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Nanoparticle Albumin-bound Thiocolchicine Dimer nab-5404

National Cancer Institute

Source

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A nanoparticle albumin-bound formulation of a thiocolchicine dimer, an inhibitor of both microtubule and topoisomerase I (TOP1), with antineoplastic and vascular disrupting activities. Upon administration of nanoparticle albumin-bound thiocolchicine dimer nab-5404, this agent binds to tubulin and inhibits its polymerization, which blocks mitotic spindle formation and leads to cell cycle arrest and tumor endothelial cell apoptosis. This disrupts the tumor vasculature and leads to tumor necrosis. In addition, nab-5404 binds to topoisomerase I (TOPI) and inhibits its activity. This results in the inhibition of the repair of single-strand DNA breaks, DNA replication, and tumor cell growth in susceptible tumor cell populations. The nanoparticle albumin-based formulation permits the albumin-mediated endocytosis of the thiocolchicine dimer by tumor cells and endothelial cells.