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Poster

## Antitumoral properties of Sorafenib, Regorafenib, Cabozantinib and Lenvatinib in 3D tumor liver cell culture



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### ABSTRACT

**Motivation:** Most researches to find effective therapies to treat cancer has been done in cell lines grown in monolayer that don't take into account the three-dimensional structure of the tumor or the interactions between the tumor cells. In cell cultures in two dimensions, all cells are exposed in the same way to the therapeutic agent, so the results are not very precise.

For this reason, it is important to develop cell culture techniques in which it is possible simulate in vivo conditions to predict more exactly the behavior and cellular interactions within the tumor. Like tumors, spheroids are three-dimensional aggregates of cancer cells that naturally form regions of hypoxia.

**Methods:** To carry out this study we have used three different cell lines: HepG2, Hep3B and Huh7. First, the cells were cultured in 96-well plates coated with agarose. The spheroids were collected on day 5, 8 (when treated with the different drugs), 10, 12 and 15. The collected spheroids were fixed with paraformaldehyde, passed through a paraffination cycle, were introduced in paraffin blocks and cut with the microtome. Other spheroids were disintegrated by trypsinization to determine the number of cells and lysates to be able to determine caspase-3 activity. The parameters that we have measured have been apoptosis, cell proliferation, cell viability, cell death, hypoxia and cell growth. In addition, was carried out a study of the expression of different growth factor receptors such as EGFR, VGFR, FGFR and PDGFR by immunodetection.

**Results:** Sorafenib and Regorafenib induced cell death and reduced cell proliferation both in 2D and 3D cultured HCC lines. These effects are higher than those observed with Cabozantinib and Lenvatinib in the same conditions. The expression of some receptors such as EGFR is reduced in the cells treated for 24 hours with sorafenib and regorafenib but no changes are observed in the cells treated with lenvatinib and cabozantinib with respect to the control.

**Conclusions:** The observed resistance of Lenvatinib and Cabozantinib treatment to the induction of cell death and cell cycle arrest in comparison with that observed with Sorafenib and Regorafenib may be related to the induction of EGFR-dependent pathway.

### REFERENCES

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