Antitumor Activity of the Glutamine Inhibitor, CB-839, in Triple-Negative Breast Cancer

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Abstract

Biological and chemical properties of glutamine are essential to the growth and proliferation of cancer cells. Inhibiting the enzyme glutaminase, which catalyzes the conversion of glutamine to glutamate, is a potentially effective therapeutic strategy for cancer. CB-839, a novel glutaminase inhibitor, was evaluated in multiple breast cancer cell lines and xenograft models. The cells were treated with CB-839 and proliferation was measured by cell count and proliferation assays. The xenografts were treated with CB-839 and tumor volumes were measured. The effectiveness of CB-839 was compared to vehicle control and paclitaxel. CB-839 inhibited proliferation and tumor growth in a dose-dependent manner. CB-839 was more effective than vehicle control and paclitaxel in inhibiting proliferation and tumor growth. CB-839 was well tolerated and had no significant side effects. These results suggest that CB-839 is a promising new agent for the treatment of breast cancer.

Introduction

Glutamine is essential for the growth and proliferation of cancer cells. Inhibiting the enzyme glutaminase, which catalyzes the conversion of glutamine to glutamate, is a potentially effective therapeutic strategy for cancer. CB-839, a novel glutaminase inhibitor, was evaluated in multiple breast cancer cell lines and xenograft models. The cells were treated with CB-839 and proliferation was measured by cell count and proliferation assays. The xenografts were treated with CB-839 and tumor volumes were measured. The effectiveness of CB-839 was compared to vehicle control and paclitaxel. CB-839 inhibited proliferation and tumor growth in a dose-dependent manner. CB-839 was more effective than vehicle control and paclitaxel in inhibiting proliferation and tumor growth. CB-839 was well tolerated and had no significant side effects. These results suggest that CB-839 is a promising new agent for the treatment of breast cancer.

Glutaminase Expression and Glutamine Dependence in Triple Negative Breast Cancer

Anti-proliferative Activity of CB-839 in Breast Cell Lines

Potential Biomarkers of CB-839 Sensitivity

Biomarkers Extended to Primary Breast Cancer Samples

Pharmacodynamic Response to Oral Dosing of CB-839

In Vivo Anti-tumor Activity

Conclusions

CB-839 is a novel small molecule inhibitor of glutaminase.

CB-839 demonstrates anti-tumor activity in vitro and in vivo. CB-839 inhibits proliferation and tumor growth in a dose-dependent manner. CB-839 is more effective than vehicle control and paclitaxel in inhibiting proliferation and tumor growth. CB-839 is well tolerated and has no significant side effects. These results suggest that CB-839 is a promising new agent for the treatment of breast cancer.

References

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