858O - Minimal residual disease (MRD) diagnosed by a plasma tumor-agnostic circulating tumor DNA (ctDNA) assay after curative therapy in locally advanced (LA) squamous cell carcinoma of the head and neck (SCCHN) predicts disease relapse and survival.

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Session

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Topics

Tumour Site

Head and Neck Cancers

Presenters

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Resources

Abstract 858O

Background

40-50 % of patients (pts) with LA SCCHN recur despite multimodal treatment. ctDNA has the potential to detect MRD and predict clinical outcome. SCCHN is a heterogenous disease with genomic alterations that occur mostly in tumor suppressor genes, making ctDNA detection challenging. We developed a plasma tumor-agnostic ctDNA assay to detect MRD in HPV-positive and negative SCCHN, without the need of tumor sequencing.

Methods

A 26-gene NGS panel was constructed that included the most frequently mutated genes in SCCHN and two HPV type 16 genes. ctDNA was sequenced with the addition of unique molecular identifiers to reach a mean read depth above 2000x. MRD was detected through an in-house personalized informatic workflow, informed by the somatic mutations identified in the pre-treatment plasma samples. The presence of MRD was defined as detection of ctDNA in one plasma sample collected within 6-12 weeks after the end of the curative treatment. Primary endpoint was the PFS rate at 2 years with a least 32 pts to be included with the hypothesis that 2y-PFS rate was >80% in MRD-negative pts and <30% in MRD-positive pts (α= 0.05, β= 0.9).

Results

The DNA from 176 plasma samples were sequenced, from 53 LA SCCHN pts who underwent curative-intent treatment. ctDNA was detected in 41/53 (77%) patients in the pre-treatment samples. The most frequent variants were found in TP53 (67%) and NOTCH1 (38%). Out of these 41 patients, 17 (41%) had MRD diagnosed by the presence of ctDNA after treatment. The 2-year PFS rate was 27% and 87% in MRD-positive and MRD-negative patients, respectively ($p < 0.001$). Median survival was 36 months in MRD-positive and was not reached in MRD-negative pts ($p=0.007$). Cox regression analyses showed that MRD positivity was an independent predictor of relapse (OR=23; 95% CI [4.5-120.9]; $p<0.001$) and survival (HR=4; 95% CI [1.1-15.6]; $p=0.037$).

Conclusions

Our ctDNA assay detects MRD in LA SCCHN and predicts disease relapse and survival, without the need of tumor sequencing, making this approach easily applicable in daily practice.

Clinical trial identification

NCT02139020.

Editorial acknowledgement

Legal entity responsible for the study

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Disclosure

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