

Peer Review File

Article information: <https://dx.doi.org/10.21037/jgo-24-71>

Reviewer A

Comment 1: Really interesting protocol, well-structured and described.

Reply 1: Thank you for taking valuable time to review our proposed manuscript and your encouraging feedback regarding our protocol.

Changes in the text: None.

Reviewer B

Comment 2: I read with great interest the study protocol for combining NHS76 with HAIP and systemic chemotherapy for patients with unresectable CRLM and ICCA. The protocol is well designed, with excellent correlative end points which will aid in understanding mechanisms of treatment effect and resistance. This protocol will provide excellent rationale for phase III comparison should it prove to meet the primary and secondary objectives.

Reply 2: Thank you for taking valuable time to review our proposed manuscript and your encouraging feedback regarding our protocol. We look forward to the results of this early phase clinical trial and hold similar hope for correlative scientific endpoints and future phase III comparisons if appropriate.

Changes in the text: None.

Reviewer C

1. Please provide the full name of “RECIST” in the Abstract and “IL-12” “IgG1” “ECOG” “CT” “MRI” “PBMcs” in the main text. Please also check through your article to make sure **all** the abbreviated terms have been defined when they **FIRST** appear in the Abstract and the main text.

We have provided the full name of the following abbreviated terms below as suggested in this editorial revision where they first appear in both the abstract and main text:

RECIST – Response Evaluation Criteria in Solid Tumors (page 3, line 55)

IL-12 – Interleukin-12 (page 4, line 75)

IgG1 – Immunoglobulin G1 (page 5, line 89)

ECOG – Eastern Cooperative Oncology Group (page 7, line 150)

CT – Computed Tomography (page 9, line 196)

MRI – Magnetic Resonance Imaging (page 9, lines 196-197)

PBMCs – Peripheral Blood Mononuclear Cells (page 10, 211)

We have checked the remainder of the manuscript text and have confirmed that all abbreviated terms have been defined when they first appear in both the abstract and main text.

2. Please add citation for the guideline in the manuscript.

be evaluated for response at eight-week intervals with CT and MRI. Response and progression will be evaluated using the revised Response Evaluation Criteria in Solid Tumors (RECIST) guideline (Version 1.1). Secondary objectives include hepatic progression-free survival (PFS), extra-hepatic PFS, and overa

We have added the appropriate citation for the RECIST v1.1 guidelines to the manuscript. This is reflected as reference number 26 (page 9, line 198; page 15, lines 330-332).

3. Please add citations for the mentioned “studies”.

“Pre-clinical studies, including colorectal cancer cell line xenografts, have demonstrated superior tumor volume growth reduction by NHS76 antibody fused to murine IL-12 (NHS-muIL12) in comparison to recombinant murine IL-12 (rmuIL-12).”

We have updated the text to include both reference 12 and an additional reference (reference 13) comparing NHS-muIL12 to rmu-IL12. These references have been added to the end of the first sentence referencing multiple studies, while only reference 12 applies to the following sentence regarding CD8 depletion and rechallenge (page 5, line 94; page 14, lines 294-296).