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CASE REPORT

Pharmacokinetic profile of irinotecan in patients with chronic kidney disease: Two cases and literature review

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Abstract

Aims: There are limited pharmacokinetic data on the use of irinotecan in patients with reduced glomerular filtration rate (GFR) and no haemodialysis. In this case report, we present 2 cases and review the current literature.

Methods: The dose of irinotecan in both patients was reduced pre-emptively due to reduced GFR. The first patient had her irinotecan dose reduced to 50%, but was nevertheless admitted to hospital because of irinotecan-induced toxicity, including gastrointestinal toxicity and neutropenic fever. The dose was reduced further to 40% for the second cycle; however, the patient was again admitted to the hospital, and irinotecan was stopped indefinitely. The second patient also had his irinotecan dose reduced to 50% and was admitted to the emergency department for gastrointestinal toxicity after the first cycle. However, irinotecan could be administered in the same dose in later cycles.

Results: The area under the curve to infinity of irinotecan and SN-38 in the first patient were comparable to those of an individual receiving 100% dose intensity. The area under the curve to infinity of irinotecan and SN-38 in patient 2 in both cycles were slightly less than reference values. Furthermore, clearance values of irinotecan and SN-38 in our patients were comparable to those without renal impairment.

Conclusion: Our case report suggests that reduced GFR may not significantly affect the clearance of irinotecan and SN-38, but can still result in clinical toxicity. Reduced initial dosing seems indicated in this patient population. Further research is needed to fully understand the relationship between reduced GFR, pharmacokinetics, and toxicity of irinotecan and SN-38.

KEYWORDS
irinotecan, pharmacokinetics, renal insufficiency, SN-38

1 | INTRODUCTION

Irinotecan is extensively used in the treatment of e.g. colorectal and pancreatic cancer. Irinotecan is the prodrug for SN-38, which is a

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topoisomerase I inhibitor. Topoisomerase is an enzyme involved in DNA replication.[1] SN-38 is at least 100 times more cytotoxic than irinotecan.[2] Eventually SN-38 is conversed into the inactive SN-38 glucuronide (SN-38G) by uridine diphosphate glucuronosyltransferase (UGT) 1A1. Variants in the *UGT1A1* gene can result in reduced enzyme activity, leading to increased risk of toxicity.[3] Furthermore, irinotecan and its metabolites are primarily faecal excreted (62.0% ± 7.60%) followed by urinary excretion (30.2% ± 6.60%).[4] Patients with reduced glomerular filtration rate (GFR; GFR < 59 mL/min per 1.73 m^2) may have increased irinotecan exposure, leading to more adverse events. The main side effects of irinotecan are neutropenia, gastrointestinal toxicity, cholinergic syndrome, anaemia, anorexia, alopecia and asthenia.

Trials of drugs in patients with reduced GFR are in general scarce. In the Summary of Product Characteristics, it is mentioned that use of Irinotecan HCl-trihydrate in patients with reduced GFR is not recommended since sufficient data is lacking.[5] Also in clinical guidelines, general statements, such as 'caution is warranted in patients with reduced GFR', do not provide guidance in how to approach dosing in these patients.[6] In daily clinical practice, this causes uncertainty on how to dose this specific patient population. Over the years, only a limited number of studies have reported on the dosing, pharmacokinetics and toxicity of irinotecan in this patient population with contrasting results and no clear dose recommendations. Venook *et al.* stated that dosing of irinotecan in patients with renal dysfunction is not clarified in their study since the doses explored were below the standard recommended doses. The 2 out of 9 patients with dose limiting toxicity in the renal dysfunction cohort had grade 4 diarrhoea and neutropenia with calculated creatinine clearances of 36 and 32 mL/min.[7] Also other studies have reported severe toxicity in patient with reduced GFR.[8] The clearance of SN-38 was reported to be lower.[9]

Because of the lack of clear dosing recommendations, dosing is mostly based on extrapolation of pharmacokinetic data of patients with normal GFR (GFR ≥90 mL/min per 1.73 m^2) and case reports. As pharmacokinetic data of irinotecan in patients with reduced GFR and without haemodialysis are limited, we hereby report 2 cases with detailed pharmacokinetic data that will add to the current knowledge on the pharmacokinetics and toxicity in this population and will provide guidance on how to dose this patient group. In addition, the current literature will be reviewed.

2 | CASE REPORTS

2.1 | Case 1

The patient was a 54-year-old Caucasian female, nonsmoker and known with hypertension, asthma and morbid obesity (body surface area [BSA; Dubois] 2.36 m^2). She received a kidney transplant in 1999 as a result of membranous glomerulonephritis. In March 2019, she was diagnosed with pT2N0M1 coecum cancer and subsequently a right hemicolectomy was performed. Radiofrequency ablation was conducted for the treatment of liver metastases. In December 2019, oxaliplatin and capecitabine were started as palliative therapy for new liver metastases. Eight days after starting chemotherapy, the patient was admitted to hospital because of nausea, vomiting and diarrhoea. Chemotherapy was altered to FOLFOX (folinic acid, 5-fluorouracil and oxaliplatin). Dose of oxaliplatin was reduced to 75% and dose of 5-fluorouracil was reduced to 50% because of reduced GFR and dihydropyrimidine dehydrogenase deficiency (*DPYD 1236G > A*), respectively. Once more, a few days after chemotherapy she was admitted to hospital because of gastrointestinal toxicity. Chemotherapy was ceased and in March 2020 radiation therapy was opted to treat the metastases.

Regrowth of metastases in segments V and VIII was observed in July 2020 and monotherapy irinotecan biweekly was chosen as palliative chemotherapy. The patient was identified to be *UGT1A1*1/*28*. Dexamethasone 4 mg was provided as part of antiemetic prophylaxis. In addition, the patient was taking ciclosporin, which is known to have a drug–drug interaction with irinotecan. The dose of irinotecan was pre-emptively reduced to 50% (90 mg/m^2, 212 mg total) due to reduced GFR (serum creatinine 201 μmol/L, GFR estimated according to the Chronic Kidney Disease Epidemiology Collaboration [eGFR] 23 mL/min/1.73 m^2). Total bilirubin level was not aberrant (13 μmol/L). Samples were obtained for pharmacokinetic analysis. Again, she was admitted to hospital as a result of gastrointestinal toxicity, neutropenic fever, acute reversible prerenal insufficiency, pancytopenia and apathy. The second irinotecan administration was postponed. After 4 days, she recovered and was discharged from hospital. Irinotecan was administered, 1 month after the first administration, in further reduced dose (60% dose reduction; 72 mg/m^2, 170 mg total). The adjustment was based on pharmacokinetic data and renal function (serum creatinine 168 μmol/L, eGFR 29 mL/min/1.73 m^2). Continuation of chemotherapy was requested by the patient as the tumour marker carcinoembryonic antigen decreased from 314.0 to 226.7 μg/L after the first cycle. One week after the administration, she was admitted to hospital due to gastrointestinal toxicity and acute kidney injury. Based on negative risk benefit analysis, irinotecan was ceased.

2.2 | Case 2

The patient was a 72-year-old Arabic male, nonsmoker and diagnosed in 2015 with pT3N3M0 sigmoid carcinoma. After resection, 8 cycles of CAPOX (capecitabine and oxaliplatin) were administered as adjuvant chemotherapy. In 2017 4 cycles of CAPOX were used for induction prior to hyperthermic intraperitoneal chemotherapy for treating peritoneal metastasis. Recurring peritoneal metastasis and suspicious lesions in the liver were detected in October 2018 and it was opted to treat these with capecitabin and bevacizumab. After the first cycle, the patient was admitted to hospital for gastrointestinal toxicity. Ultimately capecitabine was ceased indefinitely.

Due to progressive liver metastasis, monotherapy irinotecan (180 mg/m^2; 337 mg total) biweekly was started in July 2019. Serum creatinine was 150 μmol/L (eGFR 42 mL/min/1.73 m^2) at the time. The patient was identified to be *UGT1A1*1/*1*. The irinotecan dose

was reduced by 25% to 242 mg in total in December 2019 as a result of diarrhoea. In January 2020, the patient decided to pause chemotherapy. Monotherapy irinotecan was restarted in September 2020 due to growing lesions in the liver and 2 new metastases in the rectus abdominis muscle. The dose was reduced to 50% (90 mg/m^2; 165 mg total) on discretion of the patient's oncologist. GFR was reduced (serum creatinine 143 µmol/L, eGFR 42 mL/min/1.73 m^2) and total bilirubin level was within the normal range (4 µmol/L). Besides dexamethasone, no other medicines with known interactions with irinotecan were identified. Samples were obtained for pharmacokinetic analysis. After a few days the patient presented to the emergency department because of gastrointestinal toxicity. He was discharged without admission. During the second administration of irinotecan (serum creatinine 132 µmol/L, eGFR 45 mL/min/1.73 m^2), no further dose adjustment was made. No significant side effects were observed in the following 8 cycles. Carcinoembryonic antigen declined from 21.2 µg/L before starting chemotherapy to 4.9 µg/L 2 months after start irinotecan treatment.

3 | METHODS

Both patients were treated in the Leiden University Medical Center. Irinotecan and metabolite exposure measurements were performed as part of standard care for patients' safety and further guidance of dosing in the absence of clear guidelines. Informed consent was obtained from the patients to publish the results. Blood was drawn before administration, at 10 and 20 min after start administration of irinotecan and at 5, 15, 30, 60, 120, 240, 600 and 1440 min after end of infusion. Duration of the infusion was 30 min. The blood was centrifuged at 2200 g for 10 min and the plasma was extracted and stored at −20°C until transport to the bioanalytical laboratory. After transportation to the ISO15189 certified laboratory of the Erasmus University Medical Center, the samples were stored at −80°C until analysis. Irinotecan and SN-38 were measured by a validated reversed-phase high-performance liquid chromatography with fluorescence detection, as described by de Bruijn *et al.*[10]

Pharmacokinetic parameters of irinotecan and SN-38 were obtained by using noncompartmental analyses. The area under the curve (AUC) was calculated for a 24-h period (AUC_{0-24}) and for the period zero to infinity ($AUC_{0\text{-inf}}$), which was obtained by extrapolating the slope of the terminal concentration decline. Volume of distribution, total body clearance and half-life were calculated. Pharmacokinetic analysis was performed using Pkanalix 2020 (Simulations Plus, Inc., West Lancaster, CA, USA).

4 | RESULTS

The plasma concentrations of irinotecan and its metabolite SN-38 are shown in Figure 1. The pharmacokinetic parameters are presented in Table 1. The expected $AUC_{0\text{-inf}}$ of irinotecan and SN-38 in an individual receiving 180 mg/m^2 are 8000–15 000 and 250–325 ng*h/mL respectively.[4,11–14] After dose reduction, the $AUC_{0\text{-inf}}$ of irinotecan and SN-38 in patient 1 were comparable to those of an individual receiving 180 mg/m^2 (100% dose intensity) irinotecan. The $AUC_{0\text{-inf}}$ of irinotecan and SN-38 in patient 2 in both cycles were slightly less than aforementioned reference values. The clearance of irinotecan and SN-38 were comparable to those reported in the literature in both patients during both cycles.[15]

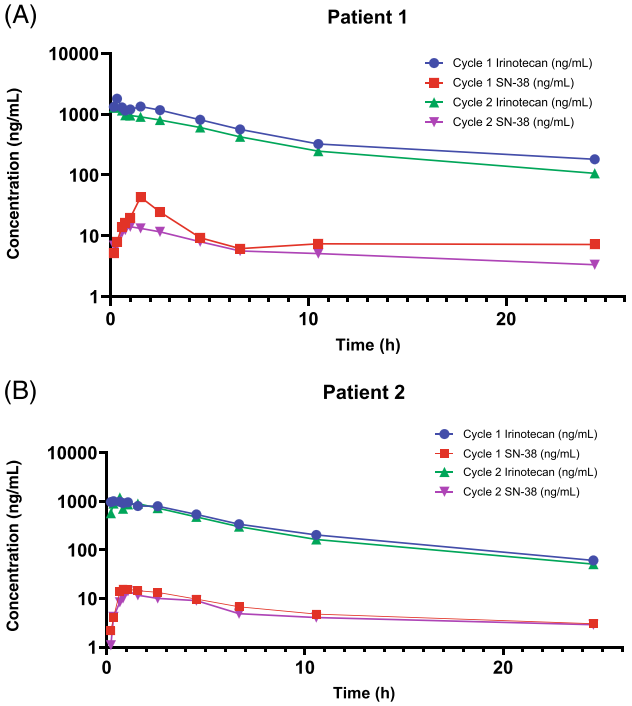

FIGURE 1 (A) Concentrations of irinotecan and SN-38 after start administration of irinotecan. Patient 1 had a glomerular filtration rate estimated according to the Chronic Kidney Disease Epidemiology Collaboration (eGFR) 23 mL/min/1.73 m^2 at the first cycle and received 90 mg/m^2 (212 mg total) irinotecan. At the second cycle she had an eGFR 29 mL/min/1.73 m^2 and received 72 mg/m^2 (170 mg total). (B) Concentrations of irinotecan and SN-38 after start administration of irinotecan. Patient 2 had an eGFR 42 mL/min/1.73 m^2 and an eGFR 45 mL/min/1.73 m^2 at the first and second cycle respectively; 90 mg/m^2 (165 mg total) irinotecan was administered in both cycles.

5 | DISCUSSION

In both patients, exposure to irinotecan and its metabolite SN-38 remained within the same order of magnitude as the average exposure of those who received the full dose (180 mg/m^2) of irinotecan, despite significant dose reductions (60 and 50%).[4,11–14] Furthermore, during both cycles, the absolute clearance of irinotecan and SN-38 fell within the range of those reported in the literature for both patients.[11,15,16]

Patient 1 exhibited high $AUC_{0\text{-inf}}$, which may be partially explained by the fact that dosing of irinotecan is based on actual BSA without dose capping, and this patient had an above-average BSA of

TABLE 1 Pharmacokinetic parameters of irinotecan and SN-38 after administration of irinotecan. Patient 1 received 50 and 40% of the recommended irinotecan dose (180 mg/m^2) during the first and second cycles, respectively. Patient 2 received 50% of the recommended irinotecan dose (180 mg/m^2) during both cycles.
V = volume of distribution; AUC = area under the concentration *vs.* time curve; CL = total body clearance; $t_{1/2}$ = elimination half-life; CL/fm = apparent clearance.

		Patient 1 Cycle 1	Patient 1 Cycle 2	Patient 2 Cycle 1	Patient 2 Cycle 2
Irinotecan					
	Dose (mg)	212	170	165	165
	Dose (mg/m^2)	90	72	90	90
	V (L)	174.6	182.8	223.6	250.1
	AUC_{0-24h} (ng*h/mL)	11 496	8299	6979	6205
	AUC_{0-inf} (ng*h/mL)	13 828	9641	7918	6988
	CL (l/h)	15,3	17,6	20,8	23,6
	$t_{1/2}$ (h)	7.9	7.2	7.4	7.3
SN-38					
	V (L)	14 449.6	22 616.3	18 032.3	26 065.9
	AUC_{0-24h} (ng*h/mL)	232	139	144	121
	AUC_{0-inf} (ng*h/mL)	466	255	220	226
	CL/fm (L/h)	454.3	666.7	748.2	727.1
	$t_{1/2}$ (h)	22.1	23.6	16.7	24.8

TABLE 2 Studies on patients receiving irinotecan who have reduced glomerular filtration rate and do not undergo haemodialysis.

Authors	Year	Number of patients	Findings of the study	Remarks
Venook *et al.*[7]	2003	35	Clearance of irinotecan and metabolites in the group with serum creatinine 1.6–5.0 mg/dL did not differ significantly compared to cohorts with serum creatinine <1.6 mg/dL.	Nine patients with reduced glomerular filtration rate (creatinine clearance varying between 21 and 60 mL/min [median 40.5]) were included.
De Jong *et al.*[8]	2008	187	A significant correlation between renal function calculated according to Cockcroft–Gault and clearance of irinotecan ($P = .05$), SN-38 ($P = .12$) and SN-38G ($P = .06$) could not be found. However, upon categorizing patients according to their renal function, those with an estimated glomerular filtration rate 35–66 mL/min exhibited a 13% lower irinotecan clearance than the group with an estimated glomerular filtration rate >98 mL/min ($P = .02$). Results from the pharmacodynamic analysis of 131 patients showed that slower creatinine clearance was associated with severe neutropenia.	Only 3 patients could be assigned to the group with the lowest creatinine clearance of 30–50 mL/min.

2.36 m^2. When calculating BSA adjusted clearance, the clearance of this patient was relatively low compared to the mean clearance in the Food and Drug Administration drug label (6.5–7.5 *vs.* 13.3–13.9 L). However, the literature has conflicting results regarding the relationship between BSA and irinotecan exposure. Poujol *et al.* reported a moderate positive correlation between irinotecan AUC and irinotecan dose ($r = 0.62$, $P < .0001$),[15] while Klein *et al.* found that BSA was not a predictor for exposure to irinotecan or SN-38.[17] Current guidelines recommend using actual body weight for calculating BSA-based dosing in obese patients to avoid underdosing.[18]

Other factors might have contributed to the high AUC_{0-inf} of irinotecan and SN-38 in patient 1. More specifically, the concurrent use of the immunosuppressive drug ciclosporin. Ciclosporin has been shown to decrease the clearance of irinotecan by 39–64% and increase the AUC_{0-24h} of SN-38 by 23–623%.[19] Nonetheless, the absolute clearance of irinotecan in patient 1 was not aberrant. Another possible contributing factor to the high AUC_{0-inf} may be that patient 1 carried the *UGT1A1*1/*28* polymorphism, which is associated with increased systemic exposure to SN-38. However, dose adjustment is not recommended by the national guideline.[20] No factors were identified in patient 2 that could significantly alter the plasma concentration of irinotecan and SN-38.

Reduced GFR could theoretically lead to increased exposure of irinotecan and its metabolites, potentially resulting in more adverse events. However, the clearance of irinotecan and SN-38 in our patients were not unusual, yet both patients experienced toxicity.

Despite the potential clinical relevance of reduced GFR in the dosing of irinotecan, there is currently a lack of literature on this subject. Table 2 provides a summary of the available literature.

Current literature is contradictory on the effect of reduced GFR on the pharmacokinetics of irinotecan and SN-38.[7–9] Dose reduction of irinotecan due to reduced GFR is currently not recommended by national and international guidelines.[6,21] Nevertheless, several studies have reported an increased risk of adverse events in patients with reduced GFR. One possible explanation for this is that elevated uraemic toxins in patients with reduced GFR may inhibit the binding of SN-38 to albumin, leading to an increase in unbound SN-38. Additionally, reduced hepatic uptake of SN-38 by OATP1Bs may contribute to this phenomenon.[22] However, further research is required to test this hypothesis, and studies with larger sample sizes are needed to clarify the effect of reduced GFR on the pharmacokinetics of irinotecan and SN-38. The current report of 2 well documented and monitored cases with impaired renal function adds to the total sample size reported in literature. In line with earlier reports these 2 cases also showed considerable toxicity with reduced doses. Although this effect could not conclusively be explained by reduced clearance caused by the impaired renal function, reduced initial dosing followed by up titration of the dosed based on toxicity seems indicated.

In conclusion, our case report suggests that reduced GFR may not significantly affect the clearance of irinotecan and SN-38, but can still result in toxicity. Current guidelines do not recommend dose reduction of irinotecan based on reduced GFR, but several studies have reported an increased risk of adverse events in such patients. Reduced initial dosing followed by up titration of the dose based on toxicity therefore seems indicated in this patient population. Further research is needed to fully understand the relationship between reduced GFR, pharmacokinetics, and toxicity of irinotecan and SN-38.

AUTHOR CONTRIBUTIONS

Chang Yue Chui and Dirk Jan A.R. Moes interpreted data. Chang Yue Chui wrote the original draft. Dirk Jan A.R. Moes performed the pharmacokinetic analysis. Dirk Jan A.R. Moes, Stijn L.W. Koolen, Jesse J. Swen and Hans Gelderblom revised the manuscript. All authors approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare they have no competing interests in the content of this article.

DATA AVAILABILITY STATEMENT

Additional data are available from the corresponding author upon reasonable request.

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REFERENCES

1. Hsiang YH, Liu LF. Identification of mammalian DNA topoisomerase I as an intracellular target of the anticancer drug camptothecin. *Cancer Res*. 1988;48(7):1722-1726.
2. Kingsbury WD, Boehm JC, Jakas DR, et al. Synthesis of water-soluble (aminoalkyl)camptothecin analogues: inhibition of topoisomerase I and antitumor activity. *J Med Chem*. 1991;34(1):98-107. doi:10.1021/jm00105a017
3. Karas S, Innocenti F. All you need to know about UGT1A1 genetic testing for patients treated with irinotecan: a practitioner-friendly guide. *JCO Oncol Pract*. 2022;18(4):270-277. doi:10.1200/OP.21.00624
4. Slatter JG, Schaaf LJ, Sams JP, et al. Pharmacokinetics, metabolism, and excretion of irinotecan (CPT-11) following I.V. infusion of [(14)C] CPT-11 in cancer patients. *Drug Metab Dispos*. 2000;28(4):423-433.
5. College ter Beoordeling van Geneesmiddelen. Irinotecan HCl-trihydraat Summary of product characteristics. Available from: https://www.geneesmiddeleninformatiebank.nl/smpc/h117260_smpc.pdf
6. Lexicomp. Irinotecan (conventional): Drug information. Available from: https://www.uptodate.com/contents/irinotecan-conventional-drug-information?search=irinotecan&selectedTitle=1~146&usage_type=panel&display_rank=1&kp_tab=drug_general&source=panel_search_result#F50990697
7. Venook AP, Enders Klein C, Fleming G, et al. A phase I and pharmacokinetic study of irinotecan in patients with hepatic or renal dysfunction or with prior pelvic radiation: CALGB 9863. *Ann Oncol*. 2003;14(12):1783-1790. doi:10.1093/annonc/mdg493
8. de Jong FA, van der Bol JM, Mathijssen RH, et al. Renal function as a predictor of irinotecan-induced neutropenia. *Clin Pharmacol Ther*. 2008;84(2):254-262. doi:10.1038/sj.clpt.6100513
9. Fujita K, Sunakawa Y, Miwa K, et al. Delayed elimination of SN-38 in cancer patients with severe renal failure. *Drug Metab Dispos*. 2011;39(2):161-164. doi:10.1124/dmd.110.035451
10. de Bruijn P, Verweij J, Loos WJ, Nooter K, Stoter G, Sparreboom A. Determination of irinotecan (CPT-11) and its active metabolite SN-38 in human plasma by reversed-phase high-performance liquid chromatography with fluorescence detection. *J Chromatogr B Biomed Sci Appl*. 1997;698(1–2):277-285. doi:10.1016/S0378-4347(97)00290-9
11. Saltz LB, Kanowitz J, Kemeny NE, et al. Phase I clinical and pharmacokinetic study of irinotecan, fluorouracil, and leucovorin in patients with advanced solid tumors. *J Clin Oncol*. 1996;14(11):2959-2967. doi:10.1200/JCO.1996.14.11.2959
12. Deyme L, Barbolosi D, Gattacceca F. Population pharmacokinetics of FOLFIRINOX: a review of studies and parameters. *Cancer Chemother Pharmacol*. 2019;83(1):27-42. doi:10.1007/s00280-018-3722-5
13. Canal P, Gay C, Dezeuze A, et al. Pharmacokinetics and pharmacodynamics of irinotecan during a phase II clinical trial in colorectal cancer. Pharmacology and molecular mechanisms Group of the European Organization for research and treatment of cancer. *J Clin Oncol*. 1996;14(10):2688-2695. doi:10.1200/JCO.1996.14.10.2688
14. U.S. Food & Drug Administration. Full prescribing information Camptosar 2022. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/020571Orig1s053lbl.pdf
15. Poujol S, Pinguet F, Ychou M, Abderrahim AG, Duffour J, Bressolle FM. A limited sampling strategy to estimate the pharmacokinetic parameters of irinotecan and its active metabolite, SN-38, in patients with metastatic digestive cancer receiving the FOLFIRI regimen. *Oncol Rep*. 2007;18(6):1613-1321. doi:10.3892/or.18.6.1613
16. Poujol S, Pinguet F, Malosse F, et al. Sensitive HPLC-fluorescence method for irinotecan and four major metabolites in human plasma and saliva: application to pharmacokinetic studies. *Clin Chem*. 2003;49(11):1900-1908. doi:10.1373/clinchem.2003.023481
17. Klein CE, Gupta E, Reid JM, et al. Population pharmacokinetic model for irinotecan and two of its metabolites, SN-38 and SN-38

glucuronide. *Clin Pharmacol Ther*. 2002;72(6):638-647. doi:10.1067/mcp.2002.129502

18. Griggs JJ, Bohlke K, Balaban EP, et al. Appropriate systemic therapy dosing for obese adult patients with cancer: ASCO guideline update. *J Clin Oncol*. 2021;39(18):2037-2048. doi:10.1200/JCO.21.00471
19. Innocenti F, Undevia SD, Ramirez J, et al. A phase I trial of pharmacologic modulation of irinotecan with cyclosporine and phenobarbital. *Clin Pharmacol Ther*. 2004;76(5):490-502. doi:10.1016/j.clpt.2004.07.016
20. KNMP Kennisbank. Irinotean UGT1A1 *1/*28-*28/*28 [updated 05-03-2018; cited 2021 10-02-2021]. Available from: https://kennisbank.knmp.nl/article/farmacogenetica/1693-1694.html
21. Kennisbank K. Irinotecan nierfunctie 2011 [cited 2022 04/01/2022]. Available from: https://kennisbank.knmp.nl/article/verminderde_nierfunctie/3452.html
22. Fujita K, Masuo Y, Okumura H, et al. Increased plasma concentrations of unbound SN-38, the active metabolite of irinotecan, in cancer patients with severe renal failure. *Pharm Res*. 2016;33(2):269-282. doi:10.1007/s11095-015-1785-0

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