Christopher's Smile

coz kids get cancer too

Registered Charity 1129906

Briefing Paper on Childhood Cancer - November 2016

Background

Childhood cancer is the biggest killer by disease of children in the western world. While significant increases in survival of children with leukaemia and lymphoma have been made in the last 20 years, the survival of children with solid tumours has not seen any marked improvement and there are some types of childhood cancer for which there is still no curative treatment. Approximately 1750 children in the UK are diagnosed with cancer each year in the UK and approximately 260 children in the UK die each year from cancer before their 15th birthday.

New Treatments – Research

The development of existing chemotherapy agents has reached a peak and the survival rate for children has plateaued. Additionally, many survivors are left with a legacy of issues caused by the extremely high levels of toxicity of their treatments or the permanent effects of radiotherapy. New treatments are urgently needed for those children who currently receive the worst prognosis. Childhood cancer is not common. Approximately 1% of cancer patients are children and therefore children constitute a tiny market for pharmaceutical companies so there are few incentives for paediatric drug development. While many of the genetic abnormalities in childhood cancers also occur in adults and children can be treated with the same drugs, paediatric drug development and trials always lag behind adults by many years.

Genetic Testing – Research

Christopher's Smile funded the development of a tumour DNA sequencing test specifically for children's tumours. The test was developed at The Institute of Cancer Research in Sutton. This test identifies abnormalities in 91 key genes in children's tumours. The test is available at The Royal Marsden NHS Foundation Trust Children's Unit as a clinical study and is already providing clinicians with data previously unobtainable in a clinical setting. The cost of each test is approximately £200. The challenge now is to roll out the availability of the test to the 20 UK paediatric oncology centres.

The 100,000 Genomes project will generate data that will be invaluable to researchers now and in the future. The information gathered will define genetic abnormalities but that does not mean that treatments will be instantly available. For some childhood cancers the genetic abnormalities are already known and have been for years but to date no drug has been developed to provide treatment.

Implementation of New Treatments

We have learnt that there is no one person, group or body outside the pharmaceutical industry whose role it is to champion the introduction of new treatments into NHS standard care. This role is not one taken up by the NIHR or the NHS England Academic Health Science Network (even though one of their core objectives is to *"Speed up adoption of innovation into practice to improve clinical outcomes and patient experience – support the identification and more rapid spread of research and innovation at pace and scale to improve patient care and local population health."*). There is also no documented process to follow in order to even plan the implementation of new treatments into front line use.

Availability of New Drugs

As stated above, children represent only a tiny proportion of cancer patients and therefore children diagnosed with cancer represent a tiny market to the global pharmaceutical industry. The pharmaceutical industry targets the largest markets for their R&D activities and want their latest drugs to go into frontline use as quickly as possible to gain maximum benefit from their patent protection. Legislation exists to make paediatric testing mandatory where a new drug shows benefit in the paediatric community. These additional studies slow down approval and where possible pharmaceutical companies obtain a waiver to circumvent paediatric testing. This can result in paediatric researchers being denied access to the very latest drugs in development until such time approval has been granted. It is only at this time that pre-clinical paediatric studies can begin – years after their adult counterparts.

Processes and Procedures

Progress is hampered by outdated processes and procedures that have not changed in years and do not take into account the information age. Why should it take 5 months to get the aforementioned genetic test for tumour tissue through ethics? Ethical approval for studies can take a very long time and duplicate effort. Why should a study have to go through ethical approval at each centre where the study is open and not have one blanket ethical approval?

Data is woefully poor. While patient confidentiality must be preserved, in this information age the numbers of children diagnosed, their cancer types and outcome statistics should be available at the touch of a button. It is not. Until processes and procedures are brought up to date to complement the new technologies that are available to all, advances in childhood cancer outcomes will always be retarded.

Leaving the European Union

With the UK leaving the European Union within 2 years of Article 50 being implemented, the UK government will need to address the UK laws that have been introduced as a result of EU legislation

The 3 pieces of EU legislation that most affect paediatric cancer research are:

- REGULATION (EC) No 1901/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004
- REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC
- REGULATION (EC) No 141/2000 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 1999 on orphan medicinal products

The following factors should be taken into account when the UK is revising its post EU legislation that impacts paediatric cancer research:

- To ensure that UK legislation does not retard or hamper UK research into paediatric cancers.
- Legislation in the UK complements the UK's intellectual and academic infrastructure to make it the first choice as a location for paediatric cancer research.
- The UK government must not assume that the 3 pieces of EU legislation shown above are fit for purpose in their current form.
- To encourage changes in research and clinical implementation processes to complement any changes in legislation.

Specific information supplied on 23rd November 2016 by Dame Glenis Willmott MEP Leader of the European Parliamentary Labour Party and Rapporteur for the EU Clinical Trials Regulations

1) **Drug mechanism of action vs cancer type:** Under the EU's Paediatric Regulation, developers must produce Paediatric Investigation Plans (PIP) for all new drugs they develop. However, PIP waivers are granted if a drug is intended to treat a disease that doesn't occur in children, and this is the case for most childhood cancers. Nevertheless, the mechanism of action of a drug for adult cancer may be effective in treating a paediatric cancer - it's the molecular abnormality that causes the cancer that is important, rather than the cancer type. Currently, too many drugs with potential to treat paediatric cancers have been granted waivers; it should be a priority to ensure that decisions on whether to investigate a medicine's potential to treat a paediatric illness is based on the drug's mechanism of action, rather than the disease type.

2) **Paediatric trials not seen as lower priority:** currently, many developers wait for a drug to show promise in the target adult population before beginning paediatric trials, meaning children wait longer for access to potentially life-saving treatments. There is also nothing to stop a developer from terminating a promising paediatric trial early if they are not getting the anticipated results in the adult population. Future regulation should ensure that paediatric trials are not seen as a lower priority.

3) **Access to cross-border trials:** cross-border trials are particularly important for rare diseases such as childhood cancer, where there are often not enough cases in one country to make a trial viable. The EU's new Clinical Trials Regulation will come into force in October 2018 and will make it much easier to carry out these cross-border trials by requiring one single application to be submitted to a central portal, rather than one in every country. In order to ensure children do to not lose access to life-saving trials, the UK should consider how we can remain part of this system post-Brexit.

Social Impact of Childhood Cancer

Childhood cancer impacts families during and after treatment. The loss of a child or ongoing post treatment issues can be too much for relationships to tolerate resulting in breakdown. We are not aware of any studies that record the rate of divorce, sibling behavioural issues or alcohol or substance excess following a child cancer diagnosis in the family.

There is also the issue of no employment protection for parents whose children have received a diagnosis of cancer or worse, a terminal diagnosis. While mothers and fathers have maternity/paternity rights when their pregnancy and subsequent childbirth has gone normally, parents of children with cancer who are dying have no protection and either continue working or face losing their job. Is this the best we can do in 2016?

Funding of Childhood Cancer Research and Initiatives

Many of the issues that hamper progress are not caused by a lack of funds. Putting more money into childhood cancer will not achieve any step change until the issues highlighted above are corrected. With outdated procedures, a lack of new drugs and no clear process or champion for taking new treatments from clinical study to front line use quickly, additional funding will not provide the change we all so desperately want.

Christopher's Smile

Christopher's Smile was set up in October 2008 after Karen and Kevin Capel lost their son, Christopher in June the same year to an aggressive medulloblastoma brain tumour. Following a 21-month battle with the disease, he passed away 9 days before his 6th birthday. The Capels wanted to find something positive in their tragedy and thought long and hard about the direction they should take.

The Capels feel strongly that new treatments are urgently needed for the 20% of children who do not survive their disease along with those children who survive but face a lifetime of post treatment issues.

Christopher's Smile does not have a specific paediatric tumour focus but instead provides funding for projects that will benefit the largest number of children possible across the childhood cancer community. The charity has awarded 6 project grants and raised over 1 million pounds.

The current research funding focus of Christopher's Smile is the development of tumour DNA sequencing for the analysis of tissue and fluid samples.

The lack of innovative targeted drugs for paediatric trials is of particular concern to the Capels. They have been actively campaigning for change on a European platform and they have addressed the European Commission and MEPs in Brussels with the overall aim to improve the outcome for children with cancer.

Our vision is for every child diagnosed with childhood cancer to not only survive, but to reach adulthood enjoying a good quality of life.

Further Reading and References

CRUK website Childhood Cancer Statistics
http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers

Office for National Statistics Cancer Registrations
http://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancerregistrationstatisticsengland/2014

10 year report by the EMA for the European Commission on the EU Paediatric Regulation
http://ec.europa.eu/health/files/paediatrics/2016_pc_report_2017/ema_10_year_report_for_consultation.pdf

Institute of Cancer Research Blog article on Paediatric Regulation
http://www.icr.ac.uk/blogs/science-talk-the-icr-blog/page-details/european-commission-misses-a-chance-to-open-a-pipeline-of-cancer-drugs-to-children

Institute of Cancer Research Blog article on developing the genetic test for children
http://www.icr.ac.uk/blogs/science-talk-the-icr-blog/page-details/how-this-icr-phd-student-is-helping-bring-personalised-medicine-to-children-with-cancer

Christopher's Smile website
http://www.christopherssmile.org.uk/