



## Reply to the Letter to the Editor Regarding “Laparoscopic Hyperthermic Intraperitoneal Chemotherapy is Safe for Patients with Peritoneal Metastases from Gastric Cancer and May Lead to Gastrectomy”

Timothy E. Newhook, MD<sup>1</sup>, and Brian D. Badgwell, MD, MS<sup>1</sup>

The University of Texas MD Anderson Cancer Center, Houston, TX

Dear Editor,

We would like to thank Drs. Eveno, Voron, and Piesson for their interest in our article “Laparoscopic Hyperthermic Intraperitoneal Chemotherapy is Safe for Patients with Peritoneal Metastases from Gastric Cancer and May Lead to Gastrectomy”, which was recently published in *Annals of Surgical Oncology*.<sup>1</sup> In regard to their comments, we appreciate the opportunity to highlight several aspects of our publication, which will help resolve any confusion.

First, we must clarify and re-emphasize the purpose of our study in order to alleviate concerns over conceptual flaws or unsupported conclusions. Following a phase II study of laparoscopic hyperthermic intraperitoneal chemotherapy (LS-HIPEC; NCT 02092298), we sought to report a more thorough evaluation of morbidity and toxicity of LS-HIPEC for patients with low-volume peritoneal disease from gastric adenocarcinoma.<sup>2</sup> Our conclusions therefore only include short-term outcomes such as safety, feasibility of repeated treatment, and the potential for subsequent gastrectomy. Indeed, as reported, LS-HIPEC has low morbidity and toxicity, and may be repeated with a low safety profile for patients in order to potentially clear peritoneal disease, as well as to identify patients with unresponsive peritoneal disease. The conclusion of our report is certainly not that LS-HIPEC is the only pathway

to gastrectomy for our patients with peritoneal metastases from gastric adenocarcinoma, but that this approach, as reported in our phase II trial, is safe and is an option that requires further validation.

Indeed, patients enrolled in the study had radiologically occult peritoneal involvement by gastric adenocarcinoma, either positive cytology or low-volume carcinomatosis. The investigators from University Hospital Lille nicely document the criticisms of laparoscopic detection of peritoneal disease or staging, and for that very reason we did not include the Peritoneal Cancer Index (PCI) in our study. Moreover, calculation of a PCI is even less reliable after repeated LS-HIPEC procedures. As all patients had radiographically occult disease, we were confident their PCI scores would be uniformly low. Lastly, we do not advocate use of the term ‘localized gastric peritoneal metastases’, however, we do agree that HIPEC in general is most beneficial in low-volume disease.

The criticism regarding the lack of HIPEC at gastrectomy for these patients is well taken, and, as discussed in our manuscript, we are incorporating this into an investigation of neoadjuvant LS-HIPEC on a pathway to gastrectomy. In this phase II clinical trial that we are currently completing (NCT02891447), patients undergo at least one LS-HIPEC followed by cytoreduction, gastrectomy, and HIPEC. We are excited to report these results in the very near future.

Patients with metastatic gastric adenocarcinoma have traditionally only been offered systemic chemotherapy or supportive care, however these are exciting times as investigators around the world push to develop innovative approaches to this deadly disease. Because of this, prospective clinical trials of treatment directed at

peritoneal disease are imperative for patients with gastric adenocarcinoma, and we greatly applaud Drs. Eveno, Voron, and Piessen's ongoing work with pressurized intraperitoneal aerosol chemotherapy (PIPAC) as yet another novel approach to what was a disease with few treatment options. We, along with patients with metastatic gastric adenocarcinoma everywhere, eagerly await their phase II trial results.

## REFERENCES

1. Newhook TE, Agnes A, Blum M, et al. Laparoscopic hyperthermic intraperitoneal chemotherapy is safe for patients with peritoneal metastases from gastric cancer and may lead to gastrectomy. *Ann Surg Oncol.* 2019;26(5):1394–1400.
2. Badgwell B, Blum M, Das P, et al. Phase II trial of laparoscopic hyperthermic intraperitoneal chemoperfusion for peritoneal carcinomatosis or positive peritoneal cytology in patients with gastric adenocarcinoma. *Ann Surg Oncol.* 2017; 24(11):3338–44.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.