Oncolytic HSV-1 rRp450

National Cancer Institute

Source

National Cancer Institute. Oncolytic HSV-1 rRp450. NCI Thesaurus. Code C90563.

A gene therapy agent containing an attenuated, replication-competent, genetically engineered mutant form of the Herpes simplex virus 1 (HSV-1) strain KOS with potential antineoplastic activity. Upon infusion into the hepatic artery, oncolytic HSV-1 rRp450 replicates in hepatocellular carcinoma (HCC) cells and exerts direct cytotoxic effects eventually disrupting cancer cell membranes and liberating progeny virions thereby infecting adjacent tumor cells. In addition, rRp450 expresses the cytochrome P450 transgene that activates oxazaphosphorines, such as cyclophosphamide (CPA). Therefore, CPA can become activated in the presence of rRp450 and exert its antineoplastic effect. rRp450 is deleted for the HSV-1 gene UL39, encoding the viral ribonucleotide reductase large subunit infected cell protein 6 (ICP6), thereby disrupting the activity of viral ribonucleotide reductase and resulting in the inhibition of nucleotide metabolism and viral DNA synthesis in nondividing cells but not in dividing cells. UL39 is replaced by the rat CYP2B1 gene, encoding a cytochrome P450 enzyme that activates oxazaphosphorines. rRp450 also expresses viral thymidine kinase, which activates the cancer prodrug ganciclovir.