Prognostic & predictive roles of cancer stem cell markers in HNSCC patients

Recent publication in the British Journal of Cancer by Dr Manoj Mahimkar's group at ACTREC proposed potential predictive biomarkers for stratifying head and neck squamous cell carcinoma (HNSCC) patients for epidermal growth factor receptor (EGFR)-targeted therapy based treatments. HNSCC are a heterogeneous group of cancers and a leading cause of mortality in India. Treatment modalities for HNSCC are decided based on the stage of the disease. However, patients respond differently to each treatment and not all patients receive benefits. Therefore, stratifying patients for suitable treatment is very important for the successful management of the disease. Biomarkers allowing the selection of the patients most suitable for a given treatment are called predictive biomarkers. EGFR-targeted therapies have shown limited success in HNSCC treatment largely due to the lack of clinically useful predictive biomarkers. Therefore, we analysed a set of protein biomarkers using immunohistochemistry for their prognostic and predictive roles in patients with locally advanced HNSCC, treated either with chemoradiation (CRT) or chemoradiation plus nimotuzumab (NCRT) in a phase III randomized trial conducted at TMH, Mumbai. Nimotuzumab is a targeted therapy against EGFR protein.

Our previous analysis published in British J Cancer showed poor prognosis in patients with high HIF1α expressing tumors when treated with CRT. Interestingly, these patients received a significant benefit when received NCRT. (Full-text access: https://rdcu.be/b7kDG). We have also demonstrated a low prevalence of transcriptionally active HPV-positive HNSCC in India. HPV-positive status was strongly associated with improved clinical outcomes in patients with OPSCC and with a distinct molecular profiles, which is published in Head & Neck (https://onlinelibrary.wiley.com/doi/10.1002/hed.26676).

In the current study, we evaluated the prognostic and predictive roles of putative CSC markers alone or in combination. The findings indicated that low complete membrane expression of CD44 and CD44v6 could predict clinical benefit from the addition of nimotuzumab to CRT treatment when compared with that from CRT alone. These biomarkers can serve for identifying patients (low CD44 or CD44v6) requiring NCRT treatment for the improved clinical outcome as well as marking for patients (high CD44 or CD44v6) that may not benefit from NCRT thus reducing overtreatment. In addition, we also showed the prognostic role of complete CD98hc membrane expression. This is the first study demonstrating the predictive roles of CD44 and CD44v6 in HPV-negative LA-HNSCC patients for anti-EGFR-based treatment response in a randomized setting. In addition, HIF1α has revealed a stronger prognostic biomarker than CD98hc. Investigating the correlation between HIF1α and putative CSC markers with clinical outcomes in HNSCC patients will greatly aid treatment decisions.