

Dear reviewers,

Thank you for your comments. We have revised the paper as you requested.

Reviewer #2544032: The manuscript gives a well-written overview of current data, supporting active chemotherapy against pancreatic cancer, even when second line therapy is needed. The chemo resistance of this cancer has generated limited investigation of second line regimens, and the present manuscript is therefore an important contribution to less nihilistic treatment attitudes. The treatment algorithm in figure 1, relating first and second line therapy for patient subgroups, is clarifying. Core tip The self-evident facts of the present manuscript should be omitted. The evidence base of OS-benefits from active treatment even in second line should be underlined. Abstract Even if there is no standard second line therapy, there are numerous options which should be optimized in each case. This seems to be the main message of the manuscript.

Response: We are glad to know that you appreciate our paper. We agree with your comment, therefore we have modified the core tip and the conclusion adding in this one a comment about the importance of second line therapy in OS.

Reviewer # 1832: The manuscript by Francesca Aroldi reviews second line treatment options for pancreatic cancer. This is a well written analysis of the (sparse) data on second line therapy for pancreatic cancer. The relevant literature is cited and discussed. This is a concise up-to-date review

Response: thank you for your comment, we are glad to have your approval.

Reviewer # 227509: This manuscript describes treatment for pancreatic cancer in terms of the second line therapy. However, there are few novel findings and the contents of this review article are limited.

Response: thank you for your comment but unfortunately in the last years only few novel findings had been discovered in this setting. We hope we 'll be able to discuss

about many new drugs in the next few years. However some news are reported about olaparib and we have added them in the text

Best regards.

Alberto Zaniboni