PP23 Integrated clinical databases to detect safety signals across products and indications

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Objective

To create integrated databases (AdVac) cross studies and indications to speed up the process of identifying recurring safety issues, especially the rare signals.

Introduction

- The use of adenoviruses (Ad) as vaccine vectors against a variety of pathogens has demonstrated their capacity to elicit strong antibody and cell-mediated immune responses cross indications
- Our company has a broad spectrum of vaccine portfolio using Ad as a vector.
- In order to increase robustness of signal detection cross studies and indications, a data pooling model is created.
- In this pooling model, all clinical data are mapped to SDTM domains and only selected data which are used in AdVac Safety Report are converted to ADaM datasets.
- The ADaM database is used to detect anticipated safety signal, while SDTM for Ad hoc signal detection.
- We update the integrated Adeno-based Vaccine (AdVac) databases including both SDTM and ADaM on an annual basis.
- The annual AdVac Report, a submission document which is similar to Investigational brochure, is published at the end of each year.

Data Flow Models

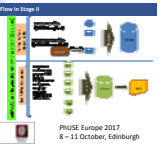
For efficiency purposes, a stage hybrid data pooling model is utilized to create the AdVac databases.

Data Flow in Stage I

- 20 legacy clinical studies from different partners (they were in different data structures and not SDTM compliant)
- First, a harmonized SDTM AdVac database was created.
- The SDTM domains related to solicited and non-solicited AEs, DM, EX were converted to ADaM database. No study specific ADaM Databases were created.
- Tables, Listings and Figures (TLFs) were created from ADaM
- Pro: an efficient process – One ADaM instead of 20 ADaM databases was generated
- Con: No trial specific rules can be applied

Data Flow in Stage II

- The AdVac ADaM Database including selected domains (AE, CM, SA, FA, VS, LB, DM, DS) is updated from individual study ADaM Datasets.
- This database is used to create the TLFs and the AdVac Report.
- In addition, a pooled AdVac SDTM database is created to include all domains (15 domains & 19 SUPP domains). This database is used for any Ad hoc questions and acts as the source for data mining.
- Pro: efficiency & data accuracy
- Con: different study specific rules may be applied so homogeneity may be an issue.



AdVac Program

Challenges

- SDTM pooling:
  - The biggest challenge was integrating and homogenize the study databases which are non-SDTM compliant. They came from different providers and greatly differ from one other.
  - Different mappings and different versions of SDTM may be used by each study.
- Analysis Dataset pooling
  - Different studies potentially use a different ADaM model, requiring harmonization with respect to variable names and content
  - Meaningful pooling is more than a technical process (decisions are needed regarding what to do with products we are not interested in, open label studies, co-administered products…)
- Disconnect between AdVac SDTM and AdVac ADaM databases

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