**DISULFIRAM AND METFORMIN COADMINISTRATION EXHIBITS ANTICANCER EFFECT ON FIBROSARCOMA IN HAMSTERS**

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**INTRODUCTION**

We investigated the effect of disulfiram and metformin on fibrosarcoma in hamsters. Aldehyde dehydrogenase (ALDH) is a cancer stem cell marker, associated with chemoresistance. Disulfiram, an alcohol aversion agent, is well known ALDH and proteasome inhibitor. Disulfiram inhibits growth of various cancer cell lines and is a candidate for repurposing in oncology.¹³.

**OBJECTIVES**

Objective of the research was to prove that coadministration of disulfiram and metformin exhibits anticancer effects in vivo on fibrosarcoma inoculated to hamsters.

**METHOD / DESIGN:**

The 40 Syrian golden hamsters of approximately 90 g, both sexes, were randomly allocated in 3 experimental and 1 control groups of 10 animals in each. 2 x 10⁶ BHK-21/C13 cells in 1ml were injected subcutaneously on the back of animals in 4 groups. The first experimental group started peroral treatment with metformin 500 mg/kg daily, second with disulfiram 200 mg/kg daily and third with combination of metformin 500 mg/kg and disulfiram 200 mg/kg daily, via gastric probe 3 days before tumor inoculation. After 19 days, when tumors were approximately 2-3 cm in control group, all animals were sacrificed, blood collected for glucose and other analyses, tumors excised, weighed, diameters measured, tumor samples pathohistologically (HE) and immunohistochemically (Ki-67, CD 31, COX IV, GLUT-1, iNOS) assessed (Figure) and main organs toxicologically analyzed, including control animals receiving metformin and disulfiram. Tumor volume was determined using the water displacement method and formula LxS²/2, L - the longest, S - the shortest diameter. Ki-67-positive cells in the tumor samples were quantified, images were taken and processed by software UTHSCSA Image Tools for Windows Version 3.00. Statistical significances were determined by the one way ANOVA.

**RESULTS**

The combination of disulfiram and metformin inhibited fibrosarcoma growth in hamsters without toxicity.

Figure. Illustration of experimental methodology. BHK fibrosarcoma immunohistochemical assessment of Ki-67 - proliferation marker protein: C – control group, M+D – group treated with combination of metformin and disulfiram.

**CONCLUSIONS**

Administration of disulfiram with metformin might be an effective and safe approach in novel nontoxic adjuvant anticancer treatment and relapse prevention antitumor therapy.

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