

British Society for Immunology Response to the House of Commons Health and Social Care Select Committee Inquiry on Future Cancer

The BSI-NCRI Cancer Immunology Group is a collaborative initiative between the British Society for Immunology (BSI) and the National Cancer Research Institute (NCRI), comprising researchers, clinicians, industry representative and patients. The group is currently developing a report linked to the Government's Life Sciences Vision that sets out the current state of, challenges to, and future priorities for immunotherapies for cancer in the UK. We will publish this report in the summer, but much of the evidence in this submission has been gleaned from working on this project so far, including discussions and roundtables with expert UK cancer immunotherapy researchers.

What are the innovations with the greatest potential to transform cancer diagnosis and treatment in the short, medium and long term?

The UK leads the world for the quality of our immunology research. With the right infrastructure and investment, we can bring this research excellence to bear on the development of new cancer immunotherapies, facilitating the smooth progress of these potentially life-saving treatments from bench to bedside to significantly improve patient care and ultimately patient survival.

Immunotherapy treatments represent a shift change in how we treat cancer and if nurtured effectively could join surgery, chemotherapy, and radiation in one of the main modes of treatments across multiple cancer types. Everybody has an immune system, so it has a universality, side effects from certain immunotherapies have the potential to be less pronounced than in other forms of treatment and, because of immune memory, there is the prospect of longer lasting remissions.

At the moment, however, patient outcomes have varied considerably in response to treatment with immunotherapy, with some responding very well but others displaying no response at all. For example, monoclonal antibodies designed to reactivate the killer function of T cells, known as immune checkpoint inhibitors, include one targeting the interaction between the programmed cell death (PD-1) receptor and its ligand (PD-L1). In theory, this should be universally effective no matter the cell type, but in practice certain types of melanomas respond well, but prostate cancers do so seldomly. In order, therefore, to identify patients for whom treatment will be effective, and those for whom treatment will not be effective, more research is required into the predictive biomarkers, which will include genes involved in mutation repair which may differ between demographics¹. Doing this will mean that unnecessary and ineffective courses of immunotherapy are no longer administered and both treatment plans and funds can be redirected towards conventional treatments that may be more effective for individual patients. Doing this will remove having to undergo side effects unnecessarily from the cancer treatment experience.

To realise this as a reality, there needs to be more investment in immunotherapy research, especially in cross-working between cancer researchers and immunologists. Much of the underlying biology behind the mechanisms through which immunotherapy works is not understood yet and this is vital to making advances in treatment; partnerships between immunologists and cancer scientists will be critical in clearing this knowledge block. There should be (1) the creation of accessible research-ready datasets that enable the long-term follow-up of patients on immunotherapies and meaningful research into mechanisms of action, immune-related adverse events (IrAEs) and co-morbidities; (2) improved access to clinical samples for robust pre-clinical models of human cancer immunity; (3) research into biomarkers for response prediction and patient stratification (as abovementioned); and (4) support of prospective cohort studies and linking them in with the wider research community.

We should also learn lessons from the COVID-19 pandemic, during which research consortia like UK-CIC took a team science approach, bringing together diverse teams when faced with a substantial challenge and showed that this approach can set the pace, drive forward the research agenda, and get results, not least through strong leadership and colossal buy in from the immunological research community. The research infrastructure that has been built up throughout the COVID-19 pandemic including deep links between industry, academia, the NHS, and clinicians that is active now, should be preserved and used or replicated to tackle other public health issues such as cancer immunotherapy research.

How best can innovations in diagnosing and treating cancer be transitioned into frontline clinical settings?

More focus should be given to upskilling the clinical oncology workforce through education in immunology, as well as targeting oncologists through education about the early detection and management of IrAEs (including in the long term); taking these steps to improve knowledge around immunotherapies would make them more practicable in a clinical environment. Only through taking steps both at the research level and in the NHS can the burgeoning benefits of immunotherapies be delivered to patients successfully and in a way that enhances the treatment experience for all involved. This fits with one of the Government's Healthcare Missions, enumerated in its Life Sciences Vision, on the development of immuno-oncology.

Additionally, there is need to greater capacity within other professions which are closely involved in cancer clinical trials. These include: additional qualified research nurses who can act as an information hub between the patient, the lab, the theatre and the pathology department; the growing need for bioinformaticians to interpret complex data; more clinical immunologists to collaborate with oncologists and provide specialist input on immune-based treatments and side-effects.

What can be learnt about innovative cancer diagnosis and treatment from international examples of best practice?

The US currently dominates immunotherapy research, followed by China, and then UK in third place with an approximate global share of 5%. The UK has two immunotherapy research centres in the global top ten and eight in the global top 50. These research centres for immunotherapies are found throughout the country, and the research infrastructure is excellent. This infrastructure, however, is not matched by the available funding reserved for immunotherapy. Funding, however, is just a small fraction of what is spent in competing countries. This is markedly different to the research ecosystem in the United States.

In 2017, Congress passed, and the President signed into law the 21st Century Cures Act, which sees \$1.8 billion funding over seven years allocated for cancer research in many areas including immunotherapy. The law also streamlined cancer-related decision-making at the Food and Drug Administration (FDA) through the formation of an Oncology Centre of Excellence, so that effective treatments can be approved more quickly, and patients can have more direct access to information about the regulatory process, which is key to bringing the public along the journey of scientific and medical advances.

Conversely, in the UK, there are challenges related to navigating the regulatory environment specific to us that hamper our position as a world leader in developing and approving immunotherapies for cancer. We are known internationally for having clinical trial regulation that is bureaucratic and

unwieldy, which slows down trials and makes them more expensive to run. Regulation such as data protection (GDPR) and rules from the Human Tissue Authority (HTA) can cause additional delays and disruptions, alongside those experienced around Material Transfer Agreements (MTAs), the process around which needs to be simplified and standardised with an expedited approval process so that they don't hinder important research. The UK could learn from countries like Spain, China, and the US in creating a more cohesive and agile path from pre-trial to treatment. We should also be strengthening links between UK academia and clinical medicine and industry at a time when it is being reported that industry backed clinical trials have decreased in number by 41% since 2017, often in favour for other countries where the regulatory environment is more amenable and navigableⁱⁱ.

President Biden has reignited his 2016 call for a 'cancer moonshot' which he launched when Vice-President. The White House has convened a 'cancer cabinet' which brings together, amongst others, the Department of Health and Human Services, National Institutes of Health, National Cancer Institute, FDA, Centers for Disease Control and Prevention, Office of Science and Technology Policy, Domestic Policy Council, Office of Management and Budget, Office of Legislative Affairs, Office of Public Engagement. Along with a dedicated co-ordinator in the White House's Executive Office of the President to help establish and advance cancer moonshot goals, the centralisation of strategy in the United States will be key to allowing co-ordinated collaboration, receiving meaningful funding, and aligning research with the regulatory environment. If the UK wishes to compete on the same level as the United States in areas like cancer immunotherapy, which has the potential to create immense patient benefit, then we need to be serious about the level of funding that is required and the need for Government to use its convening power to bring together the partners needed to deliver on this.

Is the impact of innovations in cancer diagnosis and treatment on health inequalities being sufficiently taken into account?

Immunotherapies allow care to be tailored to individuals and it is known that personalised care is able to have a positive impact on health inequalities, taking account of people's different backgrounds and preferences, with people from lower socioeconomic groups able to benefit the most from personalised careⁱⁱⁱ.

Personalised care has been shown by studies to benefit those with long term and chronic health conditions, both psychologically and physically^{iv}. It is the case however, that more research is needed to investigate which parts of personalised care planning is most effective at providing benefit for specific patient groups, including cancer patients. A personalised care plan with appropriate immunotherapies would allow a more targeted approach to individual cancers and has the potential to offer effective treatment with fewer side effects and longer remission periods.

The primary obstacle to making this a reality at the moment is the dearth of knowledge at present surrounding the predictive biomarkers which would allow clinicians to be able to identify patients that would most benefit from such interventions. There is further evidence that a one size fits all will not work with immunotherapy, for example that there may be inherent differences in treatment responses between males and females^v, which needs to be elucidated through further research in order to make sure that no population group is left behind when advances are made in this promising treatment area.

In order to address health inequalities in these areas, we should also be embedding the patient voice in research from the beginning and ensuring strong and diverse representation of patient-public

involvement (PPI) is in place so that research can benefit from understanding patient priorities on research and perspectives on how the research is designed and conducted. Utilising PPI should also be used throughout the treatment pathway.

ⁱ [Cancer immunotherapy: predicting outcomes, Genomics Education Programme, Health Education England](#)

ⁱⁱ [British Covid research led the world – why have our clinical trials fallen off a cliff, Sir Andrew Pollard, The Guardian, 26 April 2023](#)

ⁱⁱⁱ [Personalised Care – Evidence and Case Studies, NHS England](#)

^{iv} [Personalised care planning for adults with chronic or long-term health conditions, Coulter A et al., Cochrane Database Syst Rev. 2015 Mar; 2015\(3\): CD010523](#)

^v [The impact of sex and gender on immunotherapy outcomes, Klein S and Morgan R, Biol Sex Differ. 2020; 11: 24.](#)