Management of Finite Treatment for CHB: similar and different concerns with new drug classes

Working Group Update

HBV Forum 9

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Washington DC

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THE FORUM
For Collaborative Research℠

Berkeley Public Health

Background

- Functional cure:
  - Negative HBsAg, HBV DNA neg, normal ALT +/- HBsAb off-treatment
    - Requires stopping treatment to test
- Data on stopping Nrtl: mixed
- Dearth of data on stopping all treatments with new agents
  - Different MOAs of new drugs
    - Assessment of functional cure during and/or after treatment
  - Role of cccDNA and iDNA for HBsAg

Importance

- Finite treatment requires treatment discontinuation
- Consensus needed among clinical researchers, patients, pharmaceutical/diagnostic companies and regulatory agencies to inform clinical research programs
- Safety *and* Efficacy

Working Group Objective

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- Review and identify areas of consensus among stakeholders
- Identify gaps and recommend steps to fill these gaps

- Recognizing “dearth of data” on treatment discontinuation
  - Base discussions on science wrt MOA, virology, existing clinical data
  - Evolve recommendations as more data and diagnostic tools become available

Working Group Members

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SFT working group

- Project initiated December 2021 with zoom calls
- Bullet points assigned February 2022
- Manuscript prepared by writing team– August 2022

Some Consensus

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- Designing new finite duration therapeutic regimens to achieve function cure complex (differing MOA, different disease stage, no “one size fits all” approach)
- The duration and complexity of treatment regimens should be acceptable to the patient population
- New treatment regimens should achieve HBV DNA and RNA suppression, ALT normalization and significant reductions in HBsAg so that after stopping therapy there is a reasonable chance of achieving or sustaining functional cure
- No consistent predictors of response have yet been identified with therapies currently in development
- Immunological biomarkers are currently speculative
- Initial studies of finite and curative investigational therapies should focus on enrollment of patients without cirrhosis with minimal fibrosis for safety
- Different stopping criteria may need to be developed for regimens depending on whether virologic and/or immune modulators are incorporated in a treatment regimen

Future needs

- The threshold for retreating patients/study participant needs to be carefully pre-defined in the protocol based on latest data to allow adequate time to see an off-treatment response and to ensure participant safety
  - Close follow up and rapid turn around required
- Predictors of success seen with NrtI discontinuation should be evaluated in all trials
- There is a major need to be able to differentiate the source of HBsAg between iDNA and cccDNA
- All trials should include banked serum, PBMCs, RNA and DNA at baseline and end of therapy
- Pathogenesis focused trials should include FNA and liver biopsy in addition.
- New methods for measuring restoration of HBV-specific immune control are needed

Next steps

- Project initiated December 2021 with zoom calls
- Bullet points February 2022
- Manuscript collated from writing team– August 2022
  - To Regulatory and Patient Advocate October 2022
- Submit by end of 2022

Special thanks > WG Coordination End note

- Mitchell Leus

Thank You!