Combination of the Angiogenesis Inhibitor Lucitanib with Immune Checkpoint Blockade Augments Antitumor Activity in Syngeneic Models

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INTRODUCTION

• Lucitanib (E-3810) is an oral multikinase inhibitor with targets that are associated with angiogenesis and other key cancer and immune pathways.
• Angiogenesis plays a critical role in cancer growth and metastasis through tumor vascularization and also promotes immunosuppression within the tumor microenvironment.
• Therapies simultaneously targeting angiogenesis and immune checkpoint pathways have demonstrated potent antitumor activity.

RESULTS

Lucitanib Augments the Antitumor Activity of Anti-CTLA-4 in the MC38 Syngeneic Mouse Model

Antitumor Activity of Lucitanib Combined With Anti-CTLA-4 Is Similar to or Better Than That of Other Angiogenesis Inhibitor Anti-CTLA-4 Combinations

Lucitanib Enhances the Antitumor Activity of Anti-PD-1 in Several Syngeneic Models

Lucitanib Treatment Alone and in Combination with Anti-PD-1 Results in An Immune-Related Gene Expression Changes

Lucitanib Treatment Alone and in Combination with Anti-PD-1 Increases the Abundance of Intratumoral CD8+ T Cells

CONCLUSIONS

Lucitanib combined with anti-PD-1 enhances antitumor activity resulting from immune checkpoint blockade of either the CTLA-4 or PD-1 pathways in syngeneic models.

Lucitanib in combination with anti-PD-1 achieves synergistic to better additive activity than other angiogenesis inhibitors combined with anti-PD-1 in preclinical studies.

Lucitanib combined with anti-PD-1 promotes intratumoral T-cell infiltration and immune associated gene expression changes important for antitumor immunity.

Lucitanib’s antitumor mechanism of action involves both inhibiting angiogenesis and modulating immune effector activity, potentially through CD8+ T cells.

These findings provide preclinical support for clinical evaluation of lucitanib in combination with immune checkpoint inhibitors.

The combination of lucitanib and nivolumab is currently being evaluated as a treatment for patients with solid tumors (NCT04040158).

REFERENCES


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