Clinical Oncology: Case Reports

Case Report

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# Fenbendazole Enhancing Anti-Tumor Effect: A Case Series

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## Abstract

**Background:** Fenbendazole (FBZ) is a cheap and readily available anti-parasitic commonly used in veterinary medicine. FBZ belongs to the benzimidazole drug class which destabilize microtubules through a mechanism similar to the anti-oncogenic vinca alkaloids. Although there are no reported cases in the literature, there have been several anecdotal stories published on website blogs with individuals praising its ability to treat a wide variety of cancers.

**Case Presentations:** Herein we describe the cases of three patients with various genitourinary malignancies who demonstrated complete response after receiving FBZ therapy as a single or supplementary chemotherapeutic agent. In two patient scenarios, they had experienced progression of metastatic disease despite multiple lines of therapy prior to initiation of FBZ. No side effects from FBZ were reported.

**Conclusion:** FBZ appears to be a potentially safe and effective antineoplastic agent that can be repurposed for human use in treating genitourinary malignancies. Further research is necessary to define the role of FBZ as a chemotherapeutic option.

**Keywords**

Fenbendazole; Veterinary medication; Anti-parasitic; Medication repurposing; Immunotherapy; Genitourinary malignancy; Renal cell carcinoma; Urothelial carcinoma

## Introduction

There has been growing popularity in recent years for the use of Fenbendazole (FBZ) as a single agent or supplementary therapeutic to chemotherapy for those suffering with various forms of cancer. FBZ is a cheap anti-helminthic medication commonly used in veterinary practice and readily available in pet stores and off commercial websites. However, despite multiple anecdotal stories and news outlet reports for its efficacy in treating metastatic cancer, the clinical literature behind utilizing FBZ as a potential anti-neoplastic agent remains nonexistent. Existing scientific studies have primarily studied its mechanism of action through the use of animal models [1-3]. Herein, we describe three cases where patients achieved complete responses, including two who experienced progression after multiple lines of therapy, when FBZ was used alone or in combination with standard therapies.

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## Case Presentation

### Case 1

A 63-year-old Caucasian male presented with flank pain, rapid weight loss, and transient fever. Abdominal Computed Topography (CT) revealed a 3 cm left lower-pole solid renal mass. He underwent open partial nephrectomy with pathology showing pT1a high-grade clear cell Renal Cell Carcinoma (RCC). Several months later, he developed persistent left flank pain with finding of a 5.2 cm left kidney mass. Fine Needle Aspiration (FNA) biopsy redemonstrated clear cell RCC, and pazopanib 800 mg was initiated. Follow-up CT revealed a new 1.4 cm pancreatic head/body lesion, persistent left renal mass, and signs of sigmoid colitis. Given the concerns for disease progression and intolerable side effects, pazopanib was discontinued and cabozantinib was initiated. Interval Magnetic Resonance Imaging (MRI) showed stable size of recurrent left renal mass, mild decrease in 2.9 cm pancreatic head lesion, stable 1.2 cm distal pancreatic body lesion, and new 1.1 cm right posterior iliac bone lesion. Cabozantinib was ultimately discontinued due to persistent intolerable side effects. One month after discontinuation, repeat MRI showed increase in size of recurrent left renal mass, mild decrease in 2.3 cm pancreatic head lesion, stable 1.4 cm distal pancreatic body lesion, and unchanged 1.1 cm right posterior iliac bone lesion. Third-line treatment with nivolumab was initiated, and he only received three total treatments (240 mg × 3) over the course of a month due to developing severe rash and colitis. He was treated with steroids with resolution of colitis. During this time, he also started alternative therapy with FBZ 1 gm three times per week at the suggestion of one of his friends with head/neck cancer. Interval MRI imaging found near complete resolution of the previously noted left renal mass as well as decrease in pancreatic head/body and right posterior iliac spine lesions (Figure 1). Serial imaging for the past 10 months have not shown any evidence of recurrence or metastatic disease. He has continued taking FBZ without any reported side effects.

### Case 2

A 72-year-old caucasian male presented with increasing lower urinary tract symptoms and a urethral lesion. He underwent distal penectomy with pathology showing pT2 high-grade urothelial carcinoma of the urethra with focal squamous differentiation. Four years later, the patient developed a cough with finding of a 5.5 cm × 4.0 cm left hilar mass and a 1.5 cm × 1.4 cm left upper lobe nodule, with multiple abnormal AP window lymph nodes, the largest measuring 1.8 cm × 0.9 cm all avid on PET CT. Brain MRI revealed a right occipital lobe metastasis. Bronchoscopy with biopsy revealed squamous carcinoma. His presentation was felt most consistent with a lung primary and the patient was treated with gamma knife radiotherapy and carboplatin, paclitaxel, and pembrolizumab. Subsequent sequencing of the lesion from the penectomy and bronchoscopy demonstrated shared PIK3CA, RB1, CCND1 and CDKN2A alterations demonstrating that the pulmonary disease represented metastasis from urethral primary. The patient developed progressive retroperitoneal disease while on pembrolizumab maintenance and was treated with gemcitabine and cisplatin for 6 cycles over the course of 4 months with near complete response. However, interval CT imaging demonstrated increase of an

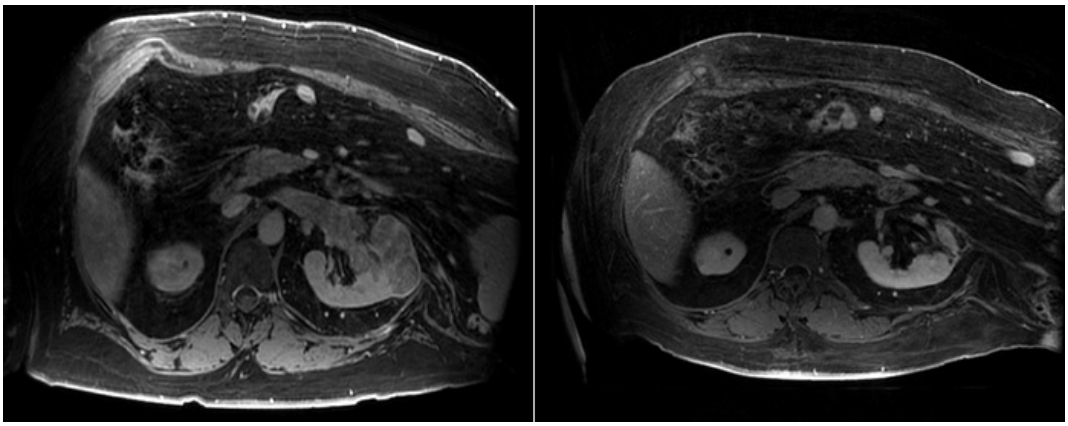

**Figure 1:** Near complete resolution of persistent left renal mass (left image) after initiation of three total doses of nivolumab and FBZ therapy 1 gm three times weekly for several months (right image).

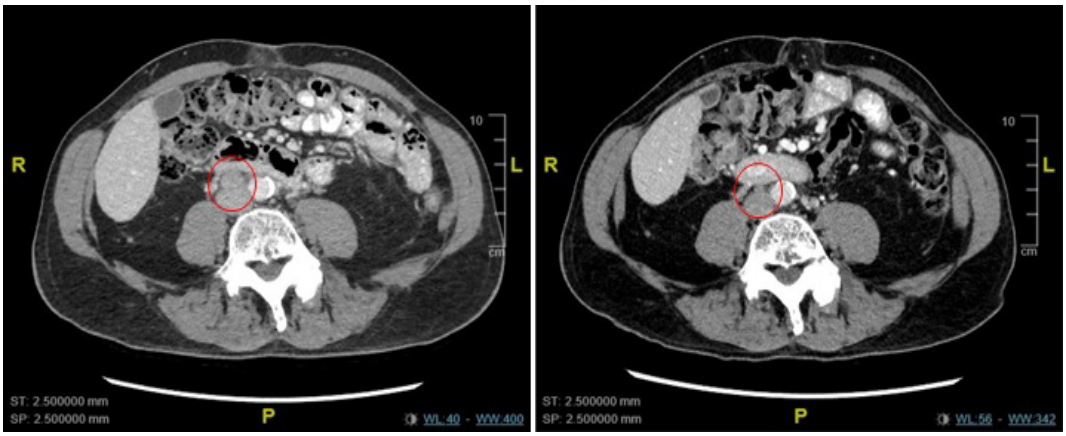


**Figure 2:** Near complete radiographic response of a 2.0 cm × 1.5 cm aortocaval node (left image) after initiation of alternative therapy including FBZ therapy 1 gm three times weekly (right image).

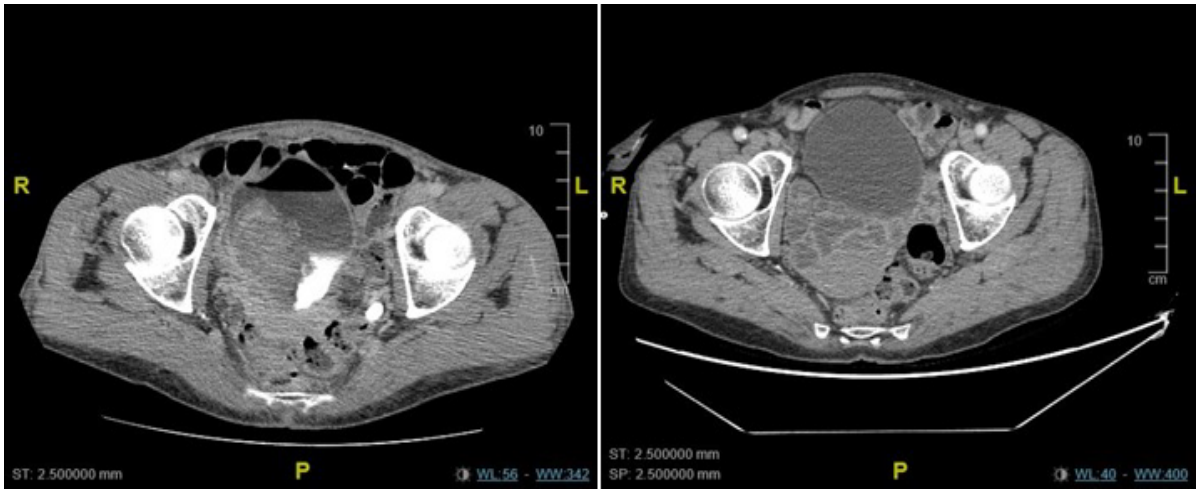


**Figure 3:** Resolution of 7.5 cm right lateral bladder mass (left image) after treatment with TURBT, Accelerated Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (AMVAC), and concurrent FBZ 1 gm three times weekly (right image).

aortocaval node from 1.2 cm × 1.0 cm on to 1.5 cm × 1.5 cm. No therapy was initiated and a subsequent scan demonstrated further increase to 2.0 cm × 1.5 cm with no evidence of progression elsewhere (Figure 2). The patient opted for complementary therapy with FBZ 1 gram orally three days per week, vitamin E 800 mg daily, curcumin 600 mg daily and CBD oil while awaiting more substantial disease progression before initiating additional systemic therapy. Serial CTs from the past 9 months showed progressive decrease in size to 0.5 cm × 0.5 cm, complete radiographic response.

### Case 3

A 63-year-old Caucasian female presented with increasing lower urinary tract symptoms and hematuria. CT imaging revealed a 7.5 cm right lateral bladder mass with extension to the right pelvic sidewall and right-sided hydronephrosis requiring percutaneous nephrostomy. There was no evidence of metastatic disease, consistent with clinical T4 tumor. Transurethral Resection of Bladder Tumor (TURBT) demonstrated a large necrotic mass with pathology confirming urothelial carcinoma with 85% squamous and 2% sarcomatoid histology. She was treated with Accelerated Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (AMVAC) for 6 cycles over the course of 4 months along with concurrent FBZ 1 gram three times weekly. Follow-up CT revealed no evidence of disease with minimal residual thickening in the right inferior bladder wall (Figure 3). She declined to proceed with cystectomy and remains on surveillance with no evidence of progression.

## Discussion

In summary, we have three patients with different primary genitourinary tumors who demonstrated complete response after receiving FBZ therapy. This raises the question of how effective FBZ can be as an anti-oncogenic agent and merits further investigation. To our knowledge, there has not been a similar case series reported.

FBZ belongs to a class of microtubule-destabilizing agents known collectively as the benzimidazoles. The ability to disrupt microtubule polymerization to induce mitotic arrest and promote apoptosis is a feature shared with the vinca alkaloids. Proposed mechanisms for FBZ's anti-tumor properties include inhibition of proteasomal activity, p53 activation, cytotoxicity via tubulin disruption, and downregulation of glycolytic enzymes crucial for cancer cell survival [1,4]. Other benzimidazoles such as albendazole possess anti-tumor properties through influencing the HIF-1-alpha pathway which is critical for VEGF expression and certain aspects of glycolysis [5]. The variety of mechanisms by which this class of medications functions may help limit the propagation of resistant cancer cell lines through targeting multiple avenues of cancer cell survival.

FBZ has been safely utilized as an anti-parasitic for various different animal species and could be repurposed for treating human malignancies. Several benzimidazoles have already shown promise for human repurposing. One example is parbendazole, which has demonstrated potential efficacy as a supplementary therapy to gemcitabine in patients with pancreatic cancer [6]. Mebendazole has been shown in case reports to be efficacious with few side effects in patients with metastatic adrenocortical carcinoma and metastatic colon cancer [7,8]. Mebendazole and flubendazole have also been shown to be effective in animal studies for glioblastoma multiforme and hematologic malignancies, respectively [9,10]. Given evidence of high tolerability and applicability to a wide range of malignancies, this warrants further investigation for FBZ and other benzimidazoles as safe chemotherapeutic options.

Prior studies have demonstrated cancer response to immune checkpoint inhibitors such as nivolumab as a third-line agent in mRCC [11]. The duration of therapy was often much longer requiring a median therapy duration of 6 months with 24% overall response rate in third-line treatment. It is possible that our first patient with mRCC would have achieved a significant response to nivolumab alone without FBZ. However, given the complete radiologic response on only 1 month of immune checkpoint inhibitor therapy, it also seems likely that FBZ played a notable role in inducing remission. This is supported by the fact that our patient has remained in extended remission while only on FBZ for nearly a year without further administration of immune checkpoint inhibitor therapy.

## Conclusion

There remains limited data with few published studies on the anti-oncogenic properties of FBZ. Other benzimidazoles have been studied to a larger extent, and the knowledge can be drawn upon to help guide future FBZ studies and to gauge the efficacy of this drug class whether as a solitary agent or in combination therapy. Given the potential benefits of FBZ with what seems to be a limited toxicity profile, further research is warranted to evaluate the clinical settings in which this medication may be beneficial and repurposed for patients with progressive genitourinary malignancy and possibly in other malignant settings as well.

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