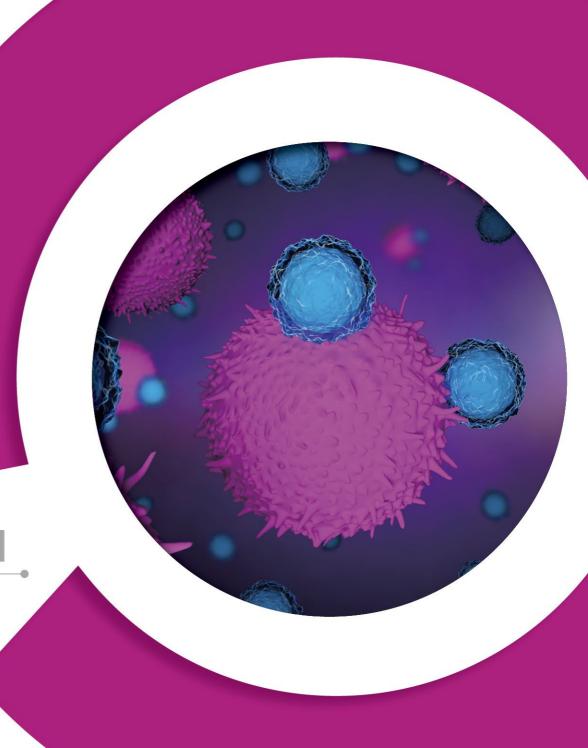
ESMO 2022 Data Read-out

INVESTOR RELATIONS 2022



September 13, 2022





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Poster Presentation at



European Society for Medical Oncology

1. NIT-110 Biomarker data (Ph.2a) Poster 1674P

- Biomarker data from the CPI-naïve arms: MSS-CRC, PaC and Ovarian cancer

Poster title:

NT-I7 plus pembrolizumab combination treatment enhances infiltration of PD-1+ T cells and provides a more immunogenic tumor microenvironment. Biomarker data from the NIT-110 study



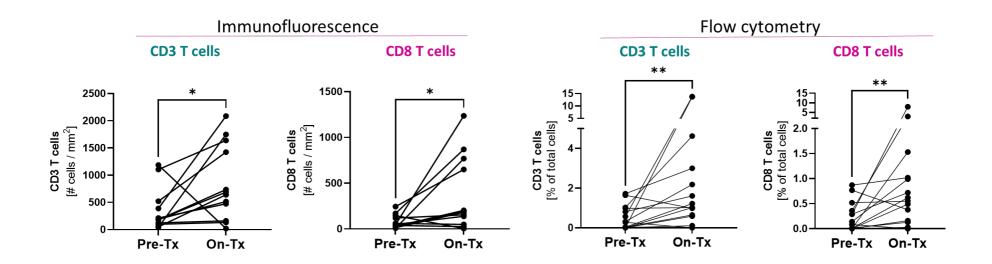
ESVO Key messages

For the first time in a clinical trial, biomarker analysis showed enhanced tumor microenvironment (TME) immunogenicity and suggested that T cells induced to infiltrate the TME by NT-I7 are tumor-specific

- 1. Biomarker data from tissue biopsy shows that the biological mechanism is linked to efficacy of pembro + NT-I7 combo in immune-cold tumors
- 2. Expansion of CD8 Tscm may be the source of T cell infiltration
- 3. Data suggests infiltrating lymphocytes may include tumor-specific CD8 T cells
- 4. A more immunogenic TME is directly associated with tumor reduction
 - the increase in the CD8-to-Treg ratio was particularly remarkable in pts with PR

Increased TIL in TME

- Pembro + NT-I7 combo favors infiltration of CD8 T cells into the TME in over 80% of analyzed tissue samples (22/27 pts)
- Over 50% of pts had a significant, over 5-fold, CD8 T cell increase after the first dose of NT-I7

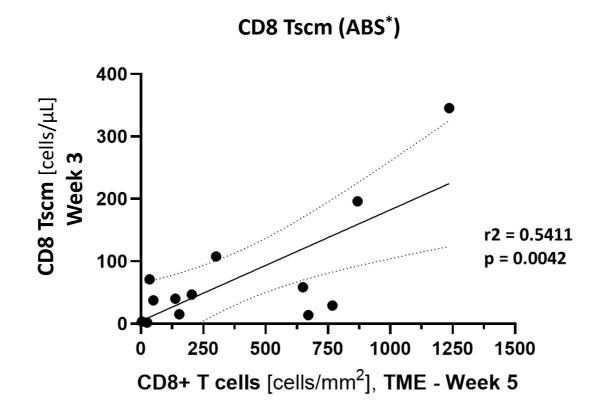


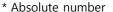
^{*} p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001



Increased Tscm associated with T cell infiltration

- The absolute number of <u>peripheral CD8 Tscm at week 3</u> is directly associated with the absolute number of <u>intratumoral CD8 T cells at week 5</u> (n = 12)
- Among all T cell subsets, CD8 Tscm are more strongly associated with the CD8 T cell infiltration into the tumor



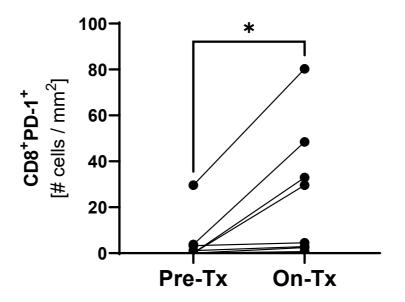




Increased tumor-specific CD8 T cells in the TME

- Tumor-infiltrating CD8 T cells express PD-1 (n = 12), suggesting that <u>tumor-specific</u> <u>CD8 T cells</u> successfully infiltrate the TME

Tumor-infiltrating CD8 T cells express PD-1

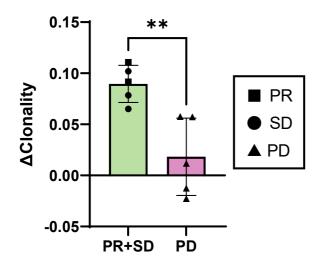


^{*} p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

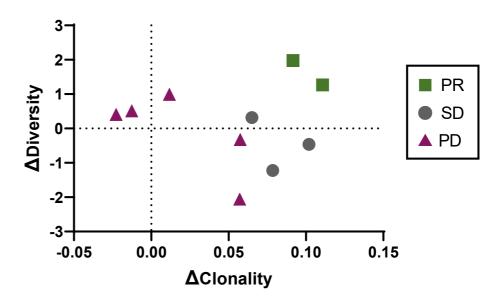
Enhanced clonality and diversity

- Pts with disease control (PR+SD) show a greater increase in intratumoral clonality than PD pts
- Increase in intratumoral clonality in the 2 PR pts was uniquely accompanied by an increase in intratumoral diversity

Intratumoral clonality



Intratumoral clonality, diversity



^{*} p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001



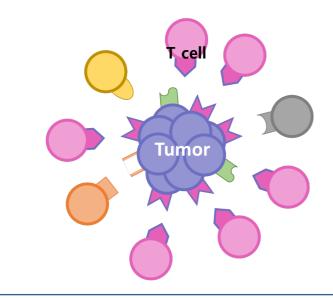
Note: T cell repertoire (clonality and diversity)

- TCR repertoire metrics includes diversity and clonality
- The analysis of the TCR repertoire has been recently considered to be a potential biomarker for patients' progression and response to therapies with immune checkpoint inhibitors

Repertoire

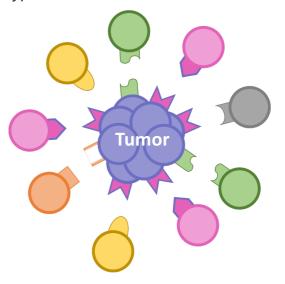
Clonality

- **Tumor-specific** clones are overrepresented
- Higher clonality suggests higher anticancer activity



Diversity

- More clones are present (tumor-specific or not)
- Higher diversity increases the ability to recognize various types of tumor cells

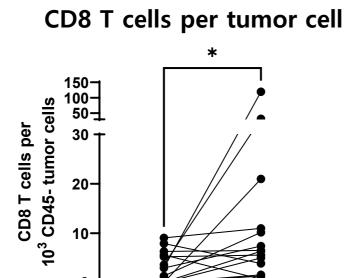


Source: Wang, X., et al., Journal for ImmunoTherapy of Cancer, 2022; 10(6), e004512. Aran, A., et, al., Cancers, 2020; 14(7), 1771.



Increased immunogenicity (1)

- The number of CD8 T cells is significantly increased and CD8-to-Treg ratio is increased in PR pts (n=12)
- Pembro+NT-I7 combo increases the number of CD8 T cells per tumor cell (n = 15)

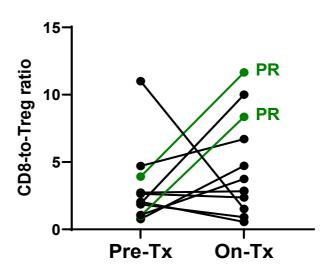


Pre-Tx

On-Tx

Number of

CD8-to-Treg ratio



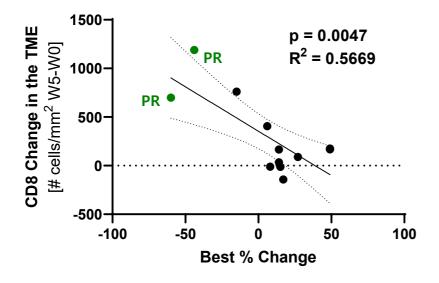
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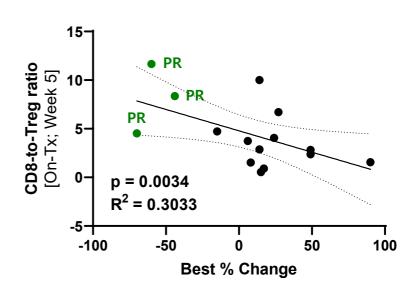
Increased immunogenicity (2)

- Magnitude of CD8 T cell infiltration is directly associated with tumor reduction (n = 12)
- CD8-to-Treg ratio at week 5 is significantly associated with the tumor reduction (n = 12)

CD8 T cell infiltration



CD8-to-Treg ratio*



* On-treatment sample from an additional PR was available for this analysis

Summary of scientific findings

- 1) Safety in both mono & combo therapies has been confirmed from 600+ pts
- 2) Tscm, which have a strong anti-tumor effect, were selectively and strongly amplified
- 3) Increase in TIL was clinically observed for multiple cancer types
- 4) TIL increased proportionally to Tscm (clinically observed)
- 5) Increases in TIL and the intratumoral CD8-to-Treg ratio led to improved clinical response

Summary of competitiveness of NT-I7

1) The world's most clinically tested T cell amplifier

- Strong and selective T cell amplification effects are consistently observed
- Less side effects, high tolerability and safety profile

2) Promising and unique partner for CPI therapy

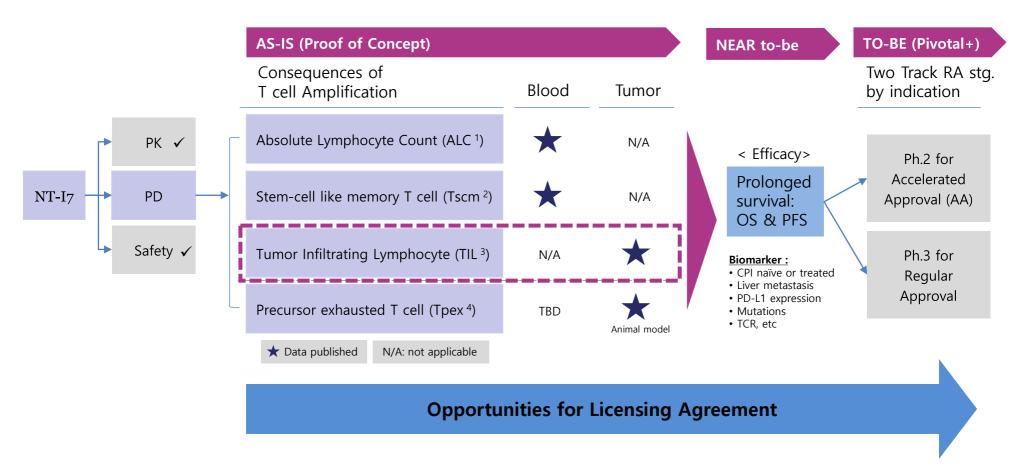
- Excellent synergistic effects with CPI were observed in non-clinical studies
- Excellent therapeutic efficacy was clinically observed in immune-cold tumors that had minimal efficacy with CPI alone (PaC and MSS-CRC)

3) A key player in various combination therapies in the immuno-oncology field

- Like PD-1 therapies, NT-I7 has the potential to play a central role in T cell-based therapies
- The most advanced clinical stage interleukin-7 pipeline with a safety profile
- Potential to become 1L, 2L, or 3L triple combo therapy where chemotherapy is the standard of care (i.e., chemotherapy + CPI + NT-I7 triple combo)
- As a strong and yet selective T cell booster, it can play an important role in various combo therapies

NT-I7 development status

- After PoC is demonstrated from 1b/2a studies, a pivotal study design will be prepared



- ALC: AACR 2018, AACR 2019, SITC 2019, ASCO 2020, SITC 2020, ASCO 2021, SNO 2021, ITC 2021, AACR 2022, Kim JH et al. Clinical & Translational Immunology; e1168 (2020), Campian JL. et al. Clin Cancer Res. 2022 Mar 15;28(6):1229-1239.
- 2. Tscm: SITC 2021, ASCO 2022
- 3. TIL: ASCO 2021, SITC 2021, ESMO GI 2022 Kim JH et al. Clinical & Translational Immunology; e1168 (2020)
- 4. Tpex: AACR 2022



Upcoming major events for 2H 2022

Estimated Data Read-Outs

(SITC) NIT-110: Selected cohorts, Pembrolizumab combo

(ASH) NIT-112: LBCL, CAR-T combo

Interim Analysis



- Society for Immunotherapy of Cancer (SITC)
- Nov. 8 Nov. 12, Boston, MA
- Oral presentation for NIT-110 / Nov.11 4:20 p.m.

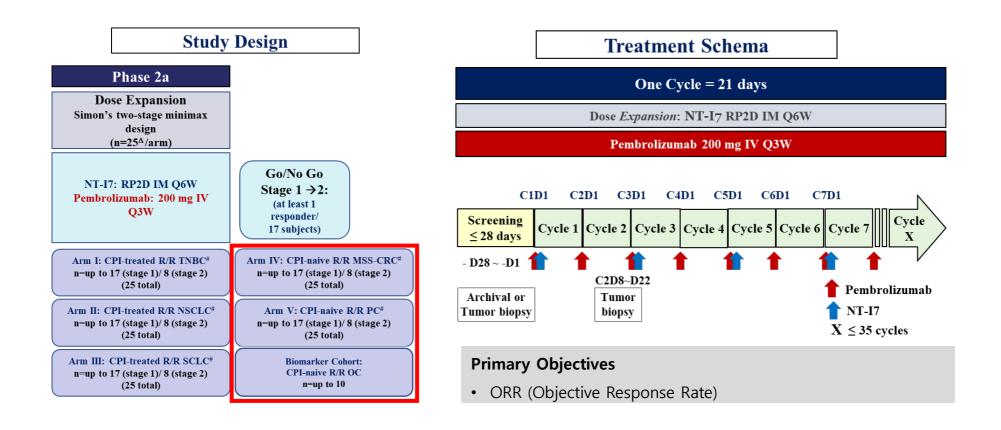


- American Society of Hematology (ASH)
- Dec. 10 Dec. 13, New Orleans, Louisiana
- NIT-112 data

^{*} Data read-out plans are subject to change

Appendix: NIT-110 study protocol

- CPI-naïve R/R solid tumors
- Pembrolizumab IV (Q3W; 200mg) + NT-I7 IM (Q6W; 1,200 μ g/kg)



THANK YOU!



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