OxPhos Inhibitor VLX600

National Cancer Institute

Source

National Cancer Institute. OxPhos Inhibitor VLX600. NCI Thesaurus. Code C118283.

A lipophilic cation-based triazinoindolyl-hydrazone compound and mitochondrial oxidative phosphorylation (OxPhos) inhibitor, with potential antineoplastic activity. Upon infusion, in normal cells and proliferating tumor cells where glucose is readily available, inhibition of OxPhos by VLX600 induces a hypoxia-inducible factor 1-alpha (HIF-1alpha)-dependent shift to, and an increase in glycolysis. Glycolysis alone does not produce enough energy to support the growth of tumor cells in this environment, and the induction of autophagy occurs. In the metabolically compromised tumor microenvironment, the availability of oxygen and glucose is limited due to poor vascularization and perfusion of tumor micro-areas. Tumor cells growing in this environment are thus unable to compensate for decreased mitochondrial function by increasing glycolysis. This leads to nutrient depletion, decreased energy production, induction of autophagy, tumor cell death and an inhibition of cell proliferation in quiescent tumor cells. Mitochondrial OxPhos, which is hyperactivated in cancer cells, plays a key role in the promotion of cancer cell proliferation.