EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Perspectives from EMA Scientific Committees

Committee of Orphan Medicinal Products - COMP

Regulatory challenges and opportunities

PCWP/HCPWP workshop on personalised medicines

Presented by Bruno Sepodes on 14 March 2017
Chairman of the Committee of Orphan Medicinal Products

Mapping conditions to treatments

The original idea:

Condition		Treatment
Gaucher's disease	→	specific enzyme replacement therapy
Leber's amaurosis	→	9-*cis*-Retinyl acetate

The "orphan logic":

Treatment - eligible population mirrors condition;

rare condition ←→ treatment for few people

Key developments that are shaping medicines evaluation

Theodore E. Woodward on the art of diagnosis (late 1940s):

"When you hear hoofbeats, think of horses not zebras"

What is a condition (disease)?

"There is a compelling case for reforming the taxonomy of human disease by moving away from traditional diagnostic criteria alone to ones that incorporate the scientific advances in molecular and genetic medicine.."

"Failure to do so perpetuates ineffective treatment in medicine…"

Nature Reviews Drug Discovery **10**, 641-642 (September 2011) | doi:10.1038/nrd3534

A call to reform the taxonomy of human disease

Ismail Kola[1] & John Bell[2]

We Are All Zebras

[From Siren® Interactive, A Dohmen Company]

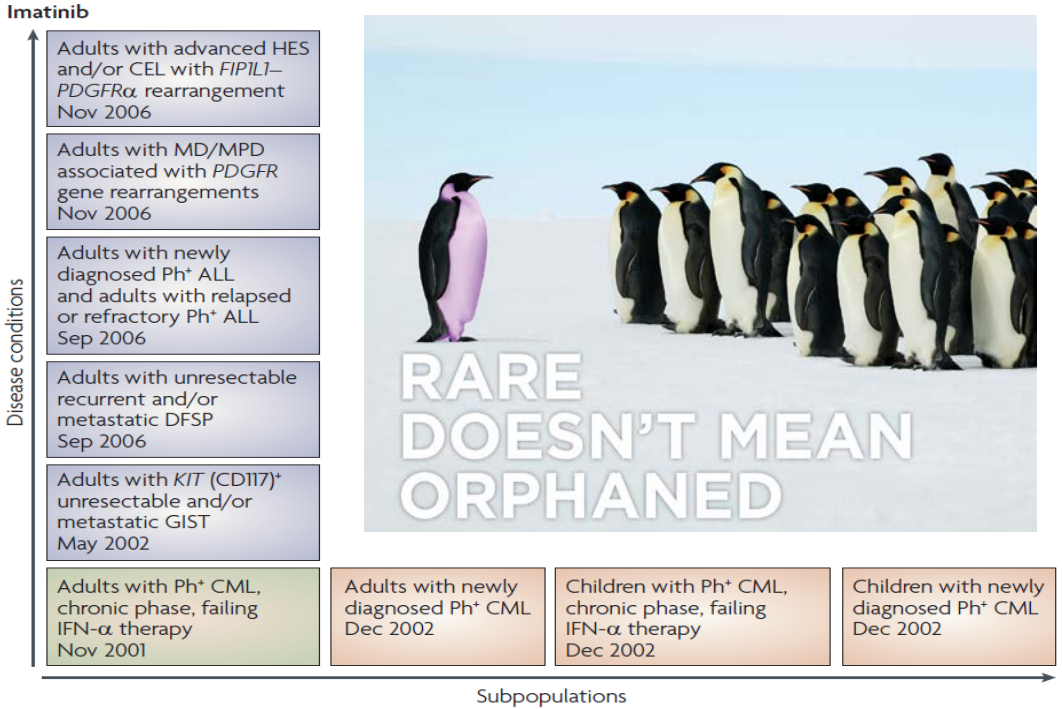
Shattering the orphan logic: ***Gleevec***

Imatinib *et al*:

Targeting not a condition but a mechanism common to many 'conditions'

(blocking the Bcr-Abl tyrosine kinase enzyme)

With progress in the understanding of molecular pathology one treatment no longer maps to one condition



[Eichler et al; Nature Rev Drug Disc; 2008]

Regulatory challenges

New Medicines

- Innovative products
- Biologicals and ATMPs (gene therapy, stem cell and tissue therapy)

Methodological Challenges

- Globalisation
- Definition of orphan condition
- Marketing authorisation procedures (full, conditional, exceptional circumstances)
- New ways to generate evidence (RWE)
- New evaluation methods (Mapp, Prime, Joint HTA-SA)

Regulatory challenges

- A new taxonomy of diseases may be needed to support the development of precision medicine (to enable better clinical trials, regulatory and reimbursement decisions, steering of on-market utilisation)
- For some clinical conditions, interpretation of the orphan rules may need further discussion, to uphold the spirit of the orphan legislation, incentivise research, but without encouraging misuse
- Both Regulation and Reimbursement rules should follow science in order to better serve the patients and society in general – [it should not be the other way round!]

RESEARCH Open Access

Use of biomarkers in the context of orphan medicines designation in the European Union

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and to justify that the criteria for orphan designation are met. The current work discusses specific examples from the experience of the COMP, where biomarkers have played a decisive role. Importantly, it identifies the proposal of sub-sets of non-rare conditions based on biomarkers as a challenging issue in the evaluation of applications. In particular two specific requirements for the candidate orphan medicines in relation to the biomarker-based subsets are highlighted: the "plausible link to the condition" and the "exclusion of effects outside the subset".

Keywords: Orphan medicinal product designation, Distinct medical entity, Biomarker

Opportunities

- Rare diseases have paved the way for some of the modern approaches to personalized medicine
- Further fragmentation of treatment-eligible populations is clearly expected to have a positive effect for public health (= precision medicine)
- Knowledge gained is eternal and will benefit drug development for rare diseases