

## **Responses for Reviewers' Comments**

### **Reviewer 1**

Many thanks for highly encouraging comments of the first reviewer.

### **Reviewer 2**

**Q1: Line 113, Please provide more description or information on high fatality of pregnant women related to acute HEV infection. Readers might wonder the possible causes or mechanism of high fatality in them.**

**Response:** The causes and possible mechanisms of high rate of mortality in pregnant women infected by HEV-1 are described in this revised manuscript (please see line 281-310)

**Q2: Please, provide current status of HEV vaccine in the manuscript.**

**Response:** The current status of HEV vaccine (Hecolin) was outlined briefly (Please see line 616).

**Q3: Please make sure the definition of ACLF used in this manuscript. The definition of ACLF differ between Asian society and Western ones.**

**Response:** The European definition, proposed by the European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF) consortium was used in this manuscript and relevant publication about this definition was cited in the main text (please see line 325)

**Q4: Please classify each treatment according to the type of illness, acute hepatitis E, ACLF, chronic hepatitis E, other extrahepatic complications.**

**Response:** Treatment section divided into three distinct subheadings consisting of ‘Treatment of acute HEV infection and ACLF’, ‘Treatment of chronic HEV infection’, and ‘Treatment of extrahepatic complications’ as consistent with your suggestion.

### **Reviewer 3**

**Q1: The manuscript has suffered a great deal of incomplete or partial information, especially in HEV molecular biology; sometimes fragmented statements with hop-on/hop-off problem.**

**Response:** The HEV molecular biology is outside the scope of this review. Therefore, we have provided only the brief information on HEV molecular biology necessary to understand other parts of this article, and refer readers to other review articles for more information on this topic. (Please see line 98). We have re-fragmented some statements in order to avoid hop-on/hop-off problem that we detected. If other hop-on/hop-off points are more precisely stated, you can be sure that we will do our best to correct them.

**Q2: Also, the language requires further polishing.**

**Response:** The manuscript language has been officially and professionally edited. If the language problems are clearly stated, we can make corrections accordingly.