Dear friends in PanCare,

We can once again enjoy a newsletter with interesting material thanks to the excellent work of Katja Baust with the assistance of Julie Byrne. It involves a lot of work and for this we are very grateful to Katja for doing this. In this issue you can read about our successful 20th PanCare meeting in Lübeck, Germany, in October 2017 generously hosted by Thorsten Langer. We have furthermore interesting reports on various topics such as the new international registration study on the late effects of proton radiotherapy, from the PanCare LIFE project on patient education on the risk of fertility impairment, the PSYNA study, and late effects after stem cell transplantation.

I hope to meet many of you in Prague in April for our 21st PanCare meeting hosted by Jarmilla Kruseova and her team

All the best,
Helena van der Pal
About 80 people from across Europe attended the semi-annual meeting held in this lovely city on the Baltic Sea in Northern Germany. The meeting was hosted by Professor Thorsten Langer, of the University of Lübeck, the venue in the Atlantic Hotel was central and met everyone’s needs. Lübeck is a small, walkable city on an island, with many buildings of historical interest and a charming residential area of alleys and tiny houses. The meeting included a symposium on endocrine late effects, and another on ototoxicity -- the way that certain chemotherapeutic agents, such as cisplatin, can cause serious hearing loss in children being treated for cancer. Guidelines are an essential component of long-term care for survivors of childhood cancer to ensure that evidence-based care is available to all survivors. The meeting heard about guidelines for care after haematopoietic cell transplant. Another symposium of interest to many concerned the various long-term follow-up projects currently
20th PanCare meeting in Lübeck, Germany, 3-5 October 2017

running in Germany, and the new proton therapy based in Aarhus, Denmark. The networking dinner was held in an old building, purchased by local philanthropists for the use of the town and university -- "Zimberei - Gemeinnützige". More information and the meeting programme is on the PanCare website at www.pancare.eu.

The next PanCare meeting will be held in Prague from 18-20 April, 2017, and is open to all. Julianne Byrne

New Proton Radiotherapy Methods and Late Effects – International Registration Study

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Proton radiotherapy is a form of radiation used in the treatment of cancer. It was developed in the 1950s and was first used for the treatment of rare eye and skull base tumors. Beginning in the 1990s proton radiotherapy machines were introduced into a hospital setting. Since then proton radiotherapy has become more available and is more often used in routine clinical work.

Conventional radiation therapy is given with high energetic X-Rays. Proton beams have the advantage that they deposit the main part of the radiation in the depth of the tumor and that there is no exit dose, thereby sparing normal tissues around the tumor. This makes proton radiotherapy attractive for the pediatric setting.

Radiotherapy is still together with surgery and chemotherapy important for cure of most pediatric solid tumors. In the last decades the survival of childhood cancer has increased, but survivors of childhood cancer suffer often from late effects that are either induced by the tumor itself or by the cancer treatment. Modern radiation therapy is increasingly employing smaller margins in normal tissues because of a precise target definition and the possibility of a very precise daily setup. With intensity modulating techniques, it is possible to avoid high doses of radiation in the surrounding normal tissues. With proton radiotherapy even lower doses of radiation can be avoided in more parts of the normal tissues while achieving the same high dose in the tumor.

This advantage of proton radiotherapy has been demonstrated in multiple virtual dosimetric studies where radiation dose plan comparisons between X-Ray and proton radiation show the normal tissue sparing potential of proton radiotherapy. But until now only few clinical studies with proton radiotherapy about late effects have been published. It is therefore important that pediatric patients treated with proton radiotherapy are enrolled into clinical trials to register outcome and toxicity.

Largescale registries are addressing this need. "In North America a pediatric proton therapy consortium will include 5000 children treated with proton radiotherapy followed with a common protocol. => continued on the next page"
The international collaboration IPPARCA (International Project on Prospective Analysis of Radiotoxicity in Children and Adolescence) is based on the German RiSK project (Registry for the Detection of Late Sequelae after Radiotherapy in Childhood and Adolescence). IPPARCA is a prospective project that studies late effects after pediatric radiotherapy by pooling data analyses from international registries. The collaboration started in 2008 between the German RiSK study and the Swedish RADTOX registry, later some institutions from Norway and Denmark joined the project. The registries are on the national level partly financed by the Swedish Childhood Cancer Foundation and the German RiSK project was financed by the German Childhood Cancer Foundation. The registries are independent from each other, but use a common dataset to collect data that can be used in future common projects. Until now only acute toxicity has been investigated from pooled data.

Children treated with X-Rays and proton radiotherapy are entered into the databases so that with sufficient follow up time we hope to be able to see the clinical impact of proton radiotherapy on late effects.

Institutions interested to know more about the IPPARCA collaboration are welcome to contact the authors.

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Reference:

Increased risk for infertility in childhood cancer patients

Following childhood cancer, founding one’s own family is of major relevance to survivors: 9 out of 10 adult childhood cancer survivors wish for their own children. However, survivors are at elevated risk for fertility impairment as a late effect of cancer treatment. In previous studies, fertility impairment was shown in one third of female and male childhood cancer survivors. Accordingly, survivors reported pregnancies significantly less often than peers from the general population. Fertility protection measures are available.

What is the current situation of patient education about fertility in Germany and use of prophylactic measures?

Only half of the survivors treated between 2000 and 2004 in Germany remembered having been informed of possible fertility impairment. Survivors who recalled having received such information, showed more initiative in family planning, such as having their fertility tested. Only 1% of the female and male participants of a Berlin survey in 2009 stated that they had used cryopreservation to protect their fertility.

How can we improve this situation?

The Patient Education – Intervention Study is part of the PanCareLIFE project.

It aims to 1) examine the current status of patient education in Austria, Czech Republic, Germany and Poland and 2) improve this situation by applying additional patient information material.

The overall aim is to inform all patients about their fertility risk and possible prophylactic measures so they can decide if they want to use them. For this purpose, patient information material consisting of leaflets and brochures was developed and is being evaluated in the intervention group of this study.
Who is being surveyed?
All newly diagnosed patients, aged 13 years and older, who are treated with chemotherapy and/or radiotherapy and their parents in eleven pediatric oncology departments in Germany, Poland, Austria and Czech Republic are invited to participate.

How is the survey being done?
The study is being conducted in two parts: 1) the control group “patient education as usual” and 2) the intervention group “patient education with additional patient information material”. In 2014/2015, patients of the control group and their parents were asked to fill out a questionnaire on patient education, their knowledge on fertility risks and preservation options as well as on utilization of fertility protection. The questionnaire was handed out three months and also six months following initial diagnosis.

First insight – results of the control group
Of the 113/142 (80%) participants in the control group (education as usual), nearly half were female (47%). Participants were 13 to 20 years old, with a median of 16 years. 16 patients refused to participate in the study, 5 had died three months after initial diagnosis, 3 had a current poor health status and 5 didn’t participate because of “other reasons”. Regarding gender, age at time of diagnosis and cancer diagnosis no significant differences were found between responders and non-responders. The majority of the adolescents reported receiving education on the risk of fertility impairment (80%) and on prophylactic measures (73%). Patients younger than 16 years recalled being informed less often than older patients (p<0.05).

According to information given by their physicians, 17% of the girls and almost half of the boys used cryopreservation. Patients aged 13 to 15 years used cryopreservation less often than older patients (p<0.05). Patients who remembered being informed about prophylactic measures used cryopreservation more often compared to those who did not (p<0.01).

We thank our patients and their families for participating in this study and are looking forward to the results of the “intervention group”.

The Patient Education – Intervention Study as part of the PanCareLIFE project has received funding from the European Union’s Framework Programme for research, technological development and demonstration under grant agreement no 602030. The project has also been supported by the Berliner Krebgesellschaft e.V. (EKPS201607) and the Kinderhilfe e.V.
Late effects in childhood cancer survivors

As a consequence of the increased success in treating childhood cancer, an increasing number of survivors may lead healthy and happy lives. However, for survivors as well as for their family and friends, suffering from cancer can be a traumatic event and, what is more, undergoing treatment means a lot of stress in every stage of life. Therefore, it is necessary to assess the late effects of a cancer diagnosis and treatment. The considerable amount of research to date has shown, for example, an increased risk of heart disease, and second cancers. Late effects can also affect mood and feelings, and include mental disorders such as depression and anxiety. To help survivors regular follow-up care is very important and should also include the psychosocial domain.

Aims of the PSYNA study

The PSYNA study was launched in 2016. It is conducted at the University Clinic in Mainz, extending and closely cooperating with the CVSS study (“Cardiac and Vascular late Sequelae in long-term Survivors of childhood cancer”). Its aims are an evaluation of a wide range of mental distress symptoms, including subjective experiences and the needs of long-term survivors relating to their after-care. Data is collected via questionnaires and in-depth interviews via telephone will gather information about survivors’ after-care, including utilisation, (unmet) needs, and survivors’ satisfaction with their care.

Further, the PSYNA study will address the following questions:

- How do survivors who make use of after-care on a regular basis differ from those who do not? (demographic, medical, and psychosocial factors)
- Which needs for information and after-care are expressed by the survivors and have those needs been met?
- How does the experience of surviving childhood cancer influence health behaviour?

Results from PSYNA will help inform interdisciplinary, risk-adjusted concepts for after-care which are in line with survivors' needs. Preliminary data analyses indicate that long-term childhood cancer survivors are more likely to suffer from a range of symptoms of mental distress (for example depression, anxiety, and panic) than a representative control population. On the other hand, the majority of participants do not report symptoms which reach clinical levels. The results speak to the need for improved after-care, especially focusing on psychosocial well-being.

by Dipl.-Psych. Mareike Ernst, University Medical Center Mainz., Mareike.Ernst@unimedizin-mainz.de
Risk factors for changes of the heart and vessels in children after hematopoietic stem cell transplantation
Rita Beier and Bianca Borchert-Mörlins, Essen and Hannover, Germany

Hematopoetic stem cell transplantation (HSCT) has become a treatment option for many diseases like lymphomas and acute leukemia, and it promises long term cure. Nowadays, due to improvements in patient supportive care, more than 80 % of children survive the first decade after transplantation. However, despite this good news, many children suffer from so-called “late effects”, that are associated with either the underlying disease or the treatment itself. These late effects are for example malfunctions of the thyroid gland, growth retardation and changes of the central nervous system. Apart from these well-known late effects, complications of the heart and vessels have been recognized in long-term survivors of HSCT. In fact, death from cardiovascular diseases (myocardial infarction, stroke) has become the third leading cause of death. These diseases were formally known to occur in the generation 50+. In addition, so-called “classical” risk factors like smoking, high blood pressure, elevated bad cholesterol and obesity are typically age dependent.

**Doctor Rita Beier** is a Pediatric Oncologist specialized in pediatric stem cell transplantation, working at the Department of Pediatric Hematology and Oncology, Essen, University Medical Center, Germany

**Doctor Bianca Borchert-Mörlins** is a cardiologist specialized in the evaluation of minimal changes in vessels and the heart, working at the Department of Pediatric Kidney-, Liver- and Metabolic diseases at the Hannover Medical School, led by Professor Anette Melk, Germany

**Do these risk factors play a role in children after HSCT** and do these risk factors have an impact on changes of the heart and vessels in these children? To approach this question we have performed a study of 64 children after...
Risk factors for changes of the heart and vessels in children after hematopoietic stem cell transplantation

-continued-

after HSCT (mean age: 13,9 +- 4,5 years, range 6-25,6 years) and looked for the presence of diverse risk factors and changes of the heart and vessels using ultrasound examination and measurements of the stiffness of arterial vessels (aorta). Elevated stiffness or loss of elasticity is a measure of arteriosclerosis.

Key Findings:
High blood pressure was present in 24 % of the children, the majority detected by using a 24-hours ambulatory blood pressure monitoring (ABPM) device. With this device, the everyday life blood pressure can be documented instead of a “shapshot” measurement in the doctor’s office. We can strongly advice to do an ABPM, even if routine blood pressure was normal, once every year.

Obesity and elevated bad cholesterol were apparent in 20% of children. Obesity defined by waist circumference was more reliable than BMI for predicting cardiovascular risk, because stiffness of the arteries was associated with elevated waist circumference in our study.

Atherosclerosis, eg. thickening of the inner layer of the vessels, which may finally lead to overt disease, was found in almost half of the children.

Sport or any kind of physical activity is beneficial in the prevention of vascular changes. Other studies have shown that exercise reduces thickening of the carotid vessels in obese children.

In most studies investigating the impact of sport, vigorous exercise with 3 sessions of one-hour training per week is required. But in our study any physical activity, even at a minimum level (eg. 30 minutes cycling, walking, playing ball), can be beneficial.

This is important because it is known that in children surviving life-threatening diseases, reintegration in sport programs is difficult.
In memory of our dear PanCare friend...

It has been three months now since we said farewell to our friend and Czech colleague Zuzana Wimmerová, the founder, thought leader and chairperson of the Brno survivors’ association Společně k úsměvu (Together Towards a Smile). Zuzana was an extraordinary person who made an exceptional mark in this world and in many people’s hearts and lives at her very young age of 25 years, when she succumbed to a late relapse of Ewing’s sarcoma.

As a cancer survivor diagnosed at 13, Zuzana believed that the experience of a young adult who had lived through cancer in childhood or teen years was so unique that it should be used for the good of other children and young adults currently combating cancer, their families, and cancer survivors suffering late effects of treatment. Her vision first led her to the study of psychology at the Brno Masaryk University where, from her early student years, she focused on the goal of helping families undergoing anticancer treatment. She chose as her bachelor thesis’ topic the Psychosocial Assessment Tool (PAT 2.0) – a screener for psychosocial risk in families of children with cancer, and was determined to follow through with its validation for the Czech Republic and introduction in Czech clinical practice. She also became very active in the European survivors’ circles and in PanCare activities. Many of you will remember her presentation “The sexuality of adolescents during oncology treatment” given at the 15th PanCare meeting in Dublin, and maintained a healthy diet.

She spoke on behalf of cancer survivors on many opportunities and public forums in the Czech Republic. Her engagement in the field of cancer survivorship resulted in the founding of the Brno survivors’ association Společně k úsměvu in 2016. Under her leadership the association established two projects – a support project for families in treatment Wise Mentor and a self-support web-based project Donate a Story. In her own story that she “donated” she promoted optimism, courage, altruism and healthy lifestyle. Leading by example, she practiced dance, yoga, cycling and backpacking.

In short, both in her early professional life and her personal life she was a source of inspiration and energy for many. Although not given the possibility to fulfil her own visions, she has generated a heartfelt commitment among her friends and colleagues to carry on her legacy.

Zuzana’s personal motto: Per aspera ad astra – Through difficulties to the stars

_Tomas Kepak and Katerina Kepakova_
The Youth Cancer Europe Foundation, formed in 2015, is a registered charity made up of 15 youth cancer organisations from across Europe which focuses on meeting the most urgent needs of young people with cancer, including age appropriate and equally accessible cancer treatment across Europe with long-term follow up and quality of survivorship, as well as acting as political and regulatory representatives of young people with cancer in the continent. Between the 24th and 27th August 2017, over 100 attendees from 22 countries gathered in Vilnius, Lithuania for YCE’s third annual meeting to discuss the most pressing issues facing young people who have successfully survived treatment for cancer or are currently undergoing treatment for it.

Among the group were young cancer patients and survivors, public policy advocates, charity workers and representatives and industry figures.

The meeting connected a new generation of patient advocates, providing a platform for people to share experiences and work on a collective action plan to transform the way the medical profession engages with young cancer patients. (Continued on the next page)
platform for people to share experiences and work on a collective action plan to transform the way the medical profession engages with young cancer patients.

Fostering direct contact between different collectives, and ensuring that the voices of patients and survivors become a key part of how treatment and after-care is shaped across the continent were a major part of the discussions. Over the course of the three days, the sessions included examples of best practice from all over Europe, highlighting the sometimes enormous differences in quality of care offered to young patients across countries; a key issue that Youth Cancer Europe is fighting to change. Panel discussions with inspirational speakers on public policy also encouraged young patients and survivors to get directly involved in policymaking and lobbying in their own countries.

The Annual General Meeting (AGM) outlined YCE’s activities for the next 18 months. This included setting up several working groups and the agreement upon specific tasks. One to organise a face-to-face capacity building session for 25 patient advocates in April 2018, aimed at helping national cancer groups influence health policies in their own countries. A second initiative to run policy events in the European Parliament in October 2018 and March 2019. A third to create easy to understand information about the latest cancer research/treatment by collaborating with scientists and researchers and promoting this material through platforms such as YouTube, social media, and the YCE website. A fourth will focus on communications, for example, telling YCE’s story and working to expand the network. A fifth will focus on fundraising.

Five board members were elected to direct these activities and support YCE on the next stage of its journey: Sarunas Narbutas (Lithuania), Emmanuel Schipor (Romania), Guy Tavori (Israel), Ania Buchacz (Austria) and Tomas Farrington (UK).

Meeting attendee Aoife Moggan (Ireland, PHOTO), added: “As a cancer survivor myself, I feel immensely passionate about the issues at hand for cancer patients and survivors throughout care. I left Vilnius confident that the palpable sense of passion and resilience of those present meant that there was going to be positive changes brought about as a result of this meeting. It fostered hope!” “I felt a quote Margaret Mead, used in an article written by Nick Smallwood (another fellow attendee at the meeting) in the British Medical Journal was particularly apt: “Never doubt that a small group of committed citizens can change the world. Indeed it is the only thing that ever has.”

For more information about Youth Cancer Europe visit http://www.youthcancereurope.org/
Upcoming meetings...

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<td>April 17-18, 2018</td>
<td>10th PanCareLIFE’s General Assembly</td>
<td>Prague, Czech Republic</td>
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<td>PanCareLIFE’s General Assembly will meet in Prague on 17-18th April, just before the PanCare Meeting.</td>
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<td>April 18-20, 2018</td>
<td>21st PanCare MEETING</td>
<td>Prague, Czech Republic</td>
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<td>The 21st PanCare Meeting will be held in Prague, Czech Republic, hosted by Jarmila Kruseova &amp; her team from the Department of Pediatric Hematology and Oncology, Charles University Prague and Motol University Hospital. Further information on the meeting will be published on the pancare website <a href="https://www.pancare.eu">https://www.pancare.eu</a> right before the meeting.</td>
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<td>June 20-22, 2019</td>
<td>International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer</td>
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<td>Further information on this meeting will be also announced on the pancare website <a href="https://www.pancare.eu">https://www.pancare.eu</a></td>
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<td>October 24-25, 2018</td>
<td>22nd PanCare MEETING</td>
<td>Institut Curie, Paris</td>
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<td>The 22st PanCare Meeting will be held in Paris, France hosted by Florent de Vathaire &amp; his team. Further information on the meeting will be published on the pancare website <a href="https://www.pancare.eu">https://www.pancare.eu</a> right before the meeting.</td>
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<td>October 26, 2018</td>
<td>PanCareLIFE Closing Meeting</td>
<td>Institute Curie, Paris</td>
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<td>For more information see <a href="http://www.pancarelife.eu">www.pancarelife.eu</a></td>
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<td>November 16-19, 2018</td>
<td>SIOP Congress</td>
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From the Editor:

This PanCare newsletter is intended to be a forum for news and updates on activities, a way for PanCare members to keep up with each other, to learn about new developments, and to participate in different activities. The Editor welcomes all submissions of interest to members, such as reports on European countries’ LTFU structures, methods and challenges, meeting announcements and reports, new publications and suggestions for columns, features and photos.

Please send submissions for future issues to the Editor at jbyrne@boyneresearch.ie