

The changing landscape of colorectal peritoneal metastases

Citation for published version (APA):

van de Vlasakker, V. C. J. (2025). *The changing landscape of colorectal peritoneal metastases: the impact of emerging treatment options*. [Doctoral Thesis, Maastricht University]. Maastricht University. <https://doi.org/10.26481/dis.20250321vv>

Document status and date:

Published: 21/03/2025

DOI:

[10.26481/dis.20250321vv](https://doi.org/10.26481/dis.20250321vv)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

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CHAPTER 11

Valorization

Valorization

This thesis describes the continuously changing landscape in the treatment of colorectal peritoneal metastases. It provides a critical analysis of current and emerging treatments of colorectal peritoneal metastases, including cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) and pressurized intra-peritoneal aerosol chemotherapy (PIPAC). Perhaps most importantly, it has tried to do so whilst taking the patient-perspective into account

The scientific impact of this thesis

A notable aspect of this research is the examination of the impact of the PRODIGE 7 trial, which has influenced global clinical practices, particularly in the use of HIPEC following neoadjuvant therapy with oxaliplatin. The study emphasizes the continuing importance of CRS in colorectal peritoneal metastasis treatment and highlights the need for more targeted research to optimize chemotherapeutic agents and delivery methods.

Additionally, the thesis explored the role of PIPAC and INTERACT in palliative care for unresectable colorectal peritoneal metastases. PIPAC has been incorporated in the medical practice in many countries all over the world. Ever since PIPAC was introduced, we have been seeing an almost exponential growth in number of PIPAC centers and PIPACs being performed. However, despite the acceptance of PIPAC in clinical practice, the safety of PIPAC-based therapy remained unclear, as it has not been assessed through prospective trials. With the results of the CRC-PIPAC-I study ePIPAC-OX monotherapy was considered safe. The safety of combinations of PIPAC and systemic therapy remained unclear, but were explored in the CRC-PIPAC-II study. Now that the safety profile of bidirectional therapy has been clarified and deemed acceptable, the road is free for prospective trials to investigate the efficacy of PIPAC-based treatment of colorectal peritoneal metastases. Besides adding to the evidence build-up of PIPAC, another important technique was investigated in this thesis. Chemotherapy can be administered intraperitoneally through a catheter. This catheter based intraperitoneal chemotherapy provides an alternative to PIPAC. The efficacy of this alternative will be explored in the INTERACT-II trial.

Another significant aspect of this thesis is the focus on patient-reported outcomes, particularly in the CRC-PIPAC-II study. This emphasis on patient perspectives in treatment planning and evaluation underscores the shift towards patient-centric outcomes, crucial for developing strategies that are clinically effective and align with patient preferences. Thereby paving the way for comparisons between patient-reported outcomes of different interventions for colorectal

peritoneal metastasis treatment. The thesis also discusses multimodal treatments, including the combination of intraoperative radiotherapy (IORT) with CRS-HIPEC, contributing to a broader understanding of integrating different treatment strategies.

The social impact of this thesis

This thesis explores the social implications of various treatment modalities for colorectal peritoneal metastases, highlighting the evolving landscape of cancer treatment. It discusses the effectiveness and controversies surrounding CRS-HIPEC, newer approaches like PIPAC, and the integration of organoid technology in treatment personalization. Each chapter contributes to the ongoing medical oncology dialogue.

The thesis underlines the role of evidence-based medicine in shaping clinical practices and policies. For instance, the critique of the PRODIGE 7 trial illustrates how scientific findings can prompt changes in medical protocols and impact healthcare economics, such as insurance reimbursement strategies. This has broad implications for patient access to treatment and the sustainability of healthcare systems. The patient-centered approach emphasized in the chapters on patient-reported outcomes, highlights the increasing importance of quality of life in cancer treatment. This aligns with societal values of patient autonomy and personalized care, advocating for treatments that extend life while preserving its quality.

The discussion on organoid technology illustrates a shift towards individualized healthcare and precision medicine. This approach could reduce the physical and financial burdens on patients by avoiding ineffective treatments, also relieving pressure on healthcare systems. Moreover, the thesis addresses the complexity of treatment decision-making in advanced cancer stages, highlighting ethical and societal challenges in balancing aggressive treatment with the risks and focusing on holistic approaches that consider medical outcomes and patient well-being.

The impact on clinical practice

Central to the discourse of the first chapter of this thesis is the debate on CRS-HIPEC reignited by the PRODIGE 7 trial. This study's findings have prompted a reevaluation of HIPEC protocols worldwide, influencing aspects like chemotherapy regimens, HIPEC perfusion times, and overall treatment approach. Despite criticisms of its design, the PRODIGE 7 trial has served as a catalyst for further research, highlighting the need for refined patient selection and optimized treatment protocols.

The exploration of PIPAC in the CRC-PIPAC-II study marks a significant stride in palliative care for patients with extensive colorectal peritoneal metastases. This study, focusing on safety, feasibility, and efficacy, underscores the potential of PIPAC as a complementary therapy,

especially when combined with systemic treatments. The outcomes indicate a favorable safety profile and encouraging response rates, though future studies are essential to establish its definitive role in colorectal peritoneal metastases management. Also, catheter-based intraperitoneal chemotherapy is revisited. The comparative efficacy, patient burden, and cost implications of these approaches remain critical areas for future research.

A novel aspect of this thesis is the integration of intraoperative radiotherapy (IORT) with CRS-HIPEC for locally advanced and recurrent rectal cancers with colorectal peritoneal metastases. The findings suggest that this combination therapy is viable and could be considered in specialized centers for selected patients, offering hope for improved outcomes in this challenging cohort. The thesis also delves into palliative tumor resection, highlighting its potential benefits over systemic therapy alone, despite higher short-term mortality rates. This finding is crucial for patient counseling and decision-making in palliative care settings.

Patient-reported outcomes form a cornerstone of this thesis, underscoring the importance of understanding treatments from the patient's perspective. The thesis advocates for more standardized and timely measurement of patient-reported outcomes, ensuring their integral role in evaluating and guiding clinical practice.