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DISCLOSURE

- I RECEIVE UNRESTRICTED GRANTS AND TRAVEL HONORARIA FROM ACTELION, BIOMARIN, GENZYME PTC, SHIRE, SYNAGEVA.

- I HAVE NO ECONOMICAL OR STOCK MARKET INTERESTS ON ANY RARE DISEASE PRODUCT

BUT ARE RARE DISEASES REALLY RARE?
Who do rare diseases affect?

30 MILLION AMERICANS

Two-thirds of Americans affected by a rare disease are children.

That’s one on every crowded elevator.

Four on every full bus.
RARE DISEASES MAIN PROBLEM: DELAYED OR DIFFICULT DIAGNOSIS

According to patients surveyed, it takes:

*On average 7.6 years in the U.S.*

According to patient/caregiver respondents, in order to get a proper diagnosis, a patient typically visits up to

*On average 5.6 y in the UK*

For a patients with a rare disease to receive a proper diagnosis

And receives **2 to 3** misdiagnoses

Data from Rare Diseases Impact Report April - 2013
A long trip to the diagnosis:
Family with 7 children, 3 of them affected by a rare disease

The diagnosis of all the brothers—by chance—due to the identification of the youngest patient starting the therapy in 2008
THE ODYSSEY OF A PATIENTS BORN IN 1988

Symptoms beginning at the age of 2 years:
- Permanent airway and ear infections (with 7 operating aids and hearing aid)
- Language Development Delay
- 5 y, 7½ years in the USA and 5 ½ years in the UK
- 5 y, Stiff fingers, shoulders, hips, and knees
- 6 y Heart valve changes
- 8 counseling from different specialists
- 11 y Hip change diagnosis (10 yrs)

Diagnosis at 20 y. after the diagnosis of the younger brother at 14 y

Counselling: Several Pediatric visits
Multiple ENT visits
Multiple Orthopedic visits
Multiple Rheumatologist
Multiple Cardiologist
Multiple Hematologist

3 WRONG DIAGNOSIS AND THERAPIES RECEIVED

Delay of Diagnosis in Rare Diseases:
- 8 counseling from different specialists
- 11 y Hip change diagnosis (10 yrs)
THE DIAGNOSIS OF NPC DISEASE

NP-C takes on average 5 YEARS to diagnose.

That’s...

1,826 DAYS
260 WEEKS
43,824 HOURS

...waiting for an answer, watching a loved one get worse

Kindly from THE GERMAN NPC ASSOCIATION
| 1. ERN BOND | European Reference Network on Rare Bone Disorders |
| 2. ERN CRANIO | European Reference Network on Rare craniofacial anomalies and ENT disorders |
| 3. Endo-ERN | European Reference Network on Rare Endocrine Conditions |
| 4. ERN EpiCARE | European Reference Network on Rare and Complex Epilepsies |
| 5. ERKNet | European Rare Kidney Diseases Reference Network |
| 6. ERN RND | European Reference Network on Rare Neurological Diseases |
| 7. ERNICA | European Reference Network on Rare inherited and congenital anomalies |
| 8. ERN LUNG | European Reference Network on Rare Respiratory Diseases |
| 9. ERN Skin | European Reference Network on Rare and Undiagnosed Skin Disorders |
| 10. ERN EURACAN | European Reference Network on Rare Adult Cancers (solid tumours) |
| 11. ERN EuroBloodNet | European Reference Network on Rare Haematological Diseases |
| 12. ERN EURO-NMD | European Reference Network for Rare Neuromuscular Diseases |
| 13. ERN EYE | European Reference Network on Rare Eye Diseases |
| 14. ERN GENTURIS | European Reference Network on Genetic Tumour Risk Syndromes |
| 15. ERN GUARD-HEART | European Reference Network on Uncommon And Rare Diseases of the HEART |
| 16. ERN ITHACA | European Reference Network on Rare Congenital Malformations and Rare Intellectual Disability |
| 17. MetabERN | European Reference Network for Rare Hereditary Metabolic Disorders |
| 18. ERN PaedCan | European Reference Network for Paediatric Cancer (haemato-oncology) |
| 19. ERN RARE-LIVER | European Reference Network on Rare Hepatological Diseases |
| 20. ERN ReCONNET | Rare Connective Tissue and Musculoskeletal Diseases Network |
| 21. ERN RITA | Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases Network |
| 22. ERN TRANSPLANT-CHILD | European Reference Network on Transplantation in Children |
| 23. VASCERN | European Reference Network on Rare Multisystemic Vascular Diseases |
| 24. ERN eUROGEN | European Reference Network on Rare and Complex Urogenital Diseases and Conditions |
WHY SHOULD WE CROSS LINK THE EUROPEAN REFERENCE NETWORKS?

|-------------------|---------------|-------------|---------------|----------|-----------|-----------|-----------|------------|----------------|--------------------|----------------|------------|----------------|---------------------|--------------|------------|---------------|----------------|----------------|-----------|---------------------|----------|----------------|

INBORN ERRORS OF METABOLISM

- Name proposed by Sir ARCHIBALD GARROD in 1908

- Observations about 4 disorders, with recurrence in families: Alcaptonuria, Pentosuria, Cystinuria and Albinism

- Investigated urine chemistry as a reflection of systemic metabolism and disease

- In 1923 he wrote his best known work: „INBORN ERRORS OF METABOLISM“
About 60%: CNS involvement/epilepsy
About 30%: Skeletal problems
About 30%: Liver Involvement
About 30%: Cardiological problems
About 25%: Kidney problems
CROSSSLINKING IS IN NATURE

Network medicine: a network-based approach to human disease
Albert-László Barabási, N. Gulbahce and J. Loscalzo,
Nature Reviews Genetics 2011: 12, 56-68
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CROSSLINKING IS IN NATURE: THE EXAMPLE OF THE METABOLIC DISEASES
ERNs MIMICK NATURE

Connected Hospital
Connected Health Information Exchanges
Connected Patient
Connected Clinician
Connected Health Authorities
Connected Life Sciences and Research
Connected Public Health
Connected Payer
1. ERNs COORDINATION
2. PATIENT COMMITMENT
3. DISEASE IDENTIFICATION
4. REGISTRY
5. DATA SHARING
6. COMMUNICATION/AWARENESS
7. EDUCATION
8. SHARED VIRTUAL COUNSELLING
9. NETWORK OF SPECIALISTS
10. INSTITUTIONAL STAKEHOLDERS
11. PAYERS
12. NATIONAL HEALTH SYSTEMS/NPRD
13. RESEARCH COORDINATION
14. GUIDELINES/PATIENT PATHWAYS
15. STANDARD OPERATING PROCEDURES
16. QUALITY INDICATORS
ONE OF THE SECRETS FOR SUCCESS OF THE CROSSLINKING: THE IT PLATFORM

CISCO 2008
OPEN TOPICS TO BE DISCUSSED

• National HCPs need to networked, continuous collaboration with the MS representatives is needed
• Sustainability of the ERNs
• Legal entity of the ERNs
• Reimbursement of the ERN activities
• Liability of Coordinators/ recognition of the Coordinator role
• The IT platform offered by the EC need to be tested according to the present HCP IT compatibility, ethical issues need to be considered properly and solved as a matter of urgency.
CONCLUSIONS

1. ERNs are not a project or a program, they are a CONCEPT* and represent (one of) the major achievement of the European spirit of collaboration, sharing and health investement in the field of rare diseases

2. ERNs group the most acknowledged centers of excellence in Europe, all sharing the same level of commitment and interest for rare diseases

3. ERNs are NOT single networks, but rather a critical mass of more than 300 hospitals and over 1000 specialised units, cross feeding each other to meet the needs of our patients.

4. Crosslinking in in the nature of the ERNs due to multidisciplinarity implications of the cared diseases.

5. The ERNs´crosslinking is instrumental to define the best way to integrate ERNs with the MS National Health Systems/National Plans for Rare Diseases and how to potentiate the Cross Border Care of our patients affected by crosslinking diseases

6. The ERNs´crosslinking is instrumental to define strategies to optimize the cost of management of patients of rare diseases

7. The Coordinators Task Force will be an unvaluable instrument for the EC to define a uniform pan-European plan for rare diseases.

* Quoted after Victoria Hedley, Newcastle, UK
ACKNOWLEDGEMENT

A warm thank to:

**DGSANTE ERN UNIT**
- Mr. Enrique Terol
- Ms. Anna Carta
- and all the ERN team

**CHAFEA**
- Ms. Hristina Mileva
- Mr. Jarek Waldigora

**DIRECTORATE GENERAL HEALTH AND FOOD SAFETY**
- Mr. Xavier Prats-Monné+
- Mr. Andrzej Rys

**COMMISIONER FOR HEALTH AND FOOD SAFETY**
- Mr. Vytenis Andriukaitis