Dear Editor,

Authors' responses to reviewers' suggestions are described below:

Reviewer #1: "Dear Authors I wish to congratulate you on an extensive and near complete review of this important topic. We all practice CHB in our clinical practice and you have rightly elaborated all the possible ways for discontinuation of therapy. There are few comments I wish to make. 1. Minor grammatical mistakes can be checked and corrected. 2. correction of "HBAg" in text as "HBsAg" is needed at certain places. 3. You can also include brief description regarding "Host dominating flare" and "Virus dominating flare". Rest all is good."

Response:

1 and 2. The authors reviewed all grammatical errors, including correction of "HBsAg".

3. The authors include the definition of host and virus dominating flare in the manuscript: "It has been suggested that decreasing levels of qHBsAg during hepatitis flare, qHBsAg decline (> 10% than the preceding level) started prior to or around the peak of ALT, may reflect host effective immune clearance of HBV is ongoing **("host-dominating flare")**; if qHBsAg keeps increasing along with ascending ALT or if qHBsAg remains high after the peak of ALT, it may reflect that immune response is failing or being ineffective **("virus-dominating flare")**".

Reviewer #2: I have read "Discontinuation of antiviral therapy in chronic hepatitis B patients" with interest. There are some comments and suggestions 1. HBeAg seroconversion in non-cirrhotic is just one possible end-point but most guideline recommend until HBsAg loss. 2. Publication cited for HBsAg loss was included small sample size, the authors did not include publication that include larger, more recent 3. Type of NUC or any predictors of relapse? 4. Recommendation of stopping NUC, even may offer some benefit but to recommend for general practice may be too early. NUC stopping should be reserved for HBeAg negative patients without baseline advanced fibrosis and in highly motivated patients who can be followed more frequently

Response:

1. The authors start to say that ideal endpoint of NUC therapy is the sustained HBsAg loss, recommended by all international societies. Considering that this endpoint is rarely achieved, we explore other alternative and feasible endpoints proposed by different societies (for both AgHBe positive and negative patients).

2. The authors included a recent publication, including a larger sample size, regarding to HBsAg loss [PMID: 33309804 DOI: 10.1016/j.cgh.2020.12.005].

3. The authors found some studies that evaluated predictors of sustained response such younger age, earlier disease stage, higher levels of ALT at baseline and at EOT, lower serum HBV DNA levels at baseline and low serum HBsAg levels at EOT or decreasing HBsAg levels during treatment. We did not find any study that evaluated the association between the type of NUC and probability of achieve HBsAg loss or relapse after stopping NUCs.

4. We changed our conclusion for: "HBsAg loss remain as the safest endpoint for discontinue NUC therapy. Due to limited HBsAg loss rate on NUC therapy, other feasible endpoints are getting interest in clinical practice. Evidence accumulating over the last decade supports the idea of stopping NUC therapy in patients with CHB who remain HBsAg positive".

Reviewer #3: Lots of English language and grammar mistakes that have to be corrected by a native English speaking person. • Current recommendations on finite NUC therapy APASL Explain what it stands for.

Response:

1. The authors reviewed all grammatical errors.

Best Regards,

Renato Medas

Rodrigo Liberal

Guilherme Macedo