Preclinical evaluation of Promitil, a novel nanoparticle formulation of Mitomycin C, in chemoradiotherapy

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Introduction

- Lipid-based prodrug of anti-cancer agent Mitomycin C (MMC)
- Developed by LipoMedix Pharmaceutical Inc.
- Currently being studied in a Phase I, dose-escalating, safety study for patients with solid tumor in Israel

Objectives

1. Evaluate the impact of drug administration and irradiation timing on efficacy
2. Evaluate the impact of dosage on efficacy in vivo
3. Evaluate the efficacy and toxicity of Promitil in vivo

Mechanism of Activation

1. Thiolytic environments, such as tumors
2. Radiation → Cell death → Apoptotic cells release cytoplasmic contents → promote thiolysis and release of MMC from the liposome-encapsulated prodrug.

Characterization of Promitil

- Cryo-TEM of Promitil
  - Size: 98.61 ± 0.27 nm by dynamic light scattering
  - Surface charge: -13.7 ± 0.49 mV

In Vivo Efficacy of Promitil

A. Best XRT timing for Promitil-CaSki

B. Dosage comparison for Promitil-CaSki

C. In vivo efficacy for Promitil-CaSki

In Vitro Efficacy of Promitil

- Dose-response assay to measure cytotoxicity of Promitil and MMC in CaSki (A) and SiHa (B). Cells were treated with indicated doses of Promitil and MMC containing an equivalent dose of MMC.

Toxicity

- Effect of Promitil and MMC on body weight

Conclusions

- Promitil showed less in vitro cytotoxicity than MMC.
- Mice can tolerate higher doses of Promitil which can improve efficacy.
- The combination of Promitil and 5-Fluorouracil resulted in the greatest radiosensitization.