Objective

C-Met is a membrane receptor with tyrosine kinase activity. Overexpression and activation lead to tumor cell migration and increased metastatic capability. It has been described as resistance mechanism in sunitinib treated RIP-Tag2 mice via hypoxia-related regulation mechanisms.

Methods

We used a TMA comprising 173 primary human pancreatic neuroendocrine neoplasms (pNEN) to assess the clinico-pathological role of c-Met expression and its relation to tumor hypoxia. Immunohistochemical stainings for c-Met, Hif-1α, CA9, GLUT1 and CD34 were correlated with established prognostic markers and outcome. C-Met and phospho-Met levels in BON1 and QGP-1 cell lines were measured by Western blot under hypoxic conditions with and without sunitinib treatment.

Results

38 of 173 pNEN showed immunohistochemical staining for c-Met. C-Met expression correlated with Hif-1α (p=0.031), MVD (p=0.023), prognostic markers, relapse (p=0.018) and survival (p=0.008). No correlation was found with CA9 (p=0.072) and GLUT1 (p=0.859). Short term upregulation under hypoxic conditions was found in BON-1. Hypoxia and sunitinib treatment had no effect on phospho-Met levels in these cell lines.

Conclusions

C-Met is expressed in a subgroup of pNEN and correlates with single hypoxia markers, prognostic markers and adverse outcome. Nonetheless, a mechanistic link between c-Met expression and activation by hypoxia or sunitinib treatment could not be detected in cell lines.