

## **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  $\mu$ M.

**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  $\mu$ M, 50% with CLM29 10  $\mu$ M, and 32% with CLM29 50  $\mu$ M. Also CLM24 in ATC-cells induced a slight but significant reduction of proliferation that was 97% with 30  $\mu$ M, and 78% with 50  $\mu$ M. CLM29 and CLM24 increased the percentage of apoptotic cells in ATC-cells dose-dependently ( $p < 0.001$ ).

The <sup>V600E</sup>BRAF mutation was observed in three ATCs; the results about the inhibition of proliferation by CLM29 and CLM24, obtained in ATC from tumors with <sup>V600E</sup>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.