THE SIOPE STRATEGIC PLAN

A European Cancer Plan for Children and Adolescents

SIOP Europe
the European Society for Paediatric Oncology

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Acknowledgements

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Preamble

The SIOPE Strategic Plan is one of the deliverables of the European Network for Cancer research in Children and Adolescents (ENCCA), a network of excellence that was run from 2011 to 2015 under the EU 7th Framework Programme for research and innovation (FP7).

This plan was first elaborated by a dedicated working group, the ENCCA Long-term Sustainability (LTS) working group. Established within the ENCCA project, this group is composed of outstanding experts in paediatric oncology: Andrea Biondi, Angelika Eggert, Lars Hjorth, Jerzy Kowalczyk, Ruth Ladenstein, Giorgio Perilongo, Rob Pieters, Kathy Pritchard-Jones, Martin Schrappe, Richard Sullivan and Gilles Vassal (working group chair).

The first document has been presented, discussed, and refined through the contributions of SIOPE Board members and partners from the ENCCA project, the European Clinical Trial Groups (ECTGs) and the National Paediatric Haematology-Oncology Societies (NaPHOS) – both parts of the European Clinical Research Council for Paediatric and Adolescent Oncology (CRC, formerly ECRC) – the ENCCA Parent Patient Advocacy Committee (PPAC), and the Europe Regional Committee of Childhood Cancer International (CCI).

On September 18th and 19th, 2014, SIOPE organized a conference in Brussels entitled '*Joining efforts for a brighter future for children and adolescents with cancer – The European roadmap to Horizon 2020*', in order to ensure the sustainability on the long-term of the results achieved in the framework of ENCCA. On this occasion, approximately 160 participants from 31 countries – representing all stakeholders (patients, survivors, parents, academia, charities, industry, regulators, EU policy-makers) – endorsed the SIOPE proposal and called for a European Cancer Plan for Children and Adolescents.

The ENCCA Scientific Advisory Board (composed of Peter Adamson, Ulrik Ringborg, Holger Schünemann) reviewed the proposal in early 2015.

The pre-final draft was approved by the SIOPE General Assembly in October 2014, by the ENCCA General Assembly in January 2015, and the final version has been approved by the SIOPE Board on May 20th, 2015.

The SIOPE Strategic Plan will be launched at the 2015 European Cancer Congress in Vienna in September 2015 and at the European Parliament during a special event of the Members of the Parliament Against Cancer (MAC) group in November 2015.

encca
European Network for Cancer research in Children and Adolescents

Executive summary

From AIEOP. Credit Attilio Rossetti photographer, Italy

Cancer in young people is rare, but it is still a major health issue in Europe. Each year, more than 6,000 young people in Europe die of cancer. There are more than 300,000 European childhood cancer survivors (in 2020, they will be nearly half a million): two-thirds of them have some late side effects of treatment, that are severe and impact on the daily life of half of those affected.

Within the European Network for Cancer research in Children and Adolescents (ENCCA), SIOPE and the European paediatric haematology-oncology community have established a long-term sustainable Strategic Plan **to increase the cure rate and the quality of survivorship for children and young people with cancer over the next ten years.** The ultimate goal is to increase the disease- and late-effect- free survival after 10 years from the disease, and beyond.

Seven medical and scientific objectives have been set up to achieve these goals:

- *Innovative treatments*: to introduce safe and effective innovative treatments (i.e. new drugs, new technologies) into standard care;
- *Precision cancer medicine*: to use improved risk classification as well as biological characteristics of both the tumour and patient (such as molecular and immunological factors) to help guide decisions on which therapies to use;
- *Tumour biology*: to increase knowledge of tumour biology and speed up translation from basic research to clinical care to benefit patients;
- *Equal access*: to bring about equal access across Europe to standard care (in both diagnosis and treatment), expertise and clinical research;
- *Teenagers and Young Adults*: to address the specific needs of teenagers and young adults (TYA), in cooperation with adult oncology;
- *Quality of survivorship*: to address the consequences of cancer treatment such as long-term side effects, to better understand the genetic background/risk of an individual, and to improve quality of life of survivors of childhood cancer;
- *Causes of cancer:* to understand the causes of paediatric cancers and to address prevention wherever possible.

SIOPE will steer and coordinate the effective implementation of this Strategic Plan, together with the European Clinical Trial Groups (ECTGs) and the National Paediatric Haematology Oncology Societies (NAPHOS) in close cooperation with the parents, patients, and survivors' advocates from the Europe Regional Committee of Childhood Cancer International (CCI).

Cross-tumour platforms and projects will facilitate this implementation: a Clinical Trial Facilitating (CTF) platform to ease setting up of clinical trials within the new EU Clinical Trial Regulation, the PICORET (Population Improvement in Childhood cancer Outcomes through Research, Evaluation and Training) outcome research project to evaluate and monitor progress in childhood cancer survival and therapy effectiveness, the QUARTET (Quality and Excellence in Radiotherapy and Imaging for Children and Adolescents with Cancer across Europe in Clinical Trials) project for quality assurance in radiation therapy, the CDDF-SIOPE-ITCC multi-stakeholder platform to improve oncology drug development for children and adolescents, and the 'Ethics, Social Science and Humanities' project to address the ethical aspects related to paediatric cancer. An efficient IT infrastructure to support e-Health and research will be developed, and a European Reference Network for paediatric patients with cancer will be created to facilitate cross-border healthcare and access to expertise.

The 'Oncopolicy' programme will ensure that the needs of young people are well taken into account into all EU policy initiatives in the field of health and research. Finally, the 'Education and Training' programme will ensure an adequate training to paediatric oncology health professionals.

Partnerships will be strengthened with patients, parents and survivors' advocates, adult oncologists as well as paediatric oncologists from other continents. 'Intelligent and transparent' public-private partnerships, recognizing the specificities of paediatric haematology-oncology, will be established with industry. The Strategic Plan's projects and structures will be funded through European and national grants, as well as by charities and industry.

In conclusion, as a result of several initiatives to involve all stakeholders and ensure that all their points of view would be taken into account in the document, this long-term sustainable Strategic Plan has achieved a broad consensus, and will serve as a **'European Cancer Plan for Children and Adolescents'.**

Gilles Vassal, SIOPE President and ENCCA Activity Coordinator

Ruth Ladenstein, SIOPE Board Member and ENCCA Coordinator

Martin Schrappe, SIOPE President-Elect and ENCCA Activity Coordinator

Kathy Pritchard-Jones, SIOPE Board Member and ENCCA Activity Coordinator

Cancer in young people in Europe

Paediatric cancer is still a major public health issue, despite high survival rates compared to adult cancers

- Each year there are **35,000 new cases** of cancer in children and adolescents in Europe (15,000 in children below the age of 15 years and 20,000 in those aged 15-24).
- 1 out of 300 new-borns will develop cancer before turning 20.
- 80% are disease-free after 5 years from diagnosis, thanks to the currently available multidisciplinary treatments:
  - Today there are approximately **300,000 EU citizens surviving a childhood cancer.** In 2020, they will be nearly half a million;
  - Two-thirds of survivors have late side effects of treatment, which are severe and impact on the daily life of half of those affected;
  - Beyond 5 years from diagnosis, disease-free survivors have higher mortality rates than their non-affected peers.
- **6,000 young people die each year of cancer.**
- Despite improving survival rates, cancer is still the first cause of death by disease beyond one year of age in the EU.
- Cancers in children differ from cancers in adults. The most frequent childhood cancers are leukaemias, tumours of the central nervous system (CNS), lymphomas and neuroblastomas. They occur from birth to adolescence, with 35% of the typical childhood cancers occurring before the age of five years.
- Considering epidemiology and outcomes, there are three main groups of paediatric cancers:
  - **Those with a good prognosis** (with a higher than 85% chance of survival after five years) under current standard multidisciplinary treatments, using cytotoxic drugs in often an intensive mode (acute lymphoblastic leukaemia, lymphomas, retinoblastoma and renal tumours). Over the last five years, the survival rates have plateaued for patients suffering from these malignancies, while treatment intensity has been reduced for some patients in order to decrease the risk of long-term sequelae;

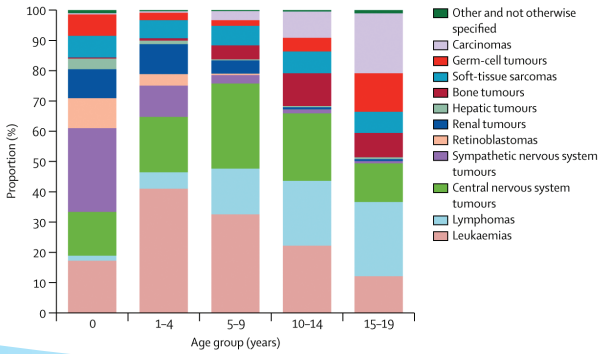


Figure 1 : Proportion of the 12 main tumour groups in children and adolescents in Europe [1]

- **Those with a poor prognosis** (~50% or less 5 year survival) such as acute myeloid leukaemia, several CNS tumours, neuroblastoma, bone and soft tissue sarcomas. Among these diseases, some have a very poor prognosis such as diffuse intrinsic pontine glioma, high-risk neuroblastoma and metastatic sarcomas;
- **The extremely rare tumours**, for which there is insufficient information on their real incidence and survival.

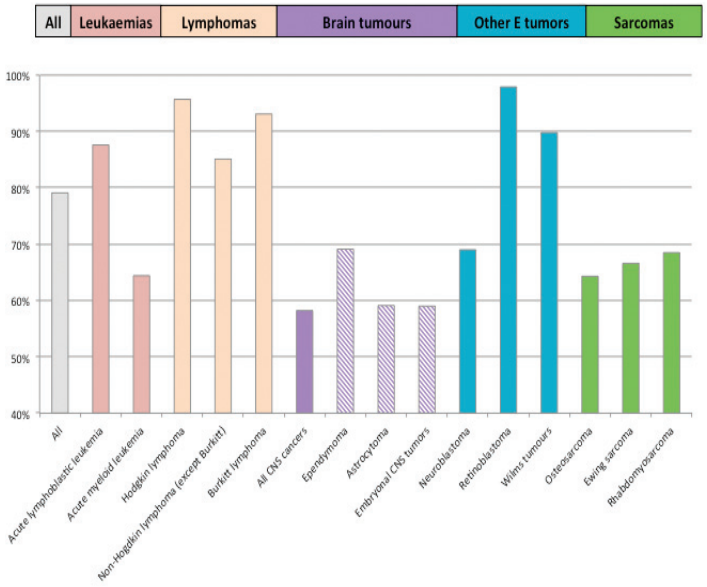


Figure 2: 5 year age-standardized survival from childhood cancers diagnosed in Europe between 2005 and 2007. Survival for retinoblastoma is calculated for 0-4 years only, and survival for osteosarcoma is calculated for 10-14 years only. Figures were region weighted and those for all cancers together and CNS cancers were adjusted by case-mix [2]

- CNS tumours (33%), leukaemias (29%) and neuroblastoma (8%) are responsible for 60% of cancer deaths amongst children aged 0 to 14 years.

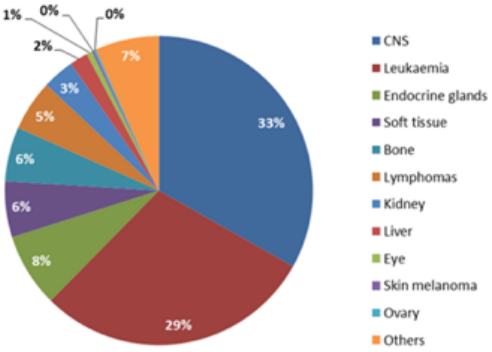


Figure 3: Cause of death by different cancer (Courtesy of Eva Steliarova-Foucher). Percentage of all cancer deaths in children (age 0-14) in all 50 areas covered by population-based cancer registries contributing data for years 2000-2007 to the European Cancer Observatory (N=6256) [3]. Causes of deaths are classified according to the ICD-10 (WHO, 1992)

Unequal access to standard care and research across Europe

- Five-year survival is generally 10 to 20% lower in Eastern Europe, a disparity that becomes even larger for cancers which already have poor outcomes [2].
- There are already standards of care for paediatric oncology treatment centres [4], but these are not applied equally across Europe [5].
- Teenagers and Young Adults (TYA) aged 15 to 24 years have very specific needs which are not equally addressed across Europe and there are still differences in their 5 years survival when compared to younger children with the same malignancy.

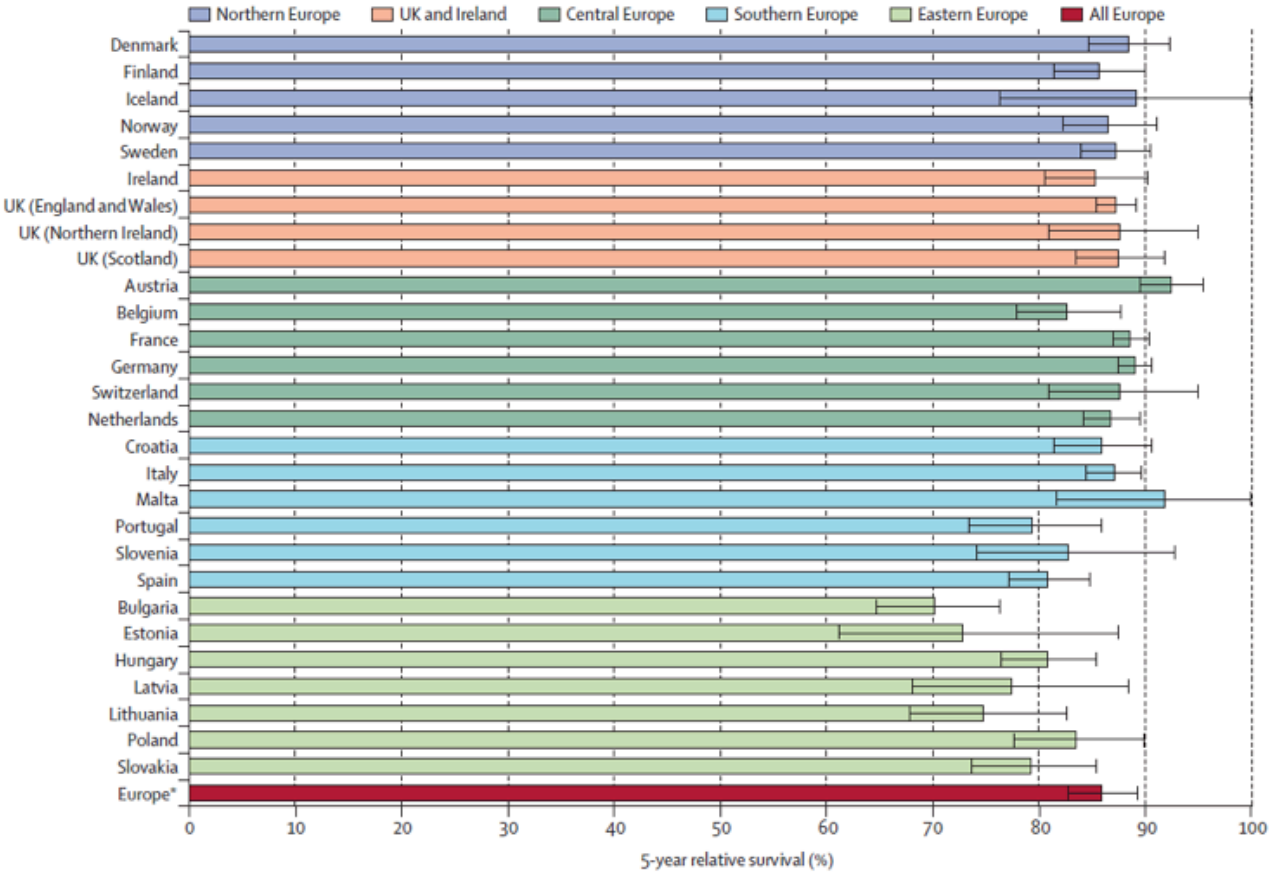


Figure 4: 5-year survival for acute lymphoid leukaemia diagnosed in 2000-2007 in European children by country
Includes data for 15 860 cases. Data adjusted by age, sex, and period of diagnosis. *Country-weighted [2].

There has been little progress regarding difficult-to-treat diseases during the last five years

- Progress has been made over the last 50 years by using intensive chemotherapy regimens (combined with surgery and/or radiotherapy in solid tumours). This includes improved outcomes in some cancers with poor prognosis such as high-risk neuroblastoma (40% survival with highly intensive chemotherapy regimens including immunotherapy) and acute myeloid leukaemia (60% survival with intensive chemotherapy and allogeneic hematopoietic stem cell transplantation).
- Patient survival has plateaued over the last five years or more for difficult-to-treat diseases, which calls for innovative treatments with new mechanisms of action to control resilient and resistant diseases.

"Children and adolescents with cancer need to be treated within clinical trials and benefit from all the facilities required by standard of care." (Marianne Naafs-Wilstra, parent advocate, VOKK, The Netherlands)

Credit Czech Working Group for Paediatric Oncology, Czech Republic

Paediatric haematology-oncology in Europe

Though the area of paediatric haematology-oncology is small, it is extremely complex and covers at least 60 different types of cancer in a population ranging from new-borns to teenagers, and even more when biological markers ("biomarkers") are considered [6].

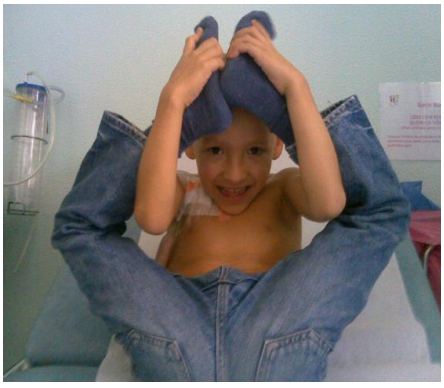
Credit Israel Society of Pediatric Hematology and Oncology (ISPHO), Israel

Strengths

- Care and research are well integrated on a daily basis, and many high-level basic and translational research teams are dedicated to paediatric malignancies.
- Approximately 350 European public specialised centres in paediatric university hospitals and comprehensive cancer centres take care of patients with a paediatric cancer, and private practice is extremely rare.
- There is a strong awareness of the needs and challenges for childhood cancer survivors, with dedicated groups (e.g. PanCare, the Pan-European network for Care of survivors after childhood and adolescent cancer) encompassing both healthcare professionals and survivors.
- Most clinical trials are run at the European level for each malignancy by well-organized European Clinical Trial Groups (ECTGs).
- Up to 90% of newly diagnosed patients are treated according to standard protocols or in prospective clinical trials. Up to 40% of patients are treated within therapeutic trials, both at diagnosis or at relapse, and clinical research is mainly led by academia, with industry-sponsored trials representing less than 5% of biomedical research.
- The paediatric haematology-oncology community is accustomed to working together since more than 50 years, with a strong track record of publishing peer reviewed research.

Weaknesses

- There is a lack of sustained and sufficient funding, with high levels of competition for funding and need for prioritisation.
- Healthcare professionals struggle to run investigator-driven clinical trials since the entry into force of the driven EU Clinical Trial Directive (2001/20/EC) in 2004.
  Although the new EU Clinical Trial Regulation (536/2014/EU) may facilitate academic research when it will be implemented (in 2016), however, it will not address all the existing challenges.
- There is still poor access to new paediatric drugs in Europe, despite the EU Paediatric Medicine Regulation (1901/2006/EC and 1902/2006/EC) – which nevertheless changed the landscape of childhood cancer drug development in Europe.
- There is insufficient integration between basic biology and clinical research, although there have been several successful EU projects (including KidsCancerKinome, EET-pipeline, ChildHope) funded within the 5th and 6th Framework Programmes.
- There are considerable disparities in Europe in the implementation of research (clinical, translational and basic) and in access to standard care, in particular for TYA.
- Paediatric haematology-oncology is not recognised as a sub-specialty in most countries.
- Parents, patients and survivors' organisations lack tools and platforms to better join forces with all stakeholders.
- A certain level of fragmentation of research remains, in spite of a long history of networking and major efforts to build together a common infrastructure.
- Paediatric haematology-oncology has grown and achieved successes so far in relative isolation in comparison with the adult oncology community.

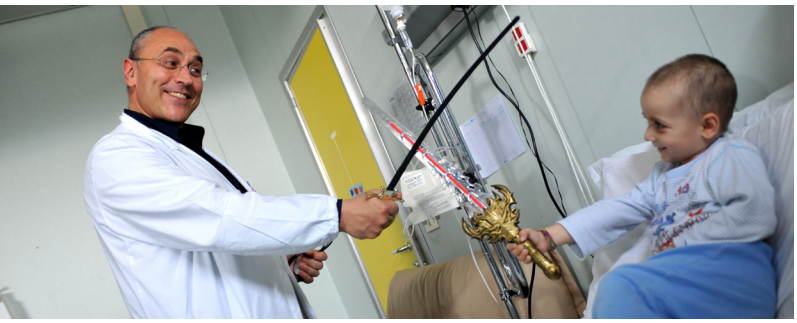


Credit Sociedade de Hemato-Oncologia Pediátrica (SHOP), Portugal

Opportunities

- The availability of high-throughput technologies that can quickly deal with large numbers of samples will allow new breakthroughs in understanding paediatric tumour biology.
- The development of effective innovative therapies (such as targeted agents and immunotherapy) in adult cancers should be applicable to the treatment of paediatric tumours.
- Paediatric haematology-oncology is now part of the EU agenda, as illustrated by ENCCA – a FP7 network of excellence structuring paediatric cancer research in Europe – and ExPO-r-Net, a DG SANTE project piloting the concept of European Reference Networks ERN) within the scope of the EU Cross-Border Healthcare Directive (2011/24/EU).

- There has been a strong commitment by the Members of the European Parliament to support the paediatric haematology-oncology agenda, for instance via their endorsement of the SIOPE-ENCCA-ICCCPO Manifesto for Paediatric Oncology.
- Advocacy groups of parents, patients and survivors advocates are increasingly well organized in Europe (through Childhood Cancer International (CCI), formerly ICCCPO) and are strongly committed and equal partners in the European care and research agenda.
- Charities in several countries are committed to support and finance research programmes on cancer in children and teenagers.



From AIEOP. Credit Attilio Rossetti photographer, Italy

"The needs of children with cancer have not been high on the political radar" (Richard Sullivan, UK)

Threats

- There is a possibility that due to factors such as a high cure rates, decision-making leaders at the European and national levels might consider that paediatric cancer is not a priority, supposing that all efforts should be concentrated only on cancer prevention in adults and on transforming cancer into a controlled chronic disease in the ageing population.
- The global economic crisis hindered the capacity of several EU Member States to improve their healthcare system to deliver standard treatments for young people with cancer.
- There is limited access to some essential medicines, due to drug shortages and to the high price of new medicines.
- Issues around the lack of collection of data in patients with diseases that have a good prognosis under standard treatment mean that the quality of care and, eventually, the probability of cure will be decreased.
- Wide-ranging EU regulatory initiatives might negatively impact the implementation of the goals of the paediatric haematology-oncology community, for example the EU General Data Protection Regulation (2012/0011(COD)) under discussion at the time of publication could impact on research and trials.

Overall goals and objectives

The overall goals over the next 10 years

- To increase the cure rate for young people who have a cancer with a poor prognosis.
- To increase the quality of life for survivors of childhood cancer.

The measure of success will be 10 years free of disease and late side effects.

The seven objectives (with equal importance and weight)

1. **Innovative treatments**: to introduce safe and effective innovative treatments (i.e. new drugs, new technologies) into standard care.
2. **Precision cancer medicine**: to use improved risk classification as well as biological characteristics of both the tumour and patient (such as molecular and immunological factors) to help guide decisions on which therapies to use.
3. **Tumour biology**: to increase knowledge of tumour biology and speed up translation from basic research to clinical care to benefit patients.
4. **Equal access**: to bring about equal access across Europe to standard care (in both diagnosis and treatment), expertise and clinical research.
5. **Teenagers and Young Adults**: to address the specific needs of teenagers and young adults (TYA), in cooperation with adult oncology.
6. **Quality of survivorship**: to address the consequences of cancer treatment such as long-term side effects, to better understand the genetic background/risk of an individual, and to improve quality of life of childhood cancer survivors.
7. **Causes of cancer**: to understand the causes of paediatric cancers and to address prevention wherever possible.

Key success factors to achieve these objectives

- Both at the European and national levels, there is a need for better integration, coordination and improved long-term sustainability of research. This is especially true when EU funding is more fragmented.
- Commitment from all funding bodies to fund projects and structures relevant to these objectives (including the European Commission, national funding bodies, charities, industry, and investors).
- The profile of paediatric haematology-oncology in the European cancer agenda should be strengthened, and its visibility increased through a more efficient communication strategy.
- A strong partnership with parents, patients and survivors, including better communication and dissemination of information.
- Levels of collaboration with adult oncology should be improved.
- Being part of the global paediatric oncology agenda and developing further collaborations with other continents.
- Building intelligent and transparent partnerships with industry.
- Effective and appropriate European regulations are vital and must be encouraged and engaged with.

Objective 1: Innovative treatments

To introduce safe and effective innovative treatments (i.e. new drugs, new technologies) into standard care.

Innovative oncology drugs with new mechanisms of action (MOA) are already available for adult cancers, and can be more effective than traditional drugs in several refractory malignancies.

From AIEOP. Credit Attilio Rossetti photographer, Italy

The field of drug development is currently expanding beyond well-studied areas like signalling pathways, to target patient's immune system, as well as their unique genetic profile and metabolism. Despite recent EU regulatory initiatives that changed the landscape of paediatric drug development in Europe for the better, access of children and adolescents with cancer to innovative therapies remains insufficient and slow [7].

Strategy

- To develop and deliver a new drug development strategy – by disease and across diseases – based on the specific biology of patients' tumour, taking into account existing therapeutic strategies implemented by the ECTGs;
- To provide a guide for efficient and innovative public-private partnerships between academia and the pharmaceutical industry, within the frame of the EU Paediatric Medicine Regulation.

Actions

1. Across Europe, increase the access of patients to new and innovative therapies, including better referral of patients, and install a molecular and immunological tumour portrait as a standard of care at the time of relapse as well as at diagnosis for patients with a high-risk and resistant diseases (link with objective 2);
2. Improve the evaluation of adult cancer drugs for use in the paediatric population, establishing a clear drugs' prioritisation and avoiding unjustified waivers (not allowing an adult drug to be translated to children);
3. Identify targets in paediatric cancers and, thus, develop specific paediatric anti-cancer drugs (link with objective 3);
4. Develop innovative technologies such a high precision radiation therapy and interventional radiology;
5. Develop innovative designs and methods for efficient studies, both in early phase and phase III clinical trials;
6. Influence changes in the relevant regulations;
7. Develop international academic collaboration and efficient cooperation with main stakeholders (patients, survivors, parents, academia, charities, industry, regulators, EU decision- and policy-makers).

The European new drug development programme will be implemented by the European consortium for Innovative Therapies for Children with Cancer (ITCC), in collaboration with the disease-specific European Clinical Trials Groups (ECTGs).

Brought about by ENCCA, the CDDF (Cancer Drug Development Forum)- SIOPE -ITCC paediatric oncology platform was created in 2013 with academia, industry, parents and regulators in order to make proposals for improving new oncology drugs development for children and adolescents [8].

Credit University of Nottingham, Children's Brain Tumour Research Centre, United Kingdom

Objective 2:
Precision cancer medicine

To use improved risk classification as well as biological characteristics of both the tumour and patient (such as molecular and immunological factors) to help guide decisions on which therapies to use.

Risk stratification is used in paediatric haematology-oncology to adapt the intensity of patients' treatment to their own individual risk of failure. It is part of standard of care, is based on the extent of the disease and, increasingly, on tumour biology and response (e.g. in neuroblastoma and leukaemias) [9] [10] [11]. There has been recent progress in the classification of severalpaediatric malignancies (such as medulloblastoma, high grade glioma, ependymoma and rhabdomyosarcoma) based on specific aspects of their biology [12]. This will lead to new "biomarkers" that can be used in clinical practice to improve risk stratification and to better adapt existing and new treatments (objective 1) to each patient.

Strategy

- To analyse the specific biology (molecular profiling) of both the patient and tumour at the point of diagnosis and throughout treatment to improve risk stratification for adapted individual treatment by identifying:
    - Patients with a high probability of cure with standard treatment, who may be proposed new or reduced interventions to decrease the risk of late effects;
    - Patients with a poor prognosis tumour to whom innovative therapies should be proposed as early as possible, to increase their probability of cure.

Actions

1. Run prospective clinical trials with innovative design and methods to confirm the use of biomarkers and algorithms in risk stratification, treatment allocation and disease monitoring;
2. Enhance the collaboration between specialists such as biostatisticians, clinicians and biologists;
3. Expand the availability and accessibility of biomarkers for clinical and research use by setting up a network of the necessary molecular laboratories;

4. Develop research in functional imaging, set up a European imaging platform as well as a platform for quality control in radiation therapy;
5. Improve data sharing, especially those that are linked, such as genomic and clinical data, and widen access of such information to researchers;
6. Facilitate international academia-led clinical trials (via facilitated submission processes, shortening the time needed from conception to launch);
7. Widen access to tumour samples and nucleic acids for researchers.

This strategy will be implemented by the ECTGs developing research in each paediatric malignancy, and it will be facilitated by the cross-tumour European platforms and programmes set up within SIOPE.

Credit Czech Working Group for Paediatric Oncology, Czech Republic

Objective 3: Tumour biology

To increase knowledge of tumour biology and speed up translation from basic research to clinical care to benefit patients.

Cancers in adults result from processes that have multiple steps, mainly following exposure to external carcinogens (tobacco, alcohol, UV, diet, etc.) and often progression over many years.

In contrast, paediatric cancers develop early in life and over a much shorter time period, suggesting that fewer and stronger events are required for progression. They are rare, and most show fewer genetic defects and a lower genetic complexity as compared to adult cancers [13]. Major progress has been made in understanding paediatric tumour biology, leading to the discovery of unique cancer hallmarks that are also involved in cancer formation in adults, such as the RB1 gene in retinoblastoma and, more recently, Histones H3 mutations in diffuse intrinsic pontine gliomas [12]. These advances have already resulted in new classification of several diseases. Additionally, the role of the immune system in controlling tumour growth is now well-established in many adult cancers, and the challenge is to translate this new findings into successful therapies.

Strategy

- To use modern and innovative technologies to further uncover the mechanisms of paediatric tumour development, progression and relapse. Also, to explore the genetic and cellular heterogeneity within the same tumour, the regulation of genes (epigenetics), and the role of the immune system, metabolism and the tumour's own surroundings (micro-environment);

- To accelerate the translation of results from research to clinical care and allow patients to benefit from new knowledge in a timely fashion.

Actions

1. Strengthen international networks of basic research teams, grouping them by different cancer types, and improve access to new pharmaceutical compounds for preclinical research;
2. Enhance interactions between bio-informaticians, system biologists and developmental biologists;
3. Increase interactions between basic scientists and clinical researchers;
4. Share the clinical-biological data generated by the introduction of technologies that analyse the biology of specific tumours (such as high-throughput sequencing and other tumour profiling technologies) between clinicians and researchers;
5. Improve the access of researchers to relevant and high quality clinically annotated biological samples (including tumour samples, circulating cells, circulating DNA);
6. Increase the involvement of patients and ents in the precision cancer medicine agenda.

Within ENCCA, several networks of tumour researchers that connect basic and translational research teams with a common interest in each paediatric malignancy have been developed.

Objective 4: Equal access

To bring about equal access across Europe to standard care (in both diagnosis and treatment), expertise and clinical research.

From AIEOP. Credit Attilio Rossetti photographer, Italy

Treating children with cancer is a complex matter, and needs the expertise of a highly specialised multidisciplinary team. Across Europe, there is a 10 to 20% difference in 5 year survival, between countries with population-based cancer registration – the differences may be much greater where no such outcome data currently exist. SIOPE led the preparation, definition and dissemination of the 'European Standards of Care for Children with Cancer', and a recent SIOPE survey within the European Partnership for Action Against Cancer (EPAAC) showed that there is a wide disparity in the implementation of these standards of care across different European countries [4].

Strategy

- To ensure that all centres in Europe that treat children and TYA with cancer meet the European Standards of Care for Children with Cancer;
- To develop pathways that, for complex treatments and rare diseases/situations, allow access to specialised expertise, specialised technologies (i.e. specialised surgery, radiotherapy techniques, haematopoietic stem cell transplantation) or clinical research (i.e. early phase trials of new treatments).

Actions

1. Build a European Reference Network (ERN) in paediatric haematology-oncology within the EU Cross-Border Healthcare Directive (2011/24/EU):
    - Create tumour boards by disease – to be considered at three levels: institutional, national and European – in order to provide advice on the best appropriate treatment and care for individual patients;
    - Identify centres that are able to deliver standard care and treatments (specialist centres) as well as hubs of coordination, which will also deliver complex treatments and specialised technology;
    - Improve referral to specialist centres and hubs of coordination within EU member states and across borders;
    - Set up an efficient e-Health and IT platform;
2. Warrant availability of essential medicines for all patients;
3. Specifically address the needs of children and adolescents with extremely rare cancers (e.g. adult cancers such as thyroid cancer, breast cancer and melanoma – occurring extremely rarely in the paediatric population – and extremely rare specific paediatric malignancies such as pleuropulmonary blastoma, etc.);
4. Ensure that paediatric cancer registries cover all European countries, in order to adequately monitor the effects of the present Strategic Plan, and ensure that each National Cancer Plan addresses the specific needs of children and adolescents with cancer;
5. Significantly improve access to palliative care for young patients at the end of their lives;
6. Provide high quality training for all health professionals across Europe, and make paediatric haematology-oncology a recognised sub-specialty.

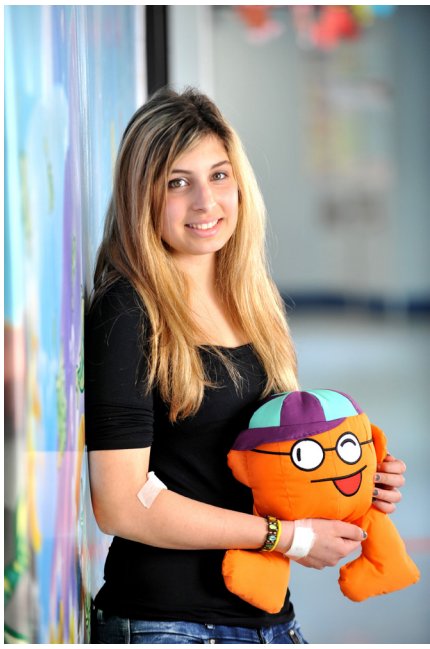
The ExPO-r-Net project, funded by DG SANTE, is currently piloting the concept of a European Reference Network (ERN) in paediatric haematology-oncology, which specifically addresses the topic of extremely rare cancers and long-term follow-up.

"All European children and young people with cancer should have access to standards of care, expertise and clinical research." (Participants at the SIOPE-ENCCA Conference, 18-19 September 2014)

Objective 5: Teenagers and Young Adults

To address the specific needs of teenagers and young adults (TYA), in cooperation with adult oncology.

Although cancer in teenagers and young adults is rare, it is a substantial cause of death in this population. Outcomes are often poorer than in younger patients with the same cancer, and several contributory factors have been identified: the type of tumours, their biology and sensitivity to current therapies, as well as the low participation of TYA in clinical trials [14] [15]. TYA have specific and unmet needs, including complex psychological and social supportive care. Their position between adult and children's services in healthcare systems does not allow for the best possible provision of care or dedicated research that could improve their quality of survival.



From AIEOP. Credit Attilio Rossetti photographer, Italy

Strategy

- To develop a comprehensive multidisciplinary European programme, tackling all issues and specific needs of the TYA population. This will be a joint integrated programme between paediatric and adult oncology, in strong partnership with patients.

Actions

1. Create a European multidisciplinary network on TYA cancers that covers care and research and includes all health professionals and patients;
2. At the national level, help the creation of TYA cancer services, which provide the required complex multidisciplinary care;
3. Define a training programme for health professionals addressing the specific needs of TYA;
4. Increase the portfolio of clinical trials for TYA, and increase their accessibility to all TYA patients;
5. Monitor progress in TYA terms of survival, using the clinical epidemiology platform (defined later in this document).

Within ENCCA a pilot project has been initiated in order to build the European Network for Teenagers and Young Adults Cancer [14].

Objective 6: Quality of survivorship

To address the consequences of cancer treatment such as long-term side effects, to better understand the genetic background/ risk of an individual, and to improve quality of life of survivors of childhood cancer.

From AIEOP. Credit Attilio Rossetti photographer, Italy

With an 80% survival at five years, the number of childhood cancer survivors (currently estimated to be more than 300,000 in Europe) is likely to continue to increase, and improving their quality of life is a major goal. Two-thirds of survivors have late-occurring side effects due to their treatments, which are severe in half of them, and have a strong impact on their daily lives. It is anticipated that in 2030 there will be around 750,000 paediatric cancer survivors in Europe.

The PanCare network was created in 2008 to address this issue [16]. PanCare is a pan-European multidisciplinary network of health professionals, survivors of paediatric cancer and their families, who collaborate to reduce the frequency, severity and impact of late treatment side effects, with the aim of ensuring that every survivor of childhood cancer receives the best possible long-term care. In addition, several survivors' associations were created recently to empower survivors and to help them tackle the issues raised above.

Credit Joke Emmerechts photographer, Belgium

Strategy

- To improve awareness of the needs of childhood cancer survivors, together with them, and facilitate research on it;
- To empower survivors to take the responsibility for their own follow-up, ensuring that they are well-informed on what to be aware of, how and when to access care and follow-up, and who to turn to if and when they need to;
- To encourage health organisations to address the issues of long-term follow-up and ease the transition to adult medicine;

- To run prospective clinical research to reduce the likelihood of long-term side effects in patients who have a good prognosis malignancy.

Actions

1. Establish guidelines for follow-up that cover all possible late-occurring side effects of current treatments;
2. Create and provide a 'Survivorship Passport' for each child and adolescent treated for cancer that will include:
    - History and summary of the patient's disease as well as treatments received;
    - Relevant follow-up measures, including precautionary measures to improve their quality of life;
    - A database to store the patient's clinical data and help monitoring and research;
3. Set up a relevant model of care to allow for a smooth transition to adult medicine (such as 'long-term follow-up clinics');
4. Increase research on late-occurring side effects (for example cardiac toxicity, secondary tumours and infertility) and on quality of survival, including societal and psychological aspects;
5. Anticipate long-term toxicities of innovative therapies, such as targeted therapies, that will be introduced in standard treatments;

Two ongoing FP7 European projects, PanCareSurFup and PanCareLIFE, carry out research on late-occurring side effects [17]. The pilot initiative of the 'Survivorship Passport' is being developed thanks to the support of ENCCA and PanCareSurFup, and the organisation of care including a virtual late-effects advisory centre, will be also addressed within the ExPO-r-NET project.

Objective 7: Causes of cancer

To understand the causes of paediatric cancers and to address prevention wherever possible.

Credit Czech Working Group for Paediatric Oncology, Czech Republic

"Why does my child have cancer?" is a crucial question for parents, which most of the time receives no answer. Relatively few causative factors have been identified so far for childhood cancers.

"Survivors of childhood cancer want a normal life."
(Sabine Karner, PPAC/CCI/PanCare, Austria)

It is estimated that 4-8% of paediatric cancers occur within a known genetic predisposition and more than 100 genetic syndromes with a risk of cancer in childhood are known. The proportion may increase as more and more rare cancer gene mutations are discovered through ongoing analyses in areas such as genomics. Some studies already suggest that up to one in four children and adolescents with a history of cancer may have a genetic predisposition condition [18]. The identification of the genetic basis of rare inherited cancers in children has revealed key pathways that are shared with sporadic tumours, even in adults. Sequencing of the whole genome will generate new information that can be used to improve care and to identify new genetic hallmarks of cancer, which can be turned into targets for new therapies.

Strategy

- To increase research focused on predisposition to childhood cancer and on the oncogenic drivers that increase the risk of childhood cancer by:
  - Using whole genome sequencing to further uncover genetic predisposition to paediatric cancers;
  - Carefully addressing the pragmatic and ethical issues of genetic testing and counselling, anticipating that DNA testing is becoming widely available;
  - Addressing questions on the environmental causes of paediatric cancer through scientifically-led and evidence-based studies.

Actions

1. Create a European consortium on genetic predisposition to childhood cancers in order to coordinate research and guide implementation of new knowledge in the clinical setting;
2. Provide guidelines and train health professionals on how to identify patients with a possible genetic predisposition, and how to inform parents;
3. Improve access to paediatric oncogeneticists and genetic testing in Europe;
4. Develop new strategies for prevention and monitoring, including through early diagnosis and screening;
5. Run high-resolution studies through the SIOPE clinical epidemiology platform (defined later in this document), to determine the role of external risk factors.

"Childhood cancer survivors in Europe should have access to adequate follow-up." (PanCare partners: Sabine Karner, Austria; Lars Hjorth, Sweden; Riccardo Haupt, Italy)