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Session 1 – Presentation 2

Rare diseases: information sources in the EU and in Slovakia
Zriedkavé choroby: informačné zdroje v EÚ a na Slovensku

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Orphanet is the most important database in the EU for rare diseases and orphan drugs for the general public. It contains information about 6 000 diseases and is freely accessible. Orphanet portal aims to offer health-care professionals, scientists, health authorities, patients and their relatives, the media and the community at large reliable, up-to-date, relevant information on rare diseases and orphan drugs.
Orphanet is managed by a board of directors representing all the countries associated with Orphanet and meets once a year. The board decides on the evolution of the database, the quality charter, the dissemination plan and the funding.
This site is designed to help improve the diagnosis, care and treatment of patients with such diseases, by providing the community at large with comprehensive, user friendly information on rare diseases in 6 languages. Features include:

- Comprehensive encyclopaedia of rare diseases
- Directory of professional services in 35 countries
- Directory of European centres of reference
- Database of orphan drugs providing information on their stage of development and availability in EU countries
- List of Expert Clinics
- List of Expert Laboratories
- Lists of research projects and clinical trials
- List of registries & biobanks

A Joint Action "Orphanet Europe" has been selected for funding in 2010 under the EU Health Programme. The French INSERM will lead the Joint Action for the following years. The expected outcome is a common European RD portal, providing European citizens with the information they need as described in the Communication "*Rare Diseases: Europe's challenge*" and in the Recommendation of the Council. The Orphanet dataset will be available for re-use in different formats to ensure dissemination of the Orphanet nomenclature of RD and maximise the use of collected information on expert services. Customised websites at national level in national language(s) will be available in order to disseminate national data at MS level. Orphanet will have the governance needed to ensure its mission at international level.

Session 1 – Presentation 2

Orphan drugs: the approach of European and Slovak regulatory institutions
Lieky na zriedkavé choroby prístup Európskych a Slovenských regulačných orgánov

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Orphan drugs are medicinal products (OMPs) intended for diagnosis, prevention or treatment of life-threatening or debilitating rare diseases. To support the development of new drugs for treatment of rare diseases as well as for future knowledge about rare diseases, in 2000 European legislation for OMPs was created (*Regulation (EC) 141/2000 and Regulation (EC) 847/2000*). It is directly applicable in each EU Member State. In connection with OMPs policy in the same year the Committee for Orphan Medicinal Products (COMP) at theEuropean Medicines Agency (EMA) was established. The Committee is responsible for reviewing applications from individuals or companies seeking OMPs designation. After designation of OMPs it might supervise the development process of OMPs due to protocol assistance. Designation of the OMPs provides further financial and market benefits to the sponsor. Actually (until February 2012) there are 62 OMP at the European market. However 1 417 applications were submitted, out of them 954 (66%) OMP designations were granted, only 18 (1%) negative opinions were given and 352 (26%) of the applicants withdraw their applications.
European support of OMP seems to be successful and turned attentions to this marginalised topic. On the other hand, there are big gaps in OMP policy at the national level and Slovakia isn't an exception. There are 32 (52%) of OMP at the Slovak market, others are available at patients named basis.
The presentation brings information about the current situation and stresses the most important points to improve availability and accessibility of OMP at the national level.

Literature: *Regulation (EC) No 141/2000 of the European parliament and of the council. Off J Eur Commun, 43, 2000, L18, p. 1-5;Regulation (EC) No 847/2000, Off J Eur Commun, 43, 2000, L103, p. 5-8;Committee for Orphan Medicinal Products and the European Medicines: European regulation on orphan medicinal products: 10 years of experience and future perspectives. Nat Rev Drug Discov 10, 5, p. 341-349. 2011*

Session 2 – Presentation 1

National registry of haemophilia and congenital bleeding disorders in Slovakia
The Rationale of registries and Data collection
Národný register hemofílie a vrodených krvácavých chorôb na Slovensku a jeho význam.

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Haemophilia and related congenital bleeding disorders represent a group of the rare diseases with severe, often life threatening bleeding manifestation, high rate of disabling complications with significant psychosocial sequelae and the high demands on the treatment. Accurate information on the disease prevalence and regional distribution of persons with bleeding disorders in each country is the prerequisite for the effective therapy and adequate lifetime comprehensive care for these patients. In Slovakia the National registry of haemophilia was established in the early 1970´s with the aim to estimate the needs for building up an efficient network of healthcare facilities providing the treatment with blood products. In 1992 the registry was computerized and it has served as the base for the establishment of the National Haemophilia Programme aimed at improving the haemophilia care in Slovakia.
The Haemophilia Registry is a database continuously collecting the key information on the persons with haemophilia and related disorders, including the relevant laboratory and clinical data, treatment patterns, complications, morbidity, mortality and social status. In 2012 the National registry accounts a total of 2150 persons with bleeding disorders, out of them 562 with haemophilia, 554 with von Willebrand diseases, 605 with Factor VII deficiency and 429 with other rare bleeding disorders.
The registry provides a lot of benefits for the persons with bleeding disorders, healthcare providers, the Health Ministry and Government as: 1) provides relevant information on the disease prevalence and distribution of patients in the country; 2) permits to assess the treatment needs and to plan the resources securing adequate treatment level nationwide; 3) serves as an effective surveillance system for monitoring of the safety of treatment with blood products; 4) allows an objective analysis and inter-regional comparisons of the standards and outcomes of care; 5) may be used as a tool for auditing clinical and laboratory services; 6) supports the close cooperation between all haemophilia treatment centres resulting in continuous progress in haemophilia care in the whole country. The National registry also allows an integrated and effective international collaboration supporting the haemophilia research on the national and international levels. All these activities have impact on the improvement of quality of life of haemophilia patients and their social and professional integration.

Session 2 – Presentation 2

National Registry for Cystic Fibrosis (CF) in Slovakia
Národný register cystickej fibrózy na Slovensku

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Slovak CF Registry was established in 1995, so that we have more than 17 years demographics, clinical and laboratory results, data and outcome of standard therapy.
In the year 2010 there were 394 CF patients with classical form of CF and 158 pts. with CF related disease. 113 pts died of CF from 80th. Median age of survival is 54.56 years. There are 3 CF centres in Slovakia (Bratislava, Banská Bystrica, Košice), each with department for children and adult patients as well. There are more than 60% pts. older than 18 years, CF is not a disease of childhood. Newborn screening of CF started in 2009 in Slovakia with 10-13 confirmed CF a year.
Efficacy of CF therapy could be evaluated according to the lung function tests, morphological changes on HRCT and CT scans of sinuses, ultrasonography of abdomen, basic anthropological parameters, immunological and laboratory results as well.
Not only life expectancy and median age of survival improved in last year's in CF patients, but quality of life did change as well. More of them did achieve high/university degree, they are employed. Some of them are married and have children.
Current symptomatic therapy is time and money consuming, but now "causal" therapy of CF is available: small molecules: CFTR correctors (Ataluren®, VX890) and CFTR potentiator (Ivafactor®-VX770). Therapy is mutation specific. After per oral application improvement of lung functions, sweat chloride, NPD was approved in long-term international studies. The importance of CF registries is also in finding appropriate patients.

Session 2 – Presentation 4

The contribution of molecular genetics for the diagnosis and treatment of hereditary cancer syndromes
Prínos molekulovej genetiky pre diagnostiku a liečbu hereditárnych nádorových syndrómov

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The identification of disease-causing genes associated with hereditary cancer risk has enabled precise diagnosis of hereditary cancer syndromes through molecular analysis. The most common cancers for which diagnostic tests are available include tumours of the colon, breast, ovary, endometrium, and endocrine glands. The most prevalent hereditary syndromes associated with these tumours are hereditary nonpolyposis colorectal cancer (HNPCC), familial adenomatous polyposis (FAP), hereditary breast and ovarian cancer (HBOC), multiple endocrine neoplasia type 2 (MEN 2) and Tuberous sclerosis complex (TSC). Identification of hereditary cancer susceptibility syndromes, increasingly using genetic testing, identifies individuals who can benefit from specific medical management options designed to address their increased risk of cancer. In many instances, identification of a hereditary cancer risk syndrome also has medical management implications for an individual already diagnosed with cancer. Significantly, testing may also identify individuals in high-risk families who did not themselves inherit cancer susceptibility, allowing them to avoid unnecessary medical interventions. A preponderance of data regarding the biology and medical manifestations of the common hereditary cancer risk syndromes has moved this area of medicine from “the bench to the bedside” in a relatively short amount of time. This rapid progress is illustrated by the examples of HNPCC, HBOC, FAP, MEN 2 and TS. This presentation uses these syndromes to illustrate the identification, implications, and management of hereditary cancer risk in Slovakia. Although there continue to be rapid advances in mutation detection strategies and medical management options for these syndromes, what is known at the present time can be utilized to enhance patient care today.

Session 2 – Presentation 5

How to create and manage a pulmonary arterial hypertension centre?
Ako vytvoriť a manažovať centrum pre pulmonálnu arteriálnu hypertenziu?

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Background: Pulmonary arterial hypertension (PAH) is a rare and devastating disease characterized by an inappropriate increase in pulmonary vascular resistance resulting in pressure overload of the right ventricle and subsequent right heart failure. Early diagnosis is important for best treatment results. Epidemiological and biological features of the disease as well as recent availability of new therapeutic options resulted in the need for systematic care for PAH patients.
Aim: To describe the patient flow and summarize the experience of the PAH centre at the National Cardiovascular Institute in Bratislava with the management of PAH patients.
Results: In 2005, the concept of comprehensive PAH management the Heart Failure and Transplant Department was suggested and adopted by the National Cardiovascular Institute, Bratislava. This management consists of several phases. Pre-hospital phase is based on screening and referral of patients with PAH suspicion and patients from risk groups (e. g. with connective tissue disease) by cardiologists, rheumatologists, and other specialists. Hospital phase includes a comprehensive diagnostic algorithm with right heart catheterization playing a pivotal role. Exact diagnosis requires a whole array of additional functional, imaging and laboratory tests. Quick referral patterns for consulting services must be available. Specific treatment is usually initiated during hospitalization. Long-term follow up is performed by the out-patient clinic and patients undergo periodic evaluation. The PAH centre is also engaged in clinical research and education activities and cooperates with patient association. Based on this long term and systematic effort, the Heart Failure and Transplant Department has been authorized as the first PAH centre by the Ministry of Healthcare in early 2012. From May 2002 to January 2012, 185 patients underwent right heart catheterization in search of PAH. Using catheterization and additional examinations, PAH was confirmed in 70 patients. At the time of diagnosis, 25% were in NYHA class II, 55% in NYHA III, and 20% in NYHA IV. The etiologic composition of the patients was as follows: 55% idiopathic PAH, 23% associated with connective tissue disease, 13% associated with congenital heart disease, and 9% other types of PAH. 6% patients were treated solely with calcium channel blockers, and specific drug treatment has been initiated in 90% of the patients and has included ambrisentan, bosentan, sildenafil, and treprostinil. 63% of patients are on combined treatment. 12 patients died and 3 patients underwent lung or heart/lung transplantation within the specified time range.
Conclusion: PAH is a rare disease and requires centralized care in a dedicated centre. PAH centre should cooperate with a wide range of specialists and perform screening, diagnosis, initiation of treatment, and long term follow–up of PAH patients. Educational and research activities are desirable. PAH patients in Slovakia receive a systematic care in a centre that conforms to the ESC criteria.

Session 2 – Presentation 6

National Centers of Expertise and the European Reference Network for Rare Diseases. Zásady tvorby expertných centier a európskej referenčnej siete

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National centers of expertise for rare diseases should provide healthcare services to patients with conditions requiring a particular concentration of resources and/or expertise provide cost-effective, high quality care and possess focal points for medical training and research, information dissemination and evaluation. There is an agreement on the following criteria for national centers of expertise for rare diseases:

- appropriate capacities to diagnose, to follow-up and manage patients with evidence of good outcomes , where applicable;
- sufficient activity and capacity to provide relevant services and maintain quality of the services provided;
- capacity to provide expert advice, diagnosis or confirmation of diagnosis, to produce and adhere to good practice guidelines and to implement outcome measures and quality control;
- demonstration of a multi-disciplinary approach;
- high level of expertise and experience documented through publications, grants or honorific positions, teaching and training activities;
- strong contribution to research and involvement in epidemiological surveillance, such as registries;
- close links and collaboration with other expert centers at national and international level and capacity to network;
- close links and collaboration with patients associations where they exist.

These designation criteria can be applied to national centers for different groups of diseases or specific diseases. Designation at country level can follow one of the following models: through a call for proposals (bottom/up), or a public health plan (top/down). The bottom/up method is more pragmatic whereas a top/down approach is more ambitious.

Session 3 – Presentation 2

Slovak Alliance of Rare Diseases (Slovak RD Alliance)
Slovenská aliancia pre zriedkavé choroby

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Introduction: Slovak RD Alliance was founded in December 2011 to promote the well-being of people living with rare diseases in Slovakia.
Aim: Alliance's mission is to improve quality of health care and social services of patients living with rare diseases and their families and to fight against the impact of rare disease on their lives. It is the network of patient associations in Slovak Republic that supports people affected by particular rare diseases.
Methods: collaborating with government, Ministry of Health, regional authorities and organizations of patients with disabilities mostly in these areas:

- Collaboration with group of experts on National plan for rare diseases in Slovakia
- Creating new professional brochure including encyclopedia and diagnostics of particular RD together with specialists in the field of rare diseases
- Mediation of health and social care
- Social counseling
- Publicity, publishing and educational training activities
- Cooperation with a team of specialists from various medical disciplines taking care of patients with rare diseases
- Educational activity
- Cooperation with international organizations (EURORDIS)
- Raising awareness for the wishes of people with rare diseases, promoting a positive attitude of the broad public towards people with rare diseases
- Providing services which are directly or indirectly to the benefit of people with rare diseases (social assistance, advice, information)

Conclusion: At this time Slovak Alliance of Rare Diseases is the network of 10 patient organizations which support people affected by rare diseases in Slovakia. One of its goals is to be one voice of patients with RD in Slovak Republic.

Session 3 – Presentation 3

Patient Empowerment
How to improve patients' orientation in the system thorough targeted education
Patient Empowerment - posilňovanie kompetencií pacientov prostredníctvom cieleného vzdelávania

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Since the economical and political changes in 1989 the patients Access to health care improved constantly and radically. The improved access was not visible always in all health care sectors, due to variability in economical and political cycles, but was present all the times since 1989.
An extraordinary phenomenon was the dramatically improved access to innovative, expensive oncology treatments (biologics, targeted therapies...) in the time 2002 – 2008. Actually, from the patient point of view, we can see a lot of negative phenomenon's, which lead – or will leave, in a short time to shortages and to deterioration of health care Access.
Literature basically identifies as main problems the poverty, administrative and geographical barriers and a lack of health education. Despite of the country of origin, we know that chronically ill patients mainly in rural areas have less Access to health care. Also the problems of unequal Access to health care are underestimated, because the universal health care coverage in EU countries is overestimated. Mostly for elderly people is the social coverage the only source how to finance health care and they suffer most from health care payments. In the internet era also grows to a huge handicap the lack of IT skills.
In Slovakia actually we identified the main problems as follows:

- Impairment of orientation in the system and information about the system
- Impairment of Access to health care
- Absence of patients point of view in declared health policy
- Hidden payments in health care services
- Lack of transparency in reimbursement procedures
- Deterioration of some epidemiological aspects
- Lack of continual patient education

The improvement of patients' social and legal competences thorough continual education seems to be the way how to improve the Access to necessary health care. In Slovakia in the years 2010 – 2011 we performed series of patient education called *Patient Empowerment*. Patients were trained to get the right information in relevant time frame, evaluate the information and use it in the communication with health care providers and the authorities.
Slovak medical university in Bratislava together with Comenius university in Bratislava starts in the year 2012 (May and November) with one day seminars for patients, patient relatives and patient advocates. The aim is to give them basic skills in rational drug use, a safe pharmacotherapy and the services in modern pharmacy. Together with these topics they seminars will cover legal responsibility, patient rights and patient duties and all aspects, how to avoid poverty due to health care payments.