Excision repair cross-complementation group 1 and 2 (ERCC1/2) variants and chemotherapy treatment outcome in Cholangiocarcinoma

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Introduction: LERCC1 and ERCC2 are major enzymes involved in nucleotide excision repair (NER). Single nucleotide polymorphisms (SNPs) affect the mRNA level and stability resulting in an alteration in protein translation. ERCC1/2 SNPs potentially association with survival in various cancers but the data in CCA was limited.

Methods: We did a retrospective review and genomic DNA analysis from FFPE tissue of patients diagnosed locally advanced or metastatic CCA who received palliative chemotherapy. The target variants included ERCC1 C19007T, C8092A and ERCC2 C312T, A2251C.

Results: Genomic DNA analysis was done in 64 patients but only 54 patients received platinum-based chemotherapy were use in the survival analysis. The ERCC1 C19007T CT variant had a trend to have better OS than wild-type (CC), 8.8 vs 6.3 months respectively, the HR was statistically significant in multivariate survival analysis (HR 0.47 (0.23-0.94), p=0.032). The ERCC1 C8092A both homozygous (AA) and heterozygous (CA) variants had shorter OS compare with wild-type (CC), 6.2, 8.0 and 9.5 months respectively, there was a trend to statistically significant between CT and CC group HR 1.83 (0.96-3.51), p=0.067. These findings also observe in response rate and disease control rate. Conversely, ERCC2 variants did not associate with the outcome.

Conclusions: ERCC1 C19007T and ERCC1 C8092A variants are associated with the overall survival but not the ERCC2 variants in cholangiocarcinoma patients receiving platinum-based chemotherapy. Longer survival is seen in ERCC1 C19007T heterozygous variant (CT) but shorter in ERCC1 C8092A variants.

Keywords: Single nucleotide polymorphisms, excision repair cross-complementation group 1 and 2, Cholangiocarcinoma, C19007T, C8092A, C312T, A2251C