**CX-839-004**: A Phase 1/2 Study of the Safety, Pharmacokinetics, and Pharmacodynamics of the Glutaminase Inhibitor CB-839 in Combination with Nivolumab in Patients with Clear Cell Renal Cell Carcinoma and Other Solid Tumors

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**CB-839 Background**

- **The Warburg Effect: Normal vs. Cancer Cell Metabolism**
- **Glutaminase Expression is Elevated in Human Tumors**

**CB-839 is a Potent Inhibitor of Glutaminase**

- **CB-839 Activity is On Target and Reversible With α-KG**
- **CB-839 is Active in Multiple Cancer Cell Types**
- **CB-839 Preferentially Inhibits Tumor Metabolism**
- **CB-839, Glutamine, and Anti-Cancer Immune Function**

**CB-839 Blocks Tumor Cell Glutamine Consumption and Restores T-Cell Division in Vitro**

**CB-839 Increases Glutamine Levels in Tumors and in Patient Blood**

**CB-839 Synergizes With Checkpoint Inhibitors In Vivo**

- **Combining CB-839 with anti-PD-L1 or anti-PD-1 showed enhanced anti-tumor activity in syngeneic models**

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**Open August 2016**

- **Primary Objectives:** Safety, tolerability, MTD/RP2D
- **Secondary Objectives:** Anti-tumor effect
- **Exploratory Objectives:** T-cell analysis, PD-L1/PD-1 expression, immunosuppression, other correlates

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**CB-839 + Nivolumab Biomarker Plan**

**Summary and Conclusions**

- **CX-839-004** is currently enrolling patients to evaluate safety, MTD/RP2D, and anti-tumor activity of CB-839 with PD-1 inhibitor nivolumab
- **Eligible patients include those with advanced ccRCC, melanoma and NSCLC, including in patients known to be refractory to nivolumab or other checkpoint inhibitors**
- **Tumor cells and immune cells compete for glutamine in the tumor microenvironment creating a metabolic checkpoint**
- **CB-839 limits glutamine metabolism by tumor cells and increases glutamine availability to immune cells**
- **CB-839 synergizes with PD-1/PD-L1 inhibition in syngeneic tumor models**

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**References**

- Gross et al (2014) Mol Cancer Ther April 1 2014; 13(4) 890-901