

ESPS Peer-review Report**Name of Journal:** World Journal of Gastrointestinal Surgery**ESPS Manuscript NO:** 9613**Title:** Downstaging and Resection Following Neoadjuvant Therapy for Fibrolamellar Hepatocellular Carcinoma**Reviewer code:** 02594499**Science editor:** Xiu-Xia Song**Date sent for review:** 2014-02-20 17:40**Date reviewed:** 2014-03-07 07:50

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

This is an interesting case of a young female with an initially considered unresectable FLHCC. Significant tumor downstaging with GEMOX allowed surgical resection. Even if not completely novel this case report highlights the potential effect of GEMOX as neoadjuvant treatment for FLHCC. Nevertheless, a ten months follow up period might be too short time to evaluate the efficacy of the treatment. Follow up protocol should be reported.

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Title: Downstaging and Resection Following Neoadjuvant Therapy for Fibrolamellar Hepatocellular Carcinoma

Reviewer code: 00910039

Science editor: Xiu-Xia Song

Date sent for review: 2014-02-20 17:40

Date reviewed: 2014-03-14 05:46

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Peer review: World Journal of Gastrointestinal Surgery "Downstaging and Resection after Neoadjuvant Therapy for Fibrolamellar Hepatocellular Carcinoma" by Fonseca GM et al. 1. General: This manuscript reports the case of a 35 year old female patient with fibrolamellar hepatocellular carcinoma (FLHCC). The tumor was initially classified as unresectable and the patient received gemcitabine in combination with oxaliplatin (GemOx). Staging by magnetic resonance tomography after 11 months of chemotherapy revealed a tumor regression, allowing for tumour resection and lymphadenectomy of the hepatic hilum. Ten months after surgery the patient showed no signs of disease recurrence. Given the rareness of FLHCC and the lack of established chemotherapy regimens for patients initially not eligible for curative resection or liver transplantation, this is an interesting report. Together with a previous report on a patient who also received curative-intended surgery after downstaging with GemOx, this report might provide guidance for further investigation of potential treatment regimens in FLHCC. However there are several concerns regarding this report: Major comments: A. Introduction: None B. Case Report 1.) Alpha-Feto Protein in this patient is reported to be highly elevated (44.395 ng/ml) which is uncommon for FLHCC. This fact should at least be discussed. 2.) Which stainings were used to confirm histopathological diagnosis of FLHCC? (please also provide a reference for the staining used). Where were the specimens evaluated? (reference center?) 3.) The authors report that "33 cycles" of GemOx were applied over a period of 11 months. No dosage or chemotherapy scheme is provided. In Hepatocellular carcinoma (HCC) two slightly different dosages of GemOx have been evaluated, however for both regimens the cycles were

repeated after 2 weeks, which is not consistent with 33 cycles in 11 months. The authors should specify dosage and schedule of the regimen used here. 3.) How was the patient classified as non-resectable? Why was liver transplantation not an option? 5.) What were the staging intervals? How was staging done (MRI or CT)? How was follow up done? How was absence of recurrence of disease 10 months after surgery evaluated? 6.) The authors state that "histological examination confirmed fibrolamellar hepatocellular with free margins". Please specify if margins were microscopically or macroscopically tumor free i.e. R0 or R1. C. Discussion 1.) Although the discussion section provides interesting information, several statements here are unspecific and at least partly not accurate. The discussion section should therefore be thoroughly rewritten giving accurate and clear information. Examples are as follows: 1.1) The authors state that for unresectable FLHCC "all known options did not show effectiveness". This is a very broad and unspecific statement that the authors do not support by a reference. (For example in Kaseb et al. Prognostic Indicators and Treatment Outcome in 94 Cases of Fibrolamellar Hepatocellular Carcinoma, Oncology 2013 Kaplan-Meier Curves for advanced FLHCC receiving chemotherapy are provided). Further the authors claim that no data on responses to different chemotherapy regimens was given in Reference 1 (Ang et al. 2013). However Ang et al. give detailed information in the text on responses to several chemotherapy regimes. This statement should therefore be corrected and information from other sources (e.g. Kaseb et al.) should be included. 1.2) It is unclear what "and evaluation of new drugs or combination treatments in clinical trials were tested" means. 1.3) The authors state that "The gemcitabine plus oxaliplatin regimen appeared to be the most promising, based on its lack of renal and hepatic toxicity in cirrhotic patients". It is unclear whether this refers to HCC treatment in general or treatment of this specific patient. It should be discussed why GemOx was use