

# Retrospective Analysis of Taxane-Based Therapy in Small Bowel Adenocarcinoma

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Disclosures of potential conflicts of interest may be found at the end of this article.

## ABSTRACT

Currently, treatment of small bowel adenocarcinoma (SBA) mirrors that of colorectal cancer (CRC). Recent genomic data have demonstrated SBA to be a genetically unique entity, suggesting that therapies not traditionally utilized in CRC should be explored. In order to further characterize the activity of taxanes in this rare cancer, we completed a single-center retrospective study. Twenty patients were found to have been treated with

taxane-based regimens (monotherapy in 3, combination therapy in 17). Median time to progression was 3.8 months (95% confidence interval [CI] 2.9–4.6), and median overall survival was 10.7 months (95% CI: 3.1–18.3). The results of this study demonstrate clinical activity from taxane-based therapy in advanced SBA and support further clinical trial investigation. *The Oncologist* 2019;24:e384–e386

## INTRODUCTION

Approximately one third of the 10,400 new cases of small bowel cancer in 2018 will be adenocarcinomas, and an estimated 27% of these patients will present with distant metastasis [1, 2]. Phase II trials have demonstrated fluoropyrimidine plus platinum-based chemotherapy to be the preferred initial regimen for metastatic disease, but optimal treatments in the second-line and beyond have not been established [3, 4].

To date, the treatment approach for small bowel adenocarcinoma (SBA) closely mirrors that for colorectal cancer (CRC). However, recent genomic data demonstrates SBA to be a unique genomic entity, differing from both gastric cancer and CRC. Specifically, the rate of APC mutations in SBA was significantly different from both gastric and CRC (27% vs. 8% and 76%, respectively), and the rate of KRAS mutations was significantly different from gastric cancer (54% vs. 14%, respectively) [5]. This suggests that classes of agents not routinely utilized in CRC treatment should be explored in SBA.

One such class, taxanes, commonly used in gastric cancer have only recently been reported in the treatment of SBA. A Phase II study of nab-paclitaxel as treatment for CpG island methylator phenotype-high CRC included 10 patients with SBA [6]. Although the treatment demonstrated a 0% response rate in patients with CRC, there was a 20% response rate in the patients with SBA. To further characterize the activity of taxanes in SBA, we

completed a single center retrospective review of patients treated with taxane-based therapy.

## MATERIALS AND METHODS

Patients treated from 2010 to 2017 at The University of Texas MD Anderson Cancer Center with SBA were reviewed. Eligible patients had advanced SBA, received greater than one cycle of a taxane-based regimen, and had a radiographic tumor response evaluation. Radiographic response was assessed retrospectively based upon the treating physician's assessment and categorized as response, stable disease, or progression. Patients with ampullary adenocarcinomas or those enrolled in a clinical trial were excluded.

Baseline characteristic data of the study population was obtained (see Table 1). Median time to progression (TTP) and median overall survival (OS) were determined using the Kaplan-Meier method. Subgroup analysis was completed for location of disease (duodenum vs. jejunum and ileum) and type of therapy (combination vs. monotherapy). Log-rank of  $p < .05$  was considered statistically significant.

## RESULTS

Three hundred and twelve patients with SBA were identified. Twenty patients were found to have been treated

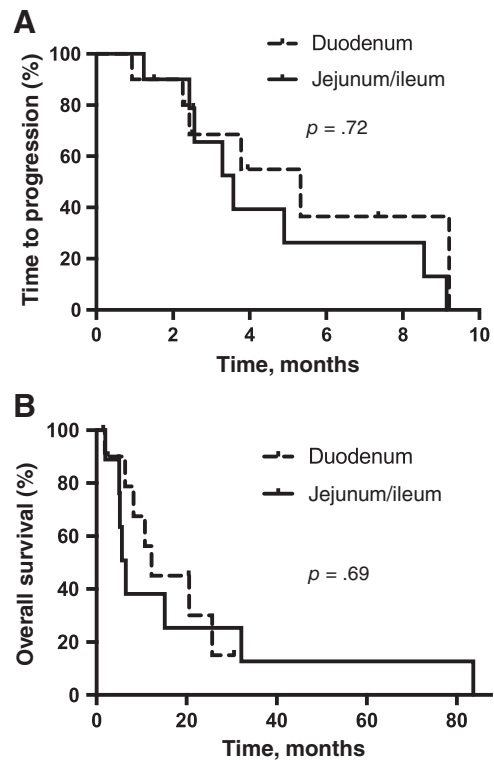
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**Table 1.** Patients' baseline characteristics

Characteristic	n (%)
Median age at diagnosis (range), yr	54 (27–75)
Female	8 (40)
Male	12 (60)
White	16 (80)
Grade	
Poor	11 (55)
Moderate	9 (45)
Stage IV at diagnosis	15 (75)
Peritoneal disease	9 (45)
Location	
Duodenum	10 (50)
Jejunum/ileum	10 (50)
Primary tumor resected	14 (70)
Predisposing condition	
Crohn disease	2 (10)
Ulcerative colitis	1 (5)
Celiac disease	2 (10)
Lynch syndrome	2 (10)
KRAS mutation	10 (50)
Previous treatment with FOLFOX or XELOX	17 (85)
Previous anti-VEGF or anti-EGFR therapy	9 (45)
Cetuximab or Panitumumab	6
Bevacizumab	4
Microsatellite status	
Microsatellite stable	11 (55)
Microsatellite instability high	4 (20)
Microsatellite unknown	6 (30)
Treatment	
Combination	17 (85)
Gemcitabine + nab-paclitaxel	6
Gemcitabine + paclitaxel	5
Gemcitabine + docetaxel	1
Fluoropyrimidine + nab-paclitaxel	4
Carboplatin + etoposide + paclitaxel	1
Monotherapy	3 (15)
Paclitaxel	2
Nab-paclitaxel	1

Abbreviations: EGFR, epidermal growth factor receptor; VEGF, vascular endothelial growth factor.

with taxane-based therapy and met inclusion criteria. Seventeen patients were treated with combination therapy (gemcitabine combination in 12, fluoropyrimidine combination in 4, and platinum combination in 1), and three were treated with monotherapy. The taxane used was paclitaxel in two and nab-paclitaxel in one. Tumor response was seen in 30%, stable disease in 35%, and progressive disease in 35% of patients. When stratified by tumor site, tumor response was 30% for duodenal and 30% for jejunal and ileal primaries. Median TTP was



**Figure 1.** Kaplan-Meier survival curves for SBA patients treated with taxane-based therapy. (A): Time to progression. (B): Overall survival.

3.8 months (95% confidence interval [CI], 2.9–4.6) and median OS was 10.7 months (95% CI, 3.1–18.3). No significant difference in TTP or OS was found between duodenum versus jejunum and ileum small bowel site ( $p = .72$  and  $.69$ , respectively; Fig. 1). No significant differences in TTP or OS were seen between various chemotherapy combinations (supplemental online Fig. 1). Of the four patients with microsatellite instability-high, three demonstrated a response to therapy.

## DISCUSSION

Classically, taxanes have not been utilized for SBA treatment, and investigations into their efficacy is lacking. To the best of our knowledge, this is the largest cohort of patients with advanced SBA treated with taxane-based therapy reported in the literature. The overall TTP supports the conclusion that taxanes have activity in SBA. Additionally, there was no significant difference between the TTP or OS in combination therapy versus monotherapy. Although 85% of patients had combination therapy, the majority were previously treated with fluoropyrimidine-based regimens, and gemcitabine has not demonstrated clinical activity in intestinal cancers [7].

In addition to establishing SBA as genetically unique compared with CRC and gastric cancer, the recent article by Schrock et al. also noted that genomic alterations were similar when comparing duodenal to jejunal and ileal small bowel locations [5]. This is consistent with our

findings, in which we found similar efficacy irrespective of small bowel tumor site.

The study is limited by the small sample size, inability to retrospectively perform RECIST tumor assessment, and single-institution nature. However, this is the largest collection of taxane-treated SBA patients in the literature. Given the rarity of this cancer, small retrospective trials such as this are beneficial to the management of

this cancer. Additional retrospective and prospective trials would help to further validate these results and support the use of taxane regimens for treatment of SBA.

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#### DISCLOSURES

The authors indicated no financial relationships.

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