Title: Identification of therapeutic targets in patients with Squamous Cell Carcinoma of the Head and Neck who progress on or after anti-PD-(L)1 therapy – A IMMUcan sub-project

Background: Nivolumab and pembrolizumab are approved for the treatment of recurrent/metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN). However, a significant number of patients are not responding to PD-(L)1 inhibitors and, ultimately, the majority of the patients will finally progress. No standard of care exists for patients who progress after platinum-based chemotherapy or PD-1 inhibitors. Median overall survival of these patients is dismal (5-6 months). Tumor molecular mechanisms and the role of the immune micro-environment implicated in disease progression on or after anti-PD1 therapy need to be better characterized to identify new therapeutic targets. This will guide the rational development of therapeutic combinations.

Trial design: IMMUcan is a European translational research study aiming at generating broad molecular and cellular profiling data of the tumor and its microenvironment from up to 3000 patients derived from 5 different cancer types: head and neck, colorectal, lung, renal and breast cancers. Collaborations with clinical trials are also possible, such as EORTC-HNCG-1559 study (UPSTREAM trial). This biomarker-driven umbrella trial enrolls patients with recurrent/metastatic SCCHN, progressing after platinum-based chemotherapy. The majority of the enrolled patients were pre-treated with PD-(L)1 inhibitors (anti-PD-(L)1 exposed patients), while a control population is also available (anti-PD-(L)1 naïve patients). Biological materials of these two distinct populations will be analyzed in IMMUcan: Whole Exome Sequencing, RNA sequencing, multiplex immunofluorescence and Imaging Mass Cytometry. The biological characteristics together with the clinical data will be analyzed to characterize the immune molecular profile of SCCHN that progress on or after anti-PD-(L)1 therapy with the final aim to identify therapeutic targets and to guide the development of rational therapeutic combinations. Those results will be completed with patients prospectively enrolled in the Head and Neck cohort of IMMUcan, via the EORTC-SPECTA infrastructure. For more information on IMMUcan, please visit https://immucan.eu/.