

In Multinational Trials Adverse Reactions should be analysed by Country or Region too

36th Annual Meeting, Society for Clinical Trials, Arlington May 2015

Krunal Pawar

Tanja Tran

Joerg Hasford

Dept. for Medical Biometry and Epidemiology,
Ludwig-Maximilians-Universitaet Muenchen, Germany

Email: has@ibe.med.uni-muenchen.de

Background

- Many items of everyday life, like foods, cars, weapons, carry highly different risks varying by country.
- Regarding pharmaceuticals different population characteristics, comorbidities, comedications and levels of health care quality may result in different ADR profiles and frequencies across countries. These may be relevant in clinical trials too.
- Although there are a few hints in the literature regional differences of ADRs are rarely considered in risk minimization actions.

Objectives

- To look for the existence of geographic variation of the profile and frequency of ADRs in the literature.
- To find out whether such variation exists exemplified for the TKI Imatinib in patients with Chronic Myeloid Leukemia.

Methods

- Screening of Medline for papers on geographic variability of ADRs (→ 2-3 papers identified only)
- Screening of Medline using the key words: CML, prospective study, Imatinib, AE, ADR, safety.
- All prospective studies with adults, Imatinib 400mg/day and quantitative, regional data on AE/ADRs were included.
- ADRs were grouped using SOCs (WHO).
- ADR-profiles were constructed using relative frequencies.

Results

- 13 prospective studies were identified, representing Asia (Japan(5), India(1)), Europe, and the USA with 2424 pts.
- Similar frequencies were reported for
 - body as a whole – general disorders
 - GI-system disorders
 - muskulo-skeletal system disorders
 - platelet, bleeding and clotting disorders
 - red blood cell disorders
 - white cell and reticuloendothelial system disorders

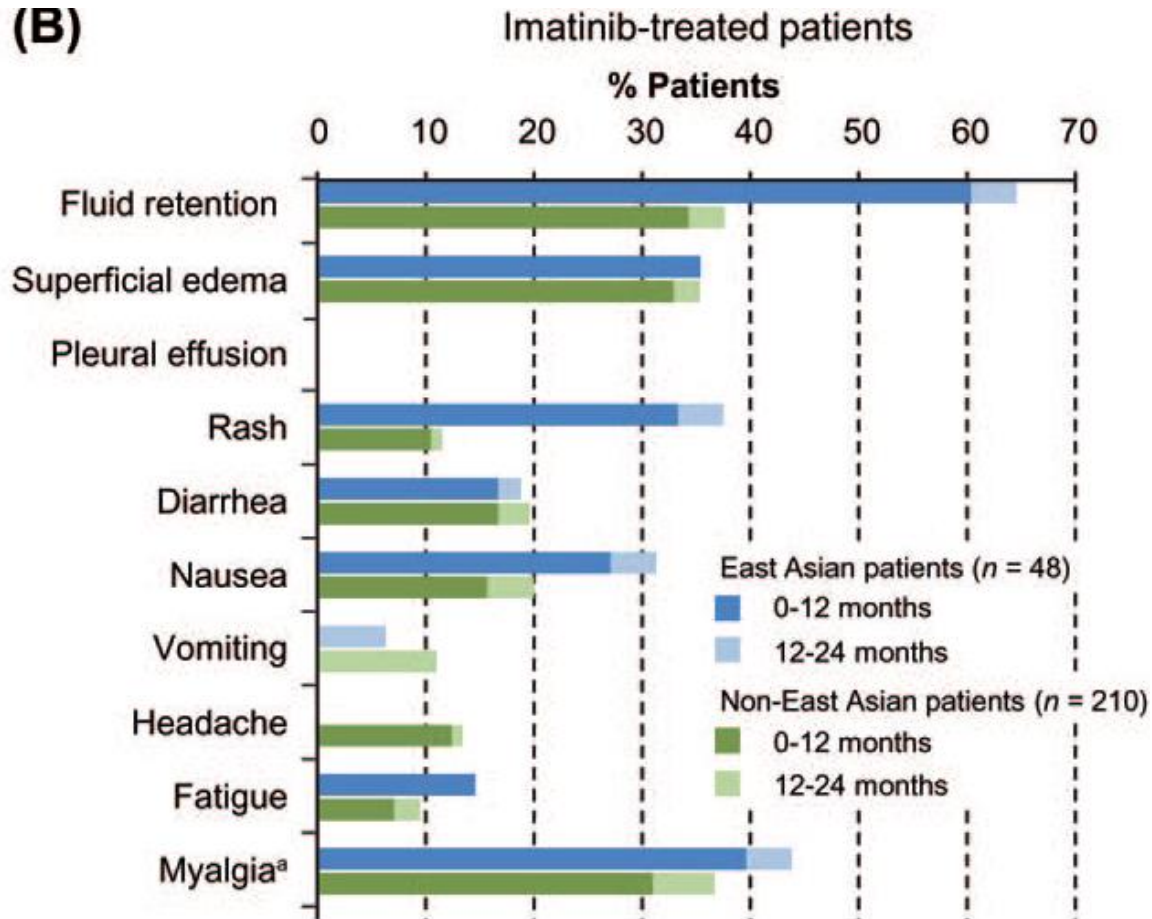
Results

- **SOCs reported more often in Asia vs EUR and USA**
 - skin and appendages disorders
 - liver and biliary system disorders
 - urinary system disorders
- **SOCs reported more often in the USA and EUR vs Asia**
 - cardiovascular disorders, general
 - central and peripheral nervous system disorders

Results

- **SOCs reported in Asia and EUR only**
 - vascular (extracardiac) disorders
 - special senses other, disorders
- **SOCs reported in EUR and USA only**
 - metabolic and nutritional disorders

Non-hematologic ADRs in East Asian vs. Non East Asian pts. DASISION-Trial



DISCUSSION

- **Strengths:**
 - prospective studies only → standardized monitoring and documentation within a study
 - SOC profiles, independent of absolute frequencies
- **Limitations:**
 - variability of monitoring and documentation across studies
 - results might reflect cultural patterns of diagnosing AE/ADR too

Conclusions and Outlook

- There were considerable geographic differences in frequencies and profiles of AE/ADR of Imatinib in 8 out of 16 System Organ Classes.
- Drug authorities should issue detailed guidelines for the monitoring, analysis and reporting of AE/ADR in clinical trials.
- There should be more emphasis on analyzing and interpreting AE/ADR reports by geographic region.