Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 78099

Title: Long survival after PD-1 inhibitor and paclitaxel in an advanced intrahepatic cholangiocarcinoma patient: case report and literature review

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05234825

Position: Peer Reviewer

Academic degree: MD

Professional title: Staff Physician

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: China

Manuscript submission date: 2022-06-23

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-07-28 08:01

Reviewer performed review: 2022-07-30 01:13

Review time: 1 Day and 17 Hours

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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The author described a case of intrahepatic cholangiocarcinoma with germline BRCA1 mutation who had no response to first line chemotherapy GemCis but had complete response to paclitaxel + anti-PD-1. The case presentation was clear and summary of literature was up to date. Some minor revision will make it better. 1. Please add more information about initial surgical plan in a patient with stage IV intrahepatic cholangiocarcinoma. In my opinion, the lung metastasis was too tiny (according to Figure 2B) to confirm it was true metastasis or non-specific nodule. Surgical resection based on initial CT scan

was reasonable but the author had better to give more information about initial decision making process. 2. The initial course was confusing. "The intrahepatic mass was subsequently excised." But according to the subsequent description and image, the tumor excision was only planned but not actually excised, right? 3. The case had image evaluation after 2 cycles of first line GemCis, approximately only 6 weeks. Is image evaluation every 6 weeks a routine practice in your institute or due to clinical signs of progression? Please describe in the case presentation section. 4. I will recommend the author to add a line graph of the dynamic change of CA199 in Figure 1A, so that readers will have more insight about the clinical course. 5. Please give a brief information about the NGS assay. Is that an approved panel or home-made panel?

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Reviewer's code: 05575380

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2022-06-23

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-08-12 15:19

Reviewer performed review: 2022-08-12 15:27

Review time: 1 Hour

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SPECIFIC COMMENTS TO AUTHORS

Dear Editor, thank you so much for inviting me to revise this manuscript about biliary tract cancer. The overall limited survival benefit provided by systemic therapies in this setting, with most patients reporting a survival rate of less than a year from the moment of diagnosis, has led to notable efforts towards the identification of novel targets and agents that could modify the natural history of these aggressive hepatobiliary malignancies. In fact, the massive use of next-generation sequencing (NGS) has led to the identification of previously unknown molecular features of CCA, including the presence of specific genetic

aberrations that have been suggested to be distinctive features of iCCA and eCCA. Among these druggable alterations, fibroblast growth factor receptor (FGFR)2 gene fusions and rearrangements, isocitrate dehydrogenase-1 (IDH-1) mutations, and BRAF mutations have been widely described in CCA patients, reporting important differences between iCCA and eCCA. In addition, immunotherapy has recently shown interesting results, as witnessed by the TOPAZ-1 trial, which has the potential to "open" the immunotherapy era for BTC. Based on these premises, the paper addresses a timely topic. The manuscript is quite well written and organized. Tables are comprehensive and clear. The introduction explains in a clear and coherent manner the background of this study. We suggest the following modifications: •

Although the authors correctly included important papers in this setting, we believe the background of emerging medical treatments as well as locoregional therapies should be better discussed and some recently published papers should be added, only for a matter of consistency (PMID: 32396398 ; PMID: 33611090 ; PMID: 32824407; PMID: 33645367) • In addition, we believe some issues deserve further discussion. In everyday clinical practice, we know that the pathologic confirmation of diagnosis is necessary before any non-surgical treatment and can be challenging in BTC, particularly in patients

affected by primary sclerosing cholangitis and biliary strictures. In fact, decisions to undertake biopsies should follow a multidisciplinary discussion, especially in potentially resectable tumors. Moreover, endoscopic imaging and tissue sampling are useful but, sadly, biopsy samples are often inadequate for molecular profiling, and in addition, tissue sampling has reported high specificity but low sensitivity in diagnosis of malignant biliary strictures. Finally, the highly desmoplastic nature of BTC limits the accuracy of cytological and pathological approaches. On the basis of these premises, in this scenario, it is urgent to develop new strategies in order to anticipate the diagnosis identifying BTC at an early, resectable stage, and to obtain sufficient material with which to perform genomic analysis. Among these strategies, liquid biopsy has received growing attention over the years, given the promising applications in cancer patients. More specifically, several studies have shown the potential role of liquid biopsy, and the authors should discuss this point, also reporting recent studies in this setting (doi: 10.3390/cells9030721; doi: 10.21873/cgp.20203). Moreover, the timeline should be enlarged and the type of systemic treatment specified, in order to help readability. The discussion should be also expanded, and a more personal perspective included. - Reference number 17 out of context. I suggest to remove it. In addition, the sentence "while the BRCA1

positivity was the rationale for taxane-based therapy" is wrong. Platinum-based chemo has a stronger rationale, why the authors talk about taxane? Please revise accordingly. We believe that major revisions are needed. The main strengths of this paper are that it addresses an interesting and very timely question and provides clear answers, with some limitations. We suggest and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points and should add some details and studies, as suggested.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 05575380

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2022-06-23

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2022-09-02 15:19

Reviewer performed review: 2022-09-02 15:20

Review time: 1 Hour

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SPECIFIC COMMENTS TO AUTHORS

The authors addressed all the queries and issues we raised. Acceptance.