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Minutes ExPO-r-Net General Assembly

Date: Friday 24 October 2014, 12:00-14:00
Venue: Canada, Toronto, Sheraton Centre Toronto Hotel, Huron Room 2nd floor

Aim: Building together a European Reference Network

ExPO-r-Net project introduction and current status
Ruth Ladenstein, Children´s Cancer Research Institute (CCRI)

Introduction to the project:
Ruth Ladenstein welcomes the participants explains the ExPO-r-Net briefly (Call, project goals, expected impact and partners) and invites the present European Clinical Research Council (ECRC) members to become collaborative partners of the project. Collaborative partners of ExPO-r-Net will be able to attend project-related meetings on the costs of the project coordinator. Tumor boards are centres of high expertise with a clear structured way and will help improve the quality of care (one objective of ExPO-r-Net). She also refers to the expected ExPO-r-Net impact of developing a clear roadmap of Pediatric Oncology Expert Reference Networks (PO-ERN) with the help of the ECRC to locate hubs of expertise throughout Europe. In this context she mentions that ExPO-r-Net is going to tackle the problem that countries with less economic outcome also have a less favourable disease outcome and that there is no structured pathway established for patients and parents who are frequently misguided. ExPO-r-Net intents to show them hubs of expertise where patients can get advice. However, it is not the intention of the project to transport an increasing number of patients cross border but to support less equipped centres with advice though structured tumor boards and enable them to learn.

Project status:
WP1 Coordination of the project, WP leader Ruth Ladenstein
The Milestones 1, Kick-off meeting and 2, Quality Assurance Plan (QUAP) were already achieved, Milestone 3, biannual consortium meetings is an ongoing process.
The QUAP contains the organisational structure of ExPO-r-Net with the Project Management Team (PMT), the Executive Committee (ExeCom) and the General Assembly (GA) consisting of ExPO-r-Net partners, ECRC chairs, SIOPE Board, PPAC, EAC and others. Ruth also gives a short overview of the project´s meeting schedule as indicated in the QUAP.

WP2 Project dissemination, WP leader Samira Essiaf
The dissemination team has already shown a lot of activity by developing a brochure, a bookmark and a banner for the SIOP congress in Toronto. ExPO-r-Net is also disseminated by dedicated E-blasts and a dedicated section in the SIOPE newsletter and a first version of the ExPO-r-Net webpage is already available (www.expornet.eu). As well, a structure for the foreseen ExPO-r-Net intranet was developed in cooperation with Günter Schreier, AIT.
So far, several meetings have taken place which add to the dissemination of ExPO-r-Net:

- ExPO-r-Net kick-off meeting
- ExPO-r-Net at the ERN conference 2014
- ExPO-r-Net at the SIOPE-ENCCA Conference 2014
- ExPO-r-Net 2nd biannual ExeCom meeting Valencia 2014
- ExPO-r-Net at the SIOP congress Toronto 2014

WP3 Project evaluation, WP leader Pam Kearns
This WP is to commence an internal evaluation plan. The so far available documents of the work packages were reviewed and feedback was given to the WP leaders. This included an interim review of the questionnaire developed in WP 4 to identify the needs of rare childhood and young people cancer types and entity subgroups and an ongoing review of the WP teleconferences in July 2014 including a TC with Enrique Terol from DG SANCO. In WP 6 an external ICPRB review of a 1st draft of principles of accreditation

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process for pediatric oncology/hematology was initiated. Until March 2015 an external evaluation plan will be determined and an external evaluation report on ExPO-r-Net is planned in December 2016.
Ruth clarifies that this evaluation is independent of the expert an accreditation process by DG SANCO for ERN.

WP4 Needs and challenges of cross border healthcare, WP leader Ruth Ladenstein
The milestone 1 to identify and to agree on potential cross border needs and challenges was already discussed at the biannual ExeCom meeting in Valencia and will also be discussed in this meeting with the European Clinical Tumor Groups (ECTG). Milestone 2, a questionnaire within the respective ECTG committees has been developed and circulated: Responses have already been achieved and a first analysis was done. Milestone 3 is to identify reference sites via the ECTG, in addition to associated and collaborative partners. At the end of the project a roadmap for public health care providers and patients should be available.

Becoming an official PO-ERN
In this context Ruth announces that DG SANCO intends to launch a call for networks in late 2015, where network proposals will be assessed and approved. ExPO-r-Net has to become an approved ERN to be eligible for later funding in 2016. For this Enrique Terol recommended to establish some (4-5) reference centres from pre-existing centres under the umbrella of ExPO-r-Net to achieve approval as an official ERN. To reach this goal some processes in the project have to be sped up. A first example PO-ERN should be established in Q3-Q3 2015 that will be extended later on. Ruth suggests that for the time being a selection of very rare tumors may simplify the identification of reference centres for a first accreditation by DG SANCO.
Contacts made with liver tumor, retinoblastoma, Wilms tumor groups as first steps how the identification process on special treatment and diagnostic identification based on special therapeutic needs can be launched with the very rare tumor clinical trial groups.

WP5 PO tumor board ERN based E-health concepts, WP leaders Adela Cañete, Günter Schreier
Since Adela Cañete presents WP5 separately, Ruth introduces this WP only briefly. She informs that the Spanish partner has circulated a questionnaire in Spain to evaluate current existing tumor boards including technical aspects. An adapted version of this questionnaire will be distributed throughout Europe. WP5 also enabled the ExPO-r-Net partners to learn that a frequently used system for virtual tumor boards is Adobe Connect (Spain, France, USA, others), whereas due to regulatory restrictions Germany uses other systems like Vidyo (Münster University). To build a suitable IT-Architecture for ExPO-r-Net as suggested by Günter Schreier DG SANCO is an active searching partner who tries to provide IT solutions and give advice.

WP6 Defining criteria to identify and certify PO expert centres, WP leader Jerzy Kowalczyk
This WP intends to identify PO centres in Europe and will be presented in detail in a separate presentation by Jerzy Kowalczyk. A glossary of terminology and definitions used for a certification process is already structured. A face to face meeting on WP6 at November 4th in Warsaw, Poland will conclude on the glossary. Jerzy foresees 7 steps containing the certification process:

- Application of a POH
- Self-assessment
- Go/no go decision
- Peer review visit and designation check
- Reporting
- Formulate improvement plan
- SIOPE Certificate

A self-assessment checklist will be developed in this WP but ExPO-r-Net will not execute an accreditation.

WP7 Cross border dimensions of long term follow up, WP leaders Lars Hjort, Riccardo Haupt
In this WP the survivorship passport will be developed to be used Europe-wide. First translations of the

English survivorship passport and the guidelines have already started with the help of professional volunteers from the United Nations as arranged by SIOPE, Olga Kozhaeva. So far, there is a priority list of languages (French, Spanish, German, Polish, Italian; Hungarian, Portuguese, Greek) which will be enlarged later on.

WP8 Integrating children with very rare tumors in an ERN, WP leader Gianni Bisogno
Finally, WP8 intends to establish a Very Rare Tumor (VRT) network tumor board and working group on rare Soft Tissue Sarcoma (STS) in collaboration with the European Paediatric Soft Tissue Sarcoma Study Group (EpSSG) until November 2014. A working meeting on this took place in Milan on the 29th September 2014 and as caveats are mentioned: i) the need of legal advice (responsibility remains with the treating clinician, tumor board gives noncommittal advice), ii) the effectiveness and the quality of the system is strictly related to the available resources. The launch of a webpage to inform families and the public about very rare tumors is expected in March 2015. Needs for this webpage will be identified via a VRT questionnaire and it will be part of the SIOPE website. Its basic structure was already developed.

Finally, Ruth ends her talk by announcing the 3rd biannual ExPO-r-Net meeting which will take place on the 6th March 2015 in Padova, Italy.

See presentation: ExPO-r-Net Project update_Ladenstein.pdf

Criteria for the definition of tumor boards

Adela Cañete, Fundacion Para La Investigacion del Hospital Universitario la Fe (HULAFE)

Adela Cañete briefly explains WP5, on which she is working together with her colleague, Pablo Berlanga and the IT expert Günter Schreier from AIT. The goal is a pediatric oncology tumor board ERN working on common standards and using IT tools based on E-health concepts for sharing and providing expertise and advice. This will also foster knowledge transfer and integrate local care teams lacking expertise or tools for specific therapeutic elements.
The IT expert analysed use cases from the European Interoperability Framework to be used by and adapted to ExPO-r-Net. He defined 4 levels of interoperability:

- Technical interoperability: need trust from the source systems (IT Administrators)
- Semantic interoperability: we need a common language – dataset standardisation
- Pragmatic interoperability: we need shared processes (workflow support)
- Juristic interoperability: need common rules (rules and rights)

The current tasks in WP5 are to learn about the state of the art by identifying current functioning tumor boards (TB). This will be achieved by a questionnaire with clinical and IT elements, which was already sent out in Spain and will be distributed throughout Europe soon (Milestone 1). This will allow specification of conceptual models and standardized IT languages resulting in the definition of Standard Operating Procedures (SOP) and roadmaps to implement the ExPO-r-Net TB (Milestone 2). In this context it is important to develop a coherent ICT strategy and devise interoperability architecture for ExPO-r-Net (Milestone 3).
Current existing virtual TB (pediatric and adult) use Adobe Connect (France, Cure-kids, USA), Vidyo (Münster) and Tandberg 2500 videoconferencing (Scotland).
The workflow of an expert advice via a virtual TB is usually as follows:

- Case submission by clinicians
- Panel assignment by a moderator
- Web review by oncologist, pathologist, radiologist, surgeon on an IT platform
- Conclusions by moderator

From the first results of the questionnaire and during the ExPO-r-Net meeting in Valencia the following important factors to be considered were raised:

- Confidentiality
- Security

→Informed consent?

- Different levels of interoperability:
  1. Data transfer
  2. Case presentation
  3. Communication
- Different complexity levels according to local/national developments and regulations

Adela closes her presentation with the notion that ExPO-r-Net does not have to reinvent the wheel but rather use and adapt already existing IT tools.

See presentation: ExPO-r-Net Criteria for def of tumor boards_Canete.pdf

Discussion:
Piotr Czauderna points out that SIOPEL works with a System as developed by CINECA, which is introduced at the SIOP congress (Rangaswami, et al., abstract No. 492). The communication is via email and easy to handle. The goal is to acquire expert´s advice within 1 week. The download of images (radiology and histology) is possible. The system could be modified for any kind of cancer. CINECA provides the central server of this IT tool and also functions as a secure database, which allows easy backtracking of cases and given advice.
Ruth Ladenstein explains that the current CINECA solution images are captured, stored and administered in a central server. In particular in cross border action a high level of data protection is needed and the issue of data storage has to be clarified (cloud vs. fixed database). It becomes more and more clear that ExPO-r-Net might not be restricted to one system but might use different options specific for certain needs.
Pam Kearns discusses with Adela that the adapted questionnaire should be first sent to the clinical trial groups and not to the centres. All agree that first the clinical trial groups will be addressed and the centres will follow to gather as much information as possible.

Virtual Tumor Board France
Dominique Valteau-Couanet, Institut Gustave-Roussy (IGR)

Ruth Ladenstein invites Dominique Valetau-Couanet to introduce the already established virtual tumor board in IGR.
Dominique explains that the TB at IGR is tumor specific. It is mandatory and consist of 4 expert centres from Ille de France which were asked to work together to give advice. First they had met in real face to face meetings which turned out to be very time-consuming and resulted in the establishment of a virtual board. Now the virtual tumor board takes place regularly and is divided to different tumor types according to a fixed meeting schedule. Different tumors like bone tumor, soft tissue tumor, leukemia, lymphoma and phase-I and II-studies are on the meeting schedule and are discussed weekly to at least once monthly. The TB discusses a large amount of patients. Every new patient is reviewed and re-discussions take place at difficult points of the treatment strategy. The meeting participants are oncologists, pediatric oncologists, radiologists, pathologists and surgeons. Each physician has to present his own patient. The board works with Adobe Connect and images and documents are shared. Under certain circumstances it is also possible to give access to a specified imaging system in the institution for interactive discussions. The conclusion of each meeting is sent to the physicians in each centre and is incorporated in the clinical data files. Since this virtual tumor board is limited to the 4 centres within one region in France, the images are not anonymised. However, an anonymization or pseudonymization may be required in cross-border virtual TB.

Discussion:
Ruth says that the IGR system is already well structured and can be a model to be further elaborated, considering the aspect of anonymization for cross border data flow. Dominique notes that a major drawback for the implementation of TB Europe-wide may be the time factor and therefore the possibility of resistance from the clinicians, since the preparation and implementation of information takes several

hours.

Quality Criteria for EU reference networks
Jerzy Kowalczyk, Medical University of Lublin (MUL)

Jerzy Kowalczyk introduces the objectives and milestones of WP6, to promote high quality patient care in paediatric oncology centres to reduce inequalities between centres and countries. A certification process is envisioned by which competency, authority and credibility is presented and confirmed. The tasks are:

- To define the terminology and definitions used for the certification process
- To describe quality certification system
- To prepare a checklist enabling self-assessment by treatment centres

A document for the definition of terminology used for the self-evaluation process (European Standards of Care for Children with Cancer, ABBREVIATIONS, TERMINOLOGY AND DEFINITIONS) is in development, its expected date of finalization will be mid-December 2014. The quality certification system will use 7 principles as already explained in the presentation of Ruth Ladenstein and Jerzy intends to define different types of Pediatric Oncology/Hematology (POH) centres:

- POH Unit (clinical facility or hospital department covering at least basic diagnostics for childhood cancer, with possibility to provide chemotherapy + formalized collaboration with other hospital specialities)
- (Specialised) Clinical POH Centre (characterised by the clinical capacity covering a sufficient degree of all diagnostics, medical, surgical and radiotherapy services and limited degree of clinical research)
- POH Research Centre (capacity in cancer research focusing on one or more areas in the field of fundamental or translational oncology)
- Comprehensive/Expert POH Centre:
    - high level of infrastructure, expertise and innovation, multidisciplinary approach using the potential of basic, translational and clinical research, clinical facilities and activities, organised in a sufficiently identifiable entity
    - maintenance of an extensive network including variety of childhood cancers, all aspects of childhood cancer care and research
    - Broad activities in the area of education and external dissemination of knowledge and innovation (related to an academic/university centre or is an academic centre)

Another milestone of WP6 will be the preparation of a checklist enabling self-assessment by treatment centres of their compliance with the European standards. The self-assessment questionnaire will contain:

- Glossary of terms and definitions
- Qualitative Part including detailed questions on general standards, strategic plan and general management, care, research innovations and developments, education and teaching as well as patients related issues
- Quantitative Part required to provide numbers related to infrastructures, including diagnostics, multidisciplinary team, facilities, human resources, research activity, education

The self-assessment questionnaire is a sensitive issue because experience showed the not all centres are willing to deliver information freely.
So far, the chairs of 18 European tumor study groups (TSG) were asked if they have a system to recognize POH centres fulfilling all necessary requirements to cooperate in the field and if these include specific requirements like special hospital facilities, a certain centre size, access to specific diagnostics etc..
Feedback was given so far by 8 TSG: EURAMOS, EWOG MDS, EXPeRT, I-BFM, LCH Studie, SIOPE-BTG, SIOPEL, SIOPE-RTSG. Except for SIOPEL no group has a system for the qualification of centres. ExPO-r-Net may use and adapt the SIOPEL questionnaire.
The approach to TSG has to be carried out on a national level. For example, Jerzy makes aware that in Germany the "Gemeinsame Bundesausschuß" (Joint Committee of stake holders in health care; short: GBA) was developed with criteria which need to be met by "Pediatric Oncology Centres". The document was activated in 2007, and revised in 2013. It may help ExPO-r-Net in the development of its certification system. Jerzy finalizes his talk with the notion that contribution from European Tumour Groups and

NaPHOS is needed and expected.

See presentation: ExPO-r-Net Quality Criteria for ERN_Kowalczyk.pdf

Discussion:
Martin Schrappe explains the "Gemeinsame Bundesausschuss" document in detail: it forces the centres to implement the needed structures and insurance is only guaranteed if the centre fulfils the criteria. This includes the mandatory involvement of patients in trials. If the criteria are not fulfilled, the centre loses its status. Jerzy states that this is already a good quality system to be adapted for ExPO-r-Net. Kathy Prichard-Jones mentions that other countries like the UK, France have similar systems. According to Jerzy, Poland has one as well. Kathy recommends to check:

- how countries accredit
- which childhood cancer centre has special treatment opportunities
- how cross boarder healthcare has to be addressed

The answers on the first point can be given by NAPHOS: what is eligible in each country.
Ruth Ladenstein takes into consideration that an aim of ExPO-r-Net is to reassure that in Eastern European countries the patient is safe to stay at home with the best advice from virtual TB. To that centres need to be identified and defined. This only works with the insight of the TSG and with the inclusion of patient´s parents and stakeholders. The clear message has to be: you do not need to go cross border except for specific treatment needs not available in the local centre.
Charlotte Niemeyer mentions that Germany does not accept small single expert centres but rather expert networks. Therefore you have to address the expert networks first.
Kathy worries that it took the countries many years to develop such systems and that ExPO-r-Net might face similar time issues, whereas Jerzy opposes that the process actually has to be sped up to become an official ERN. He suggests to identify at least 1 centre in each country where a patient can receive standardized treatment.
This is critically discussed (see below) and the ExPO-r-Net PMT rejects this approach.
Ruth summarizes the next project phases as funding action driven mechanisms:

- Early network in 2015 focussed on few entities with very rare tumors
- Official PO-ERN eligible for funding in 2016

Dominique Valetau-Couanet notes that it might be difficult to define 1 expert centre in each country because expertises are often not limited to one centre. Patients need a clear roadmap where to go for which disease. Also Kathy points out that in the case of Wilms tumor there is a multidisciplinary team.
According to Ruth the expert centre identification is a multilayer process including the view from the clinical trial groups and from other perspectives. The sharing of ideas of ExPO-r-Net with tumor groups is a starting point. Jerzy agrees that a limitation to one centre may not be applicable in certain cases.
Martin says that all the mentioned issues are highly politicial and that care has to be taken not to create sensitivities. According to him the EU expects a focus on very rare cancers. Therefore Ruth confirms the ExPO-r-Net strategy to start with very rare tumors first.
Gianni Bisogno suggests using a different terminology for expert centres, **activity coordinating centres** and not to create a list of centres with one above the other. Many centres are usually part of a network. Padova for example is in charge to coordinate the activity on very rare tumors in Italy. A similar terminology could be used.
Dominique agrees that in the case of IGR it would have been problematic if the 4 centres participating in the TB would have been rated differently.
Riccardo Haupt recommends to assemble the scientific evidence which may be cross border with the political evidence in the respective countries (could be missing in some countries).
Ruth highlights that the best execution of ExPO-r-Net is a developing process that has to be discussed and she thanks all participants for their valuable contributions in this meeting.

Survivorship passport
Riccardo Haupt, Istituto Giannina Gaslini (IGG)

Riccardo Haupt briefly updates on the survivorship passport as already outlined by Ruth Ladenstein in her presentation. The translations for the list of variables are ongoing, from technical English to lay English as well as translations from English to Italian and other countries (see above). This will be done with the help of expert volunteers. As a guideline with which to work he will consult the breast cancer recommendations and others. He will also question centres on who is an expert on late effects.

Very rare tumors in an ERN

Gianni Bisogno, Azienda Ospedaliera di Padova (AOP)

After briefly introducing the audience to the WP partners and objectives, Gianni Bisogno goes into detail by updating on the status of the establishment of a very rare tumor network tumor board. A document describing the working procedure has been written and discussed with CINECA The document needs review and external advice (Advisory Group). A website dedicated to inform families and the public will be launched in March 2015 together with SIOPE and a questionnaire on the existence and activity of cooperative groups in favour of children with very rare tumors will be distributed via Survey Monkey. In 2016 Gianni plans a European meeting to reach consensus on guidelines for very rare tumors and rare soft tissue sarcomas. On the guidelines priority list are:

- Pleuropulmonary Blastoma *(G. Bisogno*)
- Pancreatoblastoma *(E. Bien, A. Ferrari)*
- Sertoli-Leydig Tumors *(D. Schneider, G. Cecchetto)*
- Infantile Fibrosarcoma *(D. Orbach, A. Ferrari)*
- *Desmoid tumors ?*

However, only very few studies are available on very rare tumors, therefore the guidelines cannot put out a standard of care but rather remain expert recommendations.
Finally, Gianni announces again the next biannual ExPO-r-Net meeting in Padova, Italy, where he will be host.

See presentation: ExPO-r-Net Quality Criteria for ERN_Kowalczyk.pdf

Discussion:
Gianni points out that he needs external advice for the document describing the working procedure but he wonders how to identify who could give such advice. He addresses Pam Kearns if she is able to give such advice. She answers that the role of her institution in the project is to check if the WP are going in the right direction but not to give advice in every detail. However, she contacted colleagues dealing with very rare tumors. The request will be collected until the end of this year. SOPs will be defined to set up the system and for every cooperative group. She also talked with Francois Doz who intends to establish a virtual tumor board for retinoblastoma and CINECA, because their system might be applicable for very rare tumors. Howver, the CINECA system does not allow a face to face meeting, everything is done via writing. Therefore another system may be added. Pam makes aware that it is crucial to choose the best system now (Adobe Connect, CINECA-system, Vidyo) because towards the end a change will be difficult. Martin Schrappe recommends the Adobe Connect system which is used in the USA, Cure 4 kids, because it seems workable, patient oriented, with good quality of the pictures and direct communication. He announces that he heard many positive comments about it. Ruth agrees that Adobe Connect might be valuable, safe tool but Germany has to use Vidyo instead due to data protection regulations. Adela Cañete interjects that also Canada is using Adobe Connect.
Gianni mentions that a storage system is needed to see if an advice is followed. St. Judes has established such a system but the maintenance needs personnel and therefore generates costs.
Ruth Ladenstein summarizes that therefore the project will start with some trials and examples to get more funding to be re-established later on and closes the meeting.