Successful Treatment of Metastatic Fibrolamellar Hepatocellular Carcinoma with Temsirolimus In Vitro and In Vivo

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- Successfully established a FL-HCC PDX model
- Identified alteration of mTOR pathway with increased expression in metastatic lesions
- Significant in vivo response to single agent temsirolimus in FL-HCC PDX model
- mTOR overexpression in metastatic lesions seen in larger patient cohort
- mTOR Inhibition may be a beneficial treatment for metastatic FL-HCC

BACKGROUND
- Rare liver tumor with distinct morphology and a specific gene fusion
- Prognosis dependent on surgical resection
- 80-100% will recur following resection
- No recommended treatment regimens
- Patient-derived xenografts (PDXs) recapitulate original tumor and can predict therapeutic regimen efficacy

AIM
- Validate a PDX model of FL-HCC
- Identify effective therapeutic regimens

METHODS

PDX VALIDATION
1° and metastatic patient tissue was implanted into immunodeficient mice
Successfully grown tumors were harvested and stained with H&E, CD68, and CK7
Western blots were performed to assess for the presence of the characteristic fusion protein

TEMSIROLIMUS AND mTOR ACTIVITY
PDX tumors were dissociated and treated with chemo regimens and cell viability was assessed after 72 hours
Western blots were performed on patient and PDX tumors for mTOR expression
Mice were treated with one of four regimens for 30 days with biweekly assessment of tumor growth

mTOR IN PATIENT TISSUE
10 patients were identified in the pathology database with both metastatic and primary tumors available for mTOR IHC staining
Staining was scored by a pathologist
Composite Score: Density Score x Intensity Score

CONCLUSIONS
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REFERENCES