Facilitating T-cell therapy in solid tumors with oncolytic adenovirus

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Background

- Tumor-infiltrating lymphocyte (TIL) or gene-engineered T-cell therapy have efficacy limitations such as suboptimal trafficking of transformed cells to tumors.
- Lymphodepleting preconditioning and high-dose IL-2 postconditioning are major sources of toxicity in adoptive T-cell therapy protocols.
- Programmed Death (PD)-1 blockade therapy demonstrates good clinical results in only 1 in 10 TIL-treated tumors.
- TILT-123 (Ad533-EXP-D24-TNFα-IRE5-hIL-2) is an oncolytic virus designed to enable T-cell therapy coding for:
  - Human Tumor Necrosis Factor alpha (TNFα) – Increases T-cell trafficking
  - Human Interleukin-2 (IL-2) – Increases T-cell survival and growth

Results

1. Adenovirus coding for TNFα and IL-2 improves the B16.OVA growth control in combination with OT-I cell therapy

2. TILT-123 enables complete tumor regression and protection from tumor rechallenge in TIL treated hamsters

3. TILT-123 leads to regression and transduction of distant tumors in a TIL therapy setting

4. Adenovirus-mediated local IL-2 delivery is superior to postconditioning with systemic high-dose IL-2

5. TILT-123 improves the survival and efficacy of animals treated with adoptive T-cell transfer without preconditioning

6. Prime & boost adenovirus therapy regimen enables 100% survival in anti-PD-1 treated mice

Conclusions

- Adenovirus-mediated delivery of TNFα and IL-2 enables adoptive T-cell therapy using TIL therapy or gene-modified T-cells.
- TILT-123 induces systemic antitumor responses and tumor-specific memory in animals treated with TIL therapy.
- TILT-123 replaces high-dose IL-2 postconditioning and lymphodepleting preconditioning in a setting of adoptive T-cell therapy.
- Adenovirus therapy enables complete responses in animals receiving anti-PD-1 therapy.
- Clinical translation is underway to validate these hypotheses.

References

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