Workshop: measuring the impact of pharmacovigilance activities

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"Challenges of measuring the impact of pharmacovigilance processes"

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Why is it important to measure the impact of pharmacovigilance processes?

- To review of the benefits and risks of individual medicines : effectiveness of risk minimisation
- Determine what activities are successful
- Enablers and barriers for generating positive impacts

Adopted from PRAC strategy on measuring the impact of Pharmacovigilance activities, 2016

Is it possible to focus on measuring the impact in certain type of adverse drug reactions (ADRs)…?

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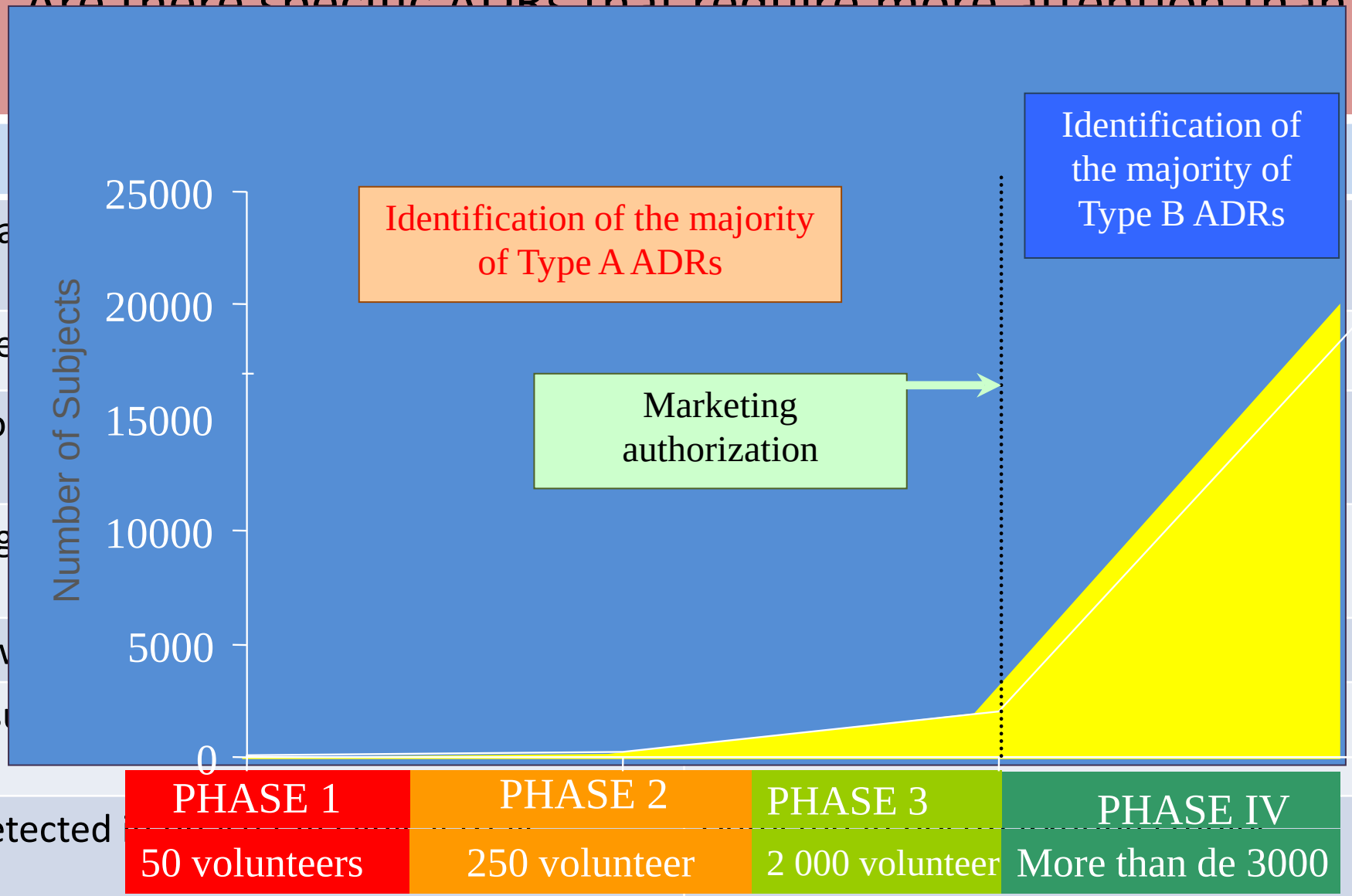
Classification of ADRs

Are there specific ADRs that require more attention than others?

TYPE A (AUGMENTED)	TYPE B (BIZARRE)
Exaggerated pharmacological effects	Not related with the pharmacological effects
Predictable	Unpredictable
Dose-related	Dose effect is unclearly defined
High incidence and morbility rates	Relatively low Incidence and morbility rates
Low mortality rates	High mortality rates
Usually reproducible in animals	Lack of animal models
Detected in phase I-III clinical trials	Detected in postmarketing studies

Adopted from Classification of Rawlins and Thompson

Classification of ADRs



Adopted from Classification of Rawlins and Thompson

Drug-Induced Liver Injury severity (ADR Type B)

- It is responsible for more than 10% of all cases of acute liver failure
- DILI is one of the most frequent reason for marketed drug withdrawal and modification of labelling
- More than 1,100 medicines, natural products, vitamins, dietary supplements, recreational and illicit compounds have been reported to cause DILI
- One of the most common reasons for attrition during drug development and adoption of post-marketing regulatory actions

What are the challenges in measuring the impact of pharmacovigilance processes? (Liver Safety Perspective)

Challenges Part I: Risk Analysis

1. Risk identification

- Optimal methods to identify DILI
- Diagnosis, causality assessment and predictive models
- At the pharmaceutical industry level
- At the regulatory level
- Access to clinical data

Potential actions

- Systematic protocols to assess DILI:
  - Guidance for special populations
  - Guidance for biological agents
- Analysis of signals during premarketing clinical trials
- Reach a consensus on terminology and define levels of evidence
- Develop standardized electronic data capture systems

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What are the challenges in measuring the impact of pharmacovigilance processes? (Liver Safety Perspective)

Challenges Part II: Risk Analysis	Potential actions

2. Risk Quantification
- DILI incidence
- Drug prescription and dispensing
 	
3. Evaluation of Risk/benefit balance
- Type of studies
- Time lag between recognition and adoption of regulatory measures
	- Promote well-designed studies
	  - Combine large clinical trial data sets during drug development
	  - Identification & Validation of mechanistic-based biomarkers
	- Personalized medicine approaches
	- Promote research based on international networking and multidisciplinary bridging (ethnicity, pharmaceutical policies..)

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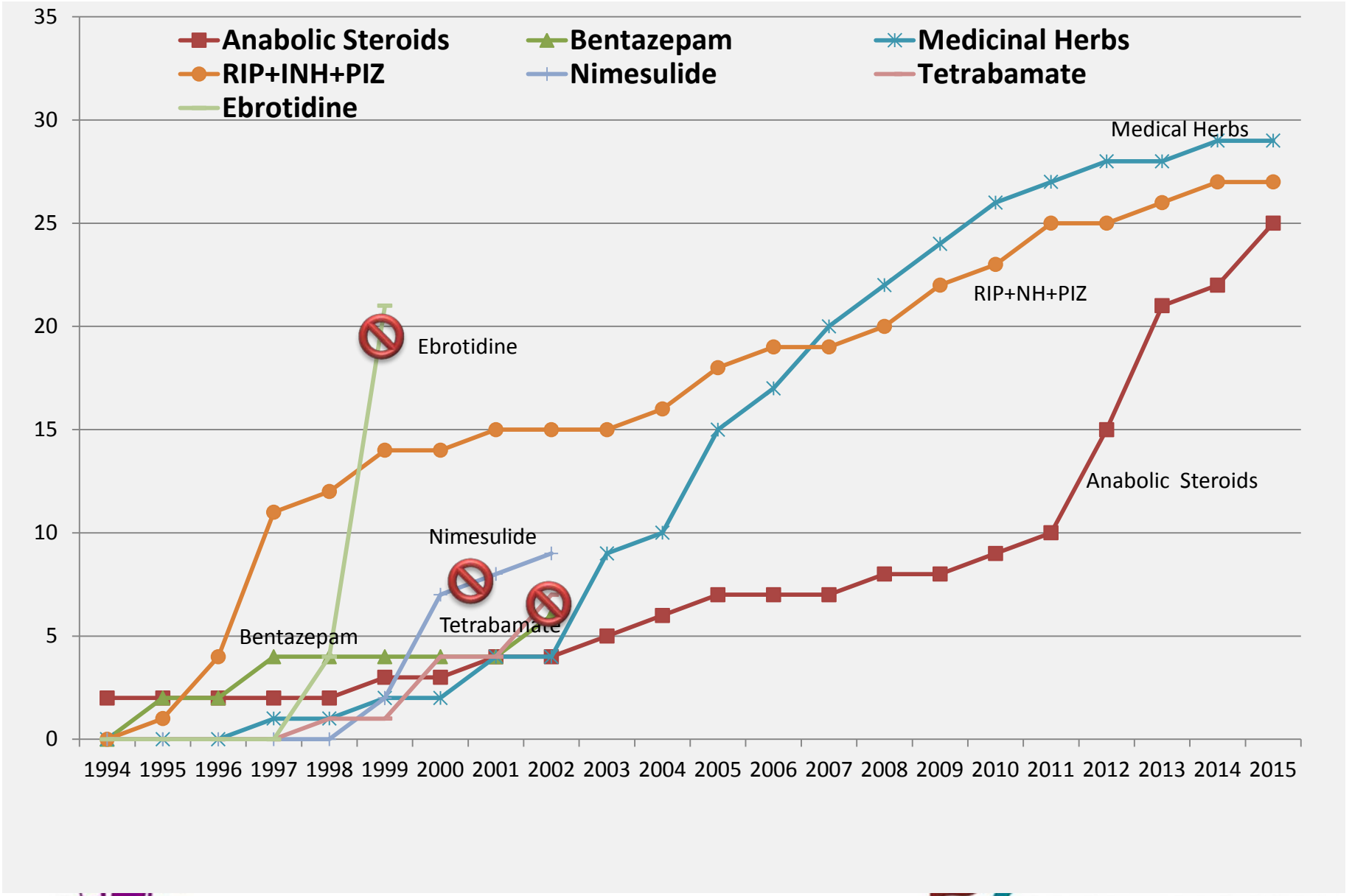
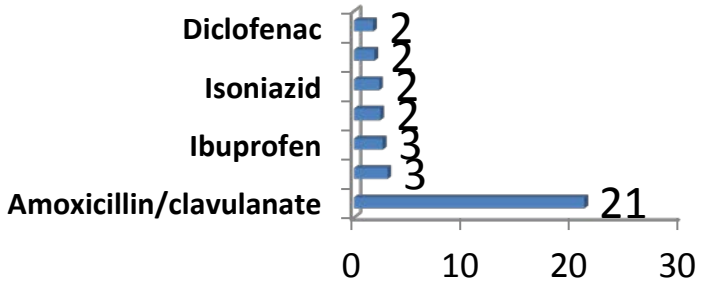
Impact of the registry on liver safety

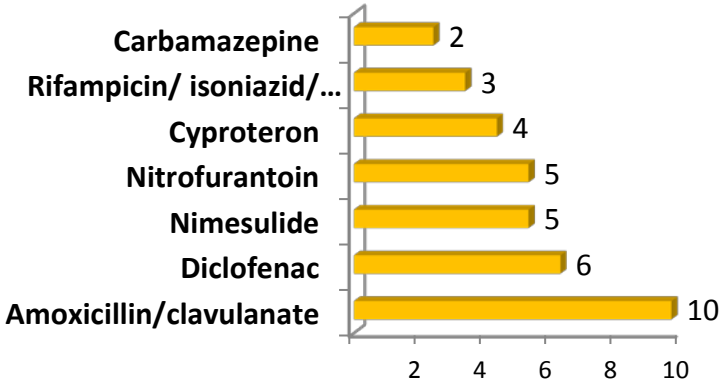


Impact of the registry on liver safety

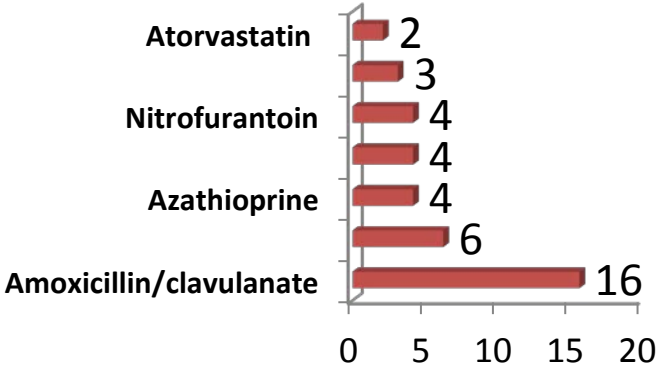
Top individual agents implicated in DILI in Spain (%)



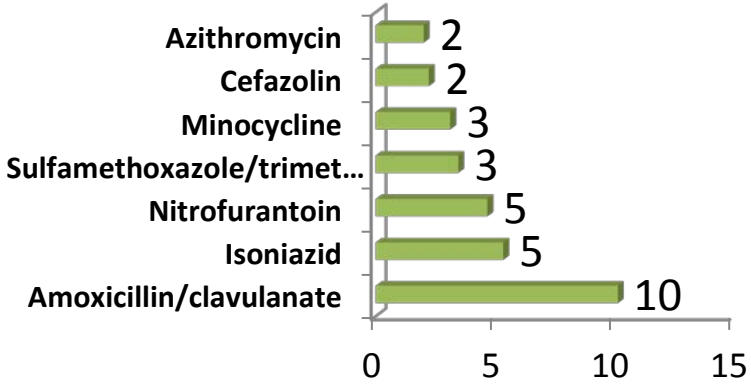
Latin America (%)



Iceland (%)



DILIN, US (%)



Bessone et al, Int J Mol Sci 2016
Chalasani et al, Gastroenterology, 2015
Björnsson et al, Gastroenterology, 2013

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Impact of the registry on liver safety

- Registries have the potential to identify signals in a more efficient way
  - Consequently, adopting regulatory measures in shorter period of time
- Registries help detect emergent problems: Autoimmune-DILI and problems related with biological agents.
- Registries support confident decision-making for regulatory agencies

How to measure the impact ?

- Measuring the time lag between signal recognition and regulatory measure adopted
- The decrease in the frequency of medication withdrawal in the post-marketing period

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