



Session III: Launch of HDV Co-infection Working Group

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HDV Working Group

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Initial Steps

- 2 conference calls to discuss potential needs in the field and direction of the working group.

Three broad areas considered

- Screening and testing
- Diagnostics
- Treatment endpoints

Screening

- Inconsistency in recommendations for screening globally
 - Risk based versus all HBsAg+
 - Underdiagnosed → missed opportunity to treat
- Viewed as an issue in U.S (and possible other non-European countries) but less so in Europe
- Optimal as our goal is to work with American and European populations

Diagnostics

- No FDA or EMA approved tests for anti-HDV or HDV RNA detection
- Impact screening/diagnostics but importantly also clinical trial
- HDV RNA decline or undetectability will be part of treatment response definition
 - If inconsistencies in tests used to define endpoints, how can be compare across studies? Have confidence that HDV RNA results have meaningful association with "hard endpoints"

Endpoints (1)

- Keep to advancing drug development: Forum has capacity to bring together academia, regulatory and pharma
- Current endpoint of 2 log reduction + ALT normalization is low bar
 - Reasonable starting point but need to consider other endpoints
 - Evidence in support of alternative endpoints
 - Sustained unquantifiable HDV RNA
 - S antigen loss
 - \pm ALT normalization

Endpoints (2)

- Beyond Bulevirtide:
 - Once bulevirtide in the market, will this become the SOC to which all others are compared?
 - What will the FDA/EMA expectations for drugs after bulevirtide?
- We need to find a balance though and not hinder drug development so none get approved

Endpoints: Specifics

- HDV endpoints was a major focus of the recent HBV AASLD-EASL Endpoints conference --- publication will be forthcoming – does this obviate need for Forum to focus on this area?
- Was there enough discussion done at Endpoints conference?
 - Need to see what is missing
 - The Forum should do more than what was discussed at this meeting
 - HBV forum could potentially do a “deeper dive” into the selection (pros/cons) of various HDV endpoints

Endpoints: Next Steps

- Currently thinking of White Paper focused on HDV endpoints
 - Robust evidence base
 - Deeper dive, particularly on areas NOT covered by Endpoints
 - More mechanistic approach

..... await the HBV Endpoints documents

Discussion/Feedback