4107 ORAL

The State of Research Into Children With Cancer Across Europe: Results of Key Opinion Leaders Survey and Innovative Policy Strategies for the Next Decade

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Background: Overcoming childhood cancers is critically dependent on the state of research. Understanding how, with whom and what the research community is doing about childhood cancers is essential for ensuring the evidence-based policies at national and European level to support children and those who care for them.
Material and Methods: As part of EUROCANCERCOMS, an EU Seventh Framework Programme (FP7)-funded project to study and integrate cancer communication across Europe, an investigation into the state of research in childhood cancers was carried out. Over a 6-week period in 2010 a comprehensive survey was conducted by SIOP Europe- the European Society for Paediatric Oncology, of 'key opinion leaders from 22 European countries working in the field of paediatric oncology to determine their subjective views on the state of paediatric oncology at both national and European level. Six questions were posed to these national experts: 1) how is paediatric oncology delivered across Europe?; 2) what are the keys issues in paediatric oncology care & research?; 3) what are the sources of funding for paediatric oncology?; 4) what is the state of patient information for paediatric oncology?; 5) what has been the impact of European funding so far?
Results: Common responses from experts included the need for an immediate re-assessment of the EU Clinical Trials Directive (2001/20/EC (EUCTD) which has negatively impacted the conduct of paediatric oncology research and increased EU funding to facilitate the running of international clinical trials. In addition, the establishment of a European registry for paediatric oncology for the collection of epidemiological data, as well as the establishment of tissue storage, and of pan-European guidelines for treatment is commonly supported. The establishment of a common European information portal in paediatric cancer care would also be useful, as it would avoid redundancies and aim at harmonisation, while providing supervision of the quality and correctness of information available on the internet.
Conclusions: Due to the common thread in the responses received, there is an urgent need to promote increased and sustained funding for these rare diseases as well as a centralisation of services and facilities, avoiding fragmentation at all levels and redundancy of the bureaucratic aspects of treating paediatric cancers, particularly by establishing a common platform or infrastructure.

Poster Presentations (Sun, 25 Sep, 14:00−16:30)
Paediatric Oncology

4108 POSTER

Detection of Micrometastases for Prognosis and Stratification for Treatment in Children With Neuroblastoma

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Background: Neuroblastoma is the most common extracranial solid tumour of childhood, which has a broad spectrum of clinical behavior, varying from aggressive malignant disease (stage 4) to spontaneous maturation and even regression (stage 4s). Metastasis to the bone marrow (BM) is a hallmark of high risk in neuroblastoma and predictive of poor prognosis for most children, except stage 4s disease. Detection of metastases in the bone marrow is crucial for specification stage of neuroblastoma and the choice of optimal treatment protocol.
Material and Methods: One hundred eighty-seven children with neuroblastoma aged 2 month − 17 years were enrolled in our study. The presence of micrometastases in BM was analyzed based on the expression of tyrosine hydroxylase (TH) gene. As biological material we used RNA derived from BM (from sternum, left and right wings of iliac bone) by acid-phenol extraction. The study was performed by the reverse-transcription polymerase-chain reaction (RT-PCR) with detection results in real time using specific primers and TaqMan fluorescent probes. Total 210 samples of BM before and on the stages of treatment have been analyzed.
Results: Expression of TH gene was found in the BM samples of 62.5% patients with neuroblastoma, which indicates the presence of micrometastases in BM. With cytology method the presence of tumour cells in BM was identified in only 47% of patients. This suggest that 15.5% of children have micrometastatic disease at diagnosis that is not detected by current routine methods. Thus, RT-PCR as a more sensitive method may improve stratification for treatment and potentially outcome. All stage IV disease was characterized by the presence of micrometastases in BM. In our study the detection of micrometastases by RT-PCR did not correlate with n-myc amplification in children with stage III or IV disease. The detection of micrometastases provides important risk information for children with low stage disease. In children aged over 1 year with advanced stage disease the detection of micrometastases in BM is predictive of rapidly progressing disease. Using the RT-PCR method in 29% of children after treatment was noted the presence of tumour cells in BM. Detection of micrometastases will probably have its biggest impact as a tool to monitor disease course and response to treatment.
Conclusions: RT-PCR is more sensitive and reliable tool for the identification of children with high risk neuroblastoma than current routine methods. Detection of micrometastases in BM helps specify prognosos, influences on choice of risk group, schedules of therapy and provides its monitoring.

4109 POSTER

Update on MTHFR Pharmacogenetics and Methotrexate Toxicity in Childhood Acute Lymphoblastic Leukemia

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Background: Acute lymphoblastic leukemia (ALL) is the most common childhood cancer, accounting for 30% of all pediatric malignancies. Remarkable progress has been made in the treatment of acute lymphoblastic leukemia (ALL): four decades ago, the cure rate was less than 10%, today it is nearly 80%.
Methotrexate (MTX) is a key component in the treatment of childhood acute lymphoblastic leukemia (ALL). MTX inhibits dihidrofolate reductase, interrupting the folic acid metabolism and affecting central enzymes of this pathway, such as methylene tetrahydrofolate reductase (MTHFR). The polymorphisms C677T and A1298C are nonsynonimous aminoacid changes that have been associated with the decreased activity of the enzyme. Previous works have associated MTHFR 1298C and 677T alleles with MTX toxicity in paediatric ALL.
The aim of the present study was to determine conclusively whether MTHFR C677T and A1298C polymorphisms play a role in the toxicity of MTX in paediatric ALL patients.
Material and Methods: DNA was extracted from blood samples of 115 paediatric ALL patients treated with the LAL/SHOP protocol. We analyzed MTHFR C677T and A1298C polymorphisms and their association with toxicity, using the Fisher exact test (p value <0.05). We performed a meta-analysis.
Results: Despite what was expected by the functional effect of both polymorphisms, we found no association with toxicity in children with B-ALL treated with the LAL/SHOP protocol. In most studies in pediatric ALL by other authors, they did not find either association with toxicity. The previously observed associations can be explained if we consider that they studied small or heterogeneous samples.
Conclusion: Considering our results and the meta-analysis performed, we dismiss MTHFR C677T and A1298C polymorphisms as predictors of toxicity in childhood acute lymphoblastic leukemia.
This project was supported by RETICS (RD/06/0020/0048) and Basque Government (GIC10/71, SAI10/03 and 2006111015). Support by SGIker (UPV/EHU) is gratefully acknowledged.