



# Tailored chemotherapy for colorectal cancer peritoneal metastases based on a drug-screening platform in patient-derived organoids: a case report

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**Background:** Peritoneal metastasis from colorectal cancer (CRC) has limited therapeutic options and poor prognosis. Systemic chemotherapy combined with cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) or pressurized intraperitoneal aerosol chemotherapy (PIPAC) have yielded initial promising results. However, standard local therapies with oxaliplatin and mitomycin are not optimal and a better individualized management of these patients remains as an unmet clinical need. Patient-derived organoid (PDO) technology allows to culture in three dimensions normal and cancer stem cells (CSC) that self-organize in multicellular structures that recapitulates some of the features of the particular organ or tumor of origin, emerging as a promising tool for drug-testing and precision medicine. This technology could improve the efficacy of systemic and intraperitoneal chemotherapy and avoid unnecessary treatments and side effects to the patient.

**Case Description:** Here we report a case of a 45-year-old man with a rectal adenocarcinoma with liver, lymph node and peritoneal metastases. The patient was treated with systemic chemotherapy (FOLFOXIRI plus Bevacizumab) and was subjected to mitomycin-based PIPAC. We generated patient-derived peritoneal carcinomatosis organoids in order to screen the activity of drugs for a personalized treatment. Both 5-FU and SN-38, the active irinotecan derivative, displayed strong cytotoxicity, while the response to oxaliplatin was much lower. Although the development of a colo-cutaneous fistulae prevented from further PIPAC, the patient continued with fluoropyrimidine maintenance treatment based on standard clinical practice and the drug-screening test performed on organoids.

**Conclusions:** Our results suggest that the peritoneal implant shows chemoresistance to oxaliplatin, while it might still be sensitive to irinotecan and 5-FU, which supports a potential benefit of these two drugs in the local and/or systemic treatment of our patient. This study shows the strength of the utility of the establishment of organoids for drug response assays and thus, for the personalized treatment of colorectal carcinomatosis patients.

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## Introduction

Approximately 17% of patients with metastatic colorectal cancer (CRC) have peritoneal carcinomatosis. However, only 2% have the peritoneum as the only site of metastasis (1,2). Peritoneal carcinomatosis in patients with CRC is considered a fatal disease with a median overall survival (OS) of 6–9 months without treatment; however, it could reach 24 months in patients subjected to palliative surgery and systemic treatment. This scenario changed with the development of cytoreductive surgery (CRS), a combination of peritonectomy procedures and multivisceral resection to accomplish the complete removal of visible disease from the abdominal cavity, followed by perfusion of hyperthermic intraperitoneal chemotherapy (HIPEC). Mitomycin or oxaliplatin are the common drugs for HIPEC for colorectal peritoneal metastases and an OS between 42 and 62 months has been reported with this multimodal approach (3). However, these promising results have not been confirmed in the recent PRODIGE7 phase 3 trial (4)

evaluating the role of HIPEC and CRS *vs.* CRS alone, and therefore the study of peritoneal carcinomatosis remains open to the assessment of new drugs and approaches (5). For patients with no possibility of CRS and HIPEC due to high peritoneal carcinomatosis index (PCI) or unresectable disease, a new technique that is increasingly being used in experienced centers is pressurized intraperitoneal aerosol chemotherapy (PIPAC). Increased penetration of chemotherapy in the tumors, reduced toxicity, an important rate of clinical responses, improves quality of life, and prolonged progression free-survival (PFS) have been reported as the most relevant benefits of this technique (6).

Organoids have recently emerged as a suitable platform to test the chemosensitivity of a variety of solid tumor types. They have the potential to avoid futile treatments and harmful side effects for the patients. Studies addressing the use of organoids to treat patients with CRC are emerging in the literature (7). Patients with CRC peritoneal metastases treated with HIPEC or PIPAC represent a unique subgroup of patients in which tumor specimen from the metastatic site can be sampled during the intervention in order to generate organoids and perform the drug-screening analysis.

We report a case of a patient with multiple colorectal peritoneal metastases that was not candidate for CRS and HIPEC due to non-resectable extent of the disease. Following standard FOLFOXIRI plus Bevacizumab treatment, the patient was subjected to palliative PIPAC. Additionally, we generated organoids from a peritoneal implant in order to determine the sensitivity to cytotoxic agents that could guide our therapeutic strategy. This case report is one of the very few studies performed in a patient with early-onset (<50 years) CRC with peritoneal carcinomatosis. We present the following article in accordance with the CARE reporting checklist (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-22-599/rc>).

## Case presentation

In January 2020, a 45-year-old man presented to the emergency room with rectal bleeding and hematuria. A

### Highlight box

#### Key findings

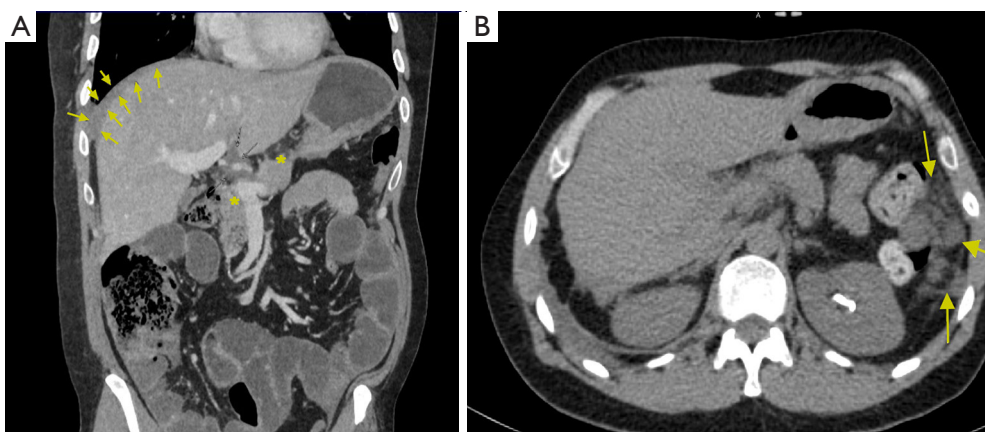
- Drug testing in organoids established from peritoneal implants are useful to select chemotherapeutic agents and avoid unnecessary treatments and side effects for colorectal cancer patients with peritoneal metastases.

#### What is known and what is new?

- Few therapeutic options exist for colorectal cancer patients with peritoneal metastases and commonly used drugs show limited beneficial effects.
- This manuscript adds the utility of patient-derived organoid technology to improve the efficacy of chemotherapy for these patients.

#### What is the implication, and what should change now?

- Organoids constitute a convenient platform for selecting chemotherapeutic drugs. Generating organoids from peritoneal implants and, if possible, from primary tumors is recommendable for a personalized clinical management of colorectal cancer patients with peritoneal metastases.



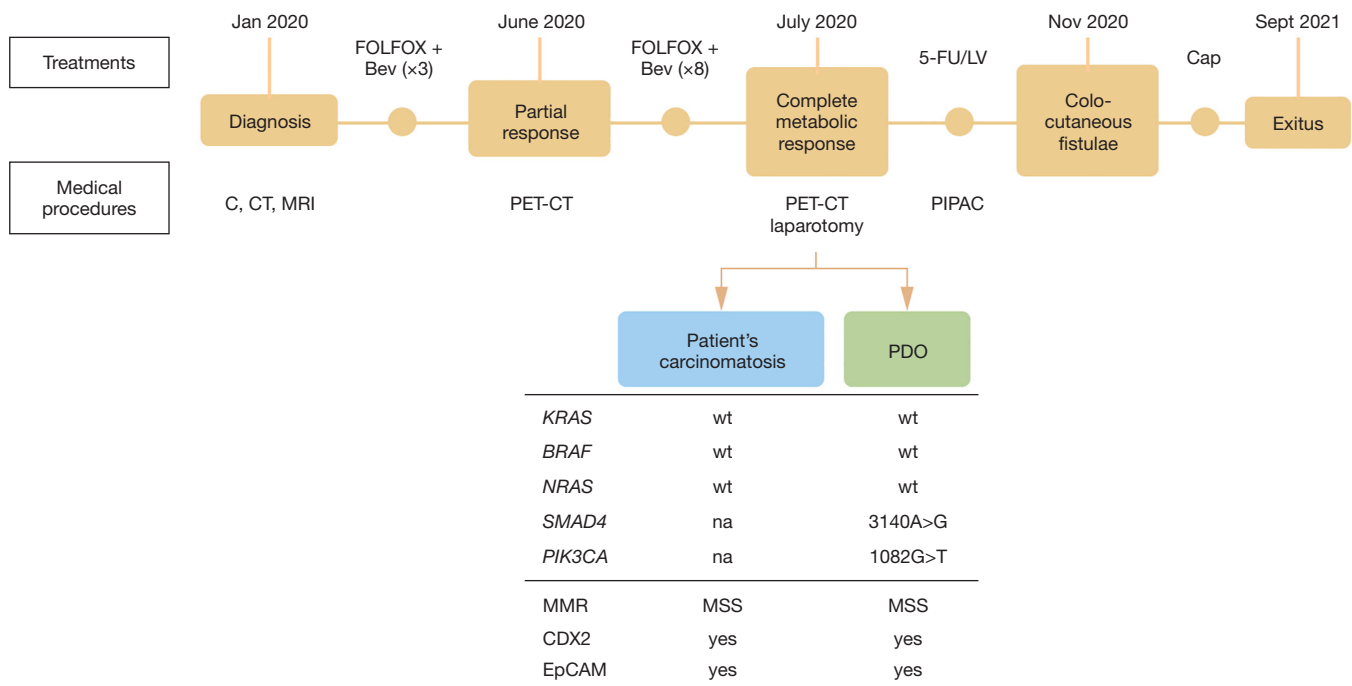
**Figure 1** Representative abdominal CT scan images prior to initiating chemotherapy with mitomycin. Coronal view (A) showing an extensive perihepatic plaque in the subphrenic region (arrows) and a hypodense mass involving the hepatic hilum and tumor nodules at the left anterior subphrenic space (asterisks). Axial view (B) showing major peritoneal nodules at the left parietocolic gutter lateral to the descending colon (arrows). These images are published with the patient's consent. CT, computed tomography.

colonoscopy performed during the diagnostic work-up revealed a histologically-confirmed upper rectal mucinous adenocarcinoma. Clinical staging evaluation with computed tomography (CT) scan and pelvic magnetic resonance imaging (MRI) classified the tumor as cT4b N2 M1 according to the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) v.8, and showed involvement of hepatic hilum and gastrohepatic lymph nodes, and a solitary liver metastasis in segment V (Figure 1). The patient started on systemic chemotherapy with FOLFOXIRI plus Bevacizumab. After 3 cycles, the positron emission tomography (PET)-CT scan showed partial morphologic and metabolic response. In July 2020, after 8 cycles and a complete metabolic response on the subsequent PET-CT scan, an exploratory laparotomy was performed. Multiple peritoneal carcinomatosis were confirmed with a PCI of 27 involving the peritoneal surface of both diaphragms, mesentery, small intestine, gallbladder, hepatic hilum, stomach and omentum. We also found scarce ascites and massive dilatation of the descending colon that required segmental colonic resection and terminal stoma creation. Anatomopathological study of the surgical piece revealed a fragment of the large intestine extensively infiltrated by a mucinous adenocarcinoma. Cytological and molecular studies showed malignant cells of a mucinous phenotype with CDX2 and EpCAM (BerEp4 positivity) expression. The tumor was microsatellite stable (MSS) and biomarker analysis revealed no mutation in *KRAS*, *NRAS* and *BRAF* genes. During laparotomy, after signing an informed

consent, a biopsy of a peritoneal metastasis was obtained to generate patient-derived organoids (PDO) (Figure 2). All procedures performed in the 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). The study was approved by the Ethics Committee of the Hospital Universitario La Paz (No. HULP-PI-3196). Written informed consent was obtained from the closer relative of the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Subsequently, the patient started on maintenance chemotherapy with 5-fluorouracil/leucovorin (5-FU/LV) plus Bevacizumab. In October 2020, the patient underwent a combination treatment protocol with systemic biweekly 5-FU/LV and PIPAC using the standard-of-care chemotherapy (mitomycin at 1.5 mg/m<sup>2</sup>) initially programmed every three months. In order to identify a personalized chemotherapy for administration during the second PIPAC procedure, and to study the putative acquisition of resistance and sensitivity to previously unused drugs, we performed low-throughput drug screening following a previously published protocol of our group that renders high reproducibility (8).

PDO from the peritoneal implant were established following the protocol previously described for primary colorectal tumors (9). The mucinous feature and low cellularity of the implant required the culture in the

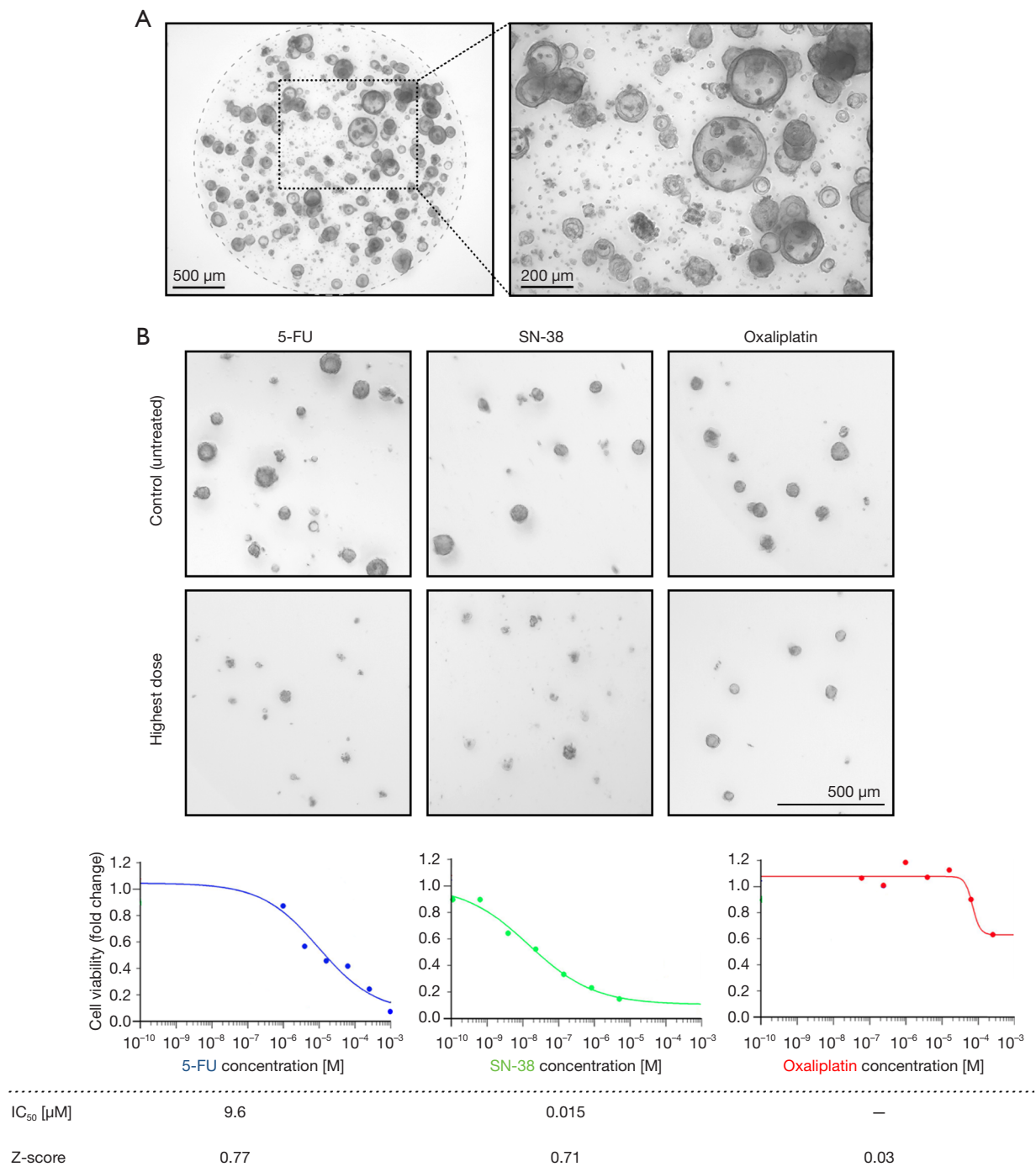


**Figure 2** Patient's clinical history timeline and mutational analysis of carcinomatosis and PDO. Table shows the modification of some genes and protein expression found in the carcinomatosis biopsy and PDO that play a relevant role in CRC. FOLFOX, folinic acid/5-fluorouracil/oxaliplatin/irinotecan; Bev, bevacizumab; 5-FU, 5-fluorouracil; LV, leucovorin; Cap, capecitabine; C, colonoscopy; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; PIPAC, pressurized intraperitoneal aerosol chemotherapy; PDO, patient-derived organoids; wt, wild type; na, not analyzed; MMR, mismatch repair status; MSS, microsatellite stable; CRC, colorectal cancer.

presence of Wnt-conditioned media and R-spondin for optimal growth (spherical) of the organoids (*Figure 3A*). For drug screening analysis, over 10 weeks after surgery, organoids were treated with 5-FU, SN-38 (7-ethyl-10-hydroxycamptothecin, the active metabolite of the DNA topoisomerase I inhibitor irinotecan) or oxaliplatin. After 4 days of treatment, PDO in cultures treated with 5-FU or SN-38 were smaller than those in control untreated cultures, a result that was less evident for cultures treated with oxaliplatin (*Figure 3B*). Cytotoxic activity of the drugs was addressed by measuring the cell viability, and the quality of the assay was checked by analyzing the Z-score, a control parameter to ensure an adequate drug-response validation (10). Under the microscope, 5-FU and SN-38 displayed relatively strong cytotoxicity ( $IC_{50} = 9.6 \mu\text{M}$  and  $IC_{50} = 0.015 \mu\text{M}$ , respectively). Contrarily, the response to oxaliplatin was much lower and no  $IC_{50}$  could be stated (*Figure 3B*). In good agreement with this, the Z-score for the assays using 5-FU and SN-38 were  $>0.5$  (excellent) but only 0.03 in the case of oxaliplatin (*Figure 3B*).

In addition, the PDO mutational analysis using the OncoPrint Comprehensive Assay v3, which contains 161 of the most relevant cancer genes, confirmed the wild-type status of *KRAS*, *NRAS* and *BRAF* previously found in the original surgical biopsy. The assay showed two genes mutated, *PIK3CA* (c.3140A>G, rs121913279) and *SMAD4* (c.1082G>T, rs377767347), which are associated to mucinous histology and aggressiveness of colorectal tumors (11,12) (*Figure 2*). In summary, these data indicate that at least the original implant had acquired resistance to oxaliplatin, while it remained sensitive to irinotecan and 5-FU, which supports therapeutic options based on single or combined treatments with these two drugs.

After the first PIPAC, the patient developed a col-cutaneous fistulae that prevented from further PIPAC treatment. In line with the results of the drug-screening in the PDO and standard clinical practice, the patient resumed systemic 5-FU/LV until February 2021, when the central venous catheter was removed due to a gram-negative bacilli catheter-related infection. The treatment was then switched



**Figure 3** Drug testing assay in patient-derived peritoneal metastasis organoids. (A) Representative phase-contrast images of peritoneal carcinomatosis-derived organoids. (B) Phase-contrast images of organoids after 4-day treatment with the highest dose of 5-FU, SN-38 or oxaliplatin used in the assays (upper panels). Graphs (dose curves) representing cell viability (fold-change *vs.* untreated cultures) of organoid treated with 5-FU (left), SN-38 (middle) and oxaliplatin (right) (lower panels). Phase-contrast images were captured with a DFC550 digital camera (Leica) mounted on an TS100 microscope (Nikon). Scale bars are indicated in the images. IC<sub>50</sub> and Z-score values are indicated for each treatment. 5-FU, 5-fluorouracil; SN-38, 7-ethyl-10-hydroxycamptothecin.

to capecitabine until September 2021, when the patient unfortunately died due to a malignant pseudo-obstruction (Figure 2).

## Discussion

Organoids were first established as a three-dimensional culture system of mouse intestinal stem cells (SC) and their cell progeny and later of human small intestine and colon normal and cancer stem cells (CSC) (13). The CSC model proposes the conversion of tissue-resident SC into CSC as the key event in tumor initiation, progression, recurrence and chemoresistance. On the basis of this model, many laboratories have established PDO from different tumor types to study the cancer biology and in several cases their predictive value in drug sensitivity testing aiming to their use for personalized treatment (14). In line with their original intestinal development, this has been particularly frequent in CRC (7,15). According to the 100% negative predictive value of drug assays in PDO models (16), the lack of effect of oxaliplatin suggested that this drug was not a valid therapeutic option for our patient.

Patients with colorectal peritoneal metastasis have a poor prognosis even when are subjected to HIPEC and/or PIPAC, usually in combination with oxaliplatin or mitomycin. Consequently, novel approaches are urgently needed. Our data show that drug sensitivity can be estimated in organoid cultures from peritoneal metastases of patients at a late stage of the tumorigenic process. This supports the establishment of peritoneal organoids as a useful platform to screen for drug activity and so for personalized treatment of patients with colorectal carcinomatosis. As the subject of this study had been treated with several cycles of chemotherapy, this is particularly promising for treatment-naïve patients or patients treated with fewer cycles of standard chemotherapy. The chance of obtaining beneficial results for the patient is clearly greater if organoids are established at early stages of the carcinomatosis process, when the number of peritoneal implants is low. During the course of our study, a report using PDO from colorectal peritoneal metastases has been published (17). This is a multicenter prospective study aimed at direct personalized therapy that describes the successful generation of organoids from 19 out of 28 patients (68%). In a timeframe comparable to our study (8 weeks), the authors performed genomic and drug profiling that resulted in a treatment change for two patients. Other studies have investigated the response to antitumoral drugs of peritoneal metastasis organoids upon xenotransplantation in mice,

which however loses clinical relevance (18).

As for primary tumors of diverse origin, the generation of organoids from peritoneal metastases needs to be optimized to increase the percentage of success to nearly 100% of normal colon tissue (15). The dependence on Wnt and R-spondin of the organoids in this study agrees with that reported for mucinous primary colorectal tumors by Sato's group (19). It suggests the vulnerability of these Wnt-dependent neoplasias to Wnt inhibitors such as those under clinical development that target porcupine, an acyltransferase enzyme required for the secretion of active Wnt factors. Interestingly, recent data from Clevers' group indicate that 5-FU induces the enrichment of colon CSC via p53-mediated Wnt activation, which contributes to tumor recurrence after treatment (20). This finding supports the use of therapeutic strategies combining 5-FU with Wnt inhibitors, which can be tested in PDO.

## Conclusions

In conclusion, our study is a proof-of-concept strategy that supports the feasibility of the use of PDO for the personalized treatment in colorectal carcinomatosis; however, the precise contribution of organoid technology needs to be addressed in further well-designed prospective clinical studies.

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## Footnote

*Reporting Checklist:* The authors have completed the CARE

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**Conflicts of Interest:** All authors have completed the ICMJE uniform disclosure form (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-22-599/coif>). IP has received a grant from ISCIII-FEDER (Spain; No. ICI20/00057). AB, AM and AFB report that they have received grants from Agencia Estatal de Investigación (Spain; No. PID2019-104867RB100/AEI/10.13039/501100011033), Instituto de Salud Carlos III (ISCIII)-Fondo Europeo de Desarrollo Regional (FEDER) (Spain; No. ICI20/00057) and ISCIII-CIBERONC (Spain; No. CIBERONC/CB16/12/00273). NRS has received two grants from ISCIII-FEDER (Spain; No. ICI20/00057) and ISCIII-CIBERONC (Spain; No. CIBERONC/CB16/12/00398). DV has been awarded with a Río Hortega contract from Sociedad Española de Oncología Médica (SEOM) (Spain) and received a grant from ISCIII-FEDER (Spain; No. ICI20/00057). DCG participates on the Board of Directors of the European Society of Surgical Oncology (ESSO) and the Board of Directors of the Spanish Society of Surgical Oncology (SEQO). The authors have no other 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 the 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). The study was approved by the Ethics Committee of the Hospital Universitario La Paz (No. HULP-PI-3196). Written informed consent was obtained from the closer relative of the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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## References

1. Ripp J, Diab O, Woodroof J, et al. Colorectal Adenocarcinoma Presenting With Isolated Metastasis to the Cortical Bone and Bone Marrow: A Case Report and Review of the Literature. *Clin Colorectal Cancer* 2021;20:e150-4.
2. Franko J, Shi Q, Meyers JP, et al. Prognosis of patients with peritoneal metastatic colorectal cancer given systemic therapy: an analysis of individual patient data from prospective randomised trials from the Analysis and Research in Cancers of the Digestive System (ARCAD) database. *Lancet Oncol* 2016;17:1709-19.
3. Parikh MS, Johnson P, Romanes JP, et al. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Colorectal Peritoneal Metastases: A Systematic Review. *Dis Colon Rectum* 2022;65:16-26.
4. Quénet F, Elias D, Roca L, et al. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy versus cytoreductive surgery alone for colorectal peritoneal metastases (PRODIGE 7): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol* 2021;22:256-66.
5. Klemptner SJ, Ryan DP. HIPEC for colorectal peritoneal metastases. *Lancet Oncol* 2021;22:162-4.
6. Alyami M, Hübner M, Grass F, et al. Pressurised intraperitoneal aerosol chemotherapy: rationale, evidence, and potential indications. *Lancet Oncol* 2019;20:e368-77.
7. Furbo S, Urbano PCM, Raskov HH, et al. Use of Patient-Derived Organoids as a Treatment Selection Model for Colorectal Cancer: A Narrative Review. *Cancers (Basel)* 2022;14:1069.
8. Costales-Carrera A, Fernández-Barral A, Bustamante-Madrid P, et al. Plocabulin Displays Strong Cytotoxic Activity in a Personalized Colon Cancer Patient-Derived 3D Organoid Assay. *Mar Drugs* 2019;17:648.
9. Fernández-Barral A, Costales-Carrera A, Buirra SP, et al. Vitamin D differentially regulates colon stem cells in patient-derived normal and tumor organoids. *FEBS J* 2020;287:53-72.
10. Zhang JH, Chung TD, Oldenburg KR. A Simple Statistical Parameter for Use in Evaluation and Validation of High Throughput Screening Assays. *J Biomol Screen* 1999;4:67-73.
11. Jin J, Shi Y, Zhang S, et al. PIK3CA mutation and clinicopathological features of colorectal cancer: a systematic review and Meta-Analysis. *Acta Oncol*

- 2020;59:66-74.
12. Liao X, Hao Y, Zhang X, et al. Clinicopathological characterization of SMAD4-mutated intestinal adenocarcinomas: A case-control study. *PLoS One* 2019;14:e0212142.
  13. Sato T, Stange DE, Ferrante M, et al. Long-term expansion of epithelial organoids from human colon, adenoma, adenocarcinoma, and Barrett's epithelium. *Gastroenterology* 2011;141:1762-72.
  14. Veninga V, Voest EE. Tumor organoids: Opportunities and challenges to guide precision medicine. *Cancer Cell* 2021;39:1190-201.
  15. Barbáchano A, Fernández-Barral A, Bustamante-Madrid P, et al. Organoids and Colorectal Cancer. *Cancers (Basel)* 2021;13:2657.
  16. Vlachogiannis G, Hedayat S, Vatsiou A, et al. Patient-derived organoids model treatment response of metastatic gastrointestinal cancers. *Science* 2018;359:920-6.
  17. Narasimhan V, Wright JA, Churchill M, et al. Medium-throughput Drug Screening of Patient-derived Organoids from Colorectal Peritoneal Metastases to Direct Personalized Therapy. *Clin Cancer Res* 2020;26:3662-70.
  18. Ubink I, Bolhaqueiro ACF, Elias SG, et al. Organoids from colorectal peritoneal metastases as a platform for improving hyperthermic intraperitoneal chemotherapy. *Br J Surg* 2019;106:1404-14.
  19. Fujii M, Shimokawa M, Date S, et al. A Colorectal Tumor Organoid Library Demonstrates Progressive Loss of Niche Factor Requirements during Tumorigenesis. *Cell Stem Cell* 2016;18:827-38.
  20. Cho YH, Ro EJ, Yoon JS, et al. 5-FU promotes stemness of colorectal cancer via p53-mediated WNT/ $\beta$ -catenin pathway activation. *Nat Commun* 2020;11:5321.

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