Patients’ role in post-marketing authorisation phase in the 21st century

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Why does it matter?

Proof of concept studies
• A few tenths

Confirmation trials
• A few hundreds

Market
• A few more hundreds, thousands
Patient population & orphan drugs

Proof of concept

Confirmation

Marketing authorisation

Target population

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Patients and off-label use

Authorised indication

Off-label uses
Often for rare diseases

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1996: highly active antiretroviral therapies to treat HIV/AIDS became available. Very rapid intake in countries that made the products available. But:

Questions:
1) What was this?
2) Was it due to drugs?
   - Class of drugs?
   - Individual drugs?
3) Was it due to disease/increased survival?
4) Could it change benefit/risk?

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2 March 1999: EMEA meeting
   - The Oversight Committee for Metabolic Disorders of HAART (with industry, academic experts, patients’ representatives)
   - 9 supportive MAH, budget: 5 746 056.3 € over 5 years

A case definition study for “lipodystrophy”

A retrospective cohort study/risk of cardiovascular events
   - Veterans Administration Database USA

A multi-cohort prospective study / cardiovascular risk

Clinical trials meta-analysis (abandoned)
   - ACTG 384, INITIO, ATLANTIC, and FIRST

Merging of 9 MAH safety databases (never started)
Results

HAART was independently associated with an 26% increased risk of myocardial infarction per year of exposure.

Lessons

- Patients’ rep. involved in each of the studies
  - design, conduct, analysis, communication
- Patients’ rep. in the oversight committee
  - Follow-up + reporting to EMEA and to patients’ community
- Total: increased transparency and trust in the assessment/decisions
- Impact on pharmacovigilance legislation
  - PASS and PAES, ADRs reporting by patients…
Why? - To Further Strengthen Pharmacovigilance

- 5% of all hospital admissions are for Adverse Drug Reactions (ADRs)
- 5% of all hospital patients suffer an ADR
- ADRs are the 5th most common cause of hospital death
- Estimated 197,000 deaths per year in EU from ADRs
- EU societal cost of ADRs amounts to Euro 79 Billion per year

Peter Harlett, EMA, Implementation of the New Pharmacovigilance Legislation
2003: EC decision to undertake an assessment of the Community system of pharmacovigilance

Both Regulation (EC) 1235/2010 and Directive 2010/84/EC have been published on 31 December 2010

July 2012: new legislation will apply
Watch out what’s (particularly) for us in the Pharmacovigilance legislation

- **Already active**
  - PhVWP, risk communication, some RMP

- **With the legislation (selection)**
  - PRAC and national equivalents
  - PASS/PAES studies
  - Patient reporting and access to Eudravigilance data (spontaneous reports)
    - Visit: [www.adrreports.eu](http://www.adrreports.eu)
  - RMP and their evaluation
  - Public hearings

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To study
- European Reference Networks for RD
- Drugs for children
- Pharmacoepidemiology

To assess
- CNAs
- MAHs
- EMA network

To inform
- Drugs
- ADRs
- Trials

Many to report
- Patients
- Healthcare professionals

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ADR reporting tools as of May 2012

- On-line reporting form
- Printed form
- No information available
- Non-EU/EEA

Q&A on suspected adverse drug reactions prepared by Eurordis DITA task force

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The DIOD project by Eurordis and partners

DAILY IMPACT OF ORPHAN DRUGS IN PATIENTS’ LIVES

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Objectives

To provide patients with information on the drugs they are taking

To collect their feedback on desired effects of the drug

To collect their feedback on undesired effects of the drug

Also useful for CHMP consultation
Benefit/risks is a matter of:

- Constrains and ease of use
- Frequency of side effects
- Efficacy including quality of life
- Severity of side effects
- Uncertainty what is known about the toxicity profile?

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Which OD to start with and how?

- Authorised products if additional monitoring
- Newly authorised OD (3-6/year)
- In MS with reporting tools and a help line
- Communication campaign Eurordis (Q&A)
1373 first-time users of pregabalin were approached in Dutch pharmacies between 1 August 2006 and 31 January 2008.

After online registration, patients received questionnaires by email 2 weeks, 6 weeks, 3 months and 6 months after the start of the drug use.

Data on patient characteristics, drug use and ADRs were collected and analysed.
Kaplan–Meier curves illustrating the incidence densities of the five most frequently reported adverse drug reactions. From the top down to the first line represents:

- increased weight
- Fatigue
- feeling drunk
- Somnolence
- dizziness

‘Survival’ pertains to those patients who did not develop particular adverse drug reaction.
How do we get organise to deliver all this?

- Large scale patients’ involvement
  - Role of EUPATI
- Large scale patients’ representatives involvement
  - Training, EUPATI
  - Time and support, cf Code du Travail

Impact assessment: “Based on the feedback of stakeholders and in an attempt to reduce costs, the final proposal for the committee structure has been revised to include a small expert committee on PhV. This results in an overall neutral effect of the committee structure changes compared to the current situation”.
To conclude

- Each person taking a yet authorised product for the first time does an experiment
  - You never know for sure if the drug is going to work for you
  - You never know which toxic effects will occur
- We need to collect more information to increase knowledge
- As patients, we need to be pharmaco-vigilant!
Thank you.