European contribution to the RWD/RWE debate

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July 2018

Sources

- UK Academy of Medical Sciences(AMS) workshops
- European Medicines Agency (EMA)
- Innovative Medicines Initiative (IMI) projects

AMS workshop 1

- Held in September 2015
- Aims

1. to explore the current acceptability of RWE in regulatory and HTA decision making
2. To address the challenges
3. To suggest practical steps to address these.

Contributors to workshop 1

- EMA
- FDA
- MHRA
- IMS Health
- NICE
- Industry

AMS Workshop 1

- Conclusions
- 1. Role of RWE in regulatory decision making remains to be defined
- 2. Being used in pharmacovigilance but less in licensing of medicines
- 3. Need for better definitions and standards to be used by all stakeholders
- 4. Need for standard IT monitoring systems

AMS Workshop 2

- Held in January 2018
- Contributors: EMA, FDA, MHRA, NICE, Industry, NAM.
- Conclusions:
- 1. In Europe, compared to U.S. ,progress has been relatively limited, being incremental rather than transformative
- 2. Many of challenges identified in 2015 remain unsolved

Access v. Evidence Debate

- Data– information– evidence-decision making
- Big Data-large sets of information which needs specialised computational tools to help analysis
- RWD-subset of Big Data relating to :
  - -Patient health status
  - -Delivery of routine health care
  - -Collected from a variety of sources

including EHRs, claims, product and disease registries, social media

Real World Evidence(1)

- RWE- evidence drawn from RWD through application of research methods
- Regulatory grade RWE
  - Define scientific question
  - identify study design
  - selection of RWD
  - data standards/analytical methods
  - compliance with regulatory standards

Real World Evidence (2)

- Uses of RWE

  - Regulators. Evaluation of product safety

  - Payers. Decisions on coverage and reimbursement

Key requirements for RWE

- Generalisability
- Relevance
- Adaptability
- Efficiency

FDA

- 21 st Century Cures Act

  - shift from preapproval RCTs to post approval RWD/RWE

  - Requires FDA to establish programme to evaluate RWE

61% NME approved in 2016 used expedited approval programmes.

81% Accelerated approvals were for cancer drugs

European Pharmacovigilance

- RWD in routine use for safety monitoring
- 2016 -1 million safety reports received on Eudravigilance network
- 2000 signals detected
- 48 validated

European efficacy study Zalmoxis

- Imunogene therapy for high risk haematological malignancies
- Phase 2 single arm study
- Historical controls using Transplantation register
- Conditional Marketing Authorisation granted
- PAES and PASS requested

European efficacy
Salford Lung Study

- Pragmatic RCT for novel treatment for COPD
- 2800 patients, 80 GPs , 130 pharmacies
- Salford Integrated Record(SIR) links primary and secondary care data
- Wider population than routine RCT

European Adaptive Licensing Pilot (1)

- Medicines Adaptive Pathways to Patients
- Prospectively planned adaptive approach to give:

- early access of patients to important new medicines for unmet medical needs, but with greater uncertainty and lower evidence requirements

- Burden of evidence shifts from pre- to post-marketing. Importance of PAES and PASS

- Involvement of company, regulator , HTA experts, payers, patients
- uses existing EU legal framework

EMA Adaptive Licensing pilot(2)

- Importance of the use of high quality RWD gathered through a prospective plan to further define benefit/ risk profile and therapeutic value of product
- In final report in July 2016, all 18 accepted pilot projects included plans for use of RWD that went beyond traditional use of registries for pharmacovigilance
- “Most of plans vague in terms of the purpose of collecting RWD to supplement RCTs”

European Medicines Agency

- March 2016, EMA and heads of Medicines Agencies formed a joint Task Force to explore how:
- To use Big Data to support innovation and medical development
- To map relevant sources of Big Data
- To identify usability and application of Big Data
- To design a Big Data roadmap
- Group has 18 months to complete work and report back

IMI funded programmes (1)

- Innovative Medicines Initiative (IMI) is an EU public – private consortium, launched in 2008, consisting of pharmaceutical companies, academia, regulators and academia. Its budget from 2014-2024 is E3 billion , half of which comes from industry. It supports 50 projects

IMI funded programmes (2)

- IMI GET REAL
- IMI PROTECT
- IMI ADAPT SMART
- IMI WEB RADR

IMI GET REAL

- 3 year project, launched in 2013 aiming to show how robust new methods of RWE collection and synthesis could be adopted early in pharmaceutical R&D and healthcare decision making to bridge the gap between efficacy and effectiveness thus getting new drugs to patients more quickly

IMI PROTECT

- (Pharmacoepidemiological Research Outcomes of Therapeutics by a European Consortium
- Aim is to strengthen the monitoring of benefit-risk of medicines in Europe, with the inclusion of patient and public involvement .
- Addresses limitations of current methods in the fields of pharmacoepidemiology and pharmacovigilance
- Output evaluated in 2016-all objectives and deliverables achieved(outcomes linked to signal detection and evaluation being implemented in routine pharmacovigilance

IMI ADAPT SMART

- A coordination and support action to facilitate and accelerate availability of MAPPS (Medicines Adaptive Pathways to Patients) related activities
- Established in 2014 for a 10 year period to develop next generation vaccines and medicines such as new antibiotics
- Built on lessons learned from first phase IMI projects started in 2008,
- Tackle Europe's growing healthcare challenges and ensure future competitiveness of Europe's pharmaceutical industry

IMI WEB RADR

- to develop a mobile app for patients and healthcare professionals to report suspected ADRs and investigate the potential for publicly available social media to identify drug safety issues
- Reports received from the mobile app will be compared with those received via established reporting schemes for completeness, quality and value for detection of safety issues
- Launched in 2014 for 3 year period and led by a consortium of experts from industry and regulatory authorities and academia

Regulatory Applications of RWE for drugs

- Safety
- Dosing
- Drug-drug interactions
- Sequence of therapies
- Subpopulations /expansion
- New indications(repurposing)
- PAES and PASS (PMR and PMC)