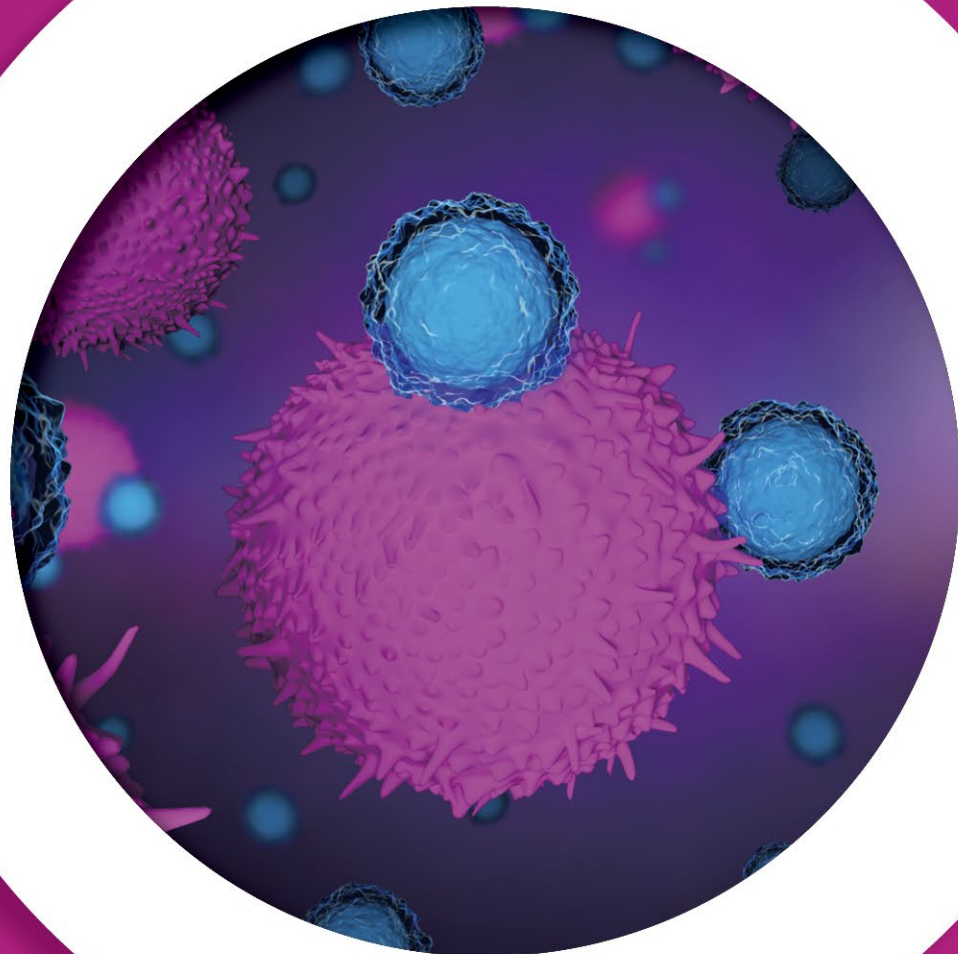


# *AACR 2022 Data Read-out*

INVESTOR RELATIONS 2022

NEOIMMUNETECH.

April, 2022



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## Poster Presentation at

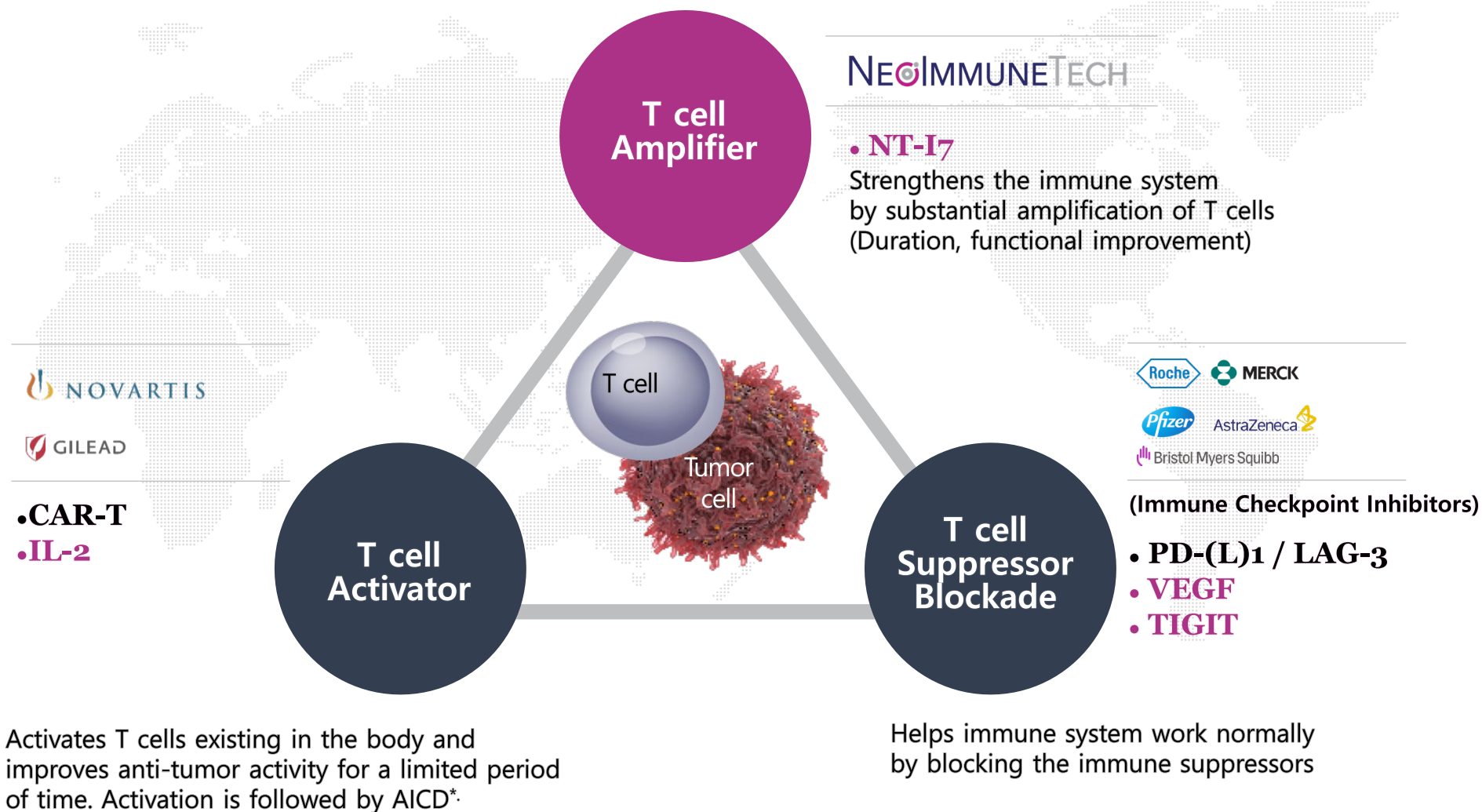
### 1. Combo therapy with Anti-TIGIT(YH29143), and anti-VEGF(Aflibercept), Poster #4172

- The anti-tumor effect of double combo therapy (NT-I7+anti-TIGIT, NT-I7+anti-VEGF)
- The anti-tumor effect of triple combo therapy (NT-I7+anti-TIGIT+anti-PD-1)
- Increase of tumor specific(PD-1<sup>+</sup> CD8<sup>+</sup>) T cells inducing anti-tumor activity in tumor

### 2. Combo therapy with hIL-2/TCB2c complex(SCL-3010), Poster #4199

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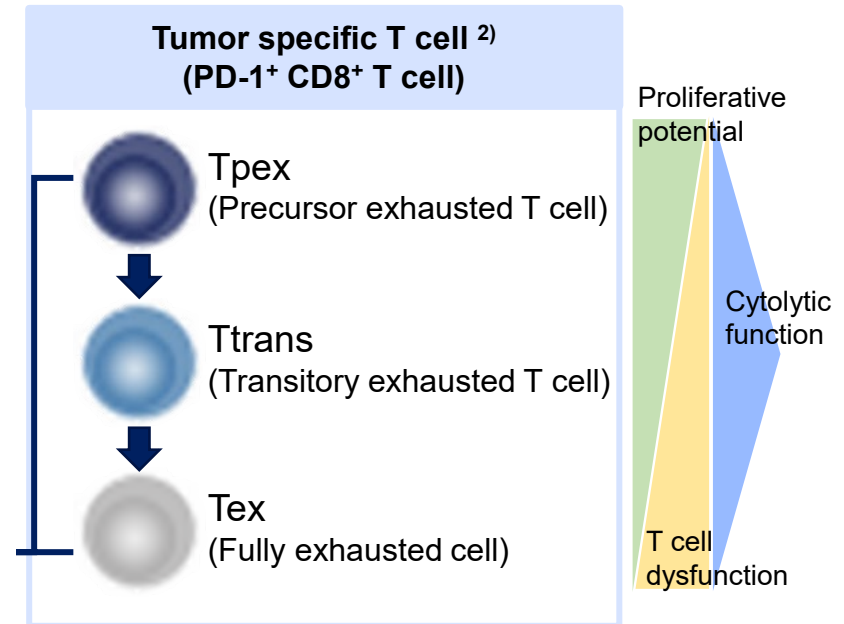
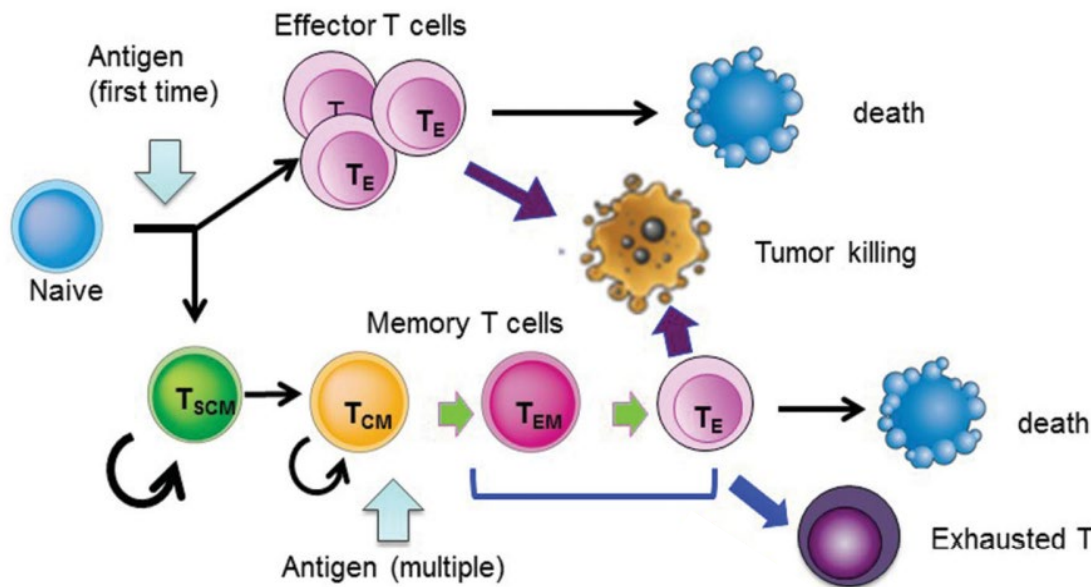
# Different mechanisms/roles in T cell based immunotherapies



\*AICD: Activation Induced Cell Death

# Classification of T cell by differentiation stages

## CD8<sup>+</sup> T cell differentiation process <sup>1)</sup>



The differentiation process is as follows:

**Tpex (Precursor exhausted T cell):** T Cell(soldier) with self-renewing ability starts to attack enemy(Tumor)

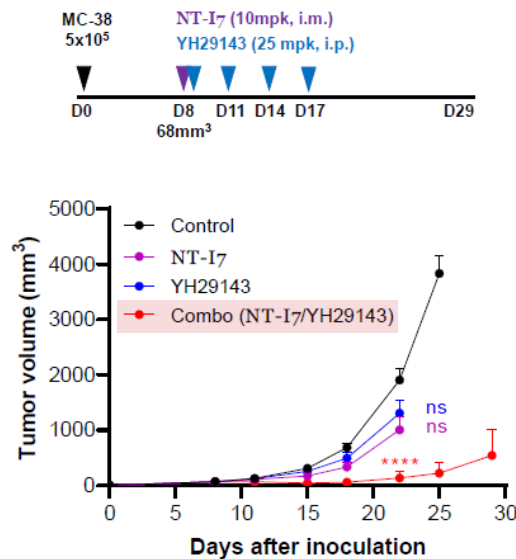
**Ttrans (Transitory exhausted T cell):** T Cell(soldier) with maximum killing(cytotoxic) capacity against enemy(Tumor)

**Tex (Fully exhausted T cell):** Dysfunctional/exhausted T cell after fighting with enemy(Tumor)

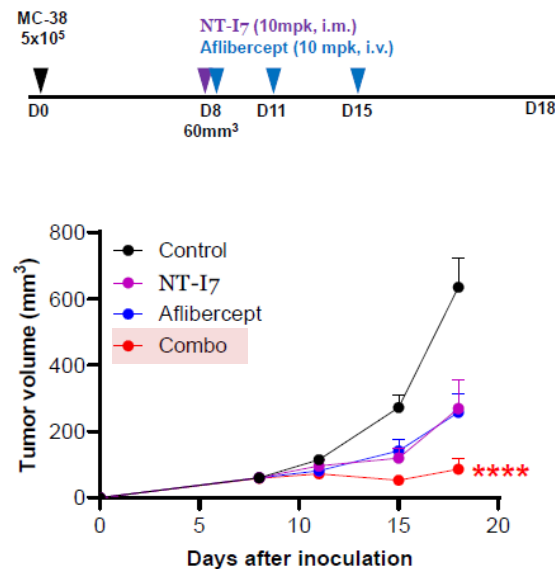
# The anti-tumor effect of NT-I7 double/triple combo therapy

- NT-I7+anti-TIGIT or anti-VEGF combo therapy showed better anti-tumor effects compared to the mono therapy of each
- **In particular, the triple combo of NT-I7+anti-TIGIT+anti-PD-1 demonstrated the strongest anti-tumor effect**

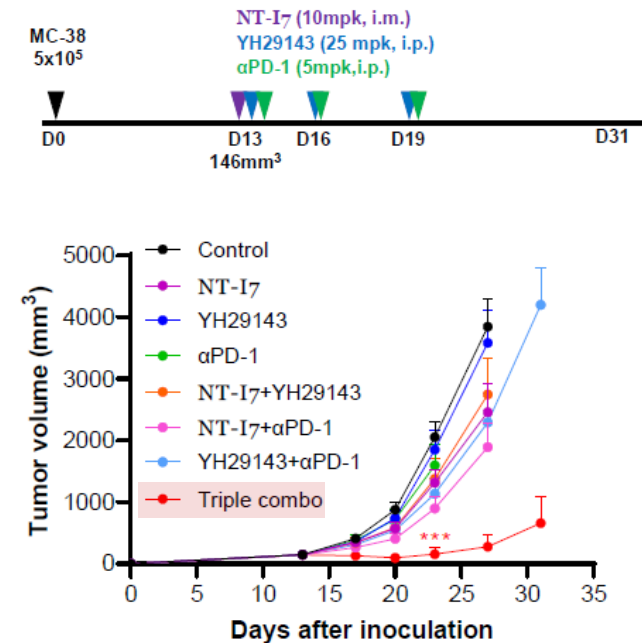
## NT-I7+anti-TIGIT



## NT-I7+anti-VEGF



## NT-I7+anti-TIGIT+anti-PD-1

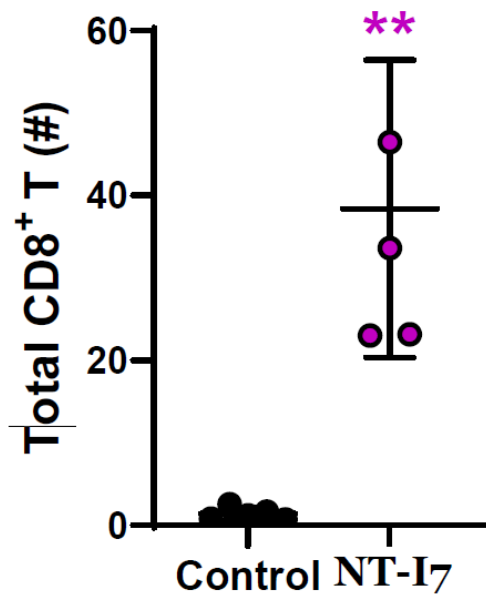


(\*p≤0.05; \*\*p ≤ 0.001; \*\*\*p ≤0.0001; \*\*\*\*p ≤0.00001)

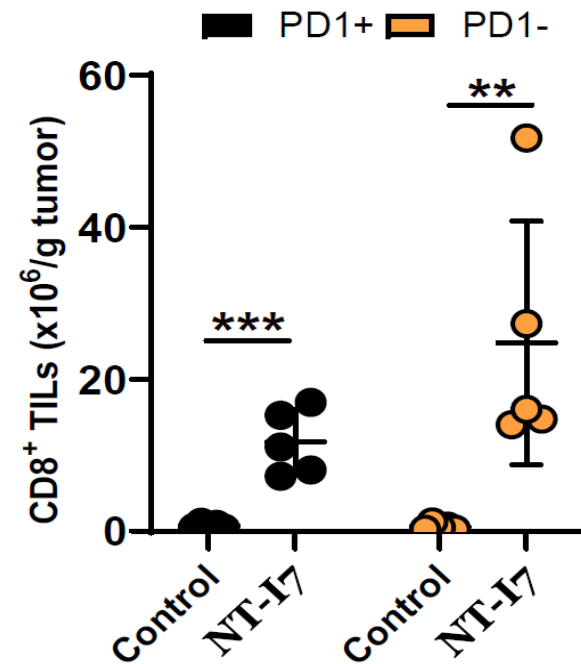
## CD8<sup>+</sup> T cell amplification in NT-I7 mono therapy

- Tumor-infiltrating CD8<sup>+</sup> T cell increased in tumor after NT-I7 injection
- Tumor-specific(PD-1<sup>+</sup>CD8<sup>+</sup>) T cell increased inducing anti-tumor effect in tumor

Tumor-infiltrating CD8<sup>+</sup> T cells



PD1<sup>+</sup> CD8<sup>+</sup> & PD1<sup>-</sup> CD8<sup>+</sup> TILs



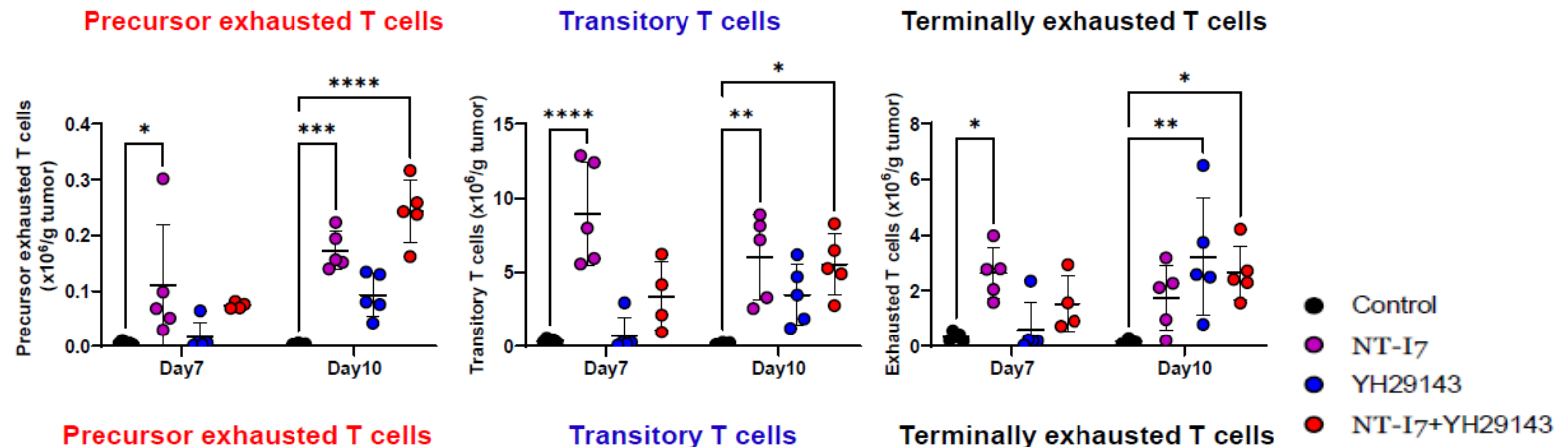
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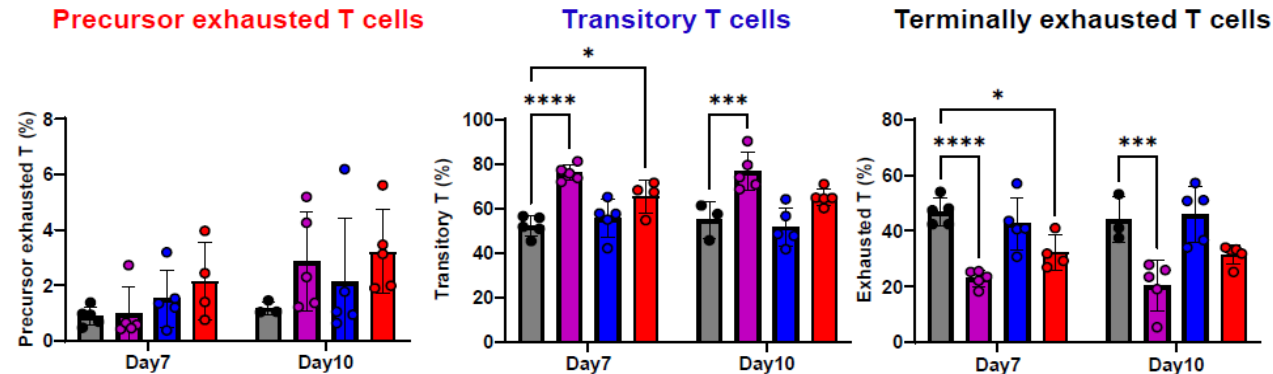
# Increase in tumor specific T cell in NT-I7+anti-TIGIT combo

- Tumor specific(PD-1<sup>+</sup> CD8<sup>+</sup>) T cell increased, closely related to anti-tumor effect
- PD-1<sup>+</sup> CD8<sup>+</sup> T cell differentiated in order of Tpex > Ttrans > Tex
- In combo therapy, as the number and ratio of Tpex, Ttrans increase, inducing sustained anti-tumor effect

# of  
Tpex, Ttrans, Tex



% of  
Tpex, Ttrans, Tex



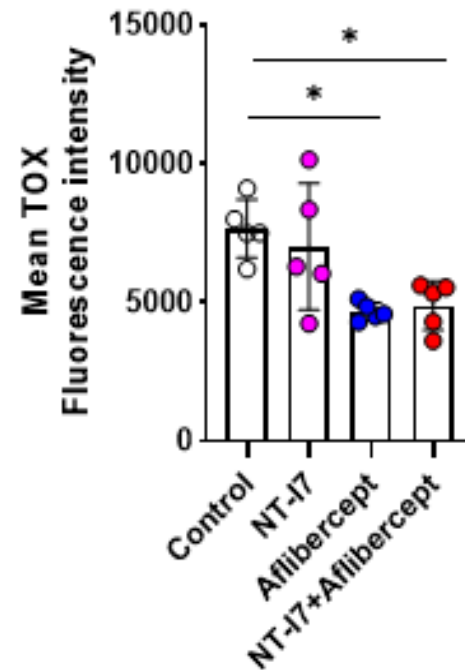
(\*p ≤ 0.05; \*\*p ≤ 0.001; \*\*\*p ≤ 0.0001; \*\*\*\*p ≤ 0.00001)



## Changes in TOX expression in NT-I7+anti-VEGF combo therapy

- TOX expression is reduced through anti-VEGF, which suppresses T cell exhaustion, and this characteristic contributes to the anti-tumor effect

### TOX expression of PD-1<sup>+</sup> CD8<sup>+</sup> T cells in tumor



(\*p≤0.05; \*\*p ≤ 0.001; \*\*\*p ≤0.0001; \*\*\*\*p ≤0.00001)



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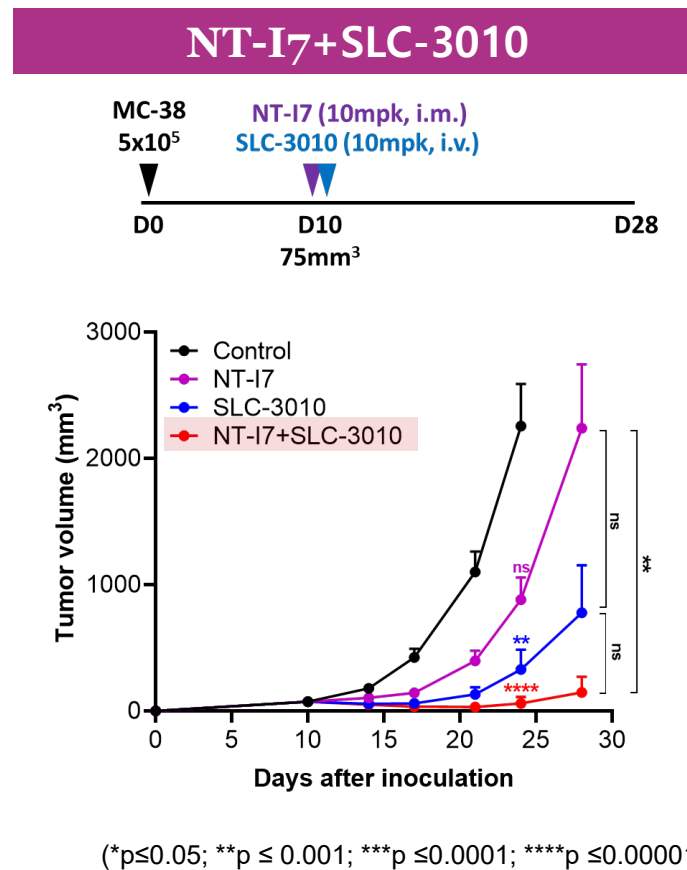
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### 2. Combo therapy with hIL-2/TCB2c complex(SCL-3010), Poster #4199

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## Anti-tumor effect in NT-I7+IL-2 combo therapy

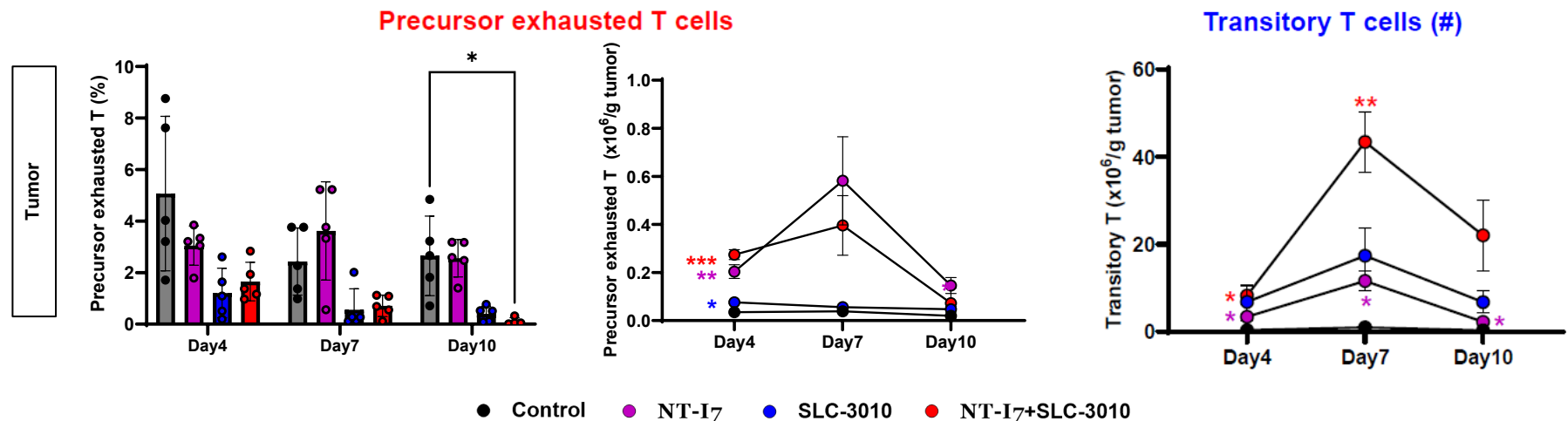
- NT-I7+IL-2 combo therapy showed the strongest anti-tumor effect among different regimens



# Increase in tumor specific T cell when NT-I7+IL-2 combo therapy

- NT-I7 increases Tpex, and IL-2 generates anti-tumor effect by differentiating Tpex into Ttrans and then Tex

## Tpex, Ttrans in Tumor



(\*p≤0.05; \*\*p ≤ 0.001; \*\*\*p ≤0.0001; \*\*\*\*p ≤0.00001)

## Key messages

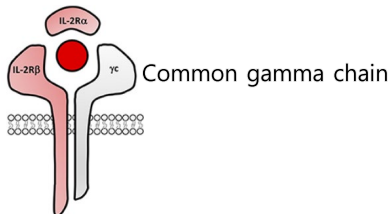
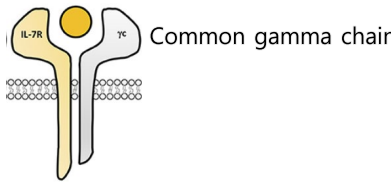


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### *NT-I7 expands its potential as an anti-tumor drug*

1. First trial of combo study with new substances(anti-TIGIT, anti-VEGF, IL-2) with anti-tumor effect
  - *NT-I7*, anti-tumor effect found in combo with all three substances
  - Anti-TIGIT demonstrated the anti-tumor effect in first time ever triple combo study with *NT-I7*
2. Deeper analysis on T cells provided to describe anti-tumor effect more in depth
  - NT-I7 tumor specific(PD-1<sup>+</sup> CD8<sup>+</sup>) T cell amplification
  - Tpex, Ttrans, closely related to anti-tumor, increased
3. Expansion of treatment potential as immuno-oncology enhancing NT-I7's clinical value

## Appendix: IL-7 vs IL-2

- IL-2 target effector T cell → Fast but short-term effect
- IL-7 target memory/naïve T cell → Long-term effect

● IL-2	VS	● IL-7
 <p>Common gamma chain</p>	<p><b>Receptor structure</b></p>	 <p>Common gamma chain</p>
<ul style="list-style-type: none"> <li>• T cell</li> </ul>	<p><b>Production</b></p>	<ul style="list-style-type: none"> <li>• Stromal cells in the bone marrow and lymphoid organs (not from T cell)</li> </ul>
<ul style="list-style-type: none"> <li>• Activated T cell</li> <li>• Regulatory T cell(Treg)</li> </ul>	<p><b>Receptor expression</b></p>	<ul style="list-style-type: none"> <li>• Naïve T cell</li> <li>• Memory T cell</li> </ul>
<ul style="list-style-type: none"> <li>• Stimulation of Effector T cell</li> <li>• Increase Treg cells</li> </ul> 	<p><b>Main function</b></p>	<ul style="list-style-type: none"> <li>• Homeostatic proliferation (Naïve/Memory T cell, increase Tscm)</li> </ul> 
<ul style="list-style-type: none"> <li>• Capillary leakage syndrome (Proleukin)</li> <li>• NKTR-214 RP2D: 0.006 mg/kg</li> </ul>	<p><b>Toxicity</b></p>	<ul style="list-style-type: none"> <li>• Tolerable</li> <li>• NT-I7 RP2D: 1.2 mg/kg</li> </ul>
<ul style="list-style-type: none"> <li>• Limitation in dosage due to toxicity (NKTR214+ Opdivo combo, RP2D: 0.006mpk)</li> <li>• Activated T cell survival for several weeks, and cell death is followed (AICD: Activation induced cell death)</li> </ul>	<p><b>Characteristic</b></p>	<ul style="list-style-type: none"> <li>• High dose (considering toxicity) (NIT-110, RP2D: 1.2mpk)</li> <li>• Tscm increase (known to survive upto 20+ years)</li> </ul>

# THANK YOU !

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