

## Peer Review File

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### Reviewer A

This is an interesting and well written review about the role and future perspective of bidirectional chemotherapy (systemic plus intra-peritoneal) in the treatment of peritoneal metastases. This is a novel, promising, and still understudied option for patients affected by disease entities difficult to treat and with a regarded prognosis. The author of the present paper is a pioneer of the comprehensive treatment of peritoneal surface malignancies. I do believe that this review will be of interest for the readers.

Reply: (Favorable comment) No comment necessary

Changes in text: None

### Reviewer B

The manuscript addresses a clinically significant topic in the field of surgical oncology—peritoneal metastases. It not only traces the historical evolution of treatment strategies but also delves into the challenges faced in managing high-grade malignancies. The inclusion of successful case studies adds value by showcasing real-world applications and successes, particularly in low-grade appendiceal mucinous neoplasms and malignant peritoneal mesothelioma.

#### Potential Benefits to Clinical Practice

1. Improved Treatment Strategies: The manuscript suggests that bidirectional chemotherapy long-term (BCLT) is an essential element for successful treatment outcomes in high-grade malignancies, offering a potential breakthrough in improving patient responses.
2. Enhanced Survival Rates: The inclusion of successful cases, especially in treating malignant peritoneal mesothelioma, highlights the potential for improved survival rates when combining CRS, HIPEC, and long-term bidirectional chemotherapy.
3. Guidance for Neoadjuvant and Adjuvant Chemotherapy: The manuscript provides insights into the optimal administration of intraperitoneal chemotherapy in both neoadjuvant and adjuvant settings. This guidance could impact clinical decision-making and contribute to better patient outcomes.
4. Consideration for Peritoneal Access Devices: By emphasizing the importance of reliable peritoneal access devices, the manuscript addresses a practical aspect that can impact the ease and safety of treatment administration.

In conclusion, the manuscript offers valuable insights into the evolving landscape of peritoneal metastases treatment, suggesting a potential paradigm shift with the incorporation of bidirectional chemotherapy long-term. The practical implications of this research could significantly benefit clinical practice by improving treatment efficacy and patient outcomes in challenging cases of high-grade malignancies.

Reply: (Favorable comment) No comment necessary

Changes in text: None