Pleura and Peritoneum 2018; 1, Special Suppl, pp sA6–sA463, September 2018 • Copyright © 2018 Walter de Gruyter GmbH, Berlin / Boston

## I.k) Peritoneal carcinomatosis from ovarian carcinoma free papers

### CO40

### A PHASE I TRIAL ASSESSING THE FEASIBILITY OF DEBULKING SURGERY FOLLOWED BY CISPLATIN-BASED HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY AND INTRAPERITONEAL BI-MONTHLY NIVOLUMAB IN ADVANCED OVARIAN CARCINOMA. THE ICONIC STUDY

**G. Freyer, C. Sajous, B. You, J. Lopez, D. Dayde, N. Medeghri, G. Witold, O. Glehen**

**Lyon University Hospital Cancer Institute - Lyon (France)**

#### Objectives

Patients with non resectable stage III-IV ovarian cancer have a poor prognosis despite neo-adjuvant chemotherapy followed by CC-0 surgery.
In advanced ovarian cancer, a Dutch team (Van Driel et al., N Engl J Med, 2018) recently reported the results of a phase 3 trial showing that debulking surgery+cisplatin-based HIPEC significantly increased PFS & OS as compared to surgery alone.
Immune checkpoint inhibitors have produced modest results in ovarian cancer, due to their moderate mutational load. A recent study showed that tumor-infiltrating lymphocytes (TILs) increased significantly from 20% to 30% after chemotherapy.
Surgery and HIPEC are likely to increase the tumor-antigen expression and the mutational load. Moreover, IP infusion will potentially enhance the immune response. Indeed some recent papers indicate that the peritoneum could be considered as a lymphoid organ, involving “milky spots”, thus able to produce a better immune response when immunotherapy is given by IP route rather than IV route.
We therefore propose to assess the feasibility of extensive debulking surgery and HIPEC followed by IP nivolumab dose escalation in patients with advanced ovarian carcinoma.

#### Methods

We will also perform ancillary studies, including:
- assessment of germline and somatic BRCA mutations
- Determination of HRD phenotype by NGS
- Quantification of tumor mutational burden on ctDNA
- Characterization of immune response in the tumor by Nanostring immuno-oncology panel

Eligible patients: Patients with advanced ovarian carcinoma in relapse, with potentially resectable peritoneal carcinomatosis.

Primary objective: To assess the tolerance of extensive debulking surgery and HIPEC followed by IP nivolumab, through a phase I study including patients at 3 dose-levels

Phase I trial: Patients will be treated according to three dose-levels of nivolumab, starting 5 to 7 days after surgery+HIPEC, through an IP catheter:

Level 1: 0.5 mg/kg IP infusion, repeated every 2 weeks for 4 infusions
Level 2: 1 mg/kg Id.
Level 3: 3 mg/kg Id.

Pleura and Peritoneum 2018; 1, Special Suppl, pp sA6–sA463, September 2018 • Copyright © 2018 Walter de Gruyter GmbH, Berlin / Boston

There will be no intra-patient dose-escalation. 6 patients will be included at each nivolumab dose-level.

The treatment will be judged feasible if limiting toxicity occurs in 1 patient or none. A cohort expansion of 12 patients will be proposed at the highest dose level

**Results**

Expected impacts: In case of favorable efficacy/tolerance ratio, other clinical studies will be proposed, in combination with IV chemotherapy and PARP inhibitors.

Pleura and Peritoneum 2018; 1, Special Suppl, pp sA6–sA463, September 2018 • Copyright © 2018 Walter de Gruyter GmbH, Berlin / Boston

## I.k) Peritoneal carcinomatosis from ovarian carcinoma free papers

### CO41

### MORBIDITY AND MORTALITY AFTER A FIRST CYTOREDUCTION WITH OR WITHOUT HIPEC IN OVARIAN CANCER IIIC-IV. PRELIMINARY RESULTS OF THE PROSPECTIVE AND RANDOMIZED CLINICAL TRIAL

**A. González Gil, Á.J. Gómez Ruiz, E. Gil Gómez, J. Gil Martínez, P. Cascales Campos**

**Carcinomatosis Unit, Department of Surgery, Hospital Universitario Virgen De La Arrixaca - Murcia (Spain)**

#### Objectives

To analyze the preliminary results regarding postoperative complications of the prospective and randomized clinical trial NCT-02328716 that evaluates the role of HIPEC in patients with peritoneal carcinomatosis of ovarian, tubal and primary peritoneal origin.

#### Methods

From March 2012 to April 2017, a total of 57 patients were evaluated and nine were excluded. The main reason of exclusion was the finding of unresectable disease during the surgery. We performed a simple blind computer randomization in two arms: administration or not of HIPEC (Cisplatino 75 mgr/$m^2$) after complete debulking.

#### Results

48 patients were included; 22 were treated with cytoreduction alone and 26 with HIPEC. The median age was 58 (67–77), PCI was 11 (4–18), and we found no statistically significant differences between the two groups. Blood transfusion was required in 15 patients (34.1%), and the average stay in recovery room was 1.4 days, with no differences between the two groups. Grade IV postoperative complications have been detected in a total of 24 patients (50%), 13 in the group without HIPEC and 11 in the group with HIPEC, 9 of them had serious complications III-V (18%), and they were the cause of the death in two patients (4.1%), one in each arm.

#### Conclusion

The administration of HIPEC with Cisplatin after complete cytoreduction in peritoneal carcinomatosis of ovarian, tubal, or primary peritoneal origin does not increase postoperative morbidity and mortality.

Pleura and Peritoneum 2018; 1, Special Suppl, pp sA6–sA463, September 2018 • Copyright © 2018 Walter de Gruyter GmbH, Berlin / Boston

## I.k) Peritoneal carcinomatosis from ovarian carcinoma free papers

### CO42

### TIME TO ADJUVANT CHEMOTHERAPY AND IMPACT ON SURVIVAL IN ADVANCED OVARIAN MALIGNANCIES: INDIAN SOCIETY OF PERITONEAL SURFACE MALIGNANCY (ISPSM) COLLABORATIVE GROUP STUDY.

**S. Zaveri[1], S. Somashekhar[1], K. Ashwin[1], C. Rohit Kumar[2], Y. Ramya[3]**

**[1]CONSULTANT SURGICAL ONCOLOGY - Bangalore (India), [2]SPECIALIST SURGICAL ONCOLOGY - Bangalore (India), [3]RESIDENT SURGICAL ONCOLOGY - Bangalore (India)**

**Objectives**

Optimal cytoreduction is the important predictor of survival outcome in patients with advanced primary epithelial ovarian carcinoma. The adjuvant chemotherapy has role in delaying and preventing the systemic relapse. However the relationship between initiation time of adjuvant chemotherapy in ovarian cancer and prognosis has remained controversial. This study was done to determine whether time from optimal cytoreductive surgery (CRS) to initiation of adjuvant chemotherapy impacts survival in advanced ovarian carcinoma.

**Methods**

Total of 164 patients with primary advanced epithelial ovarian carcinoma (Stage IIIc or selected Stage IV), who underwent optimal cytoreduction (either as upfront or interval) were included in the study. The analysis of interval between surgery and adjuvant chemotherapy and survival outcome was done.

**Results**

This was a prospective study, done in patients undergoing CRS. CRS with intraperitoneal chemotherapy either in the form of intraperitoneal port (IP) or hyperthermic intraperitoneal chemotherapy (HIPEC) was done in 118 patients (43 + 75) and CRS alone was one in 46 patients. The median interval between optimal cytoreduction and initiation of adjuvant chemotherapy was 35 days for the cohort (32 days in the CRS alone group, 34 days in CRS+IP port group and 41 days in CRS+HIPEC group). Median disease free interval (DFS) was 28, 36 and 33 months respectively in the three groups. Delay in chemotherapy, as defined by more than 40 days had significant impact on DFS in CRS alone group (36 months vs 17 months: $p = 0.02$), but had no impact in the patient who were receiving intraperitoneal chemotherapy. No statistically significant difference in the overall survival (OS) was observed in patients whose adjuvant chemotherapy was delayed (88 months versus 71 months, $p = 0.49$).

**Conclusion**

Even though there was no statistically significant difference between the median time to adjuvant chemotherapy with respect to 3 groups, delay in adjuvant chemotherapy had significant impact of DFS on patient who had not received any form of IP therapy. Whenever feasible, neoadjuvant chemotherapy and some for of IP chemotherapy should be given to advanced ovarian malignancies. However, randomised control trials are needed to define the exact impact of day in adjuvant chemotherapy in patients undergoing optimal cytoreduction.

Pleura and Peritoneum 2018; 1, Special Suppl, pp sA6–sA463, September 2018 • Copyright © 2018 Walter de Gruyter GmbH, Berlin / Boston

## I.k) Peritoneal carcinomatosis from ovarian carcinoma free papers

### CO43

### A COMPARISON OF OUTCOMES FOLLOWING TOTAL AND SELECTIVE PERITONECTOMY PERFORMED AT THE TIME OF INTERVAL CYTOREDUCTIVE SURGERY FOR ADVANCED SEROUS EPITHELIAL OVARIAN, FALLOPIAN TUBE AND PRIMARY PERITONEAL CANCER- A STUDY BY INDEPSO

**A. Bhatt[1], S. Sinukumar[2], S. Zaveri[3], F. Rajan[4], D. Damodaran[5], P. Kammer[6], S. Mehta[7]**

**[1]Zydus Hospital - Ahmedabad (India), [2]Jehangir Hospital - Pune (India), [3]Manipal Hospital - Bangalore (India), [4]Kovai Medical Center - Coimbatore (India), [5]MVR Cancer Center and Research Institute - Calicut (India), [6]Global Hospital - Hyderabad (India), [7]Saifee Hospital - Mumbai (India)**

#### Objectives

To compare clinical outcomes following total and selective peritonectomy performed during interval cytoreductive surgery (CRS) for advanced (stage III C and IVA) serous epithelial ovarian, fallopian tube and primary peritoneal cancer.

#### Methods

A retrospective analysis of patients undergoing interval CRS was performed. Data was collected from members of the Indian Network for development of peritoneal surface oncology (INDEPSO). Surgeons classified the extent of peritoneal resection as:

1. Total parietal peritonectomy (TPP) comprising of a total parietal peritonectomy including a total omentectomy. TPP was performed in order to obtain complete tumor removal or to reduce the risk of peritoneal recurrence in patients with limited disease and/or remove areas affected prior to the administration of systemic chemotherapy.
2. Selective parietal peritonectomy (SPP) comprising of removal of areas of residual disease following NACT.

The impact of the extent of peritonectomy on clinical outcomes was evaluated.

Pleura and Peritoneum 2018; 1, Special Suppl, pp sA6–sA463, September 2018 • Copyright © 2018 Walter de Gruyter GmbH, Berlin / Boston

## Results

From Jan 2013 to Dec 2017, 79 patients underwent CRS with/without intraperitoneal chemotherapy (IPC) (HIPEC-36, EPIC-22, no IPC- 21) at 5 Indian centers. 30 patients underwent TPP and 49 SPP. The median PCI was 14 (range 2–28) for TPP and 8 (range 2–30) for SPP group. A higher proportion of patients undergoing TPP had a PCI > 10 ($p < 0.001$). All patients undergoing EPIC were in the SPP group. The 90-day grade 3–4 morbidity was 16.6% in the TPP and 12.2% in the SPP group ($p = 0.58$) and in hospital mortality occurred in 1 and 3 patients in the two groups respectively ($p = 0.58$). The median ICU stay and hospital stay was 3 and 15 days and 1 and 13 days respectively in the TPP and SPP groups. A CC-0/1 resection was obtained in 29/30 undergoing TPP and in all patients undergoing SPP. All except 1 patient in the SPR group started adjuvant chemotherapy within 8 weeks of surgery. At a median follow-up of 18 months, the median disease free survival (DFS) was 37 months for SPP and 33 months for TPP ($p = 0.47$). The median overall survival (OS) was not reached in both groups. The 3-year OS was 95% in the TPP and 70.8% in the SPP group ($p = 0.06$). Grade 3–4 morbidity was an independent predictor of an inferior OS.

## Conclusion

TPP did not significantly increase the perioperative morbidity and mortality or the hospital stay as compared to SPP. There was a trend towards a increased OS in the TPP group. A longer follow-up is needed determine if there an oncological benefit of performing a TPP.