

ANSWER TO THE FIRST REVIEWER

The manuscript by Guion-Dusserre and colleagues analyzes FOLFIRINOX in elderly patients with pancreatic (PDAC) and colorectal (CRC) cancer. This retrospective study included patients over 70 years and 52 patients were treated by FOLFIRINOX, 34 had CRC and 18 had PDAC. The authors show that FOLFIRINOX toxicities were manageable and that median survival rates were comparably good. This is a well written and clinical interesting and relevant study. There are some comments/concerns that should be addressed :

1. *Can the authors give a rough estimate of how many patients of the same age group during the study period received other chemotherapies or best supportive care only? I.e. what percentage of this population are candidates for FOLFIRINOX ?*

During the same period (X -X months X patients of more than 70 years were treated for a metastatic colorectal cancer and X for a metastatic pancreatic cancer. In this populations X and Y% were treated with FOLFIRINOX based chemotherapy. We observed that patients with pancreatic cancer were more frequently treated with FOLFIRINOX that colorectal cancer because there is few therapeutic option in the context of pancreatic cancer .

2. *It is difficult to compare different PDAC or CRC cohorts regarding survival. I would not think that this is stage matched; thus, I would tone down the conclusion about better survival?*

We agree that comparing PDAC and CRC is not appropriate and does not correspond to the purpose of our study. So, we made two separate curves with overall survival for pancreatic and colorectal cancer.

Concerning time under treatment, we removed the statistical comparison and give only descriptive results for each cancer.

3. *Some French words appear in the figures. ? Some typos and grammatical errors, e.g. "commun", "initially had a reduced dose initially" should be corrected.*

We made the appropriate correction.

ANSWER TO THE SECOND REVIEWER

FOLFIRINOX in elderly patients with pancreatic or colorectal cancer. Tolerance and efficacy
Guion-Dusserre JF et al. In this article, authors showed that efficacy and safety of
FOLFIRINOX treatment for elderly patients with colorectal or pancreatic cancer. They
concluded FOLFIRINOX is a feasible treatment in elderly patients with manageable toxicity
and same efficacy with that of younger population. The paper included important points and I
agree that it is important to discuss about the safety and efficacy of recent strong
chemotherapy regimen for elderly patients in this era. However there are several points which
they should consider. Major points are two.

1. One is that there are no comparison with the younger patients. They compared the safety and efficacy data of elderly patients with reported data in literature. They should show the comparison with younger patients' data by pair matched study or something else. This comparison will strengthen their conclusion.

We did not add a control cohort of younger patients, the purpose of our study being to make a descriptive analysis of a geriatric population.

Although, when we compared our result to main studies with FOLFIRINOX, including younger patients, we observe similar rates of toxicity.

For example, concerning pancreatic cancer, in the study "FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. Conroy T. et al, *The New England Journal of Medicine*", main severe toxicities (grade 3-4) were neutropenia (45.7%), fatigue (23.6%), vomiting (14.5%), and diarrhea (12.7%) in FOLFIRINOX group.

For colorectal cancer, in the study "Phase III trial of infusional fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI) compared with infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) as first-line treatment for metastatic colorectal cancer: the Gruppo Oncologico Nord Ovest. Falcone A. et al, *J Clin Oncol*", main severe toxicities (grade 3-4) were neutropenia (50%), diarrhea (20.5%) and vomiting (7%) in FOLFIRINOX group.

As a reminder, in our study, concerning severe toxicity (grade 3-4), 32.7% of patients had neutropenia, 25% had diarrhea, 9.6% had vomiting and asthenia.

So, as mentioned in our conclusion, except diarrhea which is more frequent in our geriatric population, other toxicities seems to be similar to main studies with FOLFIRINOX in both cancer, including younger patients.

- 2. Another one is that why they used 70 years old as cut off. Also they did not describe the reason of cut off.*

We used 70 years old as cut off, because on retrospective evidence, the incidence of geriatric problems increases sharply after 70 years old in oncologic population. Almost, main oncogeriatric studies, with recommendations from the SIOG, are using the age of 70 years old as cut off for geriatric assessment and developing geriatric screening tools.

We add this explanation in the part “material and methods” with references.

- 3. In addition, they did not show the age distribution of patients. Average and Median age was about 75 years old. This suggested that most of the patients were age under 80. However, in clinical setting, treatment decision of patients over 80 are the problem. They should show the stratified analysis by dividing patients with over and under 80.*

We add a representation of age distribution in the manuscript (Table 1).

Only 9 patients were aged more than 80 years old.

We performed subgroup analysis to compare patients older than 80 years with younger. We add 2 tables with univariate and multivariate analysis by subgroup of population, for time under treatment and overall survival.

The results didn't show statistically significant difference in subgroups for age with 80 years old as cut off.

Almost, statistical results seems more interesting using a cut off as 75 years old.

However, our study staff isn't enough important to make subgroup analysis.

- 4. They should also show the difference between colorectal and pancreatic cancer patients, especially regarding the safety.*

As it is mentioned in our discussion, the primary objective of our study was to evaluate the feasibility of FOLFIRINOX in an elderly population, whatever the primary tumor, and not making a comparison between two clearly different type of cancer.

Almost there were only 18 patients with pancreatic cancer in the study.

Once again, our staff wasn't enough important to make a good comparison.