

January 10th, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15605-review.doc).

Title: Optimum chemotherapy in the management of advanced biliary tract cancer

Author: Marwan Ghosn, Hampig Raphael Kourie, Elie El Rassy, Ralph Chebib, Fadi El Karak, Colette Hanna, Dolly Nasr

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15605

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

1. Please correct introduction as Klatskin Tumors are also extrahepatic cc.
 - a. The adjustment has been made
2. Shortly discuss also the value of surgery for this malignancy.
 - a. A short discussion has been added: "in the particular case of Klatskin tumors, aggressive surgery may be performed in a curative perspective. Effectively, liver and portal vein resections are recommended in selected patients in advanced Klatskin tumors."
3. Please revise also your conclusion and change some words to delete misunderstanding. And describe more in detail your recommendations for individualised chemotherapy
 - a. According to the reviewer's comment, the following corrections were made to the conclusion:

"Despite numerous trials evaluating the chemotherapeutical regimens and targeted therapies in BTC the association of gemcitabine and cisplatin remains the gold standard in the treatment of BTC. At this time, OS is less than one year and enrolling patients in clinical trials is also recommended. New strategies should be adopted in the management of BTC. Perhaps, as the molecular biology and genetic origin of this cancer improve and become completely elucidated, personalized therapy would achieve a better outcome. Subsequently, individualized treatment can be established according to molecular profiling and epigenetics with targeted and

immunotherapy.”

4. What is your definition of advanced tumor in this specific situation? Metastatic disease or local advanced tumor (T3/4 and/or Klatskin Type III/IV)?
 - a. The following clarifications were added to the text:
 - i. “advanced stage defined as unresectable disease (metastatic or locally advanced”
 - ii. “advanced (defined as stage IVA)”
 - iii. “metastatic (defined as stage IVB)”

3 References and type settings were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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