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MEETING ABSTRACT

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Metabolic-targeted therapy with dichloroacetate and metformin: a novel treatment strategy for breast cancer

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Background: Most cancer cells produce energy by increasing aerobic glycolysis even in the presence of oxygen. This phenomenon is often referred as the Warburg effect [1]. Dichloroacetate (DCA) was observed to reverse the Warburg effect by inhibiting pyruvate dehydrogenase kinase and indirectly activating the gate-keeping enzyme pyruvate dehydrogenase. DCA shifts aerobic glycolysis towards mitochondrial glucose oxidation in cancer cells thus forcing them to attain apoptosis [2]. Metformin (Met), a widely used oral anti-diabetic agent, has been shown to have a strong anti-proliferative effect in many tumor cell lines.

Objectives: The aim of this study was to investigate the anticancer effect of DCA and Met in breast cancer *in vitro*. We hypothesized that these two agents could synergistically potentiate cytotoxic effects and induce cancer cell apoptosis.

Methods: MCF-7, MDA-MB-231 and MDA-MB-468 breast cancer cell lines were treated with different DCA and Met concentrations (1 mM, 5 mM, 10 mM and 20 mM) or their combinations. Cells were exposed to drugs for 24, 48 and 72 hours. Annexin V/PI-stained cells were analysed by flow cytometry. Flow-cytometry results were confirmed by viewing the cells under fluorescence microscope. The cell-growth-inhibitory effect of DCA, metformin and DCA–metformin was assessed by various cell viability assays.

Results: Dichloroacetate and metformin effectively sensitized breast cancer cell lines to apoptosis. The highest apoptotic cell rate was observed in MCF-7 breast cancer cell line after 24 hours of 20 mM of drug exposure.

Conclusions: This study demonstrates that targeting two key metabolic hallmarks of cancer is an effective anti-cancer strategy with therapeutic potential.

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Keywords: dichloroacetate – metformin – breast cancer – Warburg effect

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