Review of: "Resectable Pancreatic Cancer With Peritoneal Metastases: Is Cytoreduction Combined With Hipec Effective and When?"

Annalice Gandini[1]

1 Hôpital Européen Georges-Pompidou

Potential competing interests: No potential competing interests to declare.

I thank the authors for the conduction of this study, which investigates an interesting unmet need in a pathology that is still orphan of practice-changing treatments.

However, I think that there are some critical issues that need to be addressed in order to better interpret this work.

- Age should be expressed as the median.
- Between the inclusion period 2011-2018, how were patients selected? Do they represent all the patients with pancreatic cancer and peritoneal metastases who respected inclusion criteria and were referred to your center, or were they selected anyhow?
- Two patients had peritoneal carcinosis after a prior ovarian cancer, which relapses mostly on the peritoneum. No histological diagnosis was performed to better define the diagnosis. What was the histology on the surgical piece after CRS? You should not include these patients in the analysis if the diagnosis is not confirmed, and moreover, when the diagnosis is not clear, it is better to perform assessments before treatment.
- Three patients were treated with a second CRS + HIPEC after recurrence. You cannot analyze them as separate patients since the prognosis at diagnosis and at recurrence is not the same.
- Patients with liver metastases should be better defined.
- I have interpreted that some patients' primary tumors were previously resected and others at the same time of CRS; could you please define it? And which characteristics did the patients' primary tumors have? TNM, margins? Was neoadjuvant/adjuvant chemotherapy administered?
- How did you choose between the two different HIPEC regimens (gem or cis/mit)?
- After CRS + HIPEC, no literature data on systemic treatments are available since this combination of treatment is not standard. However, there could be a biological rationale for administering neoadjuvant chemotherapy, in order to give a systemic control of the disease (which is highly aggressive), defining the biological chemo-sensibility of the tumor, and evaluating clinical evolution. About adjuvant therapy, gemcitabine is not the standard, but FOLFIRINOX should be used if the patient is fit. However, there are no certain data to support this in resected advanced disease.
- It is reported that tumoral markers were assessed, but they are not presented, as well as the number of lymph nodes positive/resected.
- Toxicity should be better specified. However, a 20% rate of postoperative mortality (2/10 patients) suggests a need to

better select patients, excluding fragile patients who are more likely to have severe consequences.

- What about subsequent treatments? In order to evaluate survival, they should be noted.
- I think that results should be written more clearly, and a table including the correlation of patients' characteristics and outcomes would be appreciated to simplify comprehension.

Kind regards,