

CAF/25/36 - INDEPTH: INtegrated DEep molecular Phenotyping to improve Treatment outcomes in Head and neck cancer patients

Head and Neck Cancer (HNC) is the sixth most common cancer worldwide, responsible for over 400,000 deaths each year. In Scotland, HNC incidence (number of new cases) and mortality (number of deaths) rates are alarmingly high, the worst in the UK, with HNC being the fourth most common cancer in Scottish men. This disparity is particularly pronounced in the West of Scotland, where, despite access to state-of-the-art facilities and expert clinical teams, patient outcomes remain unacceptably poor compared to other national and international treatment centres.

Nearly all HNC develop from the cells that line the internal surfaces of the throat, mouth and tongue. Whilst tobacco and excessive alcohol consumption are established risk factors for the development of HNC, the dramatic rise in HNC cases at the back of the mouth and throat (so called Oropharyngeal Squamous Cell Carcinoma or OPSCC) over the past two decades is strongly linked to human papillomavirus (HPV) infection - the same virus associated with cervical cancer. Despite HPV vaccination programs, OPSCC cases are projected to increase until 2060.

OPSCC is routinely treated with surgery and or chemotherapy (drugs) with or without radiation treatment ((radiotherapy (RT)). Whilst these treatments can be life saving, they can have a significant detrimental impact on patients' quality of life. Although HPV-positive cancers generally respond better to treatment, a third of patients still die within five years of diagnosis. Unfortunately two-thirds of patients with HPV-negative cancers die within 5 years of diagnosis.

Despite ongoing research, we still do not understand why some HPV-positive cancers and most HPV-negative cancers respond poorly to treatment. There are also no existing tests that inform doctors and patients if the potentially damaging RT will help treat their cancers. However, a new era of technology offers hope. Molecular microscopes allow us to analyse the expression of up to 20,000 genes in individual cancer cells from diagnostic samples. Since gene expression drives cancer growth and treatment response, this technology holds immense potential.

This study will utilise these molecular microscopes to measure the genes produced in OPSCC diagnostic samples and advanced computational methods to determine what genes are potentially responsible for treatment failure and poor survival rates in West of Scotland patients. These genes themselves may be able to inform patients and doctors if RT will be effective prior to treatment, or if alternative treatments are required. Using cancer cells grown in the laboratory we will also be able to test which of these genes are required for cancer growth, potentially uncovering novel therapeutic targets. We believe that our study offers significant opportunity to improve outcomes for patients facing this devastating disease.