

## Point by point responses

June 1, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 18546-revised.doc).

Title: The role of transarterial chemoembolization in the treatment of hepatocellular carcinoma

**Author:** Kichang Han, Jin Hyoung Kim

**Name of Journal:** *World Journal of Gastroenterology*

ESPS Manuscript NO: 18546

### Editor's comments to the authors

1. Please provide language a certificate letter from a professional English language editing company

**Response:** In response to this comment, we received the English editing service and attached the language editing certificate.

2. The title must be informative, specific, and brief (Title should be no more than 10~12 words/60 bytes. Please revise it). Words should be chosen carefully for retrieval purposes. All nonfunctional words should be deleted, such as 'the', 'studies on', 'observations of', and 'roles of', etc.

**Response:** In response to this comment, we changed the title to Transarterial Chemoembolization in Hepatocellular Carcinoma Treatment: Barcelona Clinic Liver Cancer Staging System.

3. Audio core tip request

**Response:** In response to this comment, the first author made an MP3 audio file describing our core tip.

4. Please add PubMed citation numbers and DOI citation to the reference list and

list all authors. Please revise throughout.

**Response:** In response to this comment, we added the PubMed citation numbers and DOI citation to the references.

5. Not the figure, it should be the table.

Response: In response to this comment, we change the figure to the table.

#### **Reviewer 18546's comment to the authors.**

1. There are two types of TACE: one is Lip-TACE so-called conventional TACE that is performed largely in Asian countries and the other TACE using drug eluting beads (DEB) so-called DEB-TACE that is performed largely in European countries and the United states. Thus the author should state their characteristics and differences in this article.

**Response:** In response to this comment, we have stated the characteristics and differences between Lipiodol TACE and DEB-TACE and they are highlighted gray in the manuscript.

**Revision in the manuscript:** According to the BCLC system, TACE is the standard of care for both intermediate HCC. As described in the BCLC guidelines, this stratum of patients shows a survival benefit from TACE, which will be discussed later. However, in clinical practice, TACE has been widely used for different stages of HCC that extend beyond those recommended in the BCLC system (early or even advanced HCC). Irrespective of the heterogeneity in TACE techniques, chemotherapeutic agents, and treatment intervals, the term “conventional TACE” generally refers to the use of Lipiodol as an embolic material. For conventional TACE, various anticancer drugs are vigorously mixed with Lipiodol, which functions as a microvessel embolic agent, a chemotherapeutic agent carrier, and an augments of antitumor effects by promoting efflux into the portal vein<sup>[13]</sup>. As an alternative to conventional Lipiodol-based regimens, non-resorbable microspheres loaded with cytotoxic drugs can be administered intra-arterially to HCC patients. These particles are termed “drug-eluting beads” and were developed to sequester doxorubicin from solution and release it in a sustained manner. It has been reported that the amount of

chemotherapeutic agents that reach systemic circulation compared with Lipiodol-based TACE can be substantially reduced, thus sharply increasing the local drug concentration<sup>[14]</sup>.

The phase II PRECISION V trial compared doxorubicin-loaded DEBs with conventional TACE and demonstrated a significant reduction in liver toxicity and drug-related adverse events. However, to date, no prospective study has yet reported a significant difference in clinical efficacy between Lipiodol-based TACE and DEB TACE<sup>[15]</sup>.

Herein, we review the clinical implications of conventional TACE in each BCLC category.

Thank you for giving us an opportunity to revise our article. We believe that your comments have substantially improved the quality of our review article.

Sincerely yours,

*Jin Hyoung Kim*

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