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Dear Editor,

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We would like to thank you and reviewers for the helpful and constructive comments and suggestions on our manuscript entitled 'NAD(P)H:quinone oxidoreductase 1 is overexpressed in gastric cancer and associated with adjuvant chemotherapy and survival'.

Our responses to the reviewers' comments are listed below:

Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)
Conclusion: Minor revision

Specific Comments to Authors:
1. The Title "NAD(P)H:quinone oxidoreductase 1 is overexpressed in gastric cancer and associated with adjuvant chemotherapy and survival" The authors may change the title as the part "associated with adjuvant chemotherapy and survival" is not giving much meaning.

We thank the reviewer for the suggestion. The title has been revised as "NAD(P)H: quinone oxidoreductase 1 is overexpressed in gastric cancer and associated with outcome of adjuvant chemotherapy".

2. The authors aim to investigate the role of NQO1 in cancer DEVELOPMENT and PROGRESSION, and to explore the potential of NQO1 to serve as a prognostic biomarker and therapeutic target. But the results, discussion and conclusion are entirely concentrated on the Prognostic aspect only. The authors should modify this aspect as the AIM of the study is not completely reflected in the results, conclusion. Otherwise this is a very good paper and CAN BE CONSIDERED FOR PUBLICATION. Regards

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The AIM has been revised: To investigate the clinical association of NQO1 protein expression in gastric cancer and to explore the potential of NQO1 to serve as a prognostic biomarker and therapeutic target.

Reviewer #2:
Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision

Specific Comments to Authors: This study entitled 'NAD(P)H:quinone oxidoreductase 1 is overexpressed in gastric cancer and associated with adjuvant chemotherapy and survival' is a retrospective analysis that focused on investigating the associations between NQO1 protein expression status and responses to 5-FU-based adjuvant chemotherapy in patients with GC and thereby determine the potential of NQO1 to serve as a prognostic biomarker and therapeutic target. Although this study contains merit for advancing the therapy of gastric cancer, there are several problems that should be revised before publishing. Major 1. Authors should describe the procedure characteristic regarding to lymph node dissection in operation. Did every patient undergo D2 dissection in the gastrectomy?

We thank the reviewer for the precious comment. Yes, all the patients underwent the D2 dissection in the gastrectomy.

2. Were there any patients who underwent chemoradiation therapy in the participants?

We already provided the information None of the patients received chemotherapy.

3. Authors should clarify the proportion of the patients who had HER2 expression. It is possible to confirm HER2 expression by using paraffin-embedded tissue.

All the HER2 expression were determined using paraffin-embedded tissue in our previous study (https://pubmed.ncbi.nlm.nih.gov/25128063/). In the patients enrolled in this study, 17 samples were determined as strong (3+), 45 samples were determined as intermediate (2+), 49

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samples were determined as weak (1+), 37 samples were determined as negative, and 27 samples HER2 information were missing.

4. This study only analyzed the patients with adjuvant using 5-FU plus cisplatin. Although fluorinated pyrimidine has been the key drug for GC adjuvant, other effective add on therapy (fluorinated pyrimidine plus OX, DTX plus S1, SOX) are accepted in daily practice. Therefore, it seems to be difficult to conclude that GC patients with NQO1 overexpression may be suitable for adjuvant chemotherapy by just only this study's result.

We thank the reviewer for the suggestions. We agree that this result may not be sufficient to draw the conclusion that NQO1 overexpression maybe suitable for adjuvant chemotherapy, which require validations. However, as we mentioned in the manuscript, pyrimidine and platinum are the main chemo-reagents for the adjuvant chemotherapy of GC patients. And we identified NQO1 overexpression as a poor prognostic factor of GC patients who received adjuvant chemotherapy, suggesting NQO1 may associated with chemo-sensitivity, though further validation is warranted.

We look forward to hearing from you.

Sincerely yours,
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