RNR Inhibitor COH29

National Cancer Institute

Source

National Cancer Institute. RNR Inhibitor COH29. NCI Thesaurus. Code C114976.

An orally available, aromatically substituted thiazole and inhibitor of the human ribonucleotide reductase (RNR), with potential antineoplastic activity. Upon oral administration, the RNR inhibitor COH29 binds to the ligand-binding pocket of the RNR M2 subunit (hRRM2) near the C-terminal tail. This blocks the interaction between the hRRM1 and hRRM2 subunits and interferes with the assembly of the active hRRM1/hRRM2 complex of RNR. Inhibition of RNR activity decreases the pool of deoxyribonucleotide triphosphates available for DNA synthesis. The resulting decrease in DNA synthesis causes cell cycle arrest and growth inhibition. In addition, this agent may inhibit the nuclear enzyme poly (ADP-ribose) polymerase (PARP) 1, which prevents the repair of damaged DNA, and causes both the accumulation of single and double strand DNA breaks and the induction of apoptosis. RNR, an enzyme that catalyzes the conversion of ribonucleoside diphosphate to deoxyribonucleoside diphosphate, is essential for de novo DNA synthesis and plays an important role in cell growth; it is overexpressed in many cancer cell types and is associated with increased drug resistance, cancer cell growth and metastasis.