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The SIOPE strategic plan: A European cancer plan for children and adolescents

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1. Executive summary

1.1. Cancer in young people is rare, but it is still a major health issue in Europe

Each year, more than 6000 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 diagnosis, and beyond.

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

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;

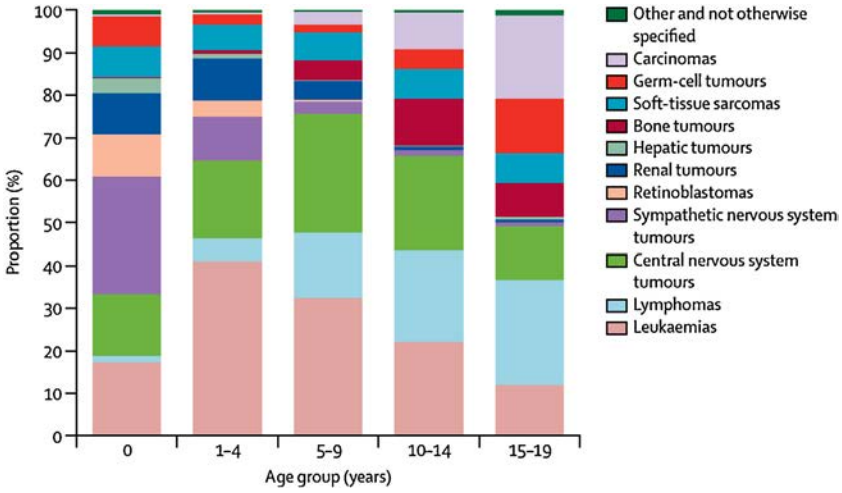

Fig. 1. Proportions of the 12 main tumour groups in children and adolescents in Europe [1].

4. Equal access: to bring about equal access across Europe to standard care (in both diagnosis and treatment), expertise and clinical research;
5. TYA: 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.

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 European 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, ACCELERATE, the CDDF-SIOPE-ITCC multi-stakeholder platform to improve oncology drug development for children and adolescents, and the 'Ethics and 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 the '**European Cancer Plan for Children and Adolescents**'.

2. Cancer in young people in Europe

2.1. 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 a 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 (Fig. 1) .
- Considering epidemiology and outcomes, there are three main groups of paediatric cancers (Fig. 2) :
  - 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 (Fig. 3) ;

- 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 a lack of information on their real incidence and survival.
- CNS tumours (33%), leukaemias (29%) and neuroblastoma (8%) are responsible for 60% of cancer deaths amongst children aged 0–14 years.

2.2. Unequal access to standard care and research across Europe

- Five-year survival is generally 10–20% lower in Eastern Europe, a disparity that becomes even larger for cancers which already have poor outcomes (Fig. 4)[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 15–24 years have very specific needs which are not equally addressed across Europe and. there are still differences in their 5 year survival when compared to younger children with the same malignancy.

2.3. 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.

3. 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].

3.1. 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.

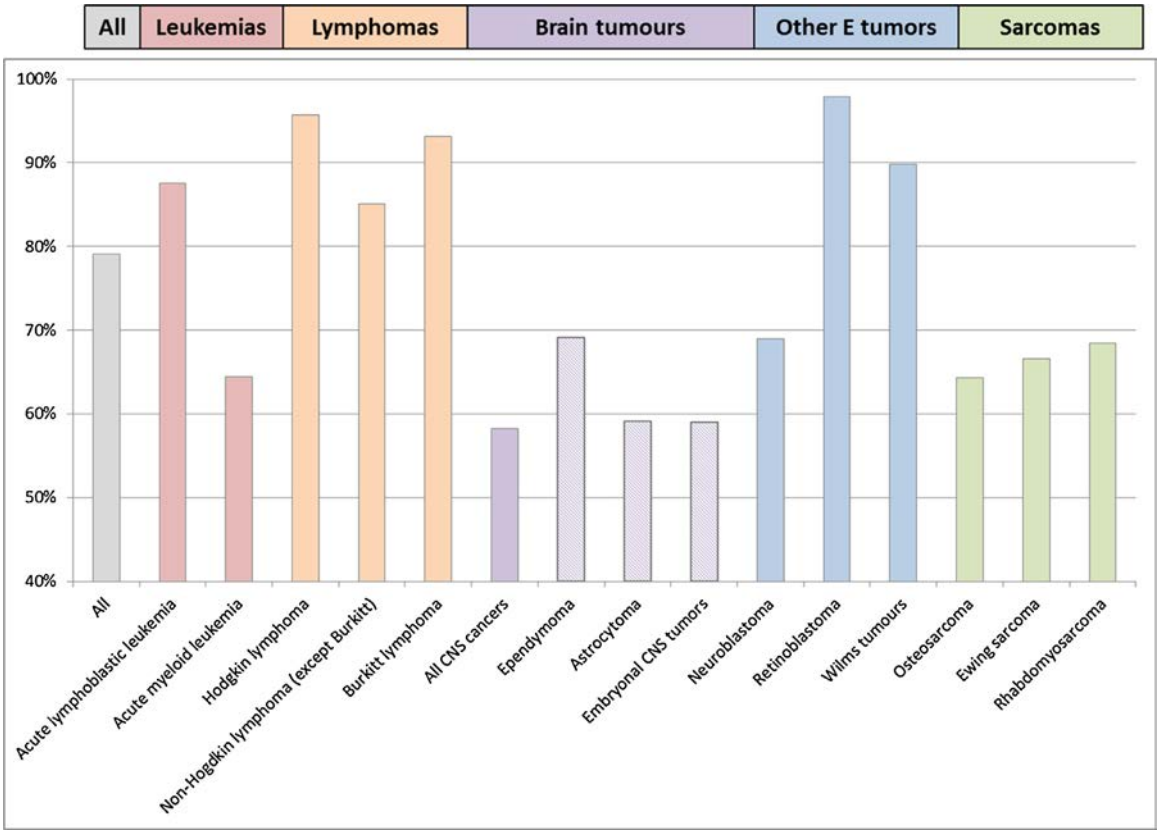

Fig. 2. 5 year age-standardised survival from childhood cancers diagnosed in Europe between 2005 and 2007. Survival for retinoblastoma is calculated for 0–4 years only, and survival for osteosarcoma is calculated for 10–14 years only. Figures were region weighted and those for all cancers together and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

- 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.

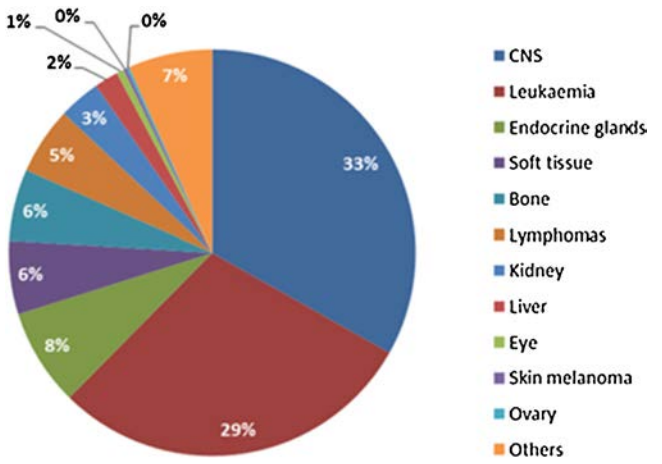

Fig. 3. Cause of death by different cancer (Courtesy of Eva Steliarova-Foucher). Percentage of all cancer deaths in children (age 0–14) in all 50 areas covered by population-based cancer registries contributing data for years 2000–2007 to the European Cancer Observatory (N = 6256) [3]. Causes of deaths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

3.2. 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 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 subspecialty in most countries.
- Parents, patients and survivors organizations 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.

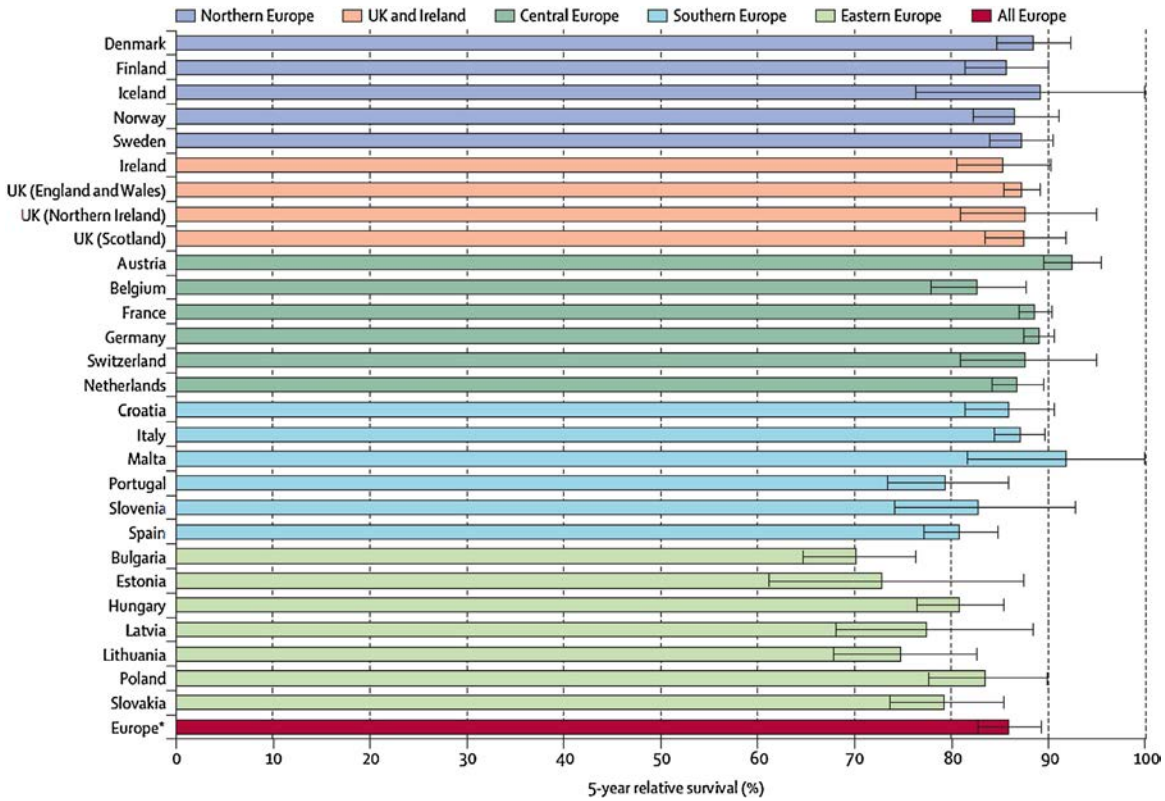

Fig. 4. 5-year survival for acute lymphoid leukaemia diagnosed in 2000–2007 in European children by country Includes data for 15 860 cases. Data adjusted by age, sex, and period of diagnosis. *Country-weighted [2].

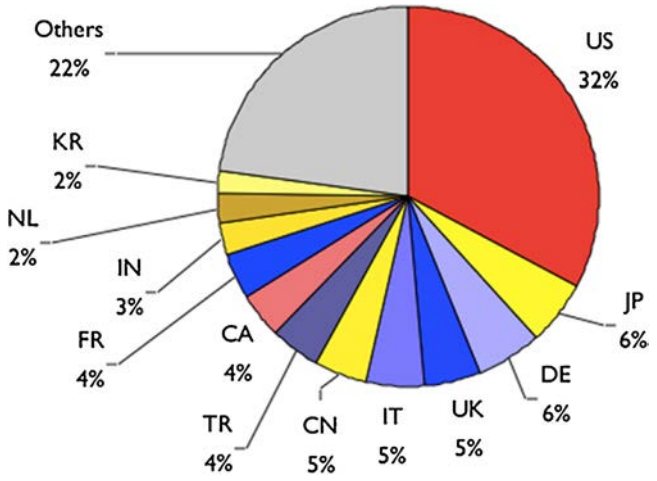

Fig. 5. Pie chart of national contributions to paediatric oncology research, 2005–2014; fractional counts. European countries coloured blue with shading; North American countries red with shading; Asian countries yellow with shading. Credit: Institute of Cancer Policy, London, UK. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

- Paediatric haematology-oncology has grown and achieved successes so far in relative isolation in comparison with the adult oncology community.

3.3. 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.

3.4. 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.

4. Overall goals and objectives

4.1. 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.

4.2. 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. TYA: 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.

4.3. 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 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.

4.4. 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. 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].

4.4.1. 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.
- Toprovide a guide for efficient and innovative public-private partnerships between academia and the pharmaceutical industry, within the frame of the EU Paediatric Medicine Regulation.

4.4.2. 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. Identifytargets in paediatric cancers and, thus, develop specific paediatric anti-cancer drugs (link with objective 3).
4. Developinnovative technologies such a high precision radiation therapy and interventional radiology.
5. Developinnovative designs and methods for efficient studies, both in early phase and phase III clinical trials.
6. Influencechanges in the relevant regulations.
7. Developinternational 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].

4.5. 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) [9–11]. There has been recent progress in the classification of several paediatric 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.

4.5.1. 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.

4.5.2. 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.

4.6. 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.

4.6.1. 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.

4.6.2. Actions

1. Strengtheninternational networks of basic research teams, grouping them by different cancer types, and improve access to new pharmaceutical compounds for preclinical research.
2. Enhanceinteractions between bio-informaticians, system biologists and developmental biologists.
3. Increaseinteractions 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. Improvethe access of researchers to relevant and high quality clinically annotated biological samples (including tumour samples, circulating cells, circulating DNA).
6. Increasethe involvement of patients and parents 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.

4.7. Objective 4: equal access

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

Treating children with cancer is a complex matter, and needs the expertise of a highly specialised multidisciplinary team. Across Europe, there is a 10–20% 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].

4.7.1. 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).

4.7.2. 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. Significantlyimprove 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.

4.8. 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 (TYA) 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.

4.8.1. 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.

4.8.2. 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].

4.9. 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.

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.

4.9.1. 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.

4.9.2. 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. Setup 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.

4.10. Objective 7: causes of cancer

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

"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. 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.

4.10.1. 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.

4.10.2. 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. Runhigh-resolution studies through the SIOPE clinical epidemiology platform (defined later in this document), to determine the role of external risk factors.

5. Coordination and implementation of the plan

SIOPE is the European Society of Paediatric Oncology and is dedicated to care, research and training in paediatric haematology-oncology as well as policy-making for decisions that impact on cancer ('oncopolicy').

Its mission is to ensure the best possible care and outcome for all children and young people with cancer in Europe, by increasing the cure rate and the quality of cure of children with cancer. More specifically, SIOPE is in charge of:

- To coordinate the implementation of the European Strategic Plan;
- To steer the integration of research, care and education, and increase funding levels;
- To ensure that the EU legislative framework facilitates the implementation of the Strategic Plan;
- To strengthen partnerships with all stakeholders.

SIOPE is the European branch of the International Society of Paediatric Oncology (SIOP) and a founding member of the European Cancer Organization (ECCO).

Currently there are 18 European Clinical Trial Groups (ECTGs) developing clinical and translational research either by an individual disease type (15 groups) or across multiple diseases (4 groups), who define and run their own research strategy according to the SIOPE Strategic Plan. In Europe there are also 25 National Paediatric Haematology-Oncology Societies (NaPHOS). The Chairs of ECTGs and NaPHOS form the SIOPE Clinical Research Council (CRC, formerly ECRC).

The European Clinical Trial Groups

By disease:

Tumour Name	Group Name	Website
Brain Tumour	SIOPE Brain Tumour Group	www.siope.eu/european-research-and-standards/european-clinical-research-council/ecrc/siope-brain-tumour-group
Ewing Tumour	EURO-E.W.I.N.G.	www.euroewing.eu/clinical-trials/ee2012-trial
Germ Cell Tumours	Germ Cell Tumours	
Hodgkin 's Lymphoma	EHL—European Hodgkins Consortium, EuroNet-PHL	www.kinderkrebsinfo.de/index_eng.html
Langerhans Cell Histiocytosis	Histiocyte Society	www.histiocytesociety.org
Leukemias and Lymphomas	I-BFM—The International BFM Study Group	www.bfm-international.org
Liver Tumours	SIOPEL—SIOPE-Epithelial Liver Tumour Study Group	www.siopel.org
Myelodysplasia	EWOG-MDS	ewog-mds.de
Neuroblastoma	SIOPEN—SIOP Europe Neuroblastoma Group	www.siopen.org
Non-Hodgkin Lymphoma	EICNHL—European Inter-group Cooperation on Childhood and Adolescent Non Hodgkin	
Osteosarcoma	EURAMOS—European and American Osteosarcoma Study Group	www.euramos.org
Renal Tumours	SIOP-RTSG—SIOP Renal Tumours Study Group	www.siop-rtsg.eu
Retinoblastoma	EURbSG—European RetinoBlastoma Group	
Soft Tissue Sarcoma	CWS—Cooperative Weichteilsarkom Studiengruppe or Cooperative soft Tissue Sarcoma StudyGroup	
Soft Tissue Sarcoma	EpSSG—European Paediatric Soft Tissue Sarcoma Study Group	www.epssgassociation.it

Across diseases:

Tumour Name	Group Name	Website
New Anticancer Agents	ITCC—Innovative Therapies for Children with Cancer	www.itcc-consortium.org
Stem Cell Transplantation	EBMT—European Group for Bone Marrow and Stem Cell Transplantation Paediatric Working Party	www.ebmt.org
Survivorship and Late Effects	PanCare—Pan-European Network of for Care of Survivors after Childhood and Adolescent Cancer	www.pancare.eu/en
Very Rare Paediatric Tumours	EXPeR—European Cooperative Study Group on Paediatric Rare Tumours)	

The National Paediatric Haematology-Oncology Societies (NaPHOS)

Country	NaPHOS/Group	Website
Austria	AGPHO (Austrian Group for Paediatric Haemato-Oncology)	www.docs4you.at
Belgium	BSPHO (Belgian Society of Paediatric Haematology Oncology)	www.bspho.be
Bulgaria	Bulgarian Society of Paediatric Oncology	
Croatia	Croatian National Group	
Czech Republic	CPH (Czech Working Group for Paediatric Oncology)	
France	SFCE (Société Française de lutte contre les Cancers et leucémies de l'Enfant et l'adolescent)	sfce.sfpediatrie.com
Germany	GPOH (Gesellschaft für Pädiatrische Onkologie und Hämatologie)	www.kinderkrebsinfo.de/gpoh_society/gpoh_who_we_are/index_eng.html
Greece	Hellenic society of Pediatric Haematology-Oncology	www.eepao.gr/
Hungary	HPOG (Hungarian Paediatric Oncology Network)	
Israel	ISPHO (Israel Society of Pediatric Hematology and Oncology)	www.ispho.org.il/english/
Italy	AIEOP (Associazione Italiana Ematologia Oncologia Pediatrica)	www.aieop.org
Latvia	Latvian Society of Paediatric Oncology	www.ihot.lt/lt/bspoh
Luxembourg (SIOPE institutional membership)	Foundation Kriibskrank Kanner	http://www.fondatioun.lu/
The Netherlands	SKION (Stichting Kinderoncologie Nederland)	www.skion.nl
Nordic countries (Denmark, Norway, Sweden, Iceland, Finland) + Lithuania	NOPHO (Nordic Society of Paediatric Haematology & Oncology)	http://nopho.org/
Poland	Polish Society of Paediatric Oncology and Haematology	
Portugal	SHOP (Sociedade de Hematologia e Oncologia Pediatrica)	www.spp.pt
Romania	Romanian Society of Paediatric Haematology-Oncology	
Serbia	Serbian Society of Haematology and Oncology	
Slovak Republic	Slovak Paediatric Association – Section of Paediatric Haemato-Oncology	
Slovenia	Slovenian Society of Paediatric Oncology	

Spain	SEHOP (Sociedad Española de Hematología y Oncología Pediátricas)	www.sehop.org
Switzerland	SPOG (Schweizerischen Pädiatrischen Onkologie Gruppe)	www.spog.ch
Turkey	TPOG (Turkish Paediatric Oncology Group)	www.tpog.org.tr
United Kingdom & Ireland	CCLG (Children's Cancer and Leukaemia Group)	www.cclg.org.uk

6. Childhood cancer from a societal perspective

From an international perspective, paediatric oncology research in Europe is in good standing. Between 2005 and 2014, there were 32,785 academic papers about paediatric oncology, representing 4.6% of all oncology papers and 7.1% of all paediatric papers. 22% of those articles came from Europe and 32% from the US (Fig. 5) [19].

In 2008, funding for paediatric oncology research was estimated, using previously validated econometric analysis of research activity [20], to be 1229 USD millions, with more than 50% from public funding, including international funding such as European framework funding and just under 20% from the pharmaceutical industry [21]. In 2013, this has been estimated to have dropped to 900 USD millions, a decline over 25% over five years.

Research output is growing, particularly in clinical research, but availability of short-term funding is getting worse despite more European programmes. In addition, most of the public policy discourse has been focused on an ageing European society and the needs of children with cancer are not high on the political radar, despite the fact that cancer is the leading cause of death by disease in the young population. Globally, childhood cancer is being heavily marginalised.

The SIOPE objectives are:

- To improve public, political and policy visibility of childhood cancer research;
- To show the existing linkage between research activity and better outcomes for children with cancer in Europe;
- To develop strategies in order to broaden research engagement;
- To address both pan-European research funding and national funding streams, as well as funding from charities.

7. Facilitating platforms and cross-tumour research projects

7.1. Platform to facilitate the implementation of ECTGs research strategy: the clinical trial facility (CTF) platform

This platform will help institutions to set up international clinical trials in the framework of the new EU Clinical Trials Regulation (536/2014/EU), and will allow researchers to share their experiences and solutions to issues related to the Regulation's implementation. It will provide templates and advice for the hurdles faced (e.g. practicalities and contracts) when implementing non-commercial clinical trials across multiple countries and sites, including the specific issues arising when trials are run in partnership with the pharmaceutical industry. Within ENCCA, a consortium of five European academic institutions has been created to speed up the implementation of early phase investigator supported trials.

7.2. Clinical epidemiology platform for outcome research—the PICORET project

The Population Improvement in Childhood Cancer Outcomes through Research, Evaluation and Training project (PICORET) will address the needs of clinical epidemiology and outcome research in paediatric haematology-oncology. Several paediatric cancers have a high survival rate with treatments that have been established through prospective European randomised trials. Population-based cancer registries measure overall but not relapse-free survival, and so there isn't sufficient information on the effectiveness of first line therapy at a population level.

PICORET will monitor the survival of all children and adolescents with cancer in Europe and evaluate progress across Europe using information from registries and observational studies that use standard treatments. Such 'non-interventional' clinical studies can assess effectiveness of biomarkers, which can be used for prognosis, and allow analysis of traditionally hard-to-research areas, such as surgical and imaging techniques. Through building enhanced clinical registry capabilities, PICORET will prospectively collect detailed clinical and biological information that can be used for quality improvement of diagnostics and treatment pathways for patients treated by a standard treatment outside of clinical trials. PICORET will monitor the survival of all children and adolescents with cancer in Europe, and will evaluate and compare the quality and effectiveness of treatments. High resolution studies will be run.

Initially, PICORET will focus on renal tumours, neuroblastoma and medulloblastoma as its first exemplars. It will develop standardised clinical guidelines as well as a standardisation and quality programme in standard care, with a special focus on infant dosing. Twinning between institutions in countries with higher and lower survival rates will be introduced. Data privacy will be carefully monitored, and the project's impact will be assessed.

7.3. Platform for quality assurance in radiotherapy—the QUARTET project

Quality assurance and quality control are mandatory when patients receive radiation therapy. This is to make sure that each patient gets the best treatment in terms of maximising effectiveness and minimising long-term side effects. However, they are not systematically performed within clinical trials and various programmes are implemented only in a limited number of EU countries.

The QUARTET project ('QUAlity and excellence in RadioTherapy and imaging for children and adolescents with cancer across Europe in clinical Trials') aims to build a radiation therapy quality assur-

ance programme across all paediatric malignancies. It will be run in partnership with the European Organisation for Research on Treatment of Cancer (EORTC) and Aquilab for patients participating in clinical trials using radiation therapy and run by ECTGs. Eventually, the platform will expand its activity to patients treated outside of clinical trials.

7.4. Multi-stakeholder platform for new paediatric oncology drug development- ACCELERATE, the CDDF-SIOPE-ITCC platform

The ACCELERATE multi-stakeholder platform (www.accelerate-platform.eu) was created in December 2013 by Cancer Drug Development Forum (CDDF), SIOPE and ITCC as a deliverable of the ENCCA project—to improve oncology drug development for children and adolescents [8].

Academia, parents and survivors, industry and regulators are equally represented and work together on the following objectives:

- To set up drug prioritisation and enable drug development, based on the mechanism of action of the drug as well as biological factors;
- To propose changes in the EU Paediatric Medicine Regulation to better address the needs of those with life threatening diseases;
- To propose new incentives for the development of specific paediatric drugs and repurposing of existing drugs;
- To implement long-term follow up measures for new oncology drugs for children and adolescents.

7.5. Ethics, Social Sciences and Humanities Programme

This is a natural development of the ethics programme set-up within ENCCA to maintain and improve the level of expertise on ethics in the field of paediatric cancer care and research. It is based on two priorities, namely to reflect the multidisciplinary nature of social sciences and humanities where suitable to paediatric oncology, and to facilitate access to appropriate expert views from professionals and from patients' representatives on ethical issues.

Following these priorities, "ethics" is meant as a multidisciplinary approach to the non-technical issues related to the care, protection, and self-realisation o of paediatric oncology-haematology patients (or former patients). It is proposed to develop a non-prescriptive, participatory and outcomes-oriented approach to these issues, harnessing the relevant knowledge and expertise in the Social Sciences and Humanities (SSH) field.

Four main topics will be addressed by this programme: (i) return of research results, (ii) personal data in care and research environments, (iii) access to medical innovation, (iv) care and healthcare pathways. The programme will be performed through objective assessment of the non-technical issues related to the care and quality of survival of children and adolescents with cancer, as well as through community-based participatory research actions within the paediatric oncology community.

In accordance with the successful implementation within ENCCA, the programme will be steered and run by a permanent contact point along with ad-hoc academic collaborations. A steering Legal and Ethical Advisory Board will peer-review the projects and the results. The following tools will be set up: (i) a thematic database of ethics expertise in Europe, identifying expert individuals and centres in Western and Eastern European Universities, (ii) a database of local initiatives for bedside and benchside ethics, accessible to professionals and patients, (iii) an initiative to establish multi-centre collaborations on non-technical interventions (fostering experience-sharing and multicentre evaluation). All this is expected to generate sustained community dialogue, concerted evidence generation as well as transverse capacity-building on non-technical domains, first of all on ethical issues.

7.6. The SIOPE portal

The portal set-up within the ENCCA project will be transferred to SIOPE after the end of the ENCCA project (December 2015). This online 'one-stop-shop' portal will support communication and interaction between everyone involved in implementing the strategic research agenda. It will serve as a resource for documentation and as a platform for information exchange.

Each patient will have a unique ID (EUPID) so that their data can be anonymised and shared between different databases. A pilot project for an integrated IT structure will allow information to be linked between sources (such as registries, clinical trial databases, hospital electronic health records) and users (such as researchers and analysts) is being developed by the IT providers of ENCCA.

Within ENCCA, a consultation IT platform has been developed for patients with haepatoblastoma (a very rare disease) by SIOPEL along with CINECA. This platform (including pathology slides and images) facilitates access to expert advice for diagnosis and treatment, including indications of liver transplant. This IT tool is further developed within the ExPO-r-Net project for retinoblastoma and extremely rare paediatric tumours, and will eventually be adapted for other diseases within the Paediatric Oncology Europe Reference Network. In addition, an IT platform for virtual tumour boards will be developed.

Based on these experiences and following those pilot projects, SIOPE and ECTGs will define how to structure the best IT environment that will allow the implementation of the Strategic Plan.

7.7. Network of biobanks

Samples from patients and tumours, which are labelled with additional clinical information, are vital for the success of the SIOPE Strategic Plan. The aim of SIOPE is therefore to support a network of biobanks that can share data electronically, in keeping with EU data protection laws. The difficulty of the task is not underestimated.

A vital step in the development of such a network within SIOPE is the introduction of a unique patient identifier (the above mentioned EUPID) for every paediatric cancer patient treated in Europe, as well as the development of standardised patient consent forms. These must be in line with national data protection laws in European countries, and allow for new developments in molecular analysis of tumour samples (particularly next-generation sequencing), as well as the wishes of patients and parents and other ethical considerations.

In addition to this, ENCCA guidelines are currently being finalised on the standards for tumour and other patient samples (e.g. blood and plasma) as well as related materials like DNA and RNA, and on the process of access and use.

8. Cross-tumour programmes

8.1. Oncopolicy programme

Several regulatory initiatives are of direct concern to paediatric haematology-oncology and the implementation of the SIOPE Strategic Plan. SIOPE has developed expertise and skills to monitor and influence the development of relevant European cancer health and research policy themes, and to ensure that the needs of the paediatric haematology-oncology community are taken into account when regulations are drafted or revised:

- Each **National Cancer Plan** should address the needs of children and adolescents with cancer, according to the European Cancer Plan.
- The **Cross Border Healthcare Directive** (2011/24/EU) was established in 2010. This is the framework for the development of the future paediatric oncology European Reference Network (via the ExPO-r-Net project).
- The **Clinical Trials Regulation** (536/2014/EU) is expected to enter into force in 2016 and to facilitate academic trials, and SIOPE will help European institutions and ECTGs to implement their trials within the new Regulation (through the CTF platform, see above) and ensure that experiences, issues and hurdles encountered in paediatric haematology-oncology are fed back to the relevant bodies.
- The **Data Protection Regulation** (2012/0011(COD)) is under discussion at the time of the publication. In its current form, it would be detrimental to outcome research in paediatric oncology – a major objective of the SIOPE Strategic Plan—as well as to the interdisciplinary research collaborations involving different institutions, in order to ensure the best quality of care to the patient. SIOPE is joining oncology stakeholders to ensure that the needs of academic research and epidemiology are taken into account.
- The **Paediatric Medicine Regulation** (1901/2006/EC and 1902/2006/EC) entered into force in 2007. The European paediatric oncology community is engaged in pushing for immediate changes to its implementation, in order to better address the unmet needs of children and adolescents with cancer. Because cooperation between all stakeholders (patients, survivors, parents, academia, industry, regulators) is crucial, ACCELERATE, the CDDF-SIOPE-ITCC multi-stakeholder paediatric platform (see above), was created to propose the immediate changes and to prepare for the revision of the Regulation, which could occur in 2017.
- In the 2015 Health programme, the European Commission called for a **Joint Action on Rare Cancers** that will be implemented jointly with EU Member States. This will provide the framework for the implementation of part of the SIOPE Strategic Plan and for cooperation with adult oncology in the field of rare cancers.

In 2014, SIOPE effectively obtained the commitment of EU institutions and civil society representatives to support young people with cancer, through their endorsement of the **SIOPE-ENCCA-ICCCPO Manifesto for Paediatric Oncology**. This document was signed by 20 members of the European Parliament, setting up objectives to advance childhood cancer research, treatment and care. After the European elections, this document became an even stronger advocacy document for SIOPE on the long-term.

Additionally SIOPE and the European paediatric haematology-oncology community will contribute to the development of oncopolicy in Europe in the fields of **multidisciplinary care**, **access to innovation** and development of **e-Health**. SIOPE will join efforts with the European CanCer Organisation (ECCO) along with European Society for Medical Oncology (ESMO) and other European societies.

8.2. Training and education programme

The aim of this programme is to encourage high quality clinical and basic research as well as the delivery of high quality care in paediatric oncology throughout Europe. This is a remit of SIOPE and focuses on the organisation of educational courses and on the revision of the training syllabus in paediatric oncology.

SIOPE is involved in several training courses to develop the knowledge of health professionals on new and state-of-the-art therapies and allow them to gain more practical skills in the treatment of paediatric malignancies:

- The SIOPE-ESO Masterclass in paediatric oncology: practice-oriented training with a focus on the application of the most recent research findings to clinical practice;
- The ECCO-AACR-ASCO workshop on “Methods in clinical cancer research” in Flims, Switzerland: introduction of junior clinical oncologists to the principles of good and innovative clinical trial design and methods;
- The SIOPE-ENCCA-ENTYAC European Course on the treatment of teenagers and young adults with cancer (TYA), centred around multiple disciplines;
- The joint SIOPE-ESMO training programme on TYA.

As part of the work of the European Academy of Paediatrics, SIOPE revised its previous syllabus with the aim of having a comprehensive document for the whole of the EU that details the requirements expected from a trainee in paediatric haematology-oncology. The new version of the syllabus proposes a programme containing core knowledge and practical aspects related to approaches for diagnosis and treatment that are essential for all trainees in paediatric haematology-oncology (available on the SIOPE website: www.siope.eu).

8.3. Communication

The SIOPE Strategic Plan relies on timely, relevant and tailored communication to target stakeholders Based on its expertise of information-sharing with members and leading EU projects' dissemination, SIOPE has set up a communication strategy, encompassing the pan-European haematology-oncology community, decision-makers and the general public.

The communication objectives are:

1. **Uniting the community:** further increasing the profile of SIOPE as the main reference point for paediatric haematology-oncology in Europe, to stimulate cross-border exchange of best practices, to strengthen existing collaborations and to develop new ones;
2. **Raising awareness:** by fostering the well-informed involvement and commitment of target stakeholders and by raising awareness of paediatric cancers across Europe in partnership with parents and survivors.
3. **Generating action:** translating the needs of the Strategic Plan as well as the SIOPE position and requests into legislative, funding, advocacy, partnership-building and further communication initiatives.

9. Partnerships

9.1. Partnership with patients, survivors and parents

Building a partnership with patients, survivors, and parents' organisations is essential to achieve the goals of SIOPE in terms of research, equal access to standard care and expertise, advocacy when new policies are developed and strategic decisions made at the national and European levels.

CCI is a worldwide childhood cancer organisation that represents families of children with cancer and childhood cancer survivor groups. SIOPE has been working with the CCI Europe Regional Committee for several years, including partnerships in several European projects and initiatives.

In 2011 the PPAC within ENCCA was created with CCI Europe Region Committee members, and consists of representatives from different national parents and survivors organisations. Since then,

they have been building networks between parent and survivor groups and organisations, disseminating health policy-related issues within Europe and improving the training of representatives of patients survivors and parents in clinical research to make them powerful advocates and partners in this field. ENCCA, SIOPE and PPAC also worked together in joint research and dissemination activities, as well as the development of a long-term sustainable strategy for paediatric oncology in Europe, the SIOPE Strategic Plan and the seven medical and scientific objectives.

SIOPE and the CCI Europe Regional Committee entered into a co-operative relationship in order to implement the European long-term Strategic Plan and to raise awareness on cancer in children and adolescents. They signed a **Memorandum of Understanding** that sets out the specific areas of cooperation along with the principles by which both parties will run the partnership. The four areas are: i) ethics and social sciences and humanities, ii) access to standard of care and expertise, iii) improvements to the regulatory and political environment at the pan-European and national level, iv) research and development.

9.2. Partnership with adult oncology

During the last 50 years, paediatric oncology has developed in relative isolation. Improving the cooperation of all paediatric haematologists and oncologists was the crucial objective so that an effective European clinical research programme could be set up and address the very specific needs of children with cancers without reference to adult cancer services.

It is now recognised that adult and paediatric oncology have a lot to share and learn from each other, and that collaboration is beneficial in order to address common goals and challenges:

- Care and research for rare cancers, in terms of innovative methodology to evaluate new treatments and in terms of health care organisation models to provide access to expertise for patients suffering from rare and extremely rare cancers;
- Care and research for TYA (see above);
- Access to essential medicines, since most anti-cancer drugs are used to treat both adult and paediatric cancers, even though there are differences in the tumours;
- European initiatives on care and research oncopolicies.

SIOPE and ESMO (the European Society of Medical Oncology) have decided to develop a joint initiative to address those topics, and established a Memorandum of Understanding to help this collaboration.

9.3. Partnership with paediatric haematology-oncology in other continents

SIOPE is part of the global paediatric oncology agenda run by the International Society of Paediatric Oncology (SIOP). Several European-centred study groups have an international scope, and bring together global investigators to participate in a common clinical trials portfolio.

The IBFM-study group is international, and patients from countries outside Europe participate to its leukaemia trials and translational research projects.

More than a hundred institutions from Europe, Asia, Central and South America, Australia and New Zealand collaborate in SIOPEL, the SIOPE-liver study group. Early drug trial groups such as ITCC in Europe, the Pediatric Oncology Experimental Therapeutics Investigator's Consortium (POETIC) and Therapeutic Advances in Childhood Leukemia and Lymphoma (TACL) in North America, the Canadian C17 network, the Australia Children's Cancer Trials group and the Children Oncology Group (COG) phase I consortium are working together to speed up the development of new anticancer agents.

SIOPEN has built with COG and neuroblastoma groups from Japan, China and Australia a large clinical and biological database of more than 9000 neuroblastoma patients in order to define and validate new staging system and new biological prognostic biomarkers through the International Neuroblastoma Research Group [9,22]. Groups such as the SIOP-Renal Tumours Study Group support clinical trials groups in other continents that run studies using the same standard treatment backbones, adapted to local circumstances.

The COG and the European Inter-group for Childhood non Hodgkin lymphoma (EICNHL) are currently running a randomised phase III clinical trial to evaluate the addition of rituximab, an anti CD20 monoclonal antibody, on standard intensive chemotherapy treatment in high-risk Burkitt's lymphoma.

The European and American Osteosarcoma Study Group (EURAMOS) has successfully completed a large phase III study with partners, which included the COG, the European Osteosarcoma Intergroup, the Cooperative Osteosarcoma Study Group, and the Scandinavian Sarcoma Group. The EURAMOS Strategy Group, made up of these four multi-national groups, as well as the relevant Australasian, French, Italian, Japanese, and Spanish osteosarcoma groups, is exploring options for collaboration on an even larger platform.

In the next 10 years, international cooperation will be reinforced to evaluate innovative targeted drugs within extremely small and rare groups (defined by biomarkers), such as children with B-RAF mutated malignancies. Even in less rare clinical situations, international randomised clinical trials will be considered more regularly to speed up evaluation of innovative therapies.

9.4. Partnership with industry

For the last 50 years, progress has been made in curing paediatric cancers by running academic trials using anti-cancer drugs that are available in hospital pharmacy departments. Pharmaceutical companies have not developed their anti-cancer agents in the paediatric population, and nearly half of drugs used daily to cure cancer in children and adolescents do not have the regulatory official authorisation, stated in the 'Summary of Product Characteristics'.

In Europe this situation has significantly changed over the last five years because regulatory initiatives, first in the U.S. and then in Europe, obliged pharmaceutical companies to test their drugs in the paediatric population when relevant. There was indeed an urgent need to access new drugs developed by pharmaceutical companies as early as possible during their development in adults, and to avoid families moving to the US to get access to innovative therapies in development.

Thanks to the EU Paediatric Medicine Regulation, pharmaceutical companies and academia have started to work together, to evaluate oncology drugs within paediatric investigation plans. This is a learning curve for everyone since pharmaceutical companies are not accustomed to working with paediatric oncologists and vice versa.

The goal is to develop 'intelligent and transparent' partnerships that recognise the specificities of paediatric haematology-oncology, i.e. a well-structured arena for clinical research, dealing with rare and complex situations, while the paediatric development of oncology drugs is, by definition, a pre-competitive research activity for pharmaceutical companies and competition to access rare patients makes no sense.

A new model of cooperation between pharmaceutical companies, academia and public-private partnership needs to be developed in order to adequately address the needs of children and adolescents with cancer and regulatory requirements. This is being addressed in ACCELERATE, the CDDF-SIOPE-ITCC paediatric

oncology platform. In addition, a strategy will be implemented to encourage investment and partnership with small pharmaceutical companies to develop drugs against specific paediatric targets.

9.5. Partnership with charities

In several EU Member States, charities are extremely efficient at fundraising to support research and care for children and adolescents with cancer. These efforts are developed at the national level and can be fragmented, with significant differences between countries.

Most research programmes are run at the European level, and there is a need to figure out how charities from different countries can be more efficient at jointly funding large and ambitious European programmes.

SIOPE will propose to charities to fund and co-fund European projects and programmes. By defining, implementing and coordinating a long term sustainable Strategic Plan, SIOPE and the European paediatric haematology-oncology are willing to provide a transparent and clear visibility to the projects that will be run within a well-defined and integrated framework.

10. Funding strategy

By definition, funding of the now established European strategy in paediatric haematology-oncology will come necessarily from several sources: the European Commission, national funding bodies, charities and foundations, industry as well as anyone willing to invest in paediatric oncology research and development.

European funding is available for research projects through Horizon 2020 calls. Projects in paediatric haematology oncology will be submitted to relevant European calls by SIOPE, groups and institutions as part of the implementation of the SIOPE Strategic Plan and referred as such in their application.

The critical hurdle encountered in paediatric haematology-oncology, as well as in other research areas, is the lack of funding for structures that are needed to run a coordinated and integrated research agenda. To this extent, in 2011 the European Commission provided €12 m to structure oncology research into children and adolescents. One of the best examples of the goals achieved is the long-term sustainable Strategic Plan described in this document. ENCCA illustrates how funding for a permanent structure is essential to achieve progress and deliver success.

ENCCA will finish on December 2015 and the decision was taken that SIOPE will run the on-going agenda. The key question is how to fund the projects, the programmes and the structures that are needed to implement the long-term sustainable strategy.

At the end of the SIOPE-ENCCA event, which shared the European Strategic Plan with all stakeholders in Brussels in September 2014, the participants decided that the SIOPE Stategic Plan should be the **European Cancer Plan for Children and Adolescents**. Implementation of this plan will show the commitment of the EU and its Member States to address childhood and adolescent cancers as a priority and a strategic objective for the European Union. Specific European initiatives will be set up to join efforts from the EU and its Member States for funding. In addition, it will allow other co-funding bodies to contribute to a pan-European initiative.

The European Cancer Plan for Children and Adolescents was officially launched last year on two occasions: first on September 26th 2015 at the European Cancer Congress, when it was presented to the scientific community, and then during a special event co-organised by SIOPE and the MAC (Members of the parliament Against Cancer) group on November 18th 2015 at the European Parliament.

11. Quotes from stakeholders

"Researchers are an essential driving force in making successful cure for childhood cancer possible." (Hermann van Rompuy, former President of the EU Council, Belgium)

"Children are desperate to enrol in new clinical trials, that in some cases can be the only hope for survival." (Glenis Willmott, Member of the European Parliament, UK)

"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)

"All national cancer plans should have provisions for children and adolescents." (Participants at the SIOPE-ENCCA Conference, 18–19 September 2014)

"The EU Data Protection Regulation is a debatable piece of legislation which could threaten childhood cancer clinical research" (Nikolaus Forgó, Institute for Legal Informatics, DE)

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

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

"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)

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

"Europe should have a European Paediatric Cancer Plan addressing both care and research." (Participants at the SIOPE-ENCCA Conference, 18–19 September 2014)

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References

[1] K. Pritchard-Jones, R. Pieters, G.H. Reaman, L. Hjorth, P. Downie, G. Calaminus, M.C. Naafs-Wilstra, E. Steliarova-Foucher, Sustaining innovation and improvement in the treatment of childhood cancer: lessons from high-income countries, Lancet Oncol. 14 (March (3)) (2013) e95–e103.

[2] G. Gatta, L. Botta, S. Rossi, T. Aareleid, M. Bielska-Lasota, J. Clavel, N. Dimitrova, Z. Jakab, P. Kaatsch, B. Lacour, S. Mallone, R. Marcos-Gragera, P. Minicozzi, M.J. Sánchez-Pérez, M. Sant, M. Santaquilani, C. Stiller, A. Tavilla, A. Trama, O. Visser, R. Peris-Bonet, EUROCARE working group childhood cancer survival in europe 1999–2007: results of EUROCARE-5–a population-based study, Lancet Oncol. 15 (January (1)) (2014) 35–47, Erratum in: Lancet Oncol. 2014,15, Februaruy (2) e52.

[3] J. Ferlay, E. Steliarova-Foucher, J. Lortet-Tieulent, S. Rosso, J. Coebergh, H. Comber, D. Forman, F. Bray, Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012, Eur. J. Cancer 49 (6) (2013) 1374–1403.

[4] J.R. Kowalczyk, M. Samardakiewicz, E. Fitzgerald, S. Essiaf, R. Ladenstein, G. Vassal, A. Kienesberger, K. Pritchard-Jones, Towards reducing inequalities: european standards of care for children with cancer, Eur. J. Cancer 50 (February (3)) (2014) 481–485.

[5] European Partnership for Action Against Cancer (EPAAC), (2015). Survey report on the Standards of Care in paediatric oncology units. [online] Available at: http://www.epaac.eu/images/END/Final_Deliverable/D4.2_Survey_report_on_the_standards_of_care_in_paediatric_oncology_units.pdf [accessed 31.01.14.].

[6] G. Vassal, E. Fitzgerald, M. Schrappe, F. Arnold, J. Kowalczyk, D. Walker, L. Hjorth, R. Riccardi, A. Kienesberger, K. Jones, M. Valsecchi, D. Janic, H. Hasle, P. Kearns, G. Petrarulo, F. Florindi, S. Essiaf, R. Ladenstein, Challenges for children and adolescents with cancer in Europe: the SIOP-Europe agenda, Pediatr. Blood Cancer 61 (9) (2014) 1551–1557.

[7] G. Vassal, C.M. Zwaan, D. Ashley, M.C. Le Deley, D. Hargrave, P. Blanc, P.C. Adamson, New drugs for children and adolescents with cancer: the need for novel development pathways, Lancet Oncol. 14 (March (3)) (2013) e117–e124.
[8] G. Vassal, R. Rousseau, P. Blanc, L. Moreno, G. Bode, S. Schwoch, M. Schrappe, J. Skolnik, L. Bergman, M.B. Bradley-Garelik, V. Saha, A. Pearson, H. Zwierzina, Creating a unique, multi-stakeholder Paediatric Oncology Platform to improve drug development for children and adolescents with cancer, Eur. J. Cancer 51 (January (2)) (2015) 218–224.
[9] P.F. Ambros, I.M. Ambros, G.M. Brodeur, M. Haber, J. Khan, A. Nakagawara, G. Schleiermacher, F. Speleman, R. Spitz, W.B. London, S.L. Cohn, A.D. Pearson, J.M. Maris, International consensus for neuroblastoma molecular diagnostics: report from the international neuroblastoma risk group (INRG) biology committee, Br. J. Cancer 100 (May (9)) (2009) 1471–1482.
[10] C.H. Pui, J.J. Yang, S.P. Hunger, R. Pieters, M. Schrappe, A. Biondi, A. Vora, A. Baruchel, L.B. Silverman, K. Schmiegelow, G. Escherich, K. Horibe, Y.C. Benoit, S. Izraeli, A.E. Yeoh, D.C. Liang, J.R. Downing, W.E. Evans, M.V. Relling, C.G. Mullighan, Childhood Acute Lymphoblastic Leukemia: Progress Through Collaboration, J. Clin. Oncol. (August) (2015), pii: JCO.2014.59.1636. [Epub ahead of print].
[11] M. Schrappe, M.G. Valsecchi, C.R. Bartram, A. Schrauder, R. Panzer-Grümayer, A. Möricke, R. Parasole, M. Zimmermann, M. Dworzak, B. Buldini, A. Reiter, G. Basso, T. Klingebiel, C. Messina, R. Ratei, G. Cazzaniga, R. Koehler, F. Locatelli, B.W. Schäfer, M. Aricò, K. Welte, J.J. van Dongen, H. Gadner, A. Biondi, V. Conter, Late MRD response determines relapse risk overall and in subsets of childhood T-cell ALL: results of the AIEOP-BFM-ALL 2000 study, Blood. 118 (August (25)) (2011) 2077–2084.
[12] A. Gajjar, S.M. Pfister, M.D. Taylor, R.J. Gilbertson, Molecular insights into pediatric brain tumors have the potential to transform therapy, Clin. Cancer Res. 20 (November (22)) (2014) 5630–5640.
[13] M.S. Lawrence, P. Stojanov, P. Polak, G.V. Kryukov, K. Cibulskis, A. Sivachenko, S.L. Carter, C. Stewart, C.H. Mermel, S.A. Roberts, A. Kiezun, P.S. Hammerman, A. McKenna, Y. Drier, L. Zou, A.H. Ramos, T.J. Pugh, N. Stransky, E. Helman, J. Kim, C. Sougnez, L. Ambrogio, E. Nickerson, E. Shefler, M.L. Cortés, D. Auclair, G. Saksena, D. Voet, M. Noble, D. DiCara, P. Lin, L. Lichtenstein, D.I. Heiman, T. Fennell, M. Imielinski, B. Hernandez, E. Hodis, S. Baca, A.M. Dulak, J. Lohr, D.A. Landau, C.J. Wu, J. Melendez-Zajgla, A. Hidalgo-Miranda, A. Koren, S.A. McCarroll, J. Mora, R.S. Lee, B. Crompton, R. Onofrio, M. Parkin, W. Winckler, K. Ardlie, S.B. Gabriel, C.W. Roberts, J.A. Biegel, K. Stegmaier, A.J. Bass, L.A. Garraway, M. Meyerson, T.R. Golub, D.A. Gordenin, S. Sunyaev, E.S. Lander, G. Getz, Mutational heterogeneity in cancer and the search for new cancer-associated genes, Nature 499 (July (7457)) (2013) 214–218.
[14] D. Stark, S. Bielack, L. Brugieres, U. Dirksen, X. Duarte, S. Dunn, D.J. Erdelyi, T. Grew, L. Hjorth, J. Jazbec, E. Kabickova, A. Konsoulova, J.R. Kowalczyk, A. Lassaletta, V. Laurence, I. Lewis, A. Monrabal, S. Morgan, G. Mountzios, P.R. Olsen, M. Renard, G. Saeter, W.T. van der Graaf, A. Ferrari, Teenagers and young adults with cancer in Europe: from national programmes to a European integrated coordinated project, Eur. J. Cancer Care (Engl.) (August) (2015).
[15] A. Potosky, L. Harlan, K. Albritton, R. Cress, D. Friedman, A. Hamilton, I. Kato, T. Keegan, G. Keel, S. Schwartz, N. Seibel, M. Shnorhavorian, M. West, X. Wu, Use of appropriate initial treatment among adolescents and young adults with cancer, JNCI J. Nat. Cancer Inst. 106 (11) (2014) (pp.dju300-dju300).
[16] L. Hjorth, R. Haupt, R. Skinner, D. Grabow, J. Byrne, S. Karner, G. Levitt, G. Michel, H. van der Pal, E. Bárdi, J.D. Beck, F. de Vathaire, S. Essig, E. Frey, S. Garwicz, M. Hawkins, Z. Jakab, M. Jankovic, B. Kazanowska, T. Kepak, L. Kremer, H. Lackner, E. Sugden, M. Terenziani, L.Z. Zaletel, P. Kaatsch, PanCare Network. Survivorship after childhood cancer: panCare: a European Network to promote optimal long-term care, Eur. J. Cancer 51 (July (10)) (2015) 1203–1211.
[17] J.F. Winther, L. Kenborg, J. Byrne, L. Hjorth, P. Kaatsch, L.C. Kremer, C.E. Kuehni, P. Auquier, G. Michel, F. de Vathaire, R. Haupt, R. Skinner, L.M. Madanat-Harjuoja, L. Tryggvadottir, F. Wesenberg, R.C. Reulen, D. Grabow, C.M. Ronckers, E. van Dulmen-den Broeder, M.M. van den Heuvel-Eibrink, M. Schindler, J. Berbis, A.S. Holmqvist, T. Gudmundsdottir, S. de Fine Licht, T.G. Bonnesen, P.H. Asdahl, A. Bautz, A.K. Kristoffersen, L. Himmerslev, H. Hasle, J.H. Olsen, Hawkins MM childhood cancer survivor cohorts in europe, Acta Oncol. 54 (May (5)) (2015) 655–668.
[18] S. Knapke, K. Zelley, K.E. Nichols, W. Kohlmann, J.D. Schiffman, Identification, management, and evaluation of children with cancer-predisposition syndromes, Am. Soc. Clin. Oncol. Educ. Book 57 (2012) 6–84.
[19] R. Sullivan, SIOPE-ICP analysis of the state of childhood cancer research: 2015 update (in press).
[20] R. Sullivan, S. Eckhouse, G. Lewison. Using bibliometrics to inform cancer research policy and spending. Chapter (5) in: Monitoring Financial Flows for Health Research 2007. Behind Global Numbers. Global Forum for Health Research. http://announcementsfiles.cohred.org/gfhr_pub/reports/2007.pdf (accessed 02.09.15.).
[21] G. Dini, R. Riccardi, J. Rascon, L. Rageliene, V. Calvagna, P. Czauderna, J.R. Kowalczyk, M.J. Gil-da-Costa, L. Norton, F. Pereira, D. Janic, J. Puskacova, J. Jazbec, A. Cañete, L. Hjorth, G. Ljungman, T. Kutluk, B. Morland, M. Stevens, D. Walker, R. Sullivan, The state of research into children with cancer across Europe: new policies for a new decade, ecancer 5 (2011) 210.
[22] N. Pinto, M. Applebaum, S. Volchenboum, K. Matthay, W. London, P. Ambros, A. Nakagawara, F. Berthold, G. Schleiermacher, J. Park, D. Valteau-Couanet, A. Pearson, S. Cohn, Advances in risk classification and treatment strategies for neuroblastoma, J. Clin. Oncol. (2015).

List of acronyms/glossary

ACCELERATE: SIOPE-ITCC-CDDF Multi-Stakeholder Platform Ïnnovation for Children with Cancer(www.accelerate-platform.eu, website under construction)
Biobank: A type of biorepository that stores biological samples (usually human) for use in research
Biomarker: Generally refers to a measurable indicator of some biological state or condition
CCI: Childhood Cancer International
CDDF: Cancer Drug Development Forum
CNS: Central Nervous System
COG: Children Oncology Group
CRC/ECRC: European Clinical Research Council for paediatric and adolescent oncology
CTF: Clinical Trial Facilitating platform
DG SANTE: Directorate General for Health and Food Safety, European Commission
EAC: (ENCCA): Ethics Advisory Committee
ECCO: European Cancer Organisation
ECTGs: European Clinical Trial Group(s) in paediatric oncology
EICNHL: European Inter-group Cooperation on Childhood and Adolescent Non Hodgkin Lymphoma
ENCCA: European Network for Cancer Research in Children and Adolescents
EORTC: European Organisation for Research and Treatment of Cancer
EPAAC: European Partnership for Action Against Cancer
ERN: European Reference Network(s)
ESMO: European society for medical oncology
EU: European Union
EURAMOS: European and American Osteosarcoma Study Group
FP5, FP6, FP7: EU 5th/6th/7th Framework Programmes for research and innovation
Horizon 2020: EU programme for research and innovation (2014–2020)
I-BFM: International BFM Study Group
ITCC: Innovative Therapies for Children with Cancer
LTS: (ENCCA) Long-term Sustainability (working group)
MAC: Members of the Parliament (MEPs) Against Cancer Group
MOA: Mechanism(s) of Action
NaPHOS: National Paediatric Haematology-Oncology Society-ies
PanCare: Pan-European network for care of survivors after childhood and adolescent cancer
PanCareSurFup: PanCare childhood and adolescent cancer SURvivor care and follow-UP studies
PICORET: Population Improvement in Childhood Cancer Outcomes Through Research, Evaluation and Training
PIP: Paediatric Investigation Plan(s)
POETIC: Pediatric Oncology Experimental Therapeutics Investigators' Consortium
PPAC: (ENCCA) Parent and Patient Advocacy Committee
QUARTET: QUAlity and excellence in RadioTherapy and imaging for children and adolescents with cancer across europe in clinical trials
SAB: (ENCCA) Scientific Advisory Board
SIOPE: SIOP Europe, the European Society for Paediatric Oncology
SIOPEL: SIOPE-Epithelial liver tumour study group
SIOPEN: SIOP Europe Neuroblastoma Group
SSH: Social Sciences and Humanities Project
TACL: Therapeutic Advances in Childhood Leukemia and Lymphoma
TYA: Teenagers and Young Adults