Cox regression analysis confirmed the survival advantage associated with chemotherapy (adjusted HR: 0.30; 95% CI: 0.17–0.52; P <0.001).

Among those treated with chemotherapy, patients who received combination regimens had a median OS of 11.10 months, compared with those receiving single-agent therapy at 5.47 months (HR: 0.51; 95% CI: 0.25–1.05; P = 0.069). Focusing specifically on fluoropyrimidine-based regimens, the doublet group achieved a median OS of 10.38 months, whereas the single-agent 5-fluorouracil (5-FU) group had a median OS of 3.35 months (HR: 0.43; 95% CI: 0.19–0.95; P = 0.036). The detailed survival outcomes stratified by regimen are presented in Table S3.

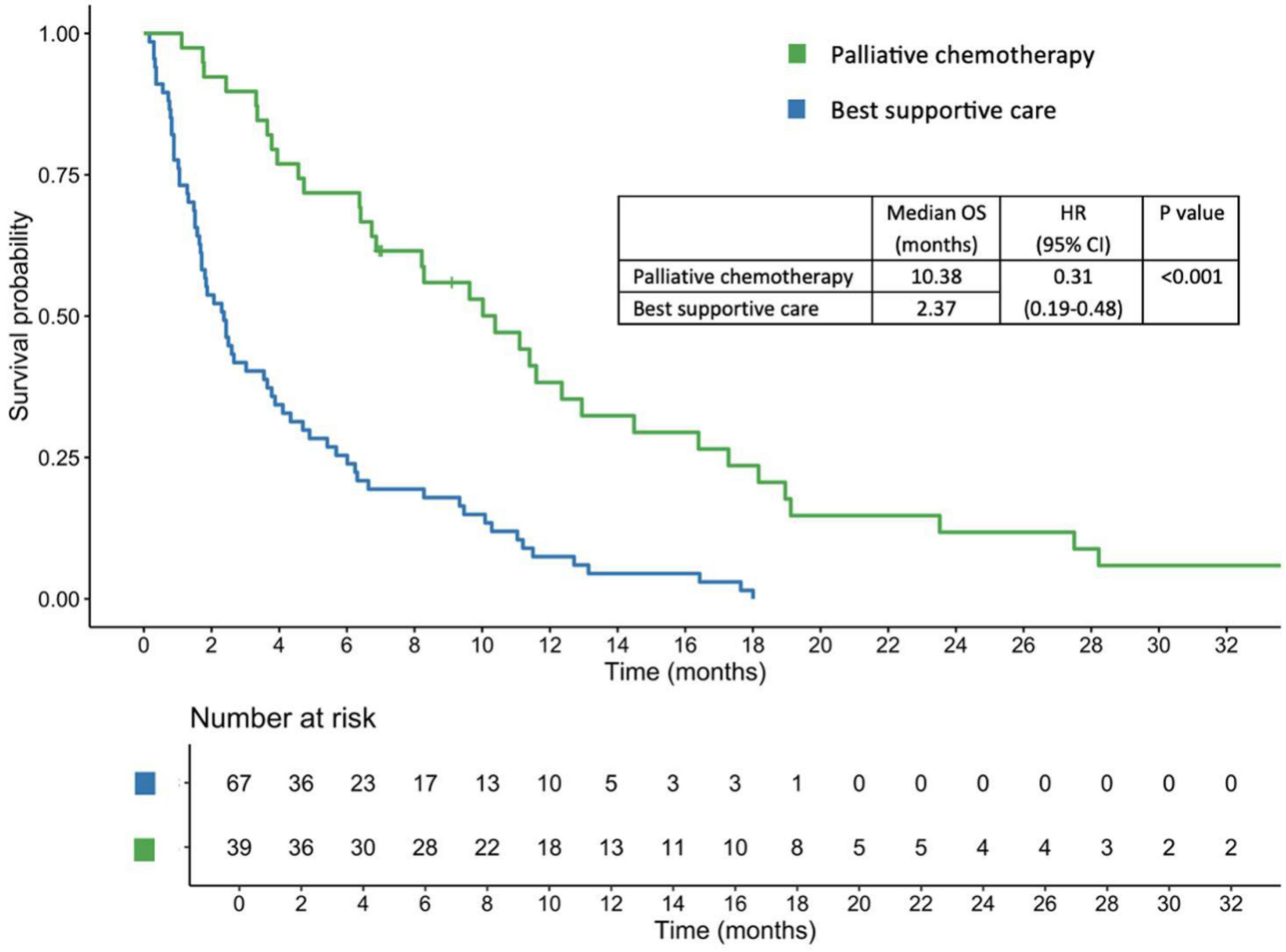

Figure 1 Overall survival between patients who received palliative chemotherapy and those who received best supportive care.

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Regarding functional status, patients with an ECOG performance status of 1 had a median OS of 10.38 months, whereas those with an ECOG performance status of 2 had a median OS of 5.57 months (HR: 0.74; 95% CI: 0.30–1.80; $P = 0.504$).

Regarding subsequent treatment, patients who proceeded to second-line chemotherapy had a notably prolonged median OS of 25.51 months, compared with those who received only first-line therapy at 8.21 months (HR: 0.14; 95% CI: 0.04–0.47; $P < 0.001$). Notably, both patients who underwent metastasectomy after initial chemotherapy remained alive at data cut-off, with follow-up durations of 46.55 and 71.35 months.

PSM Analysis of OS

To mitigate baseline imbalances between the treatment groups, a 1:1 PSM was performed using a nearest-neighbor algorithm without replacement. Matching variables included age, sex, ECOG performance status, BMI, primary tumor site, histologic grade, disease extent (metastatic vs unresectable), number of metastatic organs, and the presence of liver or peritoneal metastases. After matching, 39 patients were included in each group.

The baseline characteristics after matching are presented in Table 3. The covariates were well-balanced between the chemotherapy and BSC groups, excluding ECOG performance status, which showed a higher proportion of patients with an ECOG performance status of 1 in the chemotherapy group.

Table 3 Baseline Characteristics After Matching with Propensity Score

	Palliative Chemotherapy (n = 39)	**Best Supportive Care (n = 39)**	***P* value**
Age ≥65 years, n (%)	13 (33.3)	20 (51.3)	0.169
Male, n (%)	22 (56.4)	20 (51.3)	0.82
BMI, n (%) <18.5 kg/m^2 18.5–22.9 kg/m^2 ≥23.0 kg/m^2	 15 (38.5) 10 (25.6) 14 (35.9)	 16 (41.0) 14 (35.9) 9 (23.1)	0.409
ECOG PS, n (%) 1 ≥2	 33 (84.6) 6 (15.4)	 19 (48.7) 20 (51.3)	0.002
Location, n (%) Duodenum Non-duodenum	 30 (76.9) 9 (23.1)	 37 (94.9) 2 (5.1)	0.051
Histology differentiation, n (%) Well Moderately Poorly	 14 (35.9) 15 (38.5) 10 (25.6)	 18 (46.2) 10 (25.6) 11 (28.2)	0.461
Type of advanced stage, n (%) Metastatic disease Unresectable disease	 37 (94.9) 2 (5.1)	 34 (87.2) 5 (12.8)	0.431
Number of organ metastasis, n (%) 1 ≥2	 21 (53.8) 18 (46.2)	 22 (56.4) 17 (43.6)	1.000
Liver metastasis, n (%)	14 (35.9)	12 (30.8)	0.810
Peritoneal metastasis, n (%)	21 (53.8)	14 (35.9)	0.172

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; PS, performance status.

In the matched cohort, patients treated with palliative chemotherapy had significantly improved OS compared with those who received BSC. Median OS was 10.4 months in the chemotherapy group versus 2.6 months in the BSC group (HR: 0.36; 95% CI: 0.22–0.59; P <0.001; Figure 2).

PFS

Among patients treated with palliative chemotherapy, the median PFS was 5.95 months (95% CI: 3.02–7.82). When comparing chemotherapy regimens, those who received combination therapy had a longer median PFS of 6.34 months, compared with those treated with single-agent chemotherapy at 1.66 months (HR: 0.71; 95% CI: 0.37–1.58; P = 0.469).

For fluoropyrimidine-based regimens, median PFS was 6.34 months with a doublet regimen vs 1.61 months with single-agent 5-FU (HR: 0.69; 95% CI: 0.30–1.57; P = 0.373). The detailed PFS outcomes stratified by regimen are presented in Table S3.

Response Rate

Among patients treated with palliative chemotherapy, the overall ORR was 10.3% across all regimens (Table 4). When stratified using the treatment type, the ORR was 14.8% in patients receiving combination chemotherapy, whereas no objective response (0%) was observed in patients treated with single-agent chemotherapy.

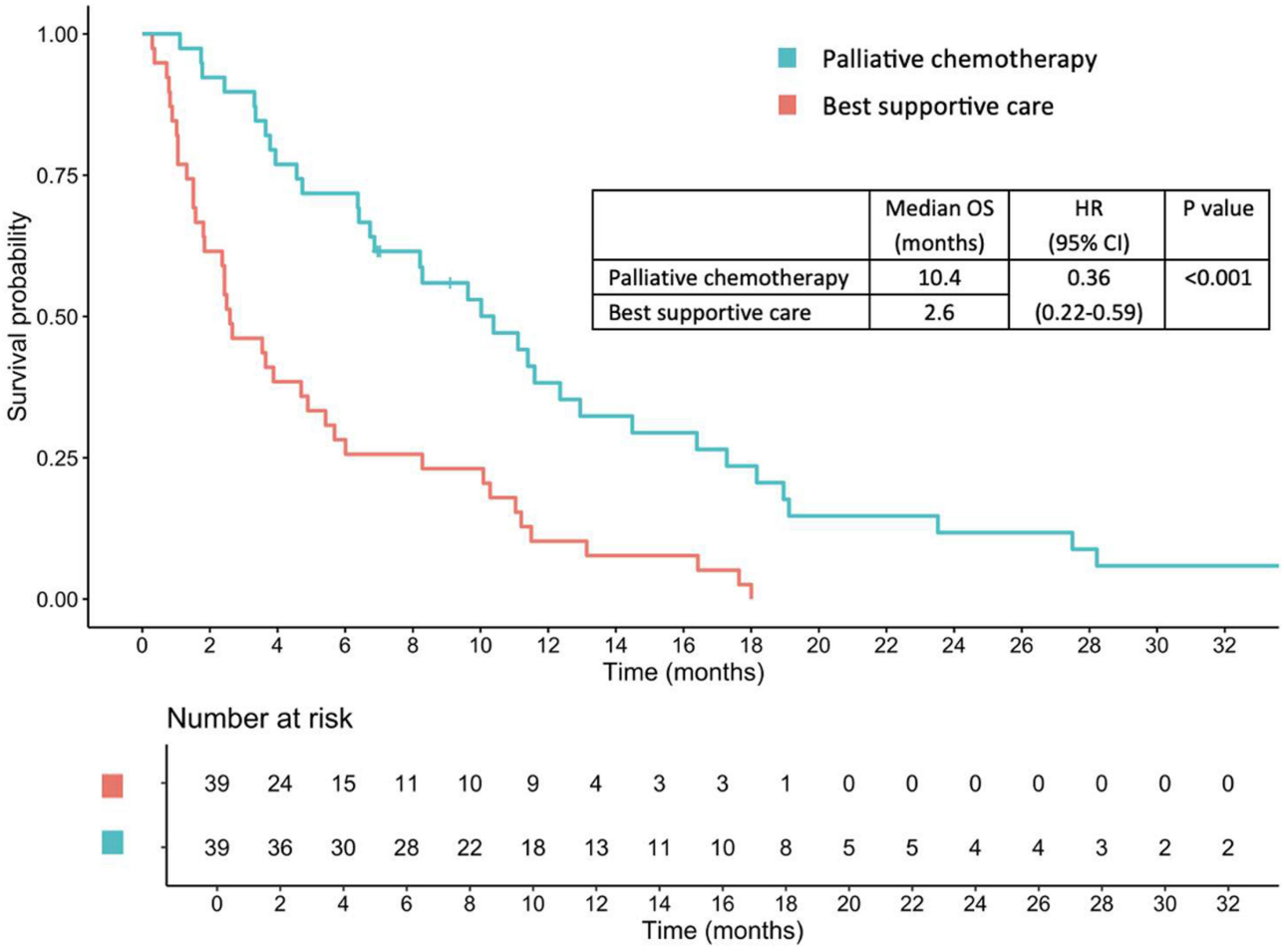

Figure 2 Overall survival between patients who received palliative chemotherapy and those who received best supportive care with propensity score-matched analysis.

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Table 4 Response Rates

Response rate, n (%)	All Chemotherapy (n = 39)	Combination Chemotherapy (n = 27)	Single-Agent Chemotherapy (n = 12)
Complete response	0	0	0
Partial response	4 (10.3)	4 (14.8)	0 (0)
Stable disease	13 (33.3)	10 (37.0)	3 (25.0)
Progressive disease	9 (23.1)	5 (18.5)	4 (33.3)
Not evaluated	13 (33.3)	8 (29.6)	5 (41.7)
Objective response rate, all patients	4/39 (10.3)	4/27 (14.8)	0 (0)
Objective response rate, assessable patients	4/26 (15.4)	4/19 (21.1)	0 (0)

Prognostic Factors for OS

The results of the prognostic analysis are summarized in Table 5. In the multivariate Cox proportional hazard regression model, several variables were independently associated with OS. Poor performance status (ECOG ≥2), poorly differentiated tumor histology, and duodenal tumor origin were significantly associated with worse survival outcomes. In contrast, palliative chemotherapy was independently associated with improved OS.

Table 5 Prognostic Factors for OS

	Univariate		Multivariate	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age ≥65 years	1.17 (0.78–1.75)	0.451	–	–
Male vs Female	0.99 (0.67–1.42)	0.959	–	–
BMI <18.5 vs ≥18.5 kg/m^2	1.18 (0.78–1.76)	0.434	–	–
ECOG PS ≥2 vs 1	2.7 (1.8–4.04)	<0.001	1.63 (1.02–2.58)	0.039
Poorly differentiation	2.69 (1.78–4.07)	<0.001	2.93 (1.84–4.68)	<0.001
CEA ≥5 ng/mL	1.1 (0.65–1.87)	0.725	–	–
CA19-9 ≥37 U/mL	0.95 (0.52–1.75)	0.871	–	–
Location: Duodenum vs others	1.85 (1.02–3.34)	0.041	1.99 (1.04–3.79)	0.037
Metastatic vs Unresectable disease	1.39 (0.76–2.55)	0.284	–	–
Number of organ metastasis ≥2 vs 1	1.11 (0.75–1.64)	0.605	–	–
Liver metastasis	1.49 (0.98–2.28)	0.065	1.54 (0.99–2.39)	0.053
Peritoneal metastasis	0.96 (0.64–1.44)	0.853	–	–
Palliative chemotherapy	0.31 (0.19–0.48)	<0.001	0.38 (0.23–0.64)	<0.001

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; PS, performance status; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19–9; CI, confidence interval; HR, hazard ratio.

Discussion

This retrospective study provides real-world evidence of the effectiveness of palliative chemotherapy and its prognostic significance in patients with advanced SBA, a rare gastrointestinal malignancy with limited treatment guidelines. Our findings revealed that systemic chemotherapy significantly improved OS compared with that of BSC, with a median OS of 10.4 months vs 2.6 months in the PSM cohort. This benefit remained significant after multivariate adjustment, reinforcing the role of systemic therapy in this understudied population.

Regarding treatment effectiveness, the median PFS of 5.95 months observed in our cohort was consistent with that of previous retrospective series[9,11,16–18] and phase II prospective single-arm trials[10,13,14] that reported a median PFS ranging from 3 to 8 months. However, owing to the absence of randomized trials in this population, there is currently no standardized first-line chemotherapy regimen for advanced SBA. Consequently, treatment strategies are usually extrapolated from gastric, ampullary, or colorectal cancer protocols. Our findings support those of previous studies,[16,18] suggesting that doublet fluoropyrimidine-based chemotherapy regimens are associated with improved PFS outcomes compared with that of single-agent regimens.

The overall ORR of 10.3% in our cohort is lower than that in some previous studies (10–50%),[10,11,13,19–21] possibly owing to the inclusion of a substantial proportion of patients receiving single-agent chemotherapy (approximately 30%) and a high proportion of non-evaluable patients (33%). The ORR for evaluable patients who received doublet chemotherapy was 21.1%, consistent with previous reports that doublet regimens provided a higher ORR than that of single-agent regimens.[16,17,21] Caution is needed when comparing results across studies because of differences in chemotherapy regimens, dosing intensities, and patient baseline characteristics.

Similarly, our data highlight the aggressiveness and poor prognosis of advanced SBA, with a median OS of <1 year, even among patients who received chemotherapy, and only 2.37 months in those treated with BSC. Our outcomes are relatively lower than those in previous retrospective studies, which reported a median OS of 12–15 months with 5-FU plus platinum-based regimens[11,19,20,22] and phase II trials showing an OS of approximately 20.4 months.[10,13] This difference may be explained by different baseline characteristics and chemotherapy regimens. A high proportion of patients with ECOG performance status ≥2, poorly differentiated tumors, and multiple organ metastases were observed in this cohort. In contrast, most patients in previous studies had ECOG 0–1 performance status ranging from 70% to 97%.[10,13] Despite variations in chemotherapy regimens, this study and existing evidence support the survival benefit of palliative chemotherapy, particularly fluoropyrimidine-based regimens and fluoropyrimidine-oxaliplatin combinations.[15]

Furthermore, our findings confirm the prognostic significance of post-progression treatments. Only 20% of patients in this study received second-line chemotherapy, and this subgroup experienced significantly prolonged survival. Although underreported in previous studies, this suggests that access to second-line therapy may be a crucial determinant of survival. In addition, two patients underwent metastasectomy following systemic therapy and remained alive with long-term follow-up, suggesting that surgical intervention may offer survival benefits in selected cases.[3,8] Although robust evidence supporting metastasectomy in advanced SBA is lacking, our findings support the need for a multidisciplinary approach in highly selected patients.

Additionally, we identified crucial prognostic factors for OS. Poor ECOG performance status (≥2), poorly differentiated histology, and primary duodenal tumors were independently associated with poor survival, which is consistent with previous findings.[4,17,23] The association between duodenal origin and poor outcomes may reflect a more advanced stage at diagnosis owing to nonspecific symptoms and complex anatomy, causing diagnostic delays.[5,24,25] Although tumor markers, including carcinoembryonic antigen and carbohydrate antigen 19–9, have been suggested as potential prognostic markers,[3,25] we could not assess their significance because of missing data in approximately half of this cohort. However, approximately half of those tested had normal tumor marker levels, suggesting the need for further evaluation of these markers in SBA.

PSM was used to minimize confounding from baseline imbalances in retrospective studies. Notably, the OS benefit of chemotherapy remained significant, even after matching was conducted. However, the ECOG performance status remained unbalanced between the groups, reflecting a real-world selection bias where patients with better functional status were more likely to receive active treatment. This study confirms the survival benefit of palliative chemotherapy,

particularly fluoropyrimidine-based doublet regimens, in patients with advanced SBA who maintain a good performance status.

Despite its strengths, including a large single-institution cohort of patients with advanced SBA, comprehensive outcome reporting (OS, PFS, and ORR), and robust statistical adjustments through multivariate and matched analyses, this study has some limitations. This retrospective design is susceptible to selection bias. Additionally, the chemotherapy cohort was relatively small, as most patients received the BSC. The heterogeneity of chemotherapy regimens further limited our ability to draw firm conclusions regarding the efficacy of specific protocols. A multicenter prospective study is required to better define optimal treatment strategies, incorporating molecular profiling to reveal predictive biomarkers for personalized therapy. Furthermore, early diagnosis, nutritional support, and interventions to enhance physical performance should be explored, as they may increase the possibility of patients receiving and benefiting from systemic treatment.

Conclusion

This study reveals that palliative chemotherapy is associated with a significant survival benefit in patients with advanced SBA compared with that of the BSC. Combination regimens, particularly fluoropyrimidine-based regimens, have the most favorable outcomes. Crucial prognostic factors such as performance status, tumor differentiation, and primary tumor location should be considered in clinical decision-making. Considering SBA's rarity, our findings provide valuable real-world evidence to guide treatment and highlight the need for prospective studies to further refine the therapeutic strategies for this disease.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Prince of Songkla University (REC.68305141/August 5, 2025).

Abbreviations

SBA, small bowel adenocarcinoma; BSC, best supportive care; OS, overall survival; PFS, progression-free survival; ORR, objective response rate; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; PSM, propensity score-matching; CI, confidence interval; HR, hazard ratio; 5-FU, 5-fluorouracil.

Data Sharing Statement

The datasets used and/or analyzed in the current study will be made available by the corresponding author upon reasonable request.

Informed Consent Statement

Patient consent was waived because of the retrospective nature of the study, and the study was approved by the Ethics Committee of the Prince of Songkla University. Patient information was anonymized for confidentiality.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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