Case Report

Fruquintinib for refractory colorectal cancer in a pre-treated 82-year-old patient achieved a progression-free survival of 25 months: a case report

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Background: Chemotherapy was recommended as the 1st or 2nd line standard of care for patients with refractory or metastatic colorectal cancer (mCRC). Extra cautions are needed for elderly patients, because cytotoxic regimens may induce unexpected adverse effects due to their impaired physical condition and tolerability. Currently, there is no evidence for the treatment in elderly patients. This case reports a new ideas to the treatment of elderly mCRC patients.

Case Description: An 82-year-old man was diagnosed with descending colon cancer and underwent radical operation revealed stage IIIB cancer (pT4aN1cM0) in June 2016, followed by adjuvant chemotherapy (6 cycles of XELOX). The disease relapsed in June 2018, and the patient was prescribed Tegafur for 6 months. In December 2018, he was admitted to hospital due to intestinal obstruction with performance status (PS) score of 3 and nutrition score (NRS2002) of 5. According to a multidisciplinary team (MDT) meeting: considering that the adverse effects of front-line treatment are dominated by myelosuppression, the general condition of the patient is currently poor. The patient received fruquintinib as the second-line treatment which was interrupted for one month due to grade 3 hypertension and proteinuria. The restarted dose was reduced from 5 to 3 mg/day and continued until the last follow-up. The disease did not progress during 25-months of Fruquintinib treatment. Unfortunately, the patient was bedridden for a long time after an accidental fall resulting in a pulmonary infection and finally died of respiratory failure in January 2021.

Conclusions: CRC patients with advanced age and poor general condition require MDT meetings and individualized treatment. Despite of an advanced age, poor physical condition, and intense tumor burden, Fruquintinib as the second-line treatment achieved satisfactory disease control in this case. Adverse events could be relieved by dose reduction. Thus, fruquintinib could be a treatment option in refractory elderly CRC patients.

Keywords: Elderly; colorectal neoplasms; comorbidity; fruquintinib; case report

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Introduction

Colorectal cancer (CRC) is one of the most frequently occurring cancers worldwide (1). Chemotherapy is the primary treatment for advanced CRC (2). Advanced age, comorbidities, and poor performance status (PS) may lead to treatment discontinuation (3), which may affect patient prognosis. Elderly patients who are also in poor general condition often have difficulty tolerating standard therapy and require dose reduction or selection of less toxic drugs. Currently, only limited evidence is available to guide the

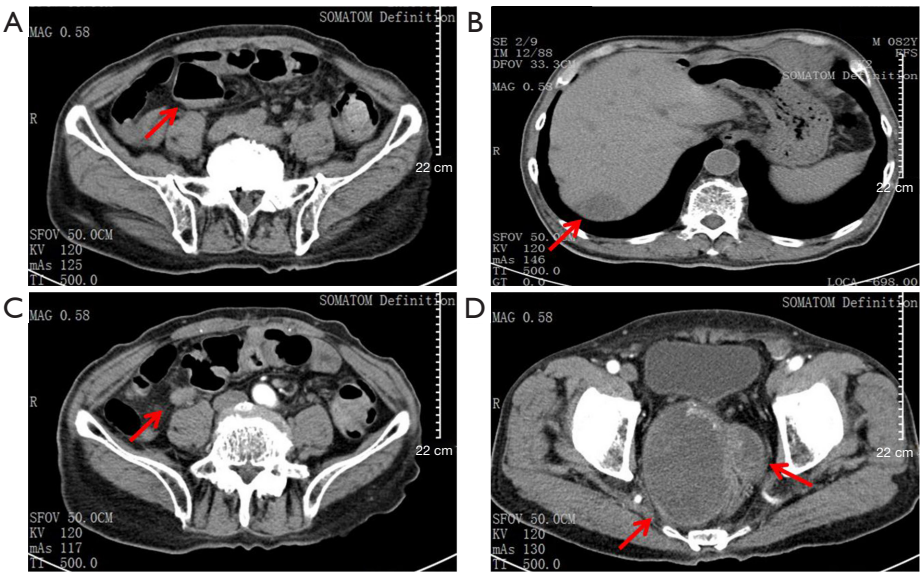

Figure 1 Abdomen CT images before fruquintinib treatment in December 2018. (A) Dilated intestinal canal with an air-liquid level, indicating intestinal obstruction (red arrow). (B) Multiple metastases in the liver (red arrow). (C) Mesenteric lymph node metastasis (red arrow). (D) Giant metastasis in the pelvic cavity (red arrows).

treatment of elderly CRC patients.

Fruquintinib is a highly selective tyrosine kinase inhibitor targeting vascular endothelial growth factor receptors and was approved in China for patients with metastatic CRC who had failed at least 2 lines of treatment (4). In this article, we report the case of an 82-year-old patient with advanced refractory CRC who received fruquintinib as the 2nd-line therapy. To date, it is the oldest metastatic colorectal cancer (mCRC) patient treated with fruquintinib, and this case provides inspiration for refractory elderly CRC patients. We present the following article in accordance with the CARE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-841/rc).

Case presentation

An 82-year-old man with a long history of hypertension was admitted to our hospital due to no defecation for 3 days in December 2018. He was diagnosed with descending colon cancer and underwent a radical operation in June 2016, followed by 6 cycles of XELOX chemotherapy. The postoperative pathological examination revealed stage IIIB cancer (pT4aN1cM0). The disease relapsed in June 2018, and the patient was prescribed Tegafur for 6 months. After front-line chemotherapy, the patient developed bone marrow suppression and mild numbness in the hands and feet.

The patient had a PS score of 3 and nutrition score (NRS2002) of 5. The patients' carcino-embryonic antigen (CEA) and carbohydrate atigen 19-9 (CA 19-9) levels were 382.27 and 68.62 ng/mL, respectively. CT showed multiple metastatic lesions, including a giant mass (10 cm) in the pelvic cavity, suggesting disease progression (see *Figure 1*).

A multidisciplinary team (MDT), including a radiologist, a colorectal surgeon, a radiotherapist, a chemotherapist, a gastroenterologist, a nutritionist, and a geriatrician, was assembled. The results of the MDT meeting were as follows: (I) The intestinal obstruction was due to the external pressure from the giant metastatic lesion at the pelvic wall. Because of the patient's advanced age and poor general condition, surgery was not considered. Fasting, fluid infusion, and enemas were applied to relieve the intestinal obstruction. (II) The patient had severe malnutrition and required 25–30 kcal/kg every day. Supplements of fish oil, ω-3, and glutamine were suggested. (III) Conservative treatment was suggested for the multiple metastases. Fruquintinib was to be applied as systemic anti-tumor therapy after the patient's general condition had been stabilized. (IV) The patient had hypertension for 30 years and was taking amlodipine 5 mg qd. The blood pressure needed to be stabilized to prevent cardiovascular adverse events (AEs) during fruquintinib treatment.

The intestinal obstruction was completely alleviated

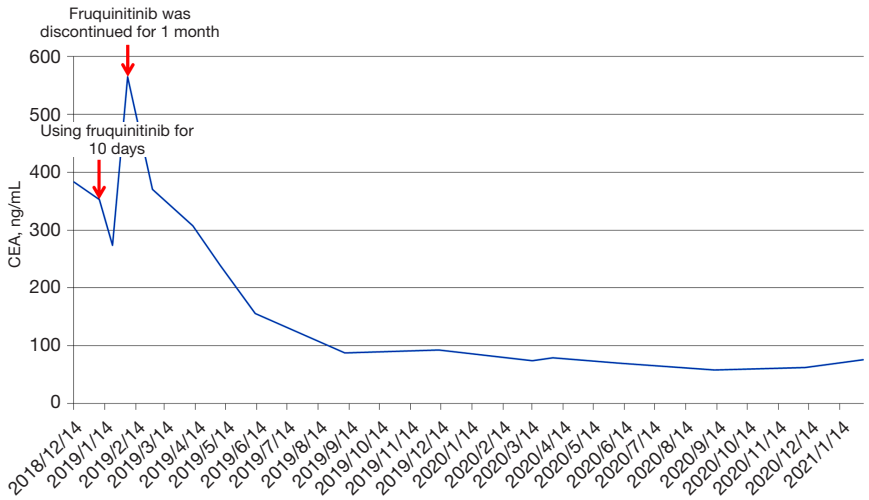

Figure 2 CEA levels during fruquintinib treatment. CEA, carcino-embryonic antigen.

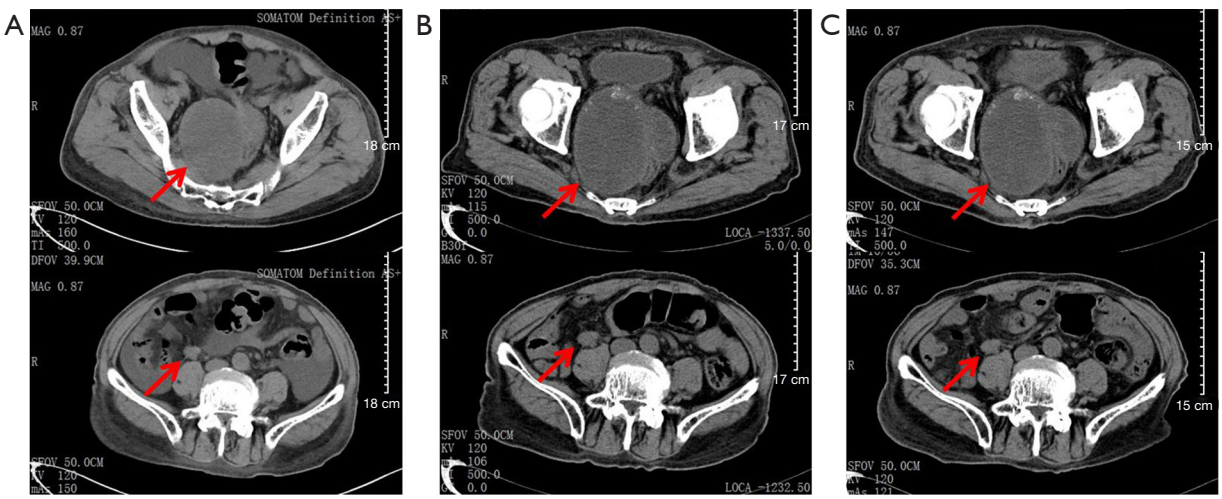

Figure 3 Abdomen CT images during follow-up at 2 months (A), 14 months (B), and 25 months (C) after fruquintinib treatment. The red arrows refer to a giant metastasis in the pelvic cavity and a mesenteric lymph node metastasis.

after symptomatic therapy, and the patient's nutritional status improved. Fruquintinib treatment (5 mg/day, D1–21, q4w) was started in December 2018. Grade 3 hypertension and proteinuria occurred 10 and 15 days after starting the treatment, respectively, and thus fruquintinib was discontinued for 1 month. Irbesartan hydrochlorothiazide, metoprolol, and nifedipine tablets, and albumin infusion were used as the symptomatic treatment. Hypertension and proteinuria gradually resolved to grade 1, and fruquintinib treatment was then re-started, but the dose was reduced to 3 mg/day. The patient's CEA levels decreased following fruquintinib administration (see *Figure 2*). The patient had no intestinal obstruction thereafter, and no disease progression was detected during the 25-month follow-up period (see *Figure 3*). However, the patient died of pulmonary infection in January 2021, which was considered a non-progression–related death. The whole treatment timeline figure is shown (see *Figure 4*).

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images.

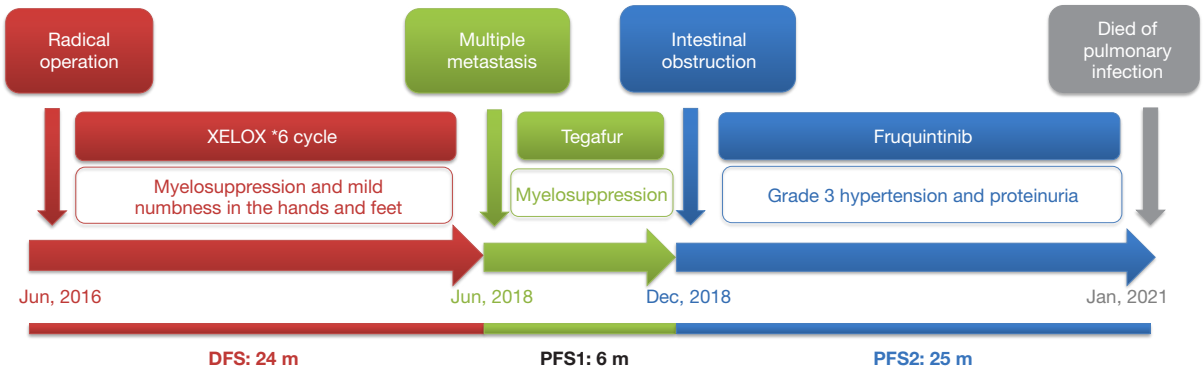

Figure 4 A timeline figure to describe the treatment history, diagnosis, treatment, treatment response and adverse events, progression and prognosis of this case. DFS, disease-free survival; PFS, progression-free survival.

A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Elderly patients have difficulties tolerating standard chemotherapy regimens. Thus, it is essential that new acceptable regimens with reliable efficacies for aged CRC patients are developed. In the present case, given the patient's general condition and impaired tolerability, single-agent chemotherapy was chosen as the 1st-line treatment when the disease recurred the 1st time. At the time of the 2nd relapse, the patient had an advanced age (82 years) and a poor physical condition (a PS score of 3); thus, treatment was challenging. As per the guidelines for CRC of the Chinese Society of Clinical Oncology (2), an MDT was assembled to control the tumor progression and improve the patient's quality of life by administering anti-tumor and symptomatic therapies. A previous study has shown fruquintinib is an effective, safe, and tolerable 3rd-line treatment for metastatic CRC (5). Thus, fruquintinib was chosen for this patient.

Grade 3 hypertension and proteinuria occurred during the treatment, and the dose reduction was given careful consideration. In the FRESCO study, the dose of fruquintinib was reduced in two 1 mg/day increments to clinically manage significant AEs (6). As the patient in this case had an underlying disease (i.e., hypertension) and severe malnutrition in addition to an advanced age, safety was the primary concern during the anti-tumor treatment. Thus, the re-start dose of fruquintinib was reduced to 3 mg/day. Notably, dose reduction requires individualized consideration, and in most cases, a primary decrease to 4 mg/day is recommended.

The most common fruquintinib-related AEs include hypertension, hand-foot-skin reaction, and proteinuria (7). Hypertension is a common AE in anti-angiogenic therapy, which is associated with a better prognosis. In metastatic CRC patients treated with bevacizumab, drug-related hypertension may be a predictor of improved survival (8,9). As the pathogenesis of angiogenesis inhibitor-related hypertension includes increased microvascular permeability, decreased endothelial renewal capacity, and the decreased production of vasodilators (10), grade 3 hypertension may suggest a favourable prognosis. The patient in the present study achieved a PFS of 25 months. Thus, while fruquintinib is not yet a standard therapy recommended for CRC, this case provides further evidence of its anti-tumor activity and safety as reported previously (6).

An 82-year-old patient with chemo-refractory CRC who received fruquintinib as the 2nd-line treatment achieved a PFS of 25 months. Typically, CRC patients with advanced age and poor general condition require MDT meetings and individualized treatment plans, and fruquintinib is effective and tolerable in these patients.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-841/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-841/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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