Immunotherapeutic potential of ST316, a peptide antagonist of β-catenin

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Abstract

Sapience Therapeutics, Inc. is a clinical-stage biotechnology company focused on the discovery and development of peptide therapeutics to address oncogenic and immuno-dysregulation that drive cancer. Our Envisage cancer antagonist, ST316, targets the interaction between β-catenin and its co-activator AP-1, a complex that drives oncogenic expression in cancers where aberrant Wnt/β-catenin pathway cell is observed. Sapience has received clearance from the FDA to proceed with a ST316 Phase I clinical trial for the treatment of solid tumors.

Introduction

Sapience Therapeutics is a clinical-stage biotechnology company focused on the discovery and development of peptide therapeutics to address oncogenic and immuno-dysregulation that drive cancer. Our Envisage cancer antagonist, ST316, targets the interaction between β-catenin and its co-activator AP-1, a complex that drives oncogenic expression in cancers where aberrant Wnt/β-catenin pathway cell is observed. Sapience has received clearance from the FDA to proceed with a ST316 Phase I clinical trial for the treatment of solid tumors.

The transcription factor β-catenin is a key player in many cellular processes, including stem cell renewal, cellular homeostasis and immunomodulation. Dysregulation of the Wnt/β-catenin pathway is frequently observed in the context of oncogenesis and immunomodulation. For instance, ST316 has been shown to inhibit expression of the β-catenin gene and mutation pathway inhibition resulting in tumor immunomodulation (TIME) in various cancers. The results presented here indicate that ST316 can be used as a potential therapeutic agent for various cancers, including breast cancer.

Results

• ST316 induces a dose-dependent shift in PBMC-derived M2 macrophage to the M1 identity and induces the M1 markers CD80 in M2 conditions.
• ST316 promotes surface expression of CD163/PD1 in β-catenin-dependent cell lines.
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• ST316 inhibits macrophage-induced CD8+ T cell activation in M2 suppressive conditions. ST316 (TAM) can be used for cell lines that are M1 and M2 markers for β-catenin.
• Flow cytometry and isotype controls are for beta-catenin. The results presented here indicate that ST316 can be used as a potential therapeutic agent for various cancers, including breast cancer.

Conclusions

These data support a model in which ST316 promotes a shift in the tumor microenvironment via multiple mechanisms, including driving macrophage polarization toward an immune-promoting phenotype, augmenting activity of cytotoxic T cells and increasing expression of checkpoint blockade such as CD163/PD1 in cancer cells.

Acknowledgments

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References

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Wnt/β-catenin in cancer and TIME

Dendritic Cell

Tumor Cell

CD8

CD4+ T cell

CD11b

Expression of Wnt Target Genes

Anti-inflammatory tumor microenvironment (TIME)

CD8 T Cell

αvβ3

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

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