

Abemaciclib

CDK4/6 inhibitor with a potent c-Met inhibitory function ¹⁾.

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, MPTOL145, 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. MPTOL145 treatment alone not only blocked autophagy activation, but also induced generation of ROS and DNA damage in a concentration-dependent manner. Importantly, MPTOL145 had a comparable penetration ability to TMZ in our blood brain barrier permeability assay. Combined MPTOL145 with abemaciclib significantly reduced cell proliferation, suppressed RB phosphorylation, and increased ROS production. In conclusion, the data suggested that blocking autophagy by MPTOL145 synergistically sensitized Glioblastoma cancer cells to abemaciclib and represents a potential therapeutic strategy for treating Glioblastoma in the future ²⁾.

in vitro analyses of two novel cell models derived from one case with NTRK-fusion revealed that combination therapy with either a MEK (trametinib) or a CDK4/6 (abemaciclib) inhibitor synergistically enhances entrectinib anticancer effects. ³⁾

The use of abemaciclib, a highly selective CDK4/6 inhibitor, effectively inhibited cell proliferation and reduced the expression of cell-cycle-related and DNA-repair-related gene expression via the suppression of RB phosphorylation, which was determined through RNA-seq and Western blot analyses. Furthermore, abemaciclib effectively induced cell death in vitro. The efficiency of abemaciclib was validated in vivo using subcutaneously implanted ependymoma tissues from patient-derived xenografts (PDXs) in mouse models. Treatment with abemaciclib showed encouraging results in preclinical pediatric ependymoma models and represents a potential therapeutic strategy for treating challenging tumors in children. ⁴⁾

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