PMDA’s initiative on real world data utilization for regulatory purposes

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Projects for promoting RWD utilization for regulatory purpose
MIHARI project

- The framework on RWD utilization for drug safety assessment in PMDA
- Formally implemented in FY2014 after completion of the pilot stage since 2009


MID-NET® project

- High quality database of hospital Information system
- Formally launched in April 2018 after completion of the pilot stage since 2011
- An important RWD for regulatory purpose including the study conducted by pharmaceutical industries

Over 4.7M patients from 23 hospitals of 10 organizations
Establishment of the MID-NET® medical information database network as a reliable and valuable database for drug safety assessments in Japan


Describing how to ensure the reliability of the database

The utilization and challenges of Japan's MID-NET® medical information database network in postmarketing drug safety assessments: A summary of pilot pharmacoepidemiological studies


Describing pilot studies and applicability of the database for drug safety assessment
- **National Claims Database (NDB)**
  - Nationwide database covering almost all Japanese individuals (~120 million)
  - Utilization on drug safety assessment formally started in September 2018 after completion of pilot stage since 2014


- **CIN (Clinical Innovation Network)**
  - PMDA-Academic collaboration for establishing the patient registries which comply with regulatory requirements.
    - Mainly target on rare-diseases (Muscular dystrophy, ALS, cancer etc.)
  - Consider related topics (data reliability, ethical, methodological etc.)
Research group on clinical outcome validation

Objective

- Efficient methods to define a clinical outcome used in MID-NET® database studies
  - Introducing machine learning process in the validation study
- Reliability of an outcome is examined in multiple hospitals for considering robustness and generalizability
  - approximately 20 safety outcomes such as anaphylaxis, interstitial pneumonia, heart failure, gastrointestinal perforation, intestinal obstruction etc.

The research grant was received from AMED (Japan Agency for Medical Research and Development)
Legislative reform for promoting RWD utilization
The ministerial ordinance and related guidelines

- The ministerial ordinance was amended to create the new category for a database study (2017)
- Several related guidelines were recently published in 2014-2019
e.g.,
  - “Basic Principles on the utilization of health information databases for Post-Marketing Surveillance of Medical Products” (June 2017, MHLW)
  - “Points to consider for ensuring data reliability on post-marketing database study for drugs“ (February 2018, MHLW)
  - “General steps for considering a post-marketing study plan of drug“ (original: February 2018, PMDA / notification: March 2019, MHLW)

- More guidelines are expected to be published in FY2019-FY2020
  - Basic principles on validation of outcome definition used in post-marketing database study (DRAFT) (available at https://www.pmda.go.jp/files/000230131.pdf)
  - Basic principle for utilization of registry data for regulatory submission (under development, finalization scheduled in FY2020)
  - Points to consider for ensuring the reliability of registry data (under development, finalization scheduled in FY2020)
Scientific Consultation

- Consultations for pharmacoepidemiological studies
  - Started in November 2017
  - Mainly focusing on post-marketing study for drug safety assessment

- Consultations for registry studies
  - Started in April 2019
  - For registry holders: mainly focusing on data reliability of the registry
  - For product developers: mainly focusing on development plan with the registry of an individual product
-International Cooperation-
International activities

- ICH
  - E6 renovation for RWD utilization
  - Pharmacoepidemiology Discussion Group
    - Strategic approach to harmonization of technical scientific requirements for pharmacoepidemiological study

- ICMRA/IPRP
  - Pharmacovigilance Task Group
    - Sharing regulatory experiences on RWD utilization

- Bilateral cooperation
  - US FDA, MHRA/CPRD, DKMA etc.
Expected utilization of RWD in pharmaceutical regulation
RWD utilization in pre- and post-approval development and benefit/risk evaluation

- examples -
- Trial feasibility
- External Control
- Risk evaluation
- Risk factor identification
- New indication
- Comparative effectiveness
- Dose optimization
- Safety monitoring

Better drug development and regulatory decision
Advancing Regulatory Science
-Regulatory Science Center in PMDA-
Past-Present

Pilot/Cluster approach

- Academic collaborations
- CDISC data analysis
- RWD utilization

4th MID-TERM plan (FY2019-FY2023)

Unified approach as the center

- More collaborations with academia and other regulatory agencies
- Cross product analysis based on accumulated data for sophisticated review and consultation
- More utilization of RWD for better benefit/risk assessment
- More regulatory guidelines corresponding to the latest science
More integration of all regulatory science activities for efficient drug development and better pharmaceutical regulation.
Thank you very much for your kind attention!!

- **PMDA web site**
  

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