A Novel Anti-angiogenesis Therapy Using Integrin Targeted Nanoparticles

Lingyun Li, Susan E. Alters, Charles A. Wartchow, Neal E. DeChene, Steven Choi, Tina Doede, Linong Huang, John S. Pease, Michael Zhang, Zhimin Shen, Amie J. Dirks, Jeffrey L. Cleland, Susan J. Knox

Department of Radiation Oncology, Stanford University Medical Center, Stanford, CA; Targesome Inc., Palo Alto, CA

Anti-angiogenesis approach using T0102

Advantages of the nanoparticle approach:
- increased half-life
- vascular confinement
- enhanced efficacy
T0102 Composition

T01: IA & T0002: Dextran-Coated Liposomes (DCL)

- **T01 (IA)**: Therapeutic and targeting agent with small molecule integrin antagonist (IA)
- Dextran coating over lipids
  - Particle size of ~100 nm

- **Coupling Site**

- **Coupling Site**

- **Exterior**
- **Interior**

- = 5% DPPE-Succinate
- = 55% DPPC
- = 40% Cholesterol

Study Design

- **Tumor model**: human M21 melanoma xenograft
- **Treatment regimen**:
  - T0102 (15 mg/kg, iv)
  - cyclo RGDFV (15 mg/kg, ip)
  - T01 (15 mg/kg, iv)
  - Buffer and placebo control

  Four doses administered every other day for a week
- **Tumor growth delay**
- **TUNEL assay and anti-CD31 staining**
- **Toxicity**
Superior efficacy of T0102 compared to free T01 (IA)

* n=9, error bars indicate ± standard error

Superior efficacy of T0102 compared to cyclo RGDfV

* n=8, error bars indicate ± standard error

* P<0.01

* P<0.05
T0102 Increases Tumor volume Quadrupling Time (TVQT)

Summary of P-values obtained using Tukey’s Pairwise Comparisons

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<th>Buffer</th>
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<th>Placebo</th>
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T0102 Induces Tumor Apoptosis and Reduces Tumor Vessel Density

- 40% reduction in vessel count with T0102 vs. control (179 vs. 299)
Summary

- T0102 significantly inhibited tumor growth, and showed superior efficacy compared to free T01 in M21 model.
- T0102 treatment caused extensive tumor apoptosis and reduced tumor vessel density ~40% in M21 model, which revealed the anti-angiogenic mechanism of this therapeutic approach.
- Necropsy data indicated that there were no gross or histopathological changes in animals following T0102 therapy.
- These encouraging results demonstrate the advantage and potential therapeutic application of active drug targeting therapy using the nanoparticle approach.

Acknowledgements

- Stanford Univ.
  - Amie Dirks
  - Susan Knox

- Targesome, Inc.
  - Susan E. Alters
  - Neal DeChene
  - Tina Doede
  - John S. Pease
  - Zhimin Shen
  - Charles Wartchow
  - Steven Choi
  - Linong Huang
  - Michael Zhang
  - Jeffrey L. Cleland

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