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Case Report

Long-Term Survival in a Patient with Metastatic Colorectal Cancer Treated with Trifluridine/Tipiracil as Late-Line Chemotherapy: A Case Report

Bülent Karabulut[a] Burcu Çakar[b]

[a]Department of Medical Oncology, Özel İzmir Kent Hospital, Izmir, Turkey; [b]Department of Medical Oncology, Ege University, Izmir, Turkey

Keywords
Long-term survival · Metastatic colorectal cancer · Trifluridine/tipiracil

Abstract
Introduction: Although long-term survival in patients with metastatic colorectal cancer (mCRC) is limited, treatments for third-line and later treatment are now recommended. We describe a patient who achieved long-term survival when they received third-line treatment with trifluridine/tipiracil (FTD/TPI). ***Case Presentation:*** The woman who was 52 years old at diagnosis of adenocarcinoma of the right colon (T3/N0/M1) with metastases to the lung, liver, ovary, and other soft tissues received first-line fluoropyrimidine-based chemotherapy (FOLFOX/FOLFIRI plus bevacizumab) intermittently for approximately 8.5 years with generally stable disease, and second-line FOLFIRI plus radiotherapy. After progression on second-line therapy, the patient initiated treatment with FTD/TPI 35 mg/m^2 twice daily on days 1–5 and 8–12 of each 28-day cycle. She received a total of 38 cycles of FTD/TPI over a period of 34 months achieving a partial response, maintained performance status, and improved quality of life. Neutropenia was successfully managed with FTD/TPI dose delays or reductions. ***Conclusion:*** This heavily pre-treated patient with mCRC demonstrated impressive long-term survival and maintenance of good quality of life with FTD/TPI treatment.

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Correspondence to:
Bülent Karabulut, onkologbk@gmail.com

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Introduction

During recent years, progress in the treatment of patients with metastatic colorectal cancer (mCRC) has led to an increase in median overall survival (mOS) to 30 months [1]. Established first- and second-line treatment options for patients with mCRC include oxaliplatin- and fluoropyrimidine-based chemotherapies and targeted anti-vascular endothelial growth factor (VEGF) and anti-epidermal growth factor receptor (EGFR) therapies [2]. However, treatment options for patients with mCRC progressing beyond first- and second-line therapy are limited [3, 4]. According to the ESMO guidelines, third-line options for mCRC include the chemotherapeutic agent trifluridine/tipiracil (FTD/TPI) [5]. This recommendation is based on data from the phase III RECOURSE study, in which mOS was 7.1 months with FTD/TPI compared with 5.3 months with placebo (HR: 0.68, $p < 0.001$) in patients with mCRC previously treated with two or more lines of therapy [6]. Observational data on real-world use of FTD/TPI, including the multinational PRECONNECT study [7–9], are generally consistent with the findings of the RECOURSE trial [10–12].

In the RECOURSE trial, although the mOS was 7.1 months, the 1-year survival was 27% (compared with 18% with placebo), and therefore, there are some patients who gain much longer survival benefits with FTD/TPI. Published cases have shown long-term survival and maintenance of quality of life (QoL) with FTD/TPI as late-line chemotherapy in other recurrent gastrointestinal cancers [13–15]. Here, we report the details of a patient with mCRC with long-term survival following treatment with FTD/TPI. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000535202).

Case Report

The case is described in detail below, and a timeline summarizing the treatment regimens and outcomes is shown in Table 1. A 52-year-old woman was diagnosed with adenocarcinoma of the right colon (T3/N0/M1) on January 22, 2008, with metastases to the lung, liver, ovary, and other soft tissues. She had KRAS-mutant mCRC. She initiated FOLFOX chemotherapy (folinic acid, 5-fluorouracil [5-FU], and oxaliplatin) and bevacizumab and underwent hemicolectomy and liver metastasectomy. After 9 months of treatment (12 cycles), her disease remained stable and treatment was stopped. Following confirmation of local progression and ovarian metastases approximately 1 year later, the patient initiated FOLFIRI (folinic acid, 5-FU, and irinotecan) chemotherapy plus bevacizumab and continued at the same dose for 6 months with stable disease. Chemotherapy was halted thereafter until October 31, 2012, when the patient initiated another course of FOLFOX chemotherapy plus bevacizumab for a lesion in the abdominal wall and achieved a partial response. After 11 months (12 cycles) of FOLFOX chemotherapy and bevacizumab, she received maintenance therapy with 5-FU-folinic acid and bevacizumab for approximately 6 weeks. A second break in therapy occurred until January 20, 2016, when the patient received 5 weeks of capecitabine and oxaliplatin, followed by 4.5 months of oxaliplatin for progression of the lesion in the abdominal wall. Consequently, progression of mCRC in August 2016 led to treatment with FOLFIRI plus radiotherapy (for 11 months), after which she experienced a second disease progression in January 2018.

Upon disease progression in January 2018, this heavily chemotherapy-treated patient was enrolled in the PRECONNECT study and began treatment with FTD/TPI. The patient met all the diagnostic criteria required to be enrolled in the PRECONNECT study [9]. Upon enrolment into this study, she exhibited signs and symptoms related to mCRC, including

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Table 1. Treatment timeline and responses

Date	Reason for treatment commencement	Treatment	Treatment duration, months	Treatment line	Response
Jan 2008	Diagnosis of adenocarcinoma of the right colon with metastases to the lung, liver, ovary, and other soft tissues	FOLFOX + bevacizumab Hemicolectomy and liver metastasectomy	9	1L	SD
Nov 2009	Local progression and ovarian metastases	FOLFIRI + bevacizumab	6		SD
Oct 2012	Lesion in the abdominal wall	FOLFOX + bevacizumab	11		PR
Nov 2013	Maintenance therapy	5-FU + folinic acid + bevacizumab	1.5		–
Jan 2016		Capecitabine + oxaliplatin	1.25		–
Mar 2016	Lesion in the abdominal wall	Oxaliplatin	4.5		–
Sep 2016	Disease progression, Aug 2016	FOLFIRI + radiotherapy	11	2L	–
Jan 2018	Second disease progression, Jan 2018. The patient was recruited into the PRECONNECT study at this time	FTD/TPI	34	3L	PR
May 2021	Evidence of disease progression	Regorafenib	Ongoing as of Dec 2021	4L	PR

1L, first-line; 2L, second-line; 3L, third-line; 5-FU, 5-fluorouracil; FOLFOX, folinic acid + 5-fluorouracil + oxaliplatin; FOLFIRI, folinic acid + 5-fluorouracil + irinotecan; FTD/TPI, trifluridine/tipiracil; PR, partial response; SD, stable disease.

anemia (grade 1), hypertension (grade 3), increased serum lactate dehydrogenase (grade 1), and lymphopenia (grade 1). Anemia was considered a consequence of being heavily pretreated with chemotherapy, and hypertension may have been a side effect of the previous anti-VEGF treatment (bevacizumab).

The patient's starting dose of FTD/TPI was 35 mg/m^2 twice daily (after morning and evening meals) on days 1–5 and 8–12 of each 28-day cycle. She received a total of 38 cycles of FTD/TPI over a period of 34 months (32 cycles in the PRECONNECT trial and 6 cycles in a post-trial access program that allowed the patient to continue treatment, even though FTD/TPI was not licensed in Turkey at the time). The relative dose intensity of FTD/TPI across the 32 cycles was 65%. The dose of FTD/TPI was delayed in 12 treatment cycles due to neutropenia as an adverse event (cycles 4, 6, 8, 9, and 14), low neutrophil count (cycles 22 and 30), unspecified adverse events (cycles 2 and 3), and non-medical reasons (cycles 7, 18, and 20). The FTD/TPI dose was reduced to 30 mg/m^2 twice daily for cycle 3 and to 25 mg/m^2 twice daily for cycle 6 and until end of treatment (both with the same schedule as the starting dose). The most severe adverse event experienced by this patient during treatment with FTD/

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TPI was grade 3/4 neutropenia. Additional adverse events reported during this patient's inclusion in the PRECONNECT trial included anemia, decreased white blood cell count, leukopenia, abdominal pain, decreased appetite, fatigue, hypocalcemia, intestinal obstruction, lymphopenia, nausea, and vomiting.

The patient had nine tumor evaluations according to the PRECONNECT study protocol and standard practice at the study site over the 34 months of treatment, and at each evaluation, she achieved a partial response. No new lesions were recorded. During the treatment period, the patient maintained an Eastern Cooperative Oncology Group (ECOG) performance status of 0 and showed improvement in QoL (mean change from baseline in European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire – Global Health Status score of ≥20 after 32 cycles).

In the PRECONNECT trial, there were no mandated regular follow-up visits planned after the end of the study. However, we do know that this patient was switched to regorafenib in May 2021, after evidence of progressive disease, and continues this treatment with achievement of partial response to date (December 2021).

Discussion

This case study reports the remarkable, long-term survival of a patient with mCRC treated with FTD/TPI as a third-line therapy. She survived for 10 years before enrolment in PRECONNECT to receive FTD/TPI. This observation of long-term survival may suggest that this patient had a nonaggressive disease. However, while most patients (69%) treated with FTD/TPI have received up to 3 previous lines of therapy [16], this patient had disease progression following five lines of chemotherapy and one line of maintenance therapy.

Despite this, the patient reported here achieved a partial response with FTD/TPI and was still alive, responding and receiving FTD/TPI 3 years after the start of FTD/TPI treatment. In comparison, in the phase III RECOURSE trial, at 16 months, only 2 of 534 patients in the FTD/TPI arm were progression-free. The patient required several dose delays or reductions due to neutropenia, but still, she was able to continue FTD/TPI in the long-term. Neutropenia is not uncommon in a patient who has received multiple lines of chemotherapy, which can suppress bone marrow function [17]. A sub-study of the RECOURSE and J003 trials indicated that patients who developed neutropenia in response to FTD/TPI had prolonged OS and progression-free survival (PFS) compared to patients who did not develop neutropenia [18]. The PRECONNECT study also found prolonged PFS in mCRC patients who developed neutropenia in response to FTD/TPI, confirming the potential for neutropenia as a predictor of response to FTD/TPI [9]. FTD/TPI-induced neutropenia was reported in most previous case studies reporting long-term PFS with FTD/TPI in mCRC patients (Table 2). The presence of FTD/TPI-induced neutropenia in this long-surviving patient, as well as previously reported patients who had a long-term response to FTD/TPI treatment (Table 2), could be further evidence of the use of neutropenia as a predictor of response to FTD/TPI in mCRC patients.

Nevertheless, the absence of major adverse events with FTD/TPI and other treatment regimens in this patient with *KRAS*-mutated mCRC suggests tumor and clinical characteristics that favor tolerability and response to FTD/TPI. For example, *KRAS*, a major oncogenic driver in multiple cancers, is mutated in 30–40% of CRC tumors and demonstrates prognostic variability depending on mutation status [19, 20]. There have been conflicting reports of the effect of *KRAS* mutations on the efficacy of FTD/TPI. A recent whole-genome analysis study suggested that mCRC patients with a *KRAS* mutation in codon 12 have poorer outcomes when treated with FTD/TPI than patients with wild-type *KRAS* [21]. However, a meta-analysis of

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Table 2. Characteristics of patients in cases of long-term PFS with FTD/TPI treatment

Publication	Patient and disease characteristics	Previous treatment	Line received FTD/TPI	Duration of PFS with FTD/TPI	*KRAS* mutational status of primary tumor	ECOG performance status	FTD/TPI adverse effects
Lin et al. [28], 2020	72-year-old man with rectal adenocarcinoma in 2012. Disease recurrence and advancement occurred in 2016 with liver and peritoneal metastases	1L: irinotecan + bevacizumab 2L: HDFL + oxaliplatin + bevacizumab	3L (in addition to radiotherapy, Yttrium-90 radioembolization and trans-arterial chemoembolization for metastases)	15 months (ongoing as of publication of case report)	*KRAS* G13D mutation	1 (at diagnosis)	Grade 3 neutropenia in response to the first dose elevation. Subsequent dose reduction improved neutropenia to grade 1. Grade 2 neutropenia seen in the latest reported FTD/TPI cycle
Orlikowska [29], 2020	57-year-old woman with sigmoidal adenocarcinoma with metastasis to the right ovary at diagnosis. Subsequent metastases to the liver and peritoneal cavity	1L: FOLFIRI 2L: FOLFOX-4 3L: LF4	4L (received FTD/TPI alone for 8 cycles, then FOLFIRI added to the regimen)	17 months (ongoing as of publication of the case report)	Not reported	1-2 during FTD/TPI treatment	Grade 3 neutropenia after first and third cycles
Skalij et al. [25], 2020	73-year-old man with rectal cancer and pelvic/abdominal metastatic lymph nodes at diagnosis. Later metastatic lesions in the liver, adrenal gland, and skeletal system	1L: FOLFIRI 2L: FOLFOX + bevacizumab 3L: capecitabine 4L: FOLFIRI 5L: capecitabine + cyclophosphamide	6L	7 months (ongoing as of publication of the case report)	No mutations in *RAS* genes	1 (at start of FTD/TPI treatment and maintained throughout)	Grade 3 neutropenia at the second cycle, treatment continued with 1/3 dose reduction
Wiśniowski [30], 2020	26-year-old woman with sigmoidal adenocarcinoma with 1/32 examined lymph nodes metastatic. Later metastases to the liver, ovaries, and peritoneal cavity	1L: FOLFOX4 2L: FOLFIRI 3L: cetuximab	4L (received FTD/TPI alone for 5 cycles then mitomycin/capecitabine added to the regimen)	8 months	Wild-type *KRAS*	Not reported. The patient reported increasing fatigue that interfered with daily duties	Grade 2 neutropenia observed during FTD/TPI treatment

Table 2 (continued)

Publication	Patient and disease characteristics	Previous treatment	Line received FTD/TPI	Duration of PFS with FTD/TPI	*KRAS* mutational status of primary tumor	ECOG performance status	FTD/TPI adverse effects
ELBassiouny [15], 2022	70-year-old woman with colorectal cancer with metastatic lymph nodes	1L: panitumumab + capecitabine 2L: bevacizumab + oxaliplatin/ capecitabine; bevacizumab + irinotecan for 1 cycle	3L	27 months (ongoing as of publication of the case report)	Wild-type *KRAS*	Not reported	No adverse reactions
Kaechele et al. [31], 2018	62-year-old man with colorectal cancer and metastases to the liver and lung. This patient exhibited pronounced hematological event history in response to treatments	1L: FOLFOX-6/ cetuximab 2L: FOLFIRI/cetuximab + 5-FU 3L: capecitabine + bevacizumab 3L: irinotecan + cetuximab (irinotecan stopped after the first cycle)	5L	10 months	Wild-type *KRAS*	1 (at start of FTD/ TPI treatment and maintained throughout)	First cycle caused grade 1 hemotoxicity, resulting in a dose reduction for cycles 2–5. Grade 4 neutropenia at the fifth cycle led to further dose reduction for remaining cycles

5-FU, 5-fluorouracil; 1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; 5L, fifth-line; 6L, sixth-line; ECOG, Eastern Cooperative Oncology Group; HDFL, high-dose 24-h infusion of 5-fluorouracil and leucovorin; FOLFOX, folinic acid + 5-fluorouracil + oxaliplatin; FOLFOX-4, 5-fluorouracil + oxaliplatin; FOLFOX-6, fluorouracil, leucovorin, oxaliplatin; FOLFIRI, folinic acid + 5-fluorouracil + irinotecan; FTD/TPI, trifluridine/tipiracil.

three clinical trials found that *KRAS* mutations in codon 12 or 13 had no detrimental effect on the beneficial response of FTD/TPI, compared to placebo, seen in mCRC patients [22]. Therefore, it is of note that the patient reported here had a *KRAS*-mutated tumor and still saw a long-term progression-free response to FTD/TPI. However, in previous case reports shown in Table 2, all patients achieved long-term PFS with FTD/TPI, with no clear pattern of *KRAS* mutational status across the cases. This illustrates the need for further work to assess how, and if, *KRAS* mutations affect patient response to FTD/TPI, due to the potential of *KRAS* mutational status as a predictive tool for clinicians.

Previous treatment with targeted therapies has been suggested to effect patient response to FTD/TPI. Studies evaluating the efficacy of FTD/TPI (RECOURSE and TERRA) found that the risk of death was reduced in patients previously treated with VEGF- and/or EGFR-targeted therapies, compared with patients not previously treated with targeted therapies [6, 23]. Bevacizumab, an anti-VEGF therapy, has recently been recommended in combination with FTD/TPI as a third-line therapy in mCRC due to the OS benefit of the combination (mOS 10.8 months vs. 7.5 months in patients treated with FTD/TPI alone) in a recent clinical trial [24]. The patient reported here had undergone multiple previous treatments with bevacizumab before taking part in the PRECONNECT study and receiving FTD/TPI. A previous case report describing long-term disease control with FTD/TPI in a 73-year-old patient with mCRC also reported anti-VEGF and anti-EGFR therapy use prior to treatment with FTD/TPI (Table 2) [25]. An additional case study described a patient with mCRC who had received bevacizumab in previous lines of therapy who went on to maintain stable disease for more than 27 months with FTD/TPI third-line treatment (Table 2) [15]. Although the effect of previous treatment with targeted therapies on the long-term survival benefit of FTD/TPI cannot be determined from this report, it poses an interesting avenue for further work.

An ECOG performance status of 0 has been previously reported to be independently associated with prolonged OS and PFS in patients treated with FTD/TPI [21, 26]. The patient in this case study maintained an ECOG performance status of 0 throughout the FTD/TPI treatment period, meaning she was fully active and able to continue with pre-disease performance [27]. Additionally, all patients in the case reports listed in Table 2 had an ECOG performance status of 0–1. This could indicate a need to stratify patients by ECOG status to highlight mCRC patients who will be "good responders" to FTD/TPI treatment in the third line. Regardless, the consistent ECOG performance status in this patient stresses the tolerance of long-term FTD/TPI and the maintenance of good QoL. This is further evidenced by the long-term survival and maintenance of good QoL with FTD/TPI treatment in heavily pre-treated with mCRC in other case studies [28].

In conclusion, this case report indicates that FTD/TPI is an effective third-line therapy for patients with mCRC. This patient represents the longest surviving individual treated with FTD/TPI, thus showing that some individuals can achieve a long-term response with FTD/TPI treatment in the third line. Future research should aim to identify factors, such as specific mutations, ECOG performance status, or previous targeted therapies, which may predict such long-term survival with FTD/TPI treatment.

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Statement of Ethics

The patient participated in the PRECONNECT study (NCT03306394). The study protocol was reviewed and approved by the Independent Ethics Committee or Institutional Review Board of each participating center, according to local regulations in place. For the patient in this case, ethical approval was granted by Gazi University Medical Faculty Ethics Committee, Ankara, Turkey (EC ID: E. Committee-E-16-1107; CA ID: 93189304-514.03.01-E.52899). The trial was conducted in accordance with the approved protocols and adhered to ethical principles contained in the Declaration of Helsinki and Good Clinical Practice guidelines. All patients gave written informed consent before participation. The patient gave specific written consent for their data to be included in this case report submission using an adapted version of the BMJ Case Reports consent form (available upon reasonable request).

Conflict of Interest Statement

Bülent Karabulut has no conflicts to report. Burcu Çakar has no conflicts to report.

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The patient in this case report was a participant in the PRECONNECT trial, sponsored by Servier.

Author Contributions

Bülent Karabulut and Burcu Çakar assume final responsibility for the work, had access to all data, contributed extensively to the writing of this case report, and gave full approval to submit this work for publication.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Hamers PAH, Elferink MAG, Stellato RK, Punt CJA, May AM, Koopman M, et al. Informing metastatic colorectal cancer patients by quantifying multiple scenarios for survival time based on real-life data. Int J Cancer. 2021;148(2):296–306. https://doi.org/10.1002/ijc.33200.
2 Cervantes A, Adam R, Rosello S, Arnold D, Normanno N, Taieb J, et al. Metastatic colorectal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2023;34(1):10–32. https://doi.org/10.1016/j.annonc.2022.10.003.
3 Vogel A, Hofheinz RD, Kubicka S, Arnold D. Treatment decisions in metastatic colorectal cancer - beyond first and second line combination therapies. Cancer Treat Rev. 2017;59:54–60. https://doi.org/10.1016/j.ctrv.2017.04.007.
4 Arnold D, Prager GW, Quintela A, Stein A, Moreno Vera S, Mounedji N, et al. Beyond second-line therapy in patients with metastatic colorectal cancer: a systematic review. Ann Oncol. 2018;29(4):835–56. https://doi.org/10.1093/annonc/mdy038.

5 Van Cutsem E, Cervantes A, Adam R, Sobrero A, Van Krieken JH, Aderka D, et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol. 2016;27(8):1386–422. https://doi.org/10.1093/annonc/mdw235.
6 Mayer RJ, Van Cutsem E, Falcone A, Yoshino T, Garcia-Carbonero R, Mizunuma N, et al. Randomized trial of TAS-102 for refractory metastatic colorectal cancer. N Engl J Med. 2015;372(20):1909–19. https://doi.org/10.1056/NEJMoa1414325.
7 Bachet JB, Wyrwicz L, Price T, Cremolini C, Phelip JM, Portales F, et al. Safety, efficacy and patient-reported outcomes with trifluridine/tipiracil in pretreated metastatic colorectal cancer: results of the PRECONNECT study. ESMO Open. 2020;5(3):e000698. https://doi.org/10.1136/esmoopen-2020-000698.
8 Ozet A, Dane F, Aykan NF, Yalcin S, Evrensel T, Ozkan M, et al. Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer: PRECONNECT Turkey. Future Oncol. 2022;18(29):3267–76. https://doi.org/10.2217/fon-2022-0455.
9 Taieb J, Price T, Vidot L, Chevallier B, Wyrwicz L, Bachet JB. Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer: final results from the phase IIIb single-arm PRECONNECT study by duration of therapy. BMC Cancer. 2023;23(1):94. https://doi.org/10.1186/s12885-022-10489-4.
10 Cheung WY, Kavan P, Dolley A. Quality of life in a real-world study of patients with metastatic colorectal cancer treated with trifluridine/tipiracil. Curr Oncol. 2020;27(5):e451–8. https://doi.org/10.3747/co.27.6533.
11 Patel AK, Abhyankar R, Brais LK, Duh MS, Barghout VE, Huynh L, et al. Trifluridine/tipiracil and regorafenib in patients with metastatic colorectal cancer: a retrospective study at a tertiary oncology center. Oncologist. 2021;26(12):e2161–9. https://doi.org/10.1002/onco.13942.
12 Zaniboni A, Barone CA, Banzi MC, Bergamo F, Blasi L, Bordonaro R, et al. Italian results of the PRECONNECT study: safety and efficacy of trifluridine/tipiracil in metastatic colorectal cancer. Future Oncol. 2021;17(18):2315–24. https://doi.org/10.2217/fon-2020-1278.
13 Hamada SKS, Komatsu S, Shibata R, Konishi T, Matsubara D, Soga K, et al. Long-term survivor with recurrent gastric cancer using trifluridine/tipiracil as a late-line chemotherapy. Gan To Kagaku Ryoho. 2020;47(13):2056–8.
14 Kania-Zembaczyńska B. Chemotherapy with trifluridine/tipiracil prolongs progression-free survival time and improves quality of life. A case report of 59-year-old woman with metastatic rectal cancer. OncoReview. 2020;10(1):18–22. https://doi.org/10.24292/01.or.120310320.
15 ELBassiouny M. Case report: long-term survival in a patient with metastatic colorectal cancer treated with trifluridine/tipiracil in the third-line setting. Front Oncol. 2023;13:1112224. https://doi.org/10.3389/fonc.2023.1112224.
16 Andersen SE, Andersen IB, Jensen BV, Pfeiffer P, Ota T, Larsen JS. A systematic review of observational studies of trifluridine/tipiracil (TAS-102) for metastatic colorectal cancer. Acta Oncol. 2019;58(8):1149–57. https://doi.org/10.1080/0284186X.2019.1605192.
17 Crawford J, Dale DC, Lyman GH. Chemotherapy-induced neutropenia: risks, consequences, and new directions for its management. Cancer. 2004;100(2):228–37. https://doi.org/10.1002/cncr.11882.
18 Yoshino T, Cleary JM, Van Cutsem E, Mayer RJ, Ohtsu A, Shinozaki E, et al. Neutropenia and survival outcomes in metastatic colorectal cancer patients treated with trifluridine/tipiracil in the RECOURSE and J003 trials. Ann Oncol. 2020;31(1):88–95. https://doi.org/10.1016/j.annonc.2019.10.005.
19 Arrington AK, Heinrich EL, Lee W, Duldulao M, Patel S, Sanchez J, et al. Prognostic and predictive roles of KRAS mutation in colorectal cancer. Int J Mol Sci. 2012;13(10):12153–68. https://doi.org/10.3390/ijms131012153.
20 Zhu G, Pei L, Xia H, Tang Q, Bi F. Role of oncogenic KRAS in the prognosis, diagnosis and treatment of colorectal cancer. Mol Cancer. 2021;20(1):143. https://doi.org/10.1186/s12943-021-01441-4.
21 Kwakman JJM, Vink G, Vestjens JH, Beerepoot LV, de Groot JW, Jansen RL, et al. Feasibility and effectiveness of trifluridine/tipiracil in metastatic colorectal cancer: real-life data from The Netherlands. Int J Clin Oncol. 2018;23(3):482–9. https://doi.org/10.1007/s10147-017-1220-0.
22 Yoshino T, Van Cutsem E, Li J, Shen L, Kim TW, Sriuranpong V, et al. Effect of KRAS codon 12 or 13 mutations on survival with trifluridine/tipiracil in pretreated metastatic colorectal cancer: a meta-analysis. ESMO Open. 2022;7(3):100511. https://doi.org/10.1016/j.esmoop.2022.100511.
23 Xu J, Kim TW, Shen L, Sriuranpong V, Pan H, Xu R, et al. Results of a randomized, double-blind, placebo-controlled, phase III trial of trifluridine/tipiracil (TAS-102) monotherapy in asian patients with previously treated metastatic colorectal cancer: the TERRA study. J Clin Oncol. 2018;36(4):350–8. https://doi.org/10.1200/JCO.2017.74.3245.
24 Prager GW, Taieb J, Fakih M, Ciardiello F, Van Cutsem E, Elez E, et al. Trifluridine-tipiracil and bevacizumab in refractory metastatic colorectal cancer. N Engl J Med. 2023;388(18):1657–67. https://doi.org/10.1056/NEJMoa2214963.
25 Skalij P, Tokajuk P, Jelski S, Wojtukiewicz MZ. Long-term disease control during TAS-102 therapy in the VI line treatment in a 73-year-old mCRC patient. A case report. OncoReview. 2020;10(1):15–7. https://doi.org/10.24292/01.or.120260320.
26 Cremolini C, Rossini D, Martinelli E, Pietrantonio F, Lonardi S, Noventa S, et al. Trifluridine/tipiracil (TAS-102) in refractory metastatic colorectal cancer: a multicenter register in the frame of the Italian compassionate use program. Oncologist. 2018;23(10):1178–87. https://doi.org/10.1634/theoncologist.2017-0573.

Case Rep Oncol 2024;17:630–639
DOI: 10.1159/000535202
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www.karger.com/cro

27 Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the eastern cooperative oncology Group. Am J Clin Oncol. 1982;5(6):649–56. https://doi.org/10.1097/00000421-198212000-00014.
28 Lin YL, Liu KL, Lin BR. Trifluridine/tipiracil in combination with local therapy may be a favorable option for refractory metastatic colorectal cancer patients: a case report. Medicine. 2020;99(43):e22780. https://doi.org/10.1097/MD.0000000000022780.
29 Orlikowska M. Remarkable prolonged progression-free survival time after therapy with trifluridine/tipiracil. A case report of 57-year-old woman with metastatic colorectal cancer. OncoReview. 2020;10(1):27–30. https://doi.org/10.24292/01.or.120250320.
30 Wisniowski R. Efficacy of trifluridine/tipiracil as IV line chemotherapy in a young woman with metastatic colorectal cancer. A case report. OncoReview. 2020;10(1):23–6. https://doi.org/10.24292/01.or.120300320.
31 Kaechele V, Hess J, Schneider-Kappus W. Beneficial treatment management with trifluridine/tipiracil in a patient with metastatic colorectal cancer and pronounced hematological event history during previous treatments. Case Rep Oncol. 2018;11(1):43–8. https://doi.org/10.1159/000486195.