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Fumagillin-Derived Polymer Conjugate XMT-1107

National Cancer Institute

Source

National Cancer Institute. *Fumagillin-Derived Polymer Conjugate XMT-1107*. NCI Thesaurus. Code C88321.

A polymeric prodrug consisting of the fumagillol-derived small molecule XMT-1191 tethered to the hydrophilic, biodegradable 70 kDa polymer poly[1-hydroxymethylethylene hydroxymethylformal] (PHF) with potential antiangiogenic and antineoplastic activities. Upon administration, fumagillin-derived polymer conjugate XMT-1107 releases XMT-1191, which may inhibit angiogenesis through the irreversible inhibition of the methionine aminopeptidase 2 (METAP2); although the exact mechanism of action has yet to be fully elucidated, this agent appears to induce cell cycle arrest in endothelial cells, inhibiting their proliferation and migration. Compared to an unconjugated fumagillin analog, XMT-1107 exhibits improved solubility and an extended half life due to its PHF backbone. METAP2, a member of the methionyl aminopeptidase family, binds two cobalt or manganese ions and protects the alpha subunit of eukaryotic initiation factor 2 (EIF2) from inhibitory phosphorylation by removing the amino-terminal methionine residue from nascent protein; this aminopeptidase may be overexpressed in a variety of tumor cell types.