

NANOTCE: A NANOPARTICLE ANTIBODY SYSTEM FOR IMMUNOTHERAPY AGAINST HETEROGENEOUS MULTIPLE MYELOMA

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Disease indication – multiple myeloma

Drug format – antibodies conjugated to nanoparticles for T-cell immunotherapy

Drug class – improved delivery platform

Research stage and Preliminary data:

In vivo:

- Efficacy - CD38/CD3 nanoTCEs significantly prolonged survival (100% survival at 40 days) and decreased tumor burden in a mouse model of MM
- Pharmacokinetics - $T_{1/2}$ of 36 hours for NanoTCEs in healthy mice (compared to 2.1 hrs for classic BiTEs)

In vitro proof of concept – in a MM cell line: NanoMuTEs and NanoTCEs both demonstrated specific binding and caused T-cell induced cell lysis; NanoMuTE's had improved binding and improved T-cell activation over NanoTCEs

Target – CD3 for T-cell engagement and multiple myeloma targets CD38, BCMA and CS1 tested to date (could be extended to additional targets)

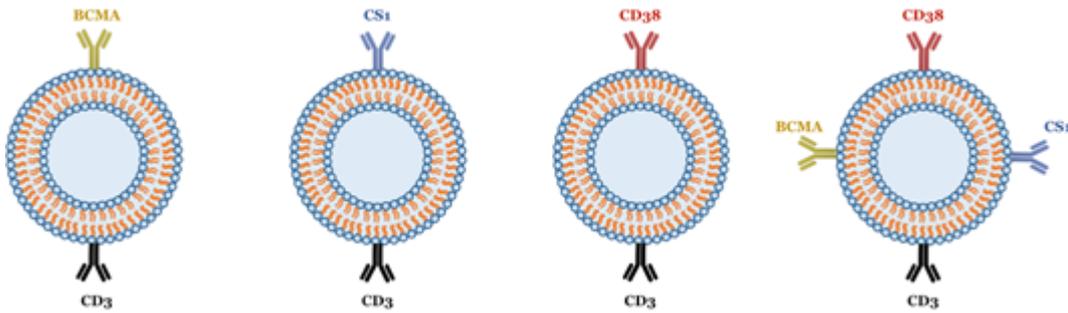
Background:

Multiple myeloma (MM) is a heterogeneous disease, with cancer cells expressing a large and dynamic repertoire of surface antigens. However, current T-cell immunotherapy strategies for MM (chimeric antigen receptor-T, “CAR-T”, and bispecific T-cell engagers, “BiTEs”) target only one antigen on the cancer cells. Over time, the non-targeted cells (known as antigen-less variants) can proliferate which can lead to relapse after treatment. This so-called “loss of antigen” occurs in 44% of patients that respond to initial multiple myeloma therapy.

Additional challenges of current T-cell immunotherapy include the short half-life of BiTE molecules and the expensive and labor intensive engineering of autologous patient CAR T-cells.

Keywords – T-cell immunotherapy, T-cell enhancer, multiple myeloma, nanoparticle, NanoTCE, NanoMuTE, bispecific, multispecific, antibody, liposome

Mode of action:



Schematic of NanoTCEs and

NanoMuTEs: NanoTCEs (first 3 figures) are liposomal nanoparticles conjugated to a cancer-targeting antibody (e.g., BCMA, CS1, CD38) and T-cell engaging antibody (CD3). NanoMuTEs (far right) are an extension of NanoTCEs, with three or more cancer-targeting antibodies designed for efficacy against heterogeneous cancer cells.

NanoTCEs (nanoparticle bispecific T-cell engager) and NanoMuTEs (nanoparticle multivalent T-cell engager) are liposome nanoparticles chemically conjugated to two or more antibodies – one (or more) antibody to target the cancer cells and the other antibody to engage and activate the T-cell. This immunotherapy system is designed to target a range of variants of the multiple myeloma with a single off-the-shelf agent. This is expected to provide enhanced antigen recognition to redirect the patient's immune system to fight the cancer while avoiding relapse from loss of antigen.

The nanoparticle-based system also improves the pharmacokinetics over traditional BiTE therapy.

Competitive edge:

- **Broad targeting** – enhanced antigen recognition compared to current T-cell therapies
 - designed to activate T-cells against heterogeneous cancer cells with a variety of cell surface antigens
 - easily add antibodies to multiple targets to NanoMuTE particle
- **Improved pharmacokinetics** – compared to conventional BiTE antibodies, NanoTCEs have longer biodistribution and half-life (36 hrs. vs. 2.1 hrs.)
- **Off-the-shelf** – unlike CAR T-cell immunotherapy (which requires individual preparation of genetically engineered autologous cells for each patient), a standard NanoTCE or NanoMuTE agent can be used for any patient who's cancer expresses the targeted marker
- **Advantages of nanoparticles:**
 - simple, low cost, scalable production
 - non-toxic liposome material

Patents - Provisional patent application filed

Website - [Azab Lab](#)