CLM29 AND CLM24, PYRAZOLOPYRIMIDINE DERIVATIVES, HAVE ANTITUMORAL ACTIVITY IN VITRO IN ANAPLASTIC THYROID CANCER, WITH OR WITHOUT BRAF MUTATION.

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Background/Purpose: We have studied the antitumoral activity of two new "pyrazolo[3,4-*d*]pyrimidine" compounds (CLM29 and CLM24) in primary anaplastic thyroid cancer cells (ATC-cells).

Methods: The antiproliferative effect was tested in ATC-cells obtained at reoperation from patients with recurrence of the tumor. The concentrations of CLM29 and CLM24 used in the *in vitro* experiments were 1, 10, 30, 50 µM.

Results: Proliferation assays in ATC-cells showed a significant reduction of proliferation after treatment with CLM29, with respect to the control, expressed as 100%, that was by 80% with CLM29 5 µM, 50% with CLM29 10 µM, and 32% with CLM29 50 µM. Also CLM24 in ATC-cells induced a slight but significant reduction of proliferation that was 97% with 30 µM, and 78% with 50 µM. CLM29 and CLM24 increased the percentage of apoptotic cells in ATC-cells dose-dependently ($p<0.001$).

The ^{V600E}BRAF mutation was observed in three ATCs; the results about the inhibition of proliferation by CLM29 and CLM24, obtained in ATC from tumors with ^{V600E}BRAF were similar to those from tumors without BRAF mutation. CLM29 inhibited migration ($p<0.001$) and invasion ($p<0.001$) of ATC-cells, while CLM24 had no significant effect.

Discussion & Conclusion: The antitumoral activity of two new "pyrazolo[3,4-*d*]pyrimidine" compounds (CLM29, CLM24) *in vitro* in ATC, independent from BRAF mutation, has been shown, opening the way to a future clinical evaluation.