**BACKGROUND AND RATIONALE**

Efficacy of the rapamycin analog, Everolimus (CC-1105), in patients with solid tumor has been demonstrated in clinical trials, and the FDA has approved this drug for the treatment of certain advanced cancers (Table 1). To evaluate the anti-tumor activity and potential benefit of Everolimus in a variety of tumor types, we initiated this Phase 1 study (Table 2). The results of this study have provided important insights into the pharmacology, safety and tolerability of Everolimus, and have informed the design of subsequent clinical trials.

**METHODS**

Phase 1 study of CB-839, a first-in-class, orally administered small molecule inhibitor of glutaminase in patients with refractory solid tumors

**STUDY SUBJECTS**

- **Eligibility:** Patients with advanced cancer, including TNBC, RCC, mesothelioma, and IDH1 mutant tumors, who had failed conventional therapies.
- **Dose:** CB-839 was administered orally in single-agent or combination regimens.
- **Design:** A modified Simon two-stage design was used to determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D).
- **Outcomes:** Efficacy, safety, and tolerability were assessed in this study.

**PHARMACOKINETICS**

- **PK:** CB-839 was well-absorbed after oral administration and achieved therapeutic levels in plasma.
- **PK-PK correlation:** There was a positive correlation between plasma exposure and clinical response.

**SAFETY AND TOLERABILITY**

- **AEs:** A total of 130 patients were enrolled, and 100 were evaluable for safety and tolerability. The most common AEs were fatigue, nausea, vomiting, diarrhea, anorexia, and muscle weakness.
- **Grade 3-4 AEs:** The most common grade 3-4 AEs were fatigue (15%), nausea (13%), and diarrhea (10%).

**CLINICAL OUTCOMES**

- **Response:** Nine of 15 evaluable patients had stable disease (SD) or better as best response.
- **Survival:** Five patients remained on CB-839 at the time of data cutoff.

**SUMMARY AND CONCLUSIONS**

- **CB-839** is a highly potent, orally administered small molecule inhibitor of glutaminase that has shown promising activity in a variety of tumor types.
- **Future studies:** Further studies will be needed to confirm the efficacy and safety of CB-839 in patients with refractory solid tumors.

**REFERENCES**

- [DeBerardinis, R., & Cheng, J. (2010).](#) Metabolism of Cancer Cells
- [Sorensen, E., & et al. (2013).](#) The Effect of CB-839 on Tumor Metabolism
- [Mittra, E. S., et al. (2015).](#) CB-839 in the Treatment of Metastatic and/or Refractory Solid Tumors
- [Erlotinib + CB-839 (C2D1 vs C1D15) and C2D1 (C1D1 and C1D15 fed on TID regimen) study results.](#)