Title : Outcomes and Biomarker-Based Predictive Analysis of Definitive Radiotherapy in Oral Cavity Squamous Cell Carcinoma

A) INTRODUCTION

Oral cavity cancer constitutes a significant health burden in India, accounting for approximately 10% of all cancers in the country. Surgery remains the mainstay of treatment with adjuvant therapies employed in cases with locally advanced disease or adverse prognostic features. However, around 30-40% patients are inoperable at presentation. For these patients, the treatment options typically range from curative treatment strategies to palliative treatment depending on extent of tumor, age, performance status, etc. Definitive radiation with or without chemotherapy offers a potentially curative option for select patients, aiming to achieve local control and improve survival outcomes. However, the outcomes associated with this approach have been inconsistent, with reports highlighting significant variability in efficacy. The poor prognosis and considerable morbidity associated with intensive chemoradiation often raise questions about its utility. This creates a recurring dilemma in multidisciplinary clinics to decide on treatment protocols for such patients. To address these challenges, it is important to evaluate the outcomes of patients with oral cavity carcinoma treated with definitive radiotherapy with/ without concurrent chemotherapy and to identify biomarkers and clinical parameters that predict favorable responses to treatment. A more precise stratification based on these factors can optimize treatment decisions and help in identifying patients who are most likely to benefit with definitive (chemo)radiation while avoiding toxicity associated with definitive (chemo)radiation for those unlikely to respond. Hence, the aim of this study is to evaluate the outcomes of patients with oral cavity squamous cell carcinoma treated with definitive (chemo)radiation and to identify biomarkers that predict treatment response, enabling more personalized and effective therapeutic strategies.

B) OBJECTIVES

Primary Objective:

- To determine prognostic factors predicting locoregional control in patients with oral cavity squamous cell carcinoma treated with definitive radiotherapy ± concurrent chemotherapy

Secondary Objectives:

- To determine overall survival (OS) and progression-free survival (PFS) in patients with oral cavity squamous cell carcinoma treated with definitive radiotherapy ± concurrent chemotherapy

- To identify blood-based and tissue-based biomarkers that predict response to definitive (chemo)radiotherapy
- To assess the patterns of failure in patients with oral cavity squamous cell carcinoma treated with definitive radiotherapy
- To evaluate the acute and late toxicities of treatment

C) **METHODOLOGY:**

Eligibility: All patients of oral cavity squamous cell carcinoma treated with curative-intent radiotherapy (with/ without chemotherapy) at our centre from the year 2015 to 2024

Study Design: Retrospective study from a prospectively collected database

Data collection: Medical records of oral cavity squamous cell carcinoma treated with curative-intent radiotherapy (with/ without chemotherapy) at our centre from the year 2015 to 2024 will be reviewed**.** Patient and tumor characteristics including age, gender, subsite, TNM staging, type of growth, extent and volume of tumor will be documented. Treatment details including administration of neoadjuvant chemotherapy, radiotherapy dose, technique, volume, concurrent chemotherapy details will be reviewed. Toxicity and outcome data will be collected from electronic medical records. The pretreatment blood parameters including leukocytes, neutrophils, lymphocytes, platelets, hemoglobin, MPV, MCV, RDW and serum albumin will be documented. Tissue biomarkers including immunohistochemical expression of p53, Ki67, E-cadherin, β2 microglobulin, MMP will be evaluated on formalin fixed paraffin embedded sections of biopsy specimens.

Statistical analysis: Data will be analyzed using SPSS version 24. Descriptive statistics will be used for baseline demographic variables, disease characteristics, treatment details and toxicities. Survival analysis will be done using Kaplan-Meier survival estimates. A univariate analysis of predictive markers will be carried out by means of logistic regression for clinical parameters and tissue based biomarkers and linear regression for blood based biomarkers. For multivariate analysis of the dependence between marker expression and LRC and OS, the Cox regression model will be used.

D) **ANTICIPATED OUTCOMES**: The study is expected to provide data on LRC and OS in patients with oral cavity squamous cell carcinoma treated with definitive (chemo)radiation. It can help in identifying clinical parameters and blood-based and tissue-based biomarkers associated with favorable treatment outcomes and help in decision-making in treatment protocols and pave the way for more personalized treatment approaches.

E) **TIMELINES**:

a) Protocol writing and IEC approval: 2-3 months
b) Data collection: 3-4 months
c) Analysis: 2-3 months
d) Manuscript writing and publication: 6-8 months