



Office of Technology Management

Therapeutic Use of Endothelin Receptor Agonists In Solid Tumors

Technology Reference

CV94

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Field

Biomedical &
Therapeutic Sciences

Key Words

Endothelin agonist

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Increased perfusion

Enhanced drug
delivery

Chemotherapy

License Status

Licensed by UIC to
Chicago Labs, Inc.

Chicago Labs, Inc.
seeking partners

Patent Status

US and PCT patents
filed

Overview

Tumor blood vessels develop differently from normal blood vessels. Single-layered endothelial cells are formed first, which do not have smooth muscle layer or innervation.

Stimulation of endothelin receptors on endothelial cells dilates the blood vessels, while those on smooth muscle layer constricts them. In the tumor tissue, endothelin receptor stimulation produces dilation of blood vessels due to lack of smooth muscle layer.

Endothelin agonists have therapeutic potential as adjuvant anticancer drugs that can increase (1) the delivery of anticancer drugs and (2) oxygenation to the solid tumors.

Technical Summary

In pre-clinical studies, endothelin infusion (selected dose) in rats did not affect systemic hemodynamics and blood flow to any organ of the body, but selectively increased blood flow to the tumor tissue. Endothelin infusion is predicted to increase efficacy and reduce toxicity of chemotherapeutic and/or radiotherapy agents by enhancing delivery of these agents to the tumor tissue.

Endothelins (ET-1, ET-2 and ET-3) when infused produce cardiovascular effects in humans. However, ET-3 produces less cardiovascular effects compared to ET-1 and ET-2. ET-1 is a nonselective ET(A) and ET(B) receptor agonist, while ET-3 is a more selective ET(B) receptor agonist. ET-3 has also been administered to humans in significantly high doses to determine its cardiovascular effects. Infusion of endothelin in humans produces cardiovascular effects, which can be blocked by usual antihypertensive drugs. The effects are reversible and last from 30 to 120 min after infusion.

Benefits

- Enhance blood flow to breast cancer tumors and
- Deliver more paclitaxel to the breast cancer tumors without affecting other tissues

Areas of Application

- Breast cancer
- Solid tumors
- Combination of endothelin agonists with cancer chemotherapy to target enhanced drug delivery of chemotherapy to breast cancer tumors.

Stage of Development

- Animal models completed