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WALES CANCER ALLIANCE

Personalised Cancer Treatments and Cancer Research in Wales

A Wales Cancer Alliance Policy Paper
Summer 2017

Personalised cancer treatments and cancer research in Wales: Overview

Advancements in molecular biology means it is now possible to sub-divide different cancer types based upon the biological variation inherent to each individual tumour. Unprecedented opportunities now exist for more accurate diagnosis, prognosis and targeted treatment of aggressive cancer.

Personalised Cancer Treatments therefore also have the potential to contribute to the Welsh Government's prudent healthcare agenda as they provide clinical effectiveness for patients - by providing evidence-based drugs for their condition, and to avoid side effects from the drugs we can predict will not work for them, and cost benefits for the NHS - by helping doctors avoid prescribing drugs that won't work for certain patients. To achieve this it is critical that Welsh government works to maximise opportunities for medical research to translate into clinical practice and provide access to innovation.

As care is proven to be much better in a research rich environment, it is vital that cancer research between the various funded resources is fully co-ordinated and embedded in NHS services and closely aligned with the ongoing Transforming Cancer Services initiatives across Wales.

Research should be focussed on the cancer types where unmet clinical needs exist, raised awareness, late diagnosis, new emerging treatments such as molecular targeted therapies, established curative treatments such as surgery and radiotherapy, and the underfunded areas of survivorship and palliative care.

Background – Personalised Cancer Treatments

Recent developments in cancer research mean that we can now separate cancer patients into different groups based on analysis of their tumours at a molecular level. As a result, we are now beginning to rationally design and develop modern medicines that target specific molecular defects with the aim to treat specific patient groups and their cancer type more appropriately. This is sometimes referred to as "stratified", "personalised" "precision" or "targeted" medicine. All cancer patients should be able to access where appropriate new targeted treatments that can more precisely target tumours reducing side effects for patients.

Molecular diagnostic tests help to detect the genetic mutations which allow us to separate patients into groups – but there is currently no clear Government policy on access to such tests within the NHS. We believe that it is critical for Welsh government to consider how to maximise opportunities to provide access to the latest innovations.

The main reason behind this shortfall in testing is that there is no national funding mechanism for these tests in Wales. Industry funds some tests, but this is not a permanent solution.

A nationally commissioned and funded service is needed. There are many more targeted medicines in the pipeline of development so it is crucial that the NHS is set up so that all suitable patients can access these tests, and therefore treatments when they become available.

We estimate that to meet current demand and future-proof the provision for molecular diagnostics across Wales, around **£1 million in annual funding** will be required. This would cover the cost per test, including reagents, consumables, staff time, and overheads. However, this amount is likely to be conservative as it does not include costs of equipment, and training.

Alongside this, there are opportunities for the NHS and Welsh government to explore other potential solutions to help deliver access to new diagnostic tests and precision medicines. These could include: enhanced horizon-scanning to improve forward planning; exploring opportunities for flexible pricing models; and explore how to assess clinical and cost effectiveness of treatments for smaller population samples.

Radiotherapy is also becoming more targeted; it is important patients that need it can access the latest radiotherapy treatments which target tumours more precisely and aggressively, and reduce side effects.

Background – Cancer Research

The Welsh Government Cancer Delivery Plan (CDP) for the NHS to 2020 acknowledges that Cancer research is critical to improve outcomes for patients and for the health of people in Wales. The CDP also says that action is needed to improve equal access to clinical trials, and to ensure that a culture of research is embedded in the NHS.

The CDP also sets an action for NHS Wales to develop a Welsh Cancer Research Strategy so we hope that the development of a Strategy will address the above issues. It will also be essential that the Strategy considers the implications that Brexit will have on research in Wales, particularly ensuring that Wales can remain attractive to researchers. The Strategy should also take into account the impact of negotiations on Wales' access to EU funding programmes and the need for current levels of funding to be maintained, in order for Wales to maintain its status as a leader in cancer research.

Cancer Delivery Plan[1]

The Welsh Government Cancer Delivery Plan for the NHS to 2020 acknowledges that the era of precision medicines and the development of integrated genetics services have the potential to radically transform the delivery of cancer care.

The Welsh Government also published its Strategy for Genomics and Precision Medicine in July 2017. The £6.8m plan aims to ensure that Wales is able to offer treatment plans by better understanding of human DNA, hopefully leading to faster access to genetic tests and targeted treatment.

Calls for Action

The Wales Cancer Alliance calls for:

1) **Longitudinal collection, and collection of samples from patients**

   Within the last 5 years it has become clear that cancers continually evolve with respect to their biological characters during the course of the disease. The inherent variation within a tumour and between tumours of a single patient or patient subgroups has been recognised as the major cause of treatment failure. Informed decisions on the biology and potential drug response of metastatic tumours are often based upon the profiles of primary tumours. Such practice is not always ideal as often there is great variation between metastatic tumours and parental primary tumours. Unfortunately, matched primary and secondary tumours from the same patient are an important yet

[1] Wales Cancer Network. Cancer Delivery Plan for Wales 2016 – 2020: The highest standard of care for everyone with cancer. Available from: http://gov.wales/docs/dhss/publications/161114cancerplanen.pdf

often unavailable resource as frequently, metastatic sites are not sampled routinely or are inaccessible. However, the new paradigm of liquid biopsies where circulating tumour cells shed from metastatic sites can be accessed through blood samples offers for the first time possibility of being able to genetically analyse previously inaccessible metastatic sites over time.

There is now a clear need to collect, where possible, repeated samples from a patient during the course of their disease and we call for strong support to be given to initiatives such as the Wales Cancer Bank and others who are striving to create longitudinal collections. The benefits of these will be great as it will enable Welsh patients to be appropriately matched with a molecular targeted therapy that better reflects their stage and state of disease driven by biology. Further, it will enable scientists in Wales and further afield to develop better cancer diagnostics, discover new drug targets and generate novel targeted anti-cancer agents pertinent to metastatic disease. Improved patient stratification and better diagnostic tests will be critical if Wales is to really deliver on the promise of personalised cancer medicine.

We would also like the Welsh Government to consider how it can improve donations of tissue samples from patients.

2) Infrastructural support for analytical platforms

In the current "omics" era, the increasing demand for and use of high-throughput and high-content technologies for the analysis of biological samples has led to the generation of masses of "Big Data". This has created a great strain on current resources in Wales both within academia and the NHS who work together to help translate these genomic technologies into mainstream clinical practice. Current bottlenecks exist that have led to delays in sample analysis and subsequent interpretation of data output.

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The Wales Cancer Alliance calls for more resources to be made available for the implementation of further platforms for both genomics and proteomics analysis so that quicker, more accurate and reliable data, of consistent quality can be acquired. Achieving these will be prudent to good healthcare and research**.** Also at present there is insufficient number of trained and skilled personnel in Wales capable of extracting clinically meaningful information from the large data sets that are being produced.

Also of equal importance there is at present a distinct lack of robust, clinically meaningful predictive biomarkers that can be used reliably by clinicians for improved targeting of these very expensive molecular targeted therapies given to patients. Often the reason why so many are deemed not cost effective. The recruitment, training and retention of more genetics, bioinformaticists or similar specialists will be vital for the integration personalised cancer treatment into standard cancer care. Although the development of adequate infrastructure will require investment, the initial outlay should in time lead to savings and greater benefit for cancer patients in Wales as they receive the very latest therapies in a more cost-efficient manner.

3) Closer Collaboration between the pharmaceutical industry, NHS and Academia

The Wales Cancer Alliance calls for greater collaboration between the pharmaceutical industry, NHS and Academia**.** Pre-treatment and post-treatment samples from the same patients are a much sought after resource, especially in the era of molecular targeted therapies where a paucity of predictive biomarkers exist, often resulting in a "scatter gun approach" for treating patients. Pharma are now recognising this and a number of funded trials are being conducted where pre- and post-treatment samples are being collected prior to and/or following other treatment modalities such as surgery or radiotherapy. Partnering with Industry will greatly facilitate the co-evolution of accompanying diagnostic tests alongside the development of targeted therapies. Tests that can predict and measure the treatment response to new drugs, in addition to conventional therapies are much needed. Greater collaboration

will also help attract Pharma and other academic leads to Wales, ensuring that Welsh patients have early access to the very latest treatments.

Fostering and strengthening of lasting partnerships with academia will help with the development of more relevant pre-clinical models (e.g. organoid culture). These will be invaluable high throughput laboratory based tools and drug screens that can be utilised by both clinicians and industry as they will better reflect patient variation and be able to discriminate different treatment responses for new emerging molecular targeted therapies, in addition to conventional treatments. As a result of these partnerships academia will also benefit from clinical and industrial expertise, increasing the translational value and enhancing the impact of their research.

4) **Better co-ordination between Local Health Boards**

The Wales Cancer Alliance is aware that unacceptable levels of cross-boundary bureaucracy exist within the Welsh healthcare system and therefore we call for greater co-ordination and collaboration between Welsh Health Boards. Increased inter-department billing and requirement of service contracts for access to patient information e.g. pathology blocks, scans etc., have led to greater time and money expenditure. The need for these extra resources has proved greatly prohibitive to pharmaceutical companies and lead academics wishing to recruit Welsh patients for ground-breaking clinical trials.

5) **Increased awareness and support of precision radiotherapy**

In recent years radiotherapy and medical imaging has made great strides in the use of new technologies to make cancer treatments with both external beam radiotherapy and molecular targeted radiotherapy (MRT) more personalised. The result has been the emergence of functional image-guided radiotherapy a new concept that lends to greater precision in the delivery of radiation medicine. The Wales Cancer Alliance calls for continued support of cutting edge initiatives that promote the delivery high precision and personalised radiotherapy such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT).

Currently there is a recognised need for a raised standard in how MRT treatments are planned and delivered as the dose of MRT delivered to the tumour site is often sporadic and inconsistent. Any improvements will in part result from better optimisation of treatments using the anatomical features and tumour characteristics of the patient such as receptor expression. Therefore greater cohesion between the Wales Cancer Bank, the PETIC centre at Cardiff University and Medical Physics and Clinical Trials Unit at Velindre Cancer Centre will help clinicians deliver more personalised and adaptive radiotherapy treatments for cancer patients in Wales.

6) **IT Systems**

The current CANISC IT System for cancer patient records infrastructure has shown to be unfit for the purpose of developing stratified medicine, so it is important that this is also urgently addressed.