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Adavosertib

National Cancer Institute

Source

National Cancer Institute. *Adavosertib*. NCI Thesaurus. Code C91725.

A small molecule inhibitor of the tyrosine kinase WEE1 with potential antineoplastic sensitizing activity. Adavosertib selectively targets and inhibits WEE1, a tyrosine kinase that phosphorylates cyclin-dependent kinase 1 (CDK1, CDC2) to inactivate the CDC2/cyclin B complex. Inhibition of WEE1 activity prevents the phosphorylation of CDC2 and impairs the G2 DNA damage checkpoint. This may lead to apoptosis upon treatment with DNA damaging chemotherapeutic agents. Unlike normal cells, most p53 deficient or mutated human cancers lack the G1 checkpoint as p53 is the key regulator of the G1 checkpoint and these cells rely on the G2 checkpoint for DNA repair to damaged cells. Annulment of the G2 checkpoint may therefore make p53 deficient tumor cells more vulnerable to antineoplastic agents and enhance their cytotoxic effect.