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PDK1 Inhibitor AR-12

National Cancer Institute

Source

National Cancer Institute. *PDK1 Inhibitor AR-12*. NCI Thesaurus. Code C88271.

An orally bioavailable, small-molecule, celecoxib-derived inhibitor of phosphoinositide-dependent kinase-1 (PDK1) with potential antineoplastic activity. Devoid of any COX inhibiting activity, PDK1 inhibitor AR-12 binds to and inhibits the phosphorylation of 3-phosphoinositide-dependent kinase-1 (PDK-1); subsequently, the phosphorylation and activation of the serine/threonine protein kinase Akt (protein kinase B or PKB) is inhibited, which may result in inhibition of the PI3K/Akt signaling pathway, inhibition of tumor cell proliferation, and the induction of tumor cell apoptosis. In addition, this agent appears to induce the activity of protein kinase R-like endoplasmic reticulum kinase (PERK), which plays a key role in the endoplasmic reticulum stress pathway. Activation and dysregulation of the PI3K/Akt signaling pathway is frequently associated with tumorigenesis and dysregulated PI3K/Akt signaling may contribute to tumor resistance to a variety of antineoplastic agents.