Berkeley School of Public Health

Forum for Collaborative HIV Research

HBV Forum 1
November 15th 2016
Hyatt Regency Hotel
Boston

www.hivforum.org

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WG Update: Treatment Combinations

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Facilitating collaborative research in drug development and health policy

Introduction

- Aim:
  - Facilitate the advancement of regulatory science for HBV combination therapy development.
- Goal:
  - To facilitate open, adaptive, iterative design for testing combinations.
- Objectives:
  - Develop a conceptual framework that provides adequate safeguards for trial participants while allowing rapid testing and innovation regarding clinical trials of new combinations.
  - Focus on how to work creatively in Phase 2 to find combinations worthy of more exhaustive testing.

Initial Activities

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- Task 1: Landscape of current regulatory guidance (HBV specific and general combination guidances):
  - Collect applicable guidances and place them into the repository.
  - Assess applicability, gaps and opportunities.
- Task 2: Landscape of current and pipeline drugs for HBV:
  - List currently known drugs in development sorted by mechanism.
  - Plan is to then consider possible combination strategies and whether novel Phase 2 endpoints will be applicable.
- Task 3: Reconsider the approach to flares:
  - Request FDA involvement from clinical team.
  - Collect flare protocols from recent or current trials.
  - Consider the roll of patient selection in mitigating this concern.

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Outcomes and Products

- Product 1: Create a white paper, suitable for publication, regarding challenges in current regulatory guidance for conducting Phase 2 combinatorial trials.
- Product 2: Map initial combination approaches with considerations of potential safety concerns and Phase 2 activity endpoints. This should help inform product 1.
- Product 3: Propose a common approach to flares occurring in clinical trials, including ongoing management and stopping rules.
  - Critical to take into account regulatory concerns around differentiation from drug induced liver injury (DILI)
  - Consider role of avoiding patients with advanced liver disease

Timelines

- Task 1 (collect regulatory guidance) and Task 2 (inventory of drugs approved or in the pipeline) are underway and will soon go out for review by the working group. These activities should complete by year-end.
- Task 3 (collection of flare protocols) just getting underway.
- As the tasks complete, sub-teams will be assembled to work on the related products. This work will commence in 2017.

Other activities

- On-going activities:
  - We plan to conduct conference calls roughly every 6 weeks.
- Additional members?
  - We have a good mix of academic and industry members and now 3 from FDA.
  - We could use additional representation from other regulatory authorities.

Questions

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