MPT0L145

MPT0L145, a highly potent PIK3C3 inhibitor

CDK4/6 inhibitors are newly FDA-approved agents to treat HER2-positive breast cancer, HER2-negative advanced, and metastatic breast cancers, and preclinical results showed that CDK4/6 inhibitors significantly reduced cell proliferation and tumor growth. However, several studies have suggested that CDK4/6 inhibitor-induced non-genetic changes caused treatment failure, including autophagy activation. Therefore, Hsieh et al. aimed to combine an autophagy inhibitor, MPT0L145, with abemaciclib to improve therapeutic efficiency. The use of abemaciclib effectively inhibited cell proliferation via suppression of RB phosphorylation and induced autophagy activation in glioblastoma cancer cells. MPT0L145 treatment alone not only blocked autophagy activation, but also induced generation of ROS and DNA damage in a concentration-dependent manner. Importantly, MPT0L145 had a comparable penetration ability to TMZ in our blood brain barrier permeability assay. Combined MPT0L145 with abemaciclib significantly reduced cell proliferation, suppressed RB phosphorylation, and increased ROS production. In conclusion, the data suggested that blocking autophagy by MPT0L145 synergistically sensitized Glioblastoma cancer cells to abemaciclib and represents a potential therapeutic strategy for treating Glioblastoma in the future [1].

1)
Hsieh TH, Liang ML, Zheng JH, Lin YC, Yang YC, Vo TH, Liou JP, Yen Y, Chen CH. Combining an Autophagy Inhibitor, MPT0L145, with Abemaciclib Is a New Therapeutic Strategy in Glioblastoma Treatment. Cancers (Basel). 2021 Dec 4;13(23):6117. doi: 10.3390/cancers13236117. PMID: 34885226; PMCID: PMC8656550.