

CORRELATION OF SOMATIC STK11 MUTATIONS WITH HISTOLOGICAL SUBTYPES AND CLINICOPATHOLOGICAL FEATURES IN GASTRIC ADENOCARCINOMA CASES DIAGNOSED IN NORTHERN PRETORIA

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Introduction: Gastric adenocarcinoma (GC) is a significant global health issue, ranked fifth in the world and the third in cancer-related mortality. Molecular alterations contribute to this tumour heterogeneity. The serine/threonine kinase 11 (*STK11*) gene is a tumour suppressor involved in cell metabolism and polarity, and can be used as a prognostic marker. The mutation in the gene, particularly in African populations, is not well-defined, and the association between somatic mutations and clinical features have not been thoroughly elucidated. This study investigated the proportion of *STK11* mutations in GC cases and their association with clinicopathological features in cases diagnosed in Northern Pretoria.

Methods: This quantitative, retrospective sub-study utilised existing data derived from a larger genomic profiling project of GC cases diagnosed in Northern Pretoria. The parent study included cases histopathologically diagnosed with GC between 01 January 2020 and 31 December 2024. Tumour samples from eligible cases had previously undergone molecular analysis using next-generation sequencing (NGS) to identify clinically relevant genomic alterations. For this sub-analysis, cases with available sequencing data and corresponding clinicopathological information were included.

Results: A total of 24 GC cases were analysed, with an overall tumour mutational burden of 117. Of these, 17 mutations involved *STK11*, which was mutated in 8 of 24 cases (33.3%). The mean age of affected patients was 61 ± 17 years, with a male predominance (75%, 6/8). Intestinal-type GC accounted for 75% of cases, with moderately differentiated tumours representing the most common histological subtype. Most cases were classified as either genomically stable (MSS) or microsatellite instability–low (MSI-L), grouped due to their similar clinicopathological, molecular, and prognostic characteristics.

Conclusion: The association of the *STK11* gene mutation with moderate differentiation and MSS/L tumours may be associated with better outcomes in GC patients. However, larger studies are needed to elucidate associations.