Berkeley School of Public Health

FORUM for Collaborative RESEARCH

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Working Group Update: Treatment Combinations

Combination Drugs Working Group

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Introduction

- Aims
  - 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

Activities

- Task 1: Landscape of current regulatory guidance (HBV specific and general combination guidances)
  - Repository created
  - Still planned is a gap analysis regarding any areas where further guidance would be helpful
- Task 2: Landscape of current and pipeline drugs for HBV
  - Spreadsheets of approved, investigational and late pre-clinical drugs created and work ongoing to populate with safety information of interest in developing combinations

Activities

- Task 3: Reconsider the approach to flares
  - Flare protocols collected from recent or current trials
  - Initial contact made with IQ DILI. Still to be determined if/how this will be combined with their work or handled separately

- New Task: Establish basic principals to be considered in combination work
  - Determined that one size fits all approach not feasible so will focus on the those issues needing to be addressed when combination work considered

Outcomes and Products

- Product 1: Create a white paper, suitable for publication, regarding challenges in current regulatory guidance for conducting Phase 2 combinatorial trials.
  - Will now be combined with basic principles discussion to provide context and depth
- Product 2: Map initial combination approaches with considerations of potential safety concerns and Phase 2 activity endpoints.
  - This proved unfeasible due to large array of potential combinations. Instead, we are mapping current drugs with a focus on calling out safety items of note for combos such as important organ tox and/or metabolic factors predicting drug:drug interactions.
  - Issue arising is paucity of public safety data available in such an immature field

Outcomes and Products

- Product 3: Propose a common approach to flares occurring in clinical trials, including ongoing management and stopping rules.
  - Still the most important safety issue that will be common to all combination trial work
  - We would expect that the manner in which the Forum will approach this will be determined prior to our next public meeting
  - Ultimately, this will merit publication, as well

Other

- On-going activities
  - Inventory spreadsheet of HBV drugs in development is now available and will add data over time
  - General principles document has been reviewed by the working group
  - IQ DILI has been engaged
- Next steps
  - Draft manuscript on General principles and gaps in regulatory guidance
  - Determine Forum approach with or without IQ DILI regarding flare issue

Questions

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Discussion