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SY-1365, a selective CDK7 inhibitor, exhibits potent anti-tumor activity against ovarian cancer models in vitro and in vivo

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Summary

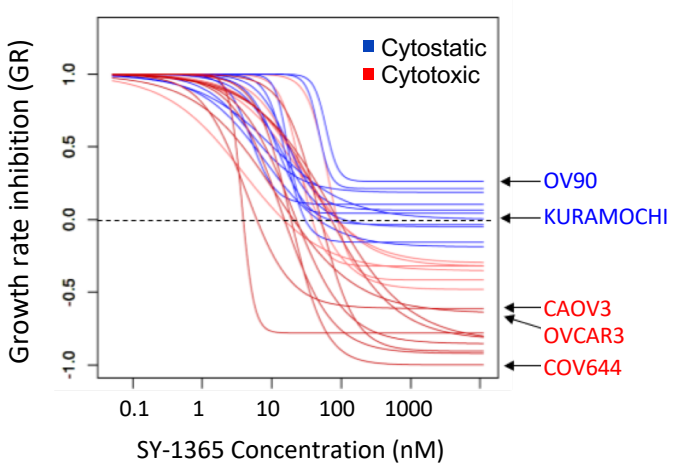
- CDK7 is a transcriptional kinase that acts as a master regulator of transcription and cell cycle progression
- Recent preclinical studies have identified CDK7 as a potentially important new therapeutic target in solid tumors, including ovarian tumors
- SY-1365, a covalent and selective inhibitor of CDK7, has been developed to exploit tumor dependencies driven by CDK7

- SY-1365 induces cytotoxicity and MCL1 protein downregulation in ovarian cancer cell lines in vitro
- SY-1365 induces tumor growth inhibition, including complete regressions, in ovarian cancer PDX models
- SY-1365 responses in preclinical models are associated with alterations in mitochondrial apoptosis and RB signaling pathways

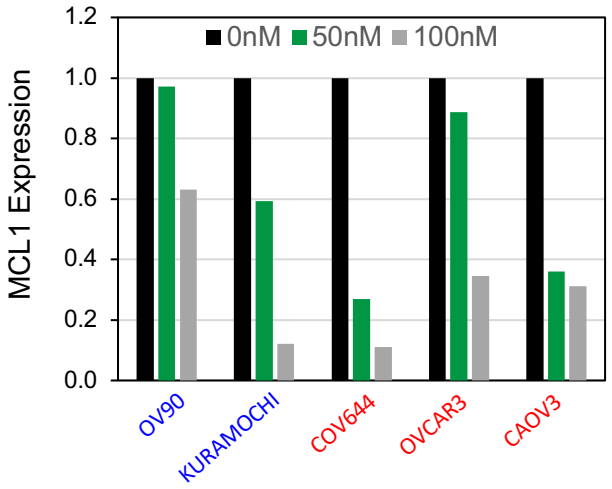
- SY-1365 is currently being assessed in a phase 1 trial in adult patients with advanced solid tumors, including expansion cohorts in patients with high-grade serous ovarian cancer (HGSOC) as a single agent and in combination with carboplatin (NCT03134638)

SY-1365 induces cytotoxicity in ovarian cancer cell lines in vitro & induces tumor growth inhibition in ovarian PDX models in vivo

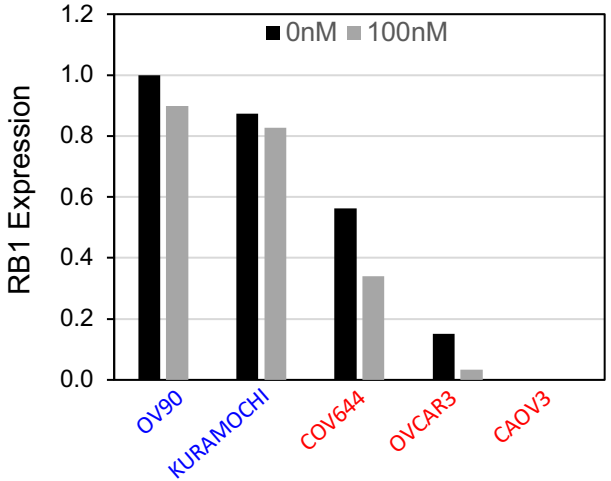
SY-1365 induces cytotoxicity in ovarian cancer cell lines



SY-1365 induces MCL1 protein downregulation in ovarian cancer cell lines



Low RB1 protein expression is associated with SY-1365 cytotoxicity in ovarian cancer cell lines



SY-1365 induces tumor growth inhibition, including complete regressions, in ovarian cancer PDX models

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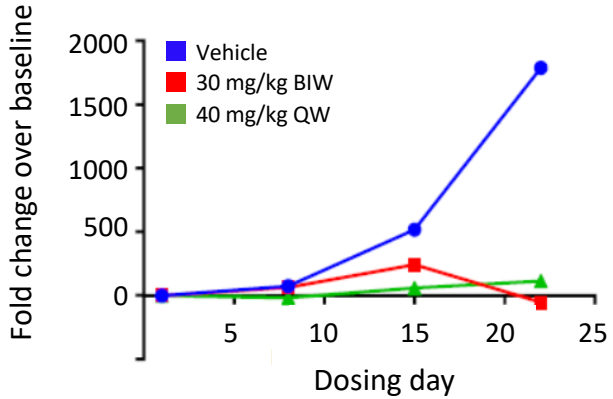
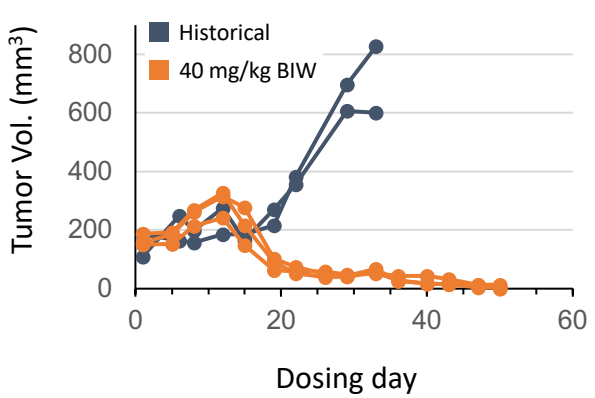


OVPDX-3



- Responses observed in 10/17 (59%) PDX models tested
- Responses observed in PDXs derived from patients treated with multiple prior therapies including platinum therapy
- Responses observed irrespective of BRCA status and/or olaparib sensitivity
- Responses associated with alterations in mitochondrial apoptosis and RB pathways