AST-MEK/ERK MAPK inhibition (PI3K) is a novel preclinical bioactivating agent activated by AKR1C3 and is currently being investigated in multiple clinical trials for the treatment of solid and hematologic cancers. Accumulation of AKR1C3 is observed in many malignancies [3,4] and the expression of AKR1C3 is associated with metastasis of cancer, poor prognosis and a low survival rate [5]. AKR1C3 is one member of the 15 gene families of ketoreductases (AKRs). Due to the high expression of AKR1C3, it is a potential target for cancer therapy. AKR1C3 catalyzes the reduction of several types of substrates, such as the physiological substrate 4-phenyl-2-butanal and several natural compounds [6-8].AKR1C3 exhibits higher catalytic efficiency towards 3424 compared to the physiological substrates. There was a marked reduction of tumor growth in a concentration dependent manner. Tumor growth inhibition of 3424 was shown to be better than or comparable to the standard of care chemotherapy. In the combination therapy, we found that AKR1C3 overexpression in many types of cancer, particularly in liver, non-small cell lung cancer, and breast cancers is associated with metastasis of cancer, poor prognosis and a low survival rate.

Results

Anti-tumor activity of 3424 in CDMX models

Anti-tumor activity of 3424 in PDX models

References


