Peer-review

Reviewer 1

There are some misspellings in the text

A: Thanks for the reviewer's hard work and we are appreciated for your advice, we have revised the manuscript and correct all the misspellings.

Reviewer 2

Overall taking to account the aim of the study, one would expect control group with treatment and to compare the results to the group without treatment. I am not sure if selection of 76 subjects without complete comparison is sufficiently informative- this may be improved by providing data from other subjecst/subgroups.

A: Thanks for the reviewer's hard work and we are appreciated for your advice. The control group with treatment is a good suggest, and we also considered about it at the time of study design, but we did not add it in this article for two reasons. As we all know NET is heterogeneous and it is not easy to find a control group with treatment has the similar baseline characteristics as the group without treatment. And the second reason is that this is retrospective study and medicine treatment for patients were non-interventional, so patients with different characteristics received individual treatment, and different treatment (SSA, targeted therapy and chemotherapy) have different PFS and efficacy. it will be difficult to make comparison in different treatment groups with different prognostic characteristics. So in this study we simplified the question and considered with one-arm study.

-The language needs to be revised in particular abstract is insufficient.

A: Thanks for the reviewer's advice, we have revised the manuscript and sufficient the abstract.

-Introduction is rather simple and relative superficial. The authors do not explain why the select only one subgroup of NENs and comparison data are not provided.

A: Thanks for the reviewer's hard work and we are appreciated for your advice. The control group with treatment is a good suggest, and we also considered about it at the time of study design, but we did not add it in this article for two reasons. As we all know NET is heterogeneous and it is not easy to find a control group with treatment has the similar baseline characteristics as the group without treatment. And the second reason is that this is retrospective study and medicine treatment for patients were non-interventional, so patients with different characteristics received individual treatment, and different treatment (SSA, targeted therapy and chemotherapy) have different PFS and efficacy. it will be difficult to make comparison in different treatment groups with different prognostic characteristics. So in this study we simplified the question and considered with one-arm study.

-Looking at the prognostic curves it is clear that active surveillance is only an option if no other therapy is available. Over 50% of patients had a progressive disease during the first 12 months. 90.7 had a progressive disease; therefore current conclusions are not truly supported by the data especially due to missing control cohort.

A: Thanks for the reviewer's hard work and we are appreciated for your advice. In our study, as the patients treated with active surveillance was not restricted with certain characteristics, we can analyze which group of patients can get benefit from active surveillance. And we found that over half of patients had a progressive disease during the first year. And for patients with favorable risk factors, the median surveillance time is 2 years, so we make the conclusion as "active surveillance might be safe for metastatic NF-PanNET patients with favorable risk factors". And indeed there is no control cohort, so we added the conclusion "further studies with larger sample size and control cohort might be needed".

-Besides progression it is also important to present the overall survival data as well.

A: Thanks for the reviewer's hard work and we are appreciated for your advice. We have described the OS data in results "outcomes of NF-PanNET patients under surveillance". 10 patients refused treatments after PD because of personal or financial problems, and 4 of them died because of disease progression. The median OS for these 10 untreated patients was not reached (range: 10-113months). The median OS for the whole cohort was also not reached.

-This was a retrospective study back to 1998. How is it possible that the authors obtained any written informed consent?

A: Thanks for the reviewer's hard work. Although some patients diagnosed at 1998, these patients make follow-up at our hospital every year and can be contacted in outpatient, so when we designed the study and evaluated their information, we asked these patients for agreement to sign the consent.

-The authors do not explain why only 76 patients received active surveillance. What about the remaining cohort subjects? What was the selection? What was the decision? Is there any comparison cohort/subgroup?

A: Thanks for the reviewer's hard work. We have explained the reason in results"patients characteristics" part. The decision to choose active surveillance in 66 patients was made jointly by the multidisciplinary team. While 10 out 76 patients choose active surveillance because they refused medical treatment as financial burden.

The remaining cohort is these receive treatment, which is not fulfilling the inclusion criteria so we did not analyze it in the article.

And the selection is explained in methods "patient selection" part. All patients had asymptomatic NF-PanNET with liver metastasis, and these who did not receive treatment were selected in the study.

And in the results part we set three subgroups based on different prognostic predictors, the patients with no risk factors, patients with one risk factor and patients with two/more factors. And we found that The mTTP in patients with no risk factors was 24 months, which was significantly longer than that in patients with one (10months) or more (6 months) risk factors.

-The authors may need to explain what is R0 resection was- only PanNET or also liver metastasis?

A: Thanks for the reviewer's suggestion. We have added the description of R0 resection in results "PanNET patients with stage IV disease, or patients with stage I-III had disease recurrence after R0 resection". In the previous description, "PanNET patients with stage IV disease or recurrence after R0 resection" means two groups of patients, one group is patients with stage IV at the diagnosis, and they are not considered R0 resection. The other group is patients without metastasis at the diagnosis, and they have recurrence after R0 resection of primary site.

The authors describe that the median active surveillance was 14 months. What were the factors influencing this time point?

A: Thanks for the reviewer's hard work. The factors influencing the time point is the time to disease prognosis and time to patients begin with treatment.

-No information is provided regarding the time point of patient's inclusion (it was 20 year study so in particular difference due to inclusion time point may be present).

A: Thanks for the reviewer's hard work. The patients' diagnosis time was 1998-2018. And as this is the retrospective study, the time point of patients inclusion is when we started to evaluate all the patients information after we designed the study. We evaluated patients who fulfill the selection criteria in these 20 years.