



Gwenaël Ferron<sup>1</sup>, Amélie Gesson-Paute<sup>1</sup>, Laurence Gladieff<sup>2</sup>, Fabienne Thomas<sup>3, 4</sup>, Etienne Chatelut<sup>3, 4</sup>, Denis Querleu<sup>1, 4</sup>

1- Department of Surgical Oncology, Institut Claudius Regaud, 20-24 Rue du Pont Pierre, 31052 Toulouse Cedex, France.

2- Department of Medical Oncology, Institut Claudius Regaud, 20-24 Rue du Pont Pierre, 31052 Toulouse Cedex, France.

3- EA3035, Institut Claudius Regaud, 20-24 Rue du Pont Pierre, 31052 Toulouse Cedex, France.

4- Paul Sabatier University, University of Toulouse

**Laparoscopically assisted Heated Intra-operative Intraperitoneal Chemotherapy (HIPEC): Technical aspect and pharmacokinetics data**

**Abstract**

*Objective.* Hyperthermic intraperitoneal chemotherapy (HIPEC) is being evaluated for patients with minimal residual or no residual disease after complete cytoreductive surgery. An experimental study on the porcine model was carried out in order to demonstrate the feasibility of the laparoscopic approach and to compare oxaliplatin pharmacokinetics during a laparoscopic assisted versus the “coliseum” technique for HIPEC.

*Methods.* In the first step, the feasibility of the peritonectomy procedure followed by HIPEC was evaluated in five adult pigs. In the second step, 10 adult pigs were selected to receive laparoscopic assisted HIPEC procedure and 10 pigs were selected for the standard HIPEC in laparotomy. The HIPEC procedure was based on 460 mg/m<sup>2</sup> of oxaliplatin for 30 minutes with a heated perfusate at 41-43°C. The HIPEC drains were placed in the upper and lower quadrants of the abdomen. Peritoneal fluid and blood samples were collected every ten minutes during the procedure and the pharmacokinetics of oxaliplatin was studied.

*Results.* For the first step, the procedure was successfully completed with an adequate intrabdominal temperature and distribution. For the second step, no major technical problems were encountered. At the end of the HIPEC, 41.5% of the chemotherapy was absorbed in the laparoscopic group compared to 33.4% in the laparotomy group ( $p = 0.0543$ ). The peritoneal oxaliplatin half-life ( $T_{1/2}$ ) was significantly shorter in the laparoscopic procedure (median value of 37.5 min versus 59.3 min,  $p = 0.02$ ). The area under the curve ratio for peritoneal / plasma reflects a faster oxaliplatin absorption through the peritoneal barrier in the laparoscopic procedure (ratio: 16.4 in the laparoscopic group versus 28.1 in the laparotomy group,  $p = 0.03$ ).

*Conclusion.* This study confirms the technical feasibility and the reliability of the laparoscopic approach for HIPEC, and improves the understanding of peritoneal drug absorption. Oxaliplatin absorption is significantly higher with laparoscopy, regarding time course in the peritoneal perfusion. Clinical application in selected patients may be expected after further experimental investigation designed to define the adequate drug dosage.