**BGB-24714, a novel oral IAP antagonist, displayed significant anti-tumor activities in preclinical models as a monotherapy and in combination with paclitaxel**

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**Background:** Evasion of apoptosis is identified as one of the essential hallmarks of cancer and upregulation of inhibitor of apoptosis proteins (IAPs) is one of the mechanisms by which tumor cells evade apoptosis. An oral SMAC mimetic and antagonist of cellular IAP1 (cIAP1) and X-linked IAP (XIAP), BGB-24714, is currently investigated in a phase 1a/1b oncology trial in patients with advanced or metastatic solid tumors (NCT05381909). Here, we evaluated the anti-tumor activity of BGB-24714 as a single agent or in combination with paclitaxel in preclinical models.

**Results:** BGB-24714 effectively inhibited cIAP1 by inducing its degradation in MDA-MB-231 cells, with an EC50 of 2.5 nM. BGB-24714 also potently antagonized the inhibitory interaction of XIAP with caspase-9 and induced caspase-9 autoactivation in MDA-MB-231 cells, with an EC50 of 23 nM. In a total of 25 breast cancer cell lines treated with TNFα, BGB-24714 potently inhibited the in vitro proliferation of 5 breast cancer cells with EC50 < 100 nM. In pharmacodynamics studies, single dose administration of BGB-24714 significantly induced degradation of cIAP1 and antagonism of the XIAP: Smac interaction in the MDA-MB-231 xenograft model in a dose dependent manner. Using the same model, BGB-24714 exhibited dose-dependent anti-tumor activities as a single agent. The tumor growth inhibition rates were 30%, 52% and 73% in low to high dosage treatment groups. Furthermore, BGB-24714 at medium dosage level demonstrated synergized anti-tumor activity in HCC1806 xenograft model when used in combination with paclitaxel. In intermittent dosing study, BGB-24714 with the intermittent dosing schedule demonstrated significant but slightly less effective anti-tumor activity than the continuous dosing schedule. In summary, BGB-24714, as a novel oral IAP antagonist, showing significant anti-tumor activities in preclinical models, which is promising and warrants the testing of the compound in human.