

Review

A comprehensive treatment for peritoneal metastases from gastric cancer with curative intent



Y. Yonemura<sup>a,b,\*</sup>, E. Canbay<sup>b</sup>, Y. Li<sup>c</sup>, F. Coccolini<sup>d</sup>, O. Glehen<sup>e</sup>,  
P.H. Sugarbaker<sup>f</sup>, D. Morris<sup>g</sup>, B. Moran<sup>h</sup>, S. Gonzalez-Moreno<sup>i</sup>,  
M. Deraco<sup>j</sup>, P. Piso<sup>k</sup>, D. Elias<sup>l</sup>, D. Batlett<sup>m</sup>, H. Ishibashi<sup>a</sup>,  
A. Mizumoto<sup>a</sup>, V. Verwaal<sup>n</sup>, H. Mahtem<sup>o</sup>

<sup>a</sup> Peritoneal Surface Malignancy Center, Kishiwada Tokushukai Hospital, Kusatsu General Hospital, Kishiwada, Shiga, Japan

<sup>b</sup> NPO to Support Peritoneal Surface Malignancy Treatment, Oosaka, 600 8189, Japan

<sup>c</sup> Department of Peritoneal Surface Oncology, Beijing Shijitan Hospital of Capital Medical University, Beijing, 100038, China

<sup>d</sup> General Surgery Papa Giovanni XXIII Hospital, Bergamo, Italy

<sup>e</sup> Département de Chirurgie Générale, Centre Hospitalier Lyon-Sud Hospices Civils de Lyon, Université Lyon, 69495, France

<sup>f</sup> Center of Gastrointestinal Malignancies, Program in Peritoneal Surface Malignancies, MedStar Washington Hospital Center, Washington, DC, 20010, USA

<sup>g</sup> Department of Surgery, St George Hospital, University of New South Wales, Australia

<sup>h</sup> Peritoneal Malignancy Institute Basingstoke, Hampshire Hospitals Foundation Trust, Adelmaston Road, Basingstoke RG24 9NA, UK

<sup>i</sup> Department of Surgical Oncology, Peritoneal Surface Oncology Program, MD Anderson Cancer Center, Madrid, Spain

<sup>j</sup> National Cancer Institute of Milan, Italy

<sup>k</sup> Krankenhaus Barmherzige Brieder, Teaching Hospital of the University of Regensburg, Regensburg, Germany

<sup>l</sup> Département de Chirurgie Générale, Institut Gustave Roussy, Villejuif, Cedex, France

<sup>m</sup> Division of Surgical Oncology, Hillman Cancer Center, 5115 Centre Ave, Pittsburgh, PA, 15232, USA

<sup>n</sup> Oncologisch GE Chirurg, Catharina, Ziekenhuis Eindhoven, The Netherlands

<sup>o</sup> Department of Surgical Sciences, Uppsala University, Övriga Samarbeten, Akademiska Sjukhuset, Ing 70 1 Tr, 751 85, Uppsala, Sweden

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Abstract

Recently, Peritoneal Surface Oncology Group International (PSOGI) developed a novel comprehensive treatment consisting of cytoreductive surgery (CRS) and perioperative chemotherapy (POC) for the treatment of peritoneal metastases (PM) from gastric cancer with curative intent. This article reviews the results of this treatment and verifies its indication.

In this strategy, peritoneal cancer index (PCI) is determined by laparoscopy, and a peritoneal port is placed. Neoadjuvant bidirectional intraperitoneal/systemic chemotherapy (NIPS) is performed for 3 cycles, and then laparotomy is performed. Cytoreductive surgery with peritonectomy procedures and hyperthermic intraperitoneal chemoperfusion (HIPEC) are performed.

Multivariate analyses showed that completeness of cytoreduction, pathologic response to NIPS and PCI level and cytologic status after NIPS, as independent prognostic factors. PCI less than cut-off level after NIPS, negative cytology after NIPS, and positive response to NIPS

\* Corresponding author. Peritoneal Surface Malignancy Center, Kishiwada Tokushukai Hospital, Kusatsu General Hospital, Kishiwada, Shiga, Japan. Tel.: +81 (0) 75 746 5895; fax: +81 (0) 75 746 5895.

E-mail address: [y.yonemura@coda.ocn.ne.jp](mailto:y.yonemura@coda.ocn.ne.jp) (Y. Yonemura).

were identified as the indications for comprehensive treatment. Patients who hold these criteria should be considered as the candidates for CRS and HIPEC.

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## Introduction

Even though, gastrectomy combined with D2 lymph node dissection remains the international standard to improve survival in advanced stages of gastric cancer, management of peritoneal metastases (PM) from gastric cancer still needs to be optimized worldwide.

PM are detected in 30% of patients with advanced gastric cancer. Until the early 1990s, PM has been considered as terminal stage of the diseases, and patients with PM were treated with palliative systemic chemotherapy or best supportive care. In the late 1990s, selected patients with PM were restaged and recategorized as local disease limited to the peritoneal cavity.

Since the first meeting of the Peritoneal Surface Oncology Group International (PSOGI) in 1998 in London, PSOGI proposed a novel comprehensive treatment strategy consisting of cytoreductive surgery (CRS) and perioperative chemotherapy (POC) in the treatment of PM originated from intra-abdominal malignancies.<sup>1,2</sup> Cytoreductive surgery with peritonectomy procedures and/or systemic chemotherapy alone are ineffective in patients with PM from gastric cancer. In contrast, the comprehensive treatment consisting of intraperitoneal chemotherapy applications with aggressive surgery improves long-term survival, because invisible metastasis left behind even complete cytoreduction could be achieved. Complete cytoreduction is essential to obtain maximum effect of hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) early postoperative intraperitoneal chemotherapy (EPIC) and/or postoperative systemic/intraperitoneal chemotherapy.<sup>3–8</sup> This comprehensive treatment became a gold standard of care with cure in selected patients with PM from colorectal cancer and pseudomyxoma peritonei.<sup>9–11</sup> The English National Institute for Health and Clinical Excellence (NICE) reviewed all published case series of patients with colorectal peritoneal metastases, with an overall survival rate of 19%, and concluded that this comprehensive treatment with cytoreductive surgery and HIPEC is an appropriate strategy for selected colorectal-cancer patients with PM.<sup>12</sup>

Malignant potential is higher in gastric cancer compared with colorectal cancer or pseudomyxoma peritonei, and patients with gastric cancer often develop PM with lymph node and/or hematogenous metastases. In contrast to the treatment for pseudomyxoma peritonei, the treatment for gastric cancer takes into consideration to control of distant

metastasis other than PM. Accordingly, the effects of the comprehensive treatment for gastric cancer-patients with PM remains controversial, and the treatment is still considered to be an experimental one.<sup>9</sup>

This review verifies the survival effects and selection criteria of the comprehensive treatment for gastric cancer patients with PM. All the authors gained approval to perform the comprehensive treatment for peritoneal metastases from the Ethical Committee of their respective hospitals and institutions. In our institution, approval was got at 2008, No. is H-20-09.

## Outline of the comprehensive treatment for gastric cancer with PM

As shown in Fig. 1, the comprehensive treatment consists of laparoscopic evaluation of the tumor load in the peritoneal cavity, perioperative chemotherapy (POC) and CRS. POC includes laparoscopic hyperthermic intraperitoneal chemotherapy (LHIPEC), neoadjuvant intraperitoneal/systemic chemotherapy (NIPS), hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC), extensive intraoperative peritoneal lavage (EIPL), early postoperative intraperitoneal chemotherapy (EPIC) and late postoperative systemic chemotherapy.<sup>9</sup>

Diagnostic laparoscopy is performed to determine the peritoneal cancer index (PCI), and is followed by histologic and cytologic analysis.<sup>13,17</sup>

By the late 2000s, CRS and HIPEC were performed following diagnostic laparotomy.<sup>3–5</sup> However, complete cytoreduction is difficult when the PCI score is high or there is extensive involvement of the small bowel mesentery. To reduce the PCI and to preserve an intact peritoneal surface as much as possible, neoadjuvant LHIPEC and neoadjuvant intraperitoneal and systemic induction chemotherapy (NIPS) were developed.

Just after laparoscopic diagnosis, extensive intraoperative peritoneal lavage (EIPL) using physiological saline delivered by a HIPEC machine was performed to wash away non-adherent peritoneal cancer cells.<sup>16</sup> LHIPEC was done using 4 L of saline with anti-cancer drugs heated to 42–43 °C.<sup>17</sup> After LHIPEC, a peritoneal port system was introduced into the lower abdomen and the tip was placed in the *cul-de-sac*. NIPS was performed through a port system starting 2 weeks after LHIPEC, and patients were treated with 3 cycles of NIPS.<sup>18–20</sup>

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