Written evidence submitted by Dr Elizabeth Marsh, University of Derby (ECS0007)

Background

I am a scientist and Senior Lecturer in Molecular and Cellular Biology at the University of Derby. I lead a research team of scientists and Head and Neck clinicians which aims to understand the mechanisms of how Human Papillomavirus (HPV) causes Head and Neck Squamous Cell Carcinoma (HNSCC), to improve outcomes for patients. We investigate this aim through three research approaches: informing therapeutic approaches, improving diagnostic tools, and through education to raise awareness of oral HPV amongst clinicians, dentists, and the general public.

Response to 'Cancer Services' Consultation

I am responding to the invitation for written evidence for the Health and Social Care Committee's expert panel; however, I am a basic scientist and I do not work within the NHS, as such I write with respect to the fundamental science, rather than from a clinical perspective.

Policy Area: Innovation and Technology

Safer and more precise treatments including advanced radiotherapy techniques and immunotherapies will continue to support improvements in survival rates

Was the commitment met overall?

HPV-positive HNSCC is a distinct disease from 'conventional' (HPV-negative) HNSCC. Patients with HPV-positive cancer often present very late and are diagnosed with cystic metastatic disease, which is treated in clinic in the same manner as HPV-negative HNSCC, despite evidence that individuals with HPV-positive cancer respond better to treatment. Given that the standard treatment regimen has huge negative impacts on the quality of life of these patients, there are grounds to revise this treatment regimen for HPV-positive disease, to improve morbidity and mortality rates for these individuals.

However, until we understand the mechanisms by which HPV causes HNSCC, we are unable to target specific genes with novel, or re-purposed, curative drugs. For instance, recent clinical trials in both the UK and US to de-escalate treatment for HPV-positive HNSCC were ended early as patients in the treatment arm who were given the EGFR-inhibitor, cetuximab (an immunotherapy), were found to result in worse, tumour control than the control (the usual treatment regimen of cisplatin-chemotherapy) arm (Gillison et al., 2019, Mehanna et al., 2019). Clearly, this highlights that such advances to meet this commitment need to be underpinned by fundamental science and investment to achieve a specific evidence base for HPV-positive HNSCC.

An alternative approach to meet this commitment for HPV-positive HNSCC is a clinical trial presently recruiting 1100 participants that aims to de-intensify treatment and improve dysphagia (swallowing difficulties) outcomes for individuals with HPV-positive disease; Post-operative Adjuvant Treatment for HPV-positive Tumours (PATHOS). This trial is principally led by Professors Mererid Evans and Terence Jones (Velindre NHS Trust and the University of Liverpool, respectively). However, it is an international trial, and is multicentre within the UK, including at University Hospitals of Derby and Burton, and is registered with ClinicalTrials.gov as NCT02215265. After surgery, 'at risk' individuals (determined by histology) are randomised into trial groups in which their radiotherapy and chemotherapy dose is reduced. The outcome measures are overall survival and swallowing function (Owadally et al., 2015), which will reveal how post-operative treatment can be effectively reduced to preserve efficacy, whilst reducing horrific and long-term side effects for patients that have significant impact upon quality of life.

The full commitment (3.62) does not specifically address all cancer types, including HPV-positive HNSCC, that are in need of safer and more precise treatments. Instead, it prioritises ovarian cancer, and committed £130 million to upgrade radiotherapy machines across England; to both of these specific details I am unable to comment. However, the commitment itself gave no clear or fixed deadline for implementation. The outcomes of the PATHOS trial, which we anticipate will directly result in HPV-positive HNSCC patients being offered treatment with fewer side effects, are not expected until April 2027. Although timely deadlines are useful, it must be recognised that research of this nature takes significant periods of time, and that this should therefore be reflected within the NHS Long Term Plan.

Was the commitment effectively funded?

The PATHOS trial is funded by the Stand up to Cancer campaign for Cancer Research UK. Further funding was awarded to PATHOS by UK Research and Innovation (UKRI) in 2020 to facilitate subsequent investigations using whole genome sequencing for therapeutic and diagnostic targets.

This trial is a hugely positive step towards improving survival outcomes for individuals with HPV-positive HNSCC; but, as outlined above, the development of such Phase II and III interventions need to be supported by basic science, which is notoriously underfunded. For instance, our group aims to understand the progressive development of HPV infections within healthy, precancerous tissues, and how this leads to HNSCC; yet less than 2% of research funding is allocated to projects for the whole remit of Head and Neck cancer. This funding is insufficient.

Did the commitment achieve a positive impact for patients?

Once the outcomes of the PATHOS trial are published, we will be in a position to state whether this approach has achieved a positive impact for patients. Given that HPV-positive HNSCC is more common in men than women, the PATHOS results are likely to have a positive effect upon men who present late at clinic, often with late-onset disease, especially when the HPV vaccination programme is also considered; boys have only been offered this vaccination since 2019 and are therefore at increased risk of HPV-positive cancers than their female counterparts. Incidentally, the implementation of the vaccination programme itself over the past two years has been severely disrupted by school closures due to COVID-19.

The time and investment required for approaches to overhaul treatment regimens and identify novel targets are significant, and further stretched when the country is responding to a global pandemic and resources are redistributed to this priority. Therefore, defined objectives to address the commitment to “curative treatment with fewer side effects and shorter treatment times” will undoubtedly improve outcomes for patients with HPV-positive HNSCC, as well as other cancers.

Was it an appropriate commitment?

It was appropriate and necessary to commit to safer and more precise treatments and treatment advances for cancer patients, and such a commitment will improve morbidity and mortality outcomes for these individuals. The commitment itself has some specifics which will be measurable as to whether the outcome has been met or not – for instance the upgrade of radiotherapy machines, and commission of proton beam facilities. However, the remainder is quite broad, and lacks detail as to how the commitment will be reached.

There is a significant need to improve outcomes for individuals with HPV-positive HNSCC, as well as other cancers, as diagnosis is often late, and treatments have significant negative impacts on patients’ quality of life. To address this need, further understanding of cancer biology through fundamental science enquiry is essential. In addition to describing the ‘natural history’ (prevalence,

pathogenesis, and persistence) of HPV within the oropharynx, one of the aims of our work is to describe a series of biomarkers that may be prognostic diagnostic tools or novel treatment targets that will improve outcomes for patients. Without the resources needed to innovate, research, and implement new diagnostic tools and treatments for cancer patients, a commitment such as this cannot be met.

References

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