TWO MULTI-TARGET PYRAZOLOPYRIMIDINE DERIVATIVES WITH ANTI-NEOPLASTIC PROPERTIES ARE ACTIVE AGAINST MEDULLARY THYROID CANCER IN VITRO: CLM3 AND CLM94

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Background/Purpose: The aims of this study were to evalute the anti-neoplastic and anti-angiogenic activity of CLM3, and a new compound (CLM94), in human primary medullary thyroid cancer (P-MTC) cells, and in the MTC cell line TT harbouring a *RET* C634W activating mutation, *in vitro*.
Methods: The CLM3 and CLM94 anti-proliferative and proapoptotic effects (5, 10, 30, 50 µmol/L) were tested in P-MTC cells obtained at surgery and in TT cells.
Results: CLM3 and CLM94 (10 µmol/L, 30 µmol/L or 50 µmol/L) inhibited significantly ($P < 0.001$) the proliferation of TT cells, increased the percentage of apoptosis in cells dose-dependently ($P < 0.001$), while had no effect on migration and invasion. CLM3 and CLM94 (10 µmol/L, 30 µmol/L or 50 µmol/L) inhibited significantly ($P < 0.001$) the proliferation of P-MTC, increased the percentage of apoptosis in cells dose-dependently ($P < 0.001$), while had no effect on migration and invasion. The inhibition of proliferation by CLM3 and CLM94 were similar in P-MTC cells with/without *RET* mutation. Furthermore, CLM3 and CLM94 significantly decreased *VEGF-A* expression in the TT cell line.
Discussion & Conclusion: In this study CLM3 and CLM94, two "pyrazolo[3,4-*d*]pyrimidine" compounds, have shown their anti-tumor activity in MTC *in vitro*, opening the way to a future clinical evaluation.