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ORIGINAL ARTICLE – CANCER RESEARCH

MET canonical transcript expression is a predictive biomarker for chemo-sensitivity to MET-inhibitors in hepatocellular carcinoma cell lines

Abstract Purpose Long interspersed nuclear element 1 (LINE-1 or L1) is a dominant non-long terminal repeat (non-LTR) retrotransposon in the human genome that has been implicated in the overexpression of MET. Both the canonical MET and L1-MET transcripts are considered to play a role in hepatocellular carcinoma (HCC) development. The aim of this study was to assess the utility of canonical MET, L1-MET, and MET protein expressions as predictive biomarkers for chemo-sensitivity to METinhibitors in HCC cell lines in vitro. Additionally, we assessed their expression in tumour tissues from Egyptian HCC patients. Methods MET and L1-MET expressions were assessed by qRT-PCR in six liver cancer cell lines (SNU-387, SNU-475, SK-HEP-1, PLC/PRF/5, SNU-449 and SNU-423) and 47 HCC tumour tissues. MET protein expression was measured by western blot in cell lines and immunohistochemistry in the tumours. Cell proliferation assay was used to assess the efect of crizotinib and tivantinib on the six liver cancer cell lines in correlation with the expression of MET, L1-MET and MET. Results The antitumor efect of crizotinib and tivantinib correlated with MET gene expression but not with L1-MET transcript or MET protein expressions. No signifcant diference was observed between HCC tumours and non-tumour samples in MET and L1-MET transcripts expression. There were no signifcant correlations between the 2-year overall survival rate and the MET, L1-MET transcripts and the MET protein expression. Conclusion MET RNA expression could be useful biomarker for tivantinib and crizotinib targeted therapy in HCC. The value of assessment of MET protein expression is limited.

Keywords MET gene · L1-MET transcript · MET protein · Hepatocellular carcinoma · Crizotinib · Tivantinib