Safe management of sequential chemotherapy in a hemodialysis patient with metastatic colorectal cancer: A case report

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Abstract. Managing chemotherapy in hemodialysis (HD) patients is clinically challenging due to altered pharmacokinetics and a higher risk of severe toxicity. Evidence on drug selection and dose titration in cancer patients undergoing HD is limited. The present study reported the case of a patient with metastatic colorectal cancer who safely received first-to third-line chemotherapy while on maintenance HD. Treatment was individualized based on drug characteristics and the dialysis schedule. Initial therapy consisted of reduced-dose capecitabine (1,000 mg/m^2/day, days 1-14) plus oxaliplatin (70 mg/m^2, day 1) in a 21-day cycle, which was administered for 2 cycles. This was followed by 14 cycles of irinotecan monotherapy (day 1 of a 14-day cycle); the dose was initiated at 120 mg/m^2 and gradually reduced to 105 mg/m^2 and then 90 mg/m^2 based on toxicity. Third-line treatment involved 5 cycles of regorafenib (days 1-21 of a 28-day cycle), which was initiated at 40 mg/day and increased to 80 mg/day after confirming safety and tolerability. No life-threatening adverse events occurred during the treatment course. This case suggests that chemotherapy can be administered safely in selected HD patients when treatment is individualized, taking into account drug characteristics, dialysis-related factors and patient tolerance.

Introduction

Malignant tumors are now the third leading cause of death among hemodialysis (HD) patients in Japan (1). Therefore, appropriate cancer management in HD patients is increasingly important for improving clinical outcomes. Colorectal cancer (CRC), the second leading cause of cancer-related death in Japan, is among the most frequently observed malignancies in the HD population (2,3). Systemic treatment for metastatic CRC (mCRC) has advanced substantially in the general population. However, treatment selection remains challenging due to disease heterogeneity and the presence of distinct molecular subtypes. Traditionally, management relied on 5-fluorouracil (5-FU)-based chemotherapy; more recently, targeted therapies tailored to specific molecular subtypes and primary tumor location have been developed (4). In addition, immune checkpoint inhibitors have become an established option for selected patients with mismatch repair-deficient or microsatellite instability-high tumors (4). These advances have improved survival outcomes, with 5-year survival rates approaching 26% in mCRC cohorts (5).

However, patients undergoing HD are frequently excluded from clinical trials (6). Consequently, data on safety, efficacy, optimal dosing and appropriate timing of dialysis in relation to systemic therapy remain limited, and no standardized treatment strategy has been established for this population.

In HD patients, the pharmacokinetics of anticancer drugs are profoundly influenced by drug-specific characteristics, such as molecular weight, plasma protein binding and volume of distribution (7). Consequently, several cytotoxic agents and molecularly targeted agents commonly used for the treatment of mCRC require strict dose modifications in this setting, and chemotherapy in HD patients must be carefully individualized based on pharmacokinetic considerations and clinical tolerance (8). Accumulating these individualized clinical management data is an essential step toward establishing evidence-based, standardized therapies for the HD population.

The present study reported on the case of an HD patient with mCRC who was safely treated with sequential chemotherapy through individualized dose and schedule modifications.

Case report

A 61-year-old man with CRC underwent laparoscopy-assisted low anterior resection with D3 lymph node dissection at an external hospital in April 2014. Histopathological examination revealed adenocarcinoma staged as pT3N1M0 (pStage IIIB) according to the Union for International Cancer Control TNM Classification, 7th edition (9). The patient received adjuvant chemotherapy with S-1 for 4 months, followed by uracil/tegafur for 5 months. In November 2018, the patient developed a hepatic recurrence in segment S5, which was

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treated with partial hepatectomy. A right lower lobectomy was performed for a new pulmonary recurrence in February 2020. After 8 months, the patient underwent partial transverse colectomy, partial hepatectomy and cholecystectomy for hepatic and peritoneal recurrences, followed by oral uracil-tegafur plus leucovorin therapy (exact dosing regimen could not be confirmed from the available records at an external hospital).

HD was initiated in August 2023 because of progressive chronic renal failure secondary to focal segmental glomerulosclerosis. In October 2024, imaging revealed multiple metastatic lesions involving the abdominal wall, right lung, liver and the region adjacent to the hepatic portion of the inferior vena cava. Later that month, as the previous hospital lacked experience administering chemotherapy to patients undergoing dialysis, the patient was referred to our university hospital (Nara Medical University Hospital, Kashihara, Nara, Japan) to evaluate the safe administration of anticancer therapy under HD.

The patient had an Eastern Cooperative Oncology Group performance status (PS) of 0 (10). Molecular analysis of the recurrent colorectal tumor was performed on a formalin-fixed paraffin-embedded surgical specimen resected in October 2020. Analysis using the MEBGEN RASKET-B kit (Medical & Biological Laboratories) demonstrated wild-type status for *KRAS*, *NRAS*, and *BRAF*. Additionally, a multiplex PCR-based assay for microsatellite instability (MSI) demonstrated a microsatellite-stable (MSS) status. Given the tumor characteristics (left-sided, *RAS*/*BRAF* wild-type) and PS, continuous-infusion 5-FU-based doublet chemotherapy combined with an anti-epidermal growth factor receptor (EGFR) antibody would typically be considered a first-line treatment option. However, these regimens require a 46-h continuous infusion of 5-FU and close coordination with HD (11,12), which was logistically challenging because the dialysis facility was located ~1 h from our hospital. In addition, FOLFOX (folinic acid, 5-FU and oxaliplatin) is often administered with HD initiated soon after oxaliplatin infusion, and the addition of an anti-EGFR antibody would have further prolonged treatment time (11,12). Therefore, these regimens were considered impractical, and reduced-dose capecitabine plus oxaliplatin (XELOX) was initiated in November 2024.

The capecitabine and oxaliplatin doses were reduced to 1,000 mg/m^2/day for 14 days (50% of the standard dose) and 70 mg/m^2 on day 1 (54% of the standard dose), respectively, based on previous reports (13,14). The patient underwent HD three times weekly (Monday, Thursday and Saturday), and each chemotherapy cycle started on Monday morning before HD. Blood counts, renal function and electrolytes were monitored weekly.

After the first cycle, the patient experienced fatigue [Grade 2; Common Terminology Criteria for Adverse Events (CTCAE) v5.0 (15)]. Platelet count decreased (Grade 2; CTCAE v5.0, platelet count, 6.6x10^4/μl; institutional reference range, 15.8-34.8x10^4/μl) and hyperkalemia (serum K^+, 7.0 mEq/l; institutional reference range, 3.6-4.8 mEq/l). Sodium polystyrene sulfonate (15 g/day) controlled the hyperkalemia. Following a 1-week delay to allow platelet count recovery, the second cycle was initiated. Grade 2 fatigue persisted and Grade 2 platelet count decreased recurred during the second cycle (platelet count, 5.9x10^4/μl). The patient completed two cycles of XELOX without any serious adverse events. After 2 months of XELOX therapy, serum carcinoembryonic antigen (CEA) levels (institutional reference range, ≤5.0 ng/ml) increased, and computed tomography (CT) showed that the previously identified abdominal wall dissemination, liver metastases and the lesion adjacent to the right side of the hepatic portion of the inferior vena cava had become enlarged (data not shown). Although these findings met the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 criteria for stable disease (16), the overall clinical effect was deemed insufficient and the treatment strategy was changed.

Irinotecan monotherapy was initiated as second-line treatment for unresectable recurrent rectal cancer in February 2025. The dialysis schedule remained unchanged. As no validated HD-specific dosing algorithm exists for patients undergoing HD, irinotecan was initiated at 120 mg/m^2 (80% of the standard dose) on a biweekly schedule. Subsequent dose adjustments were made pragmatically based on the patient's observed toxicity. *Uridine diphosphate glucuronosyltransferase 1A1* (*UGT1A1*) genotyping for **28* and **6* was performed by SRL, Inc., using a PCR-based assay. Despite the patient being homozygous wild-type for both *UGT1A1*28* and *UGT1A1*6*, diarrhea (Grade 3; CTCAE v5.0) occurred. The dose was subsequently reduced to 105 mg/m^2 (70% of the standard dose) from the second cycle. As Grade 2 diarrhea persisted, the dose was further reduced to 90 mg/m^2 (60% of the standard dose) from the fifth cycle. The patient received a total of 14 cycles over 7 months. Follow-up CT revealed a new left pulmonary metastasis (data not shown), meeting the RECIST version 1.1 criteria for progressive disease (PD), leading to discontinuation of irinotecan.

Regorafenib was initiated as third-line treatment in September 2025 at 40 mg/day on a 3-weeks-on/1-week-off schedule, based on a previous report (17). This starting dose corresponded to 25% of the standard dose and the dialysis schedule remained unchanged. Although the patient developed hypertension (Grade 3; CTCAE v5.0), it was successfully managed with oral amlodipine 5 mg as needed when systolic blood pressure was ≥160 mmHg.

After confirming tolerability, the dose was escalated to 80 mg/day (50% of the standard dose) from the second cycle. The patient completed a total of five cycles. Subsequent CT revealed a new right pulmonary metastasis (data not shown) meeting RECIST version 1.1 criteria for PD, leading to discontinuation of regorafenib.

Since January 2026, the patient has received best supportive care. The patient was alive at the last confirmed follow-up in March 2026. Serum CEA levels and the clinical timeline of events are summarized in Fig. 1, and a detailed chemotherapy timeline under HD is presented in Table I.

Discussion

The management of cancer in HD patients remains challenging due to altered pharmacokinetics and limited evidence regarding optimal chemotherapy dosing (18). Studies suggest that cancer development in HD patients does not necessarily reduce overall survival (3,19), indicating that chemotherapy can be feasible and effective in carefully selected patients. In the CANDY study, 28% of 178 chronic dialysis patients

Table I. Chemotherapy regimens and associated adverse effects in a patient undergoing hemodialysis.

Treatment time	Note or regimen	Details	Adverse effects (CTCAE v5.0)
November 2024-January 2025	1st-2nd cycle of XELOX	Capecitabine 1,000 mg/m^2 (50% dose), oxaliplatin 70 mg/m^2 (54% dose)	Fatigue (G2), platelet count decreased [G2; PLT nadir 6.6x10^4/μl (C1D15), 5.9x10^4/μl (C2D15)], hyperkalemia [G3; K^+ 7.0 mEq/l (C1D8)]
January 2025	SD	Treatment discontinued on the basis of clinical judgment despite SD	-
February 2025	1st cycle of Irinotecan	120 mg/m^2 (80% dose)	Diarrhea (G3)
March 2025	2nd-4th cycle of Irinotecan	105 mg/m^2 (70% dose)	Diarrhea (worst grade: G3, subsequently improving to G2)
May-August 2025	5th-14th cycle of Irinotecan	90 mg/m^2 (60% dose)	Diarrhea (worst grade: G2, subsequently improving to G1)
August 2025	PD	New left pulmonary metastasis and increase in target lesion size	-
September 2025	1st cycle of Regorafenib	40 mg/day (25% dose)	Hypertension (G3)
September 2025-January 2026	2nd-5th cycle of Regorafenib	80 mg/day (50% dose)	Hypertension (G3)
January 2026	PD	New right pulmonary metastasis	-
January 2026	BSC	-	-

Tumor response was evaluated according to the Response Evaluation Criteria in Solid Tumors (version 1.1). Adverse events are summarized for each treatment period and represent the worst grade observed during that period, as defined by the CTCAE v5.0. CTCAE, Common Terminology Criteria for Adverse Events; G, grade; PLT, platelets; C, cycle; D, day; SD, stable disease; CEA, carcinoembryonic antigen; PD, progressive disease; BSC, best supportive care; XELOX, capecitabine plus oxaliplatin.

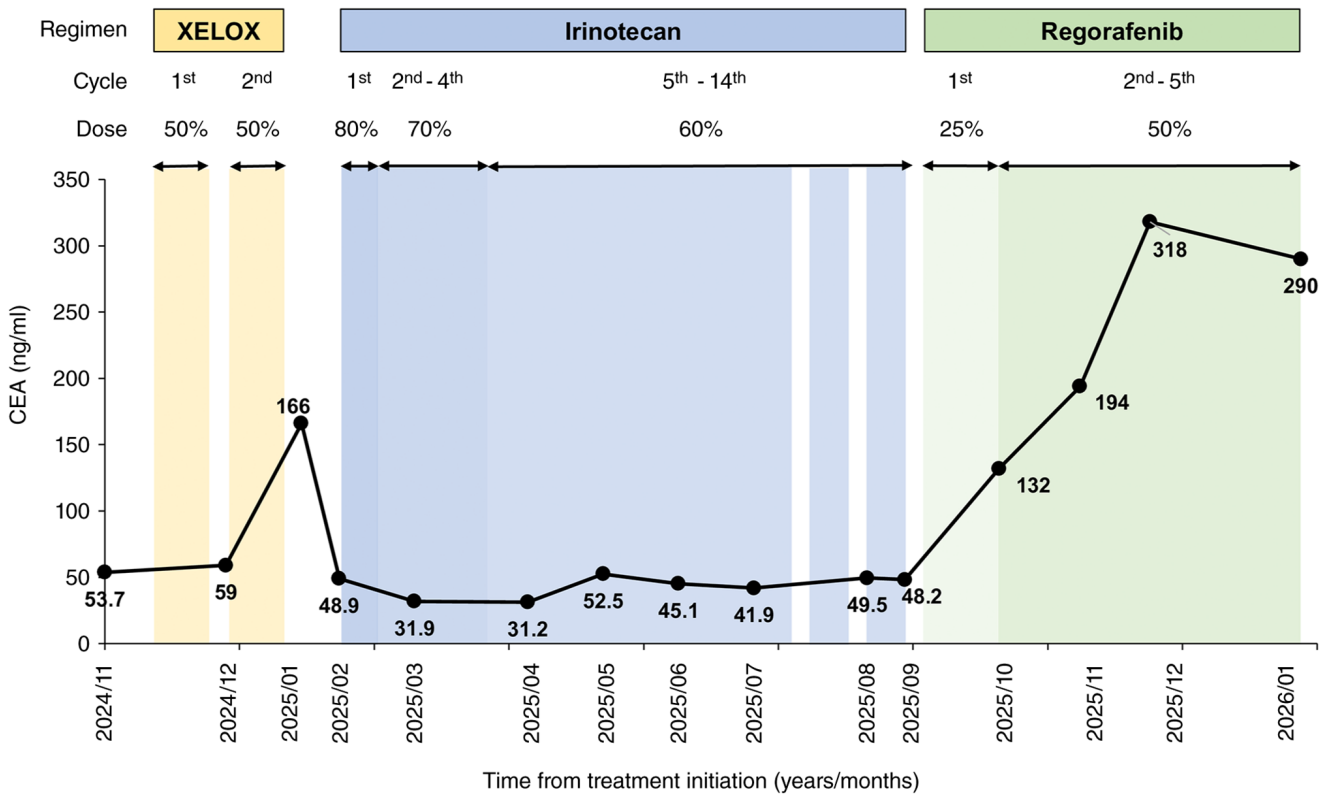

Figure 1. Course of chemotherapy and corresponding serum CEA levels. Colored areas represent treatment cycles for each regimen; each cycle included a treatment period followed by a rest period. CEA, carcinoembryonic antigen; XELOX, capecitabine plus oxaliplatin.

who developed cancer received chemotherapy, underscoring the importance of individualized treatment plans based on each drug's pharmacologic properties and available pharmacokinetic data (20).

Capecitabine, a component of the XELOX regimen, is contraindicated in patients with severe renal impairment (creatinine clearance <30 ml/min) and is generally avoided (18). Pharmacokinetic data support this approach, demonstrating increased exposure to capecitabine metabolites-particularly 5'-deoxy-5-fluorouridine and α-fluoro-β-alanine-in patients with kidney impairment (21). In a retrospective study, patients who initiated HD during capecitabine treatment tolerated a ~50% dose reduction without severe toxicity (22). Accordingly, capecitabine was administered at 50% of the standard dose in the present case to ensure safety. However, drug removal during HD could potentially reduce antitumor efficacy, which remains a limitation.

Oxaliplatin is predominantly excreted renally and biphasic elevation of plasma free platinum concentrations has been reported in HD patients (23). As platinum compounds rapidly bind to plasma proteins and erythrocytes shortly after infusion, initiating dialysis 1-1.5 h post-infusion is commonly practiced and described in previous reports (24-26). With dose reduction and early dialysis, the area under the curve for free platinum may be slightly higher than in non-HD patients, while peak concentrations remain comparable, resulting in acceptable toxicity profiles (26). Furthermore, previous studies indicate that oxaliplatin is generally administered at reduced doses (e.g., 60-85 mg/m^2) in patients undergoing HD, although higher doses (e.g., up to 100 mg/m^2) have also been reported (13,14,23). This variability underscores the lack of consensus and suggests that the optimal oxaliplatin dose in HD patients remains uncertain. In the present case, oxaliplatin was administered at 70 mg/m^2 (54% of the standard dose) in the morning, followed by HD in the afternoon at a local clinic. Adverse events were manageable and treatment was safely continued. These findings suggest that careful dose adjustment and appropriate HD timing can enhance the safety of oxaliplatin in HD patients. However, the progression-free survival (PFS) observed with XELOX in the present case was shorter than that reported with standard XELOX in non-HD populations (27). This finding suggests that early HD may have reduced the antitumor activity by removing unbound platinum before adequate tissue distribution, particularly in the context of dose reduction. Nevertheless, as pharmacokinetic analysis was not performed in the present case, the relationship among HD timing, adverse events and antitumor efficacy remains speculative.

Irinotecan is primarily metabolized in the liver to its active metabolite SN-38, which is glucuronidated by UGT1A1 and excreted in bile (28). As SN-38 is highly protein-bound and poorly cleared by dialysis, the timing of dialysis is unlikely to substantially affect its pharmacokinetics (29). Previous reports have described the safe administration of irinotecan at reduced doses (50-100 mg/m^2) in HD patients under clinical monitoring (30,31). For example, a weekly regimen of 50-80 mg/m^2 (3 weeks on, 1 week off) led to stable disease in an HD patient with mCRC (32). These favorable outcomes highlight the clinical utility of dose reduction. Conversely, severe toxicity has also been reported with irinotecan-based chemotherapy in HD patients; notably, one HD patient with mCRC developed grade 4 diarrhea and neutropenia after irinotecan at 180 mg/m^2, which ultimately resulted in death (33). Mechanistically, uremic toxins associated with severe renal failure can inhibit the hepatic uptake of SN-38, delaying its clearance and exacerbating toxicity (34). In the present case, treatment was initiated at 120 mg/m^2 to avoid potential underdosing; however, Grade 3 diarrhea developed despite the absence of common UGT1A1 risk polymorphisms. Accordingly, the dose was reduced stepwise to 105 mg/m^2 and then 90 mg/m^2 based on tolerability. The resulting PFS was ~7 months, which appears favorable compared with outcomes reported in the general mCRC population (35).

Regorafenib frequently induces early severe toxicities. The ReDOS trial demonstrated that stepwise dose escalation from 80 mg/day improves treatment continuation (36). Regorafenib is metabolized primarily in the liver, and its major active metabolites (M-2 and M-5) are highly protein-bound; therefore, hemodialysis is unlikely to substantially enhance drug elimination (37). In one reported case, regorafenib initiated at 40 mg/day was associated with early hypotension, altered mental status, abdominal pain and leukocytosis at the beginning of the second cycle, ultimately progressing to septic shock and cardiomyopathy requiring intensive care (17). By contrast, a recent case report described regorafenib initiation at 80 mg/day with escalation to 160 mg/day in an HD patient with mCRC, with acceptable tolerability (38). In the present case, therapy was initiated at 40 mg/day and escalated to 80 mg/day after confirming tolerability. Starting at a low dose, gradual titration and frequent monitoring minimized toxicity while maintaining treatment continuity. Rapid dose escalation may be considered if adverse events remain tolerable to prevent underdosing and loss of efficacy. In the present case, PFS was ~5 months, exceeding the median PFS reported in previous studies (39,40) and suggesting a relatively favorable outcome.

Several limitations should be acknowledged. Pharmacokinetic analyses were not performed for any of the administered agents and dose adjustments were based on prior reports and clinical tolerance rather than direct pharmacokinetic data. In addition, the patient's excellent PS may have contributed to the favorable tolerability profile. Finally, the limited efficacy observed with first-line therapy suggests a potential trade-off between safety-oriented dose reduction and antitumor activity.

In conclusion, this case demonstrates that sequential systemic therapy is feasible in a patient with mCRC undergoing HD when dosing and administration schedules are appropriately adjusted. In particular, it highlights the importance of individualized treatment strategies based on drug characteristics, dialysis timing and patient tolerability in HD patients for whom standard regimens are difficult to apply. Although limited to a single case, these findings contribute to the scarce literature on the management of mCRC in patients undergoing HD. Further clinical data are needed to establish effective treatment strategies for this growing HD patient population.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

RS and MT confirm the authenticity of all the raw data. Conceptualization of the manuscript was performed by RS. Data acquisition and interpretation were carried out by RS, NH, YK, YY, MO, SO and MT. The original draft was written by RS, and writing, review and editing were conducted by RS and MT. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work to ensure the accuracy and integrity of any part of the study.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The patient was informed that all identifying information would be removed to maintain anonymity.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this paper, ChatGPT-5 (https://chatgpt.com/) was used for spell checking and grammar checking. The authors then reviewed and edited the content as necessary and assume full responsibility for the final manuscript.

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