MRD in head and neck cancer: circulating tumor and HPV DNA

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Definitive treatment for locoregionally advanced head and neck squamous cell cancer (HNSCC) is delivered using a combination of surgery, radiotherapy and systemic therapy, depending on the location of the primary tumor and other factors. The detection of circulating tumor DNA (ctDNA) after definitive treatment, or molecular residual disease (MRD), is associated with recurrence in different tumor types, including HNSCC. Multiple assays are currently being investigated at Princess Margaret Cancer Centre in the MRD setting in HNSCC, including human papillomavirus (HPV) next-generation sequencing (HPV-seq) which offers both genotyping and ultrasensitive quantification of HPV ctDNA in HPV-related HNSCC. Evaluation of MRD in both HPV-related and HPV-unrelated HNSCC can be performed using ultrasensitive mutation-based tumor-informed and tumor agnostic assays, as well as non-mutation-based assays such as cfMeDIP-seq. We previously showed in the PRE-MERIDIAN study that ctDNA detection using a tumor-informed assay (RaDaR) in locoregionally advanced HNSCC patients after surgery, definitive radiotherapy or chemoradiotherapy, is associated with disease recurrence within 1 year (Sanz-Garcia et al. Cell Death Differ, 2024). To date, the impact of MRD interception prior to clinical or radiological progression in HNSCC is uncertain. The MERIDIAN study is an investigator-initiated, randomized phase II, open label, study to assess the efficacy of Rilvegostomig, a monovalent bispecific TIGIT/PD-1 antibody versus observation in patients with MRD, defined as detectable ctDNA in plasma after definitive treatment, for high risk locoregionally advanced HNSCC (NCT05414032). In addition to using a tumor-informed assay for evaluation of MRD and molecular response, MERIDIAN also plans to explore HPV-seq and cfMeDIP-seq, as well as other circulating biomarkers to correlate with relapse-free survival.