Increasing the cytotoxic effectivity of 5FU, Irinotecan and Oxaliplatin on pancreatic cancer cells through combination with the novel anticancer agent GP-2250 in vitro

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Background: The oxathiazinan derivative GP-2250 has a selective cytotoxic effect on various tumor entities in vitro and in vivo. As part of a clinical Phase I trial, the substance is currently administered in combination with Gemcitabine after FOLFIRNOX treatment. Especially in combination with Gemcitabine, GP-2250 showed a distinct synergy, enhancing the effectivity of Gemcitabine and reducing the occurrence of secondary resistances, without amplification of adverse events in vivo [1].

Methods: To evaluate, if GP-2250 might also enhance the efficiency of the FOLFIRINOX Regimen, the cytotoxicity of 5FU, Irinotecan and Oxaliplatin in combination with GP-2250 was evaluated in vitro. Pancreatic cancer cell lines were seeded for an MTT cytotoxicity assay and treated with the single substances and their combinations. After incubation time of 48 h, the cell viability was measured and the synergy was evaluated according to the Chou-Talalay combination index.

Result: Combination of GP-2250 with all three chemotherapeutic substances did indeed increase their cytotoxic effect significantly and displayed a promising synergism.

Discussion: This indicates that GP 2250 may also be a promising option to improve the effectivity of the FOLFIRINOX regimen.

Conclusion: The results form a solid foundation for further in vivo studies to validate the synergy and to get a first assessment of the toxicity.

1 Buchholz, M. and Strotmann, J et al.: New Therapy Options for Neuroendocrine Carcinoma of the Pancreas—The Emergent Substance GP-2250 and Gemcitabine Prove to Be Highly Effective without the Development of Secondary Resistances In Vitro and In Vivo. Cancers 2022, 14, 2685. https://doi.org/10.3390/cancers14112685