Efficacy and safety of NT-I7, long-acting interleukin-7, plus pembrolizumab in patients with advanced solid tumors: results from the Phase 2a study

Aung Naing, MD[1], Hirva Mamdani, MD[2], Minal Barve, MD[3], Melissa L. Johnson, MD[4], Daniel Morgensztern, MD[5], Anthony J. Olszanski, MD[6], Robert A. Wolff, MD[1], Shubham Pant, MD[1], Scott Kopetz, MD; PhD[1], Marya Chaney, PhD[7], Tolani Adebanjo, PhD[8], Jean Fan, MD, MSc[8], Richard D. Kim, MD[9]

[1]M.D. Anderson Cancer Center, Houston, TX, USA. [2]Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit, USA. [3]Mary Crowley Cancer Research, Dallas, USA. [4]Sarah Cannon/Tennessee Oncology, PLLC, Nashville, USA. [5]Washington University, St. Louis, USA. [6]Fox Chase Cancer Center, Philadelphia, USA. [7]Merck & Co., Inc., Rahway, NJ, USA. [8]NeoImmuneTech, Inc., Rockville, USA. [9]Moffitt Cancer Center, Tampa, USA.

BACKGROUND

Checkpoint inhibitors (CPIs) are usually ineffective in patients (pts) with immunologically cold tumors, such as microsatellite stable colorectal cancer (MSS-CRC) or pancreatic cancer (PDAC), and in pts progressing despite prior PD-1/PD-L1 inhibition. The addition of NT-I7, a long-acting IL-7, to pembrolizumab (pembro) may overcome resistance in these tumor types.

Here, we report the combination of NT-I7 plus pembrolizumab (pembro) in CPI-naïve MSS-CRC and PDAC cohorts, and patients (pts) with CPI-treated triple-negative breast cancer (TNBC), non-small cell lung cancer (NSCLC), and small cell lung cancer (SCLC) cohorts of this ongoing phase 2a trial.

STUDY OBJECTIVES

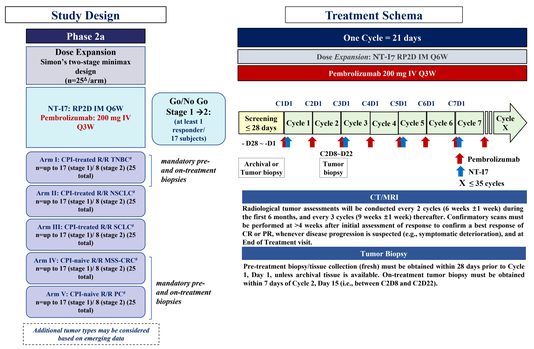
Primary objectives

- To assess the preliminary anti-tumor activity of NT-I7 in combination with pembrolizumab in subjects with CPI-treated R/R tumors (TNBC, NSCLC, SCLC), and CPI-naïve R/R tumors (MSS-CRC and PDAC), based on Objective Response Rate (ORR) per RECIST v1.1 and iRECIST.

Secondary objectives

- To further assess anti-tumor activity of NT-I7 in combination with pembrolizumab in these patient populations based on Duration of Response (DoR), Disease Control Rate (DCR), Progression-Free Survival (PFS), and Overall Survival (OS) by RECIST v1.1 and iRECIST.
- To evaluate immunogenicity of NT-I7 administered in combination with pembrolizumab in these patient populations.

STUDY DESIGN



Pts with CPI-naïve relapsed/refractory (R/R) MSS-CRC and PDAC, and CPI-treated R/R TNBC, NSCLC, and SCLC, were enrolled. NT-I7 (efineptakin alfa) 1200 µg/kg intramuscularly every 6 weeks and 200 mg pembro intravenously every 3 weeks were administered until disease progression/unacceptable toxicity.

- The study used Simon's minimax two-stage design seeking ≥1 responder of 17 evaluable patients in stage 1 for expansion.
- Stage II will enroll additional 8 evaluable patients.

RESULTS – CLINICAL DATA

Subject disposition and characteristics

- As of 15 April 2022, 106 patients were enrolled in the study. 81 patients were evaluable for safety and efficacy; efficacy-evaluable patients must have had 1 post-baseline scan result.
- Median age was 69.9 years [range, 29-83]; ECOG PS 0 (22.6%), PS 1 (77.4%).
- All patients had at least 1 prior line of therapy, and 89.4% of patients had ≥ 2 prior lines of therapy in the recurrent/metastatic setting.

Table 1. Baseline characteristics

Characteristics	Categories	TNBC (n = 10)	NSCLC (n = 28)	SCLC (n = 7)	MSS-CRC (n = 29)	PDAC (n = 32)	Total (n = 106)
Age, year, median (range)	-	52.5 (34, 68)	66.0 (29, 83)	64.0 (51, 72)	56.0 (35, 81)	66.0 (31, 81)	60.9 (29, 83)
Gender, n (%)	Male Female	- 10 (100)	20 (71.4) 8 (28.6)	4 (57.1) 3 (42.9)	19 (65.5) 10 (34.5)	16 (5.0.0) 16 (50.0)	59 (55.7) 47 (44.3)
ECOG Performance Status, n (%)	0 1	3 (30.0) 7 (70.0)	3 (10.7) 25 (89.3)	0 7 (100)	8 (27.6) 21 (72.4)	10 (31.3) 22 (68.8)	24 (22.6) 82 (77.4)
No. of previous lines of therapy, n (%)	1 ≥ 2	1 (10.0) 7 (70.0)	2 (7.1) 25 (89.3)	0 6 (85.8)	1 (3.4) 28 (96.5)	3 (9.4) 29 (90.6)	7 (6.6) 82 (89.4)
Stage at diagnosis, n (%)	1 2 3 4 Unknown	1 (10.0) 4 (40.0) 4 (40.0) 0 1 (10.0)	1 (3.6) 2 (7.1) 7 (25.0) 18 (64.3) 0	0 0 1 (14.3) 6 (85.7) 0	0 2 (6.9) 8 (27.6) 18 (62.1) 1 (3.4)	7 (21.9) 6 (18.8) 5 (15.6) 14 (43.8) 0	9 (8.5) 14 (13.2) 25 (23.6) 56 (52.8) 2 (1.9)
No. of subjects with liver metastasis, n (%)	-	4 (40.0)	5 (17.9)	3 (42.9)	23 (79.3)	25 (78.1)	60 (56.6)

ECOG: Eastern Cooperative Oncology Group

Safety

- NT-I7-related adverse events (AEs) occurred in 79 (74.5%) pts, including 60 (56.6%) Grade (G)1-2, 18 (17.0%) G3, and 1 (0.9%) G4.
- There were no NT-I7-related G5 AEs.

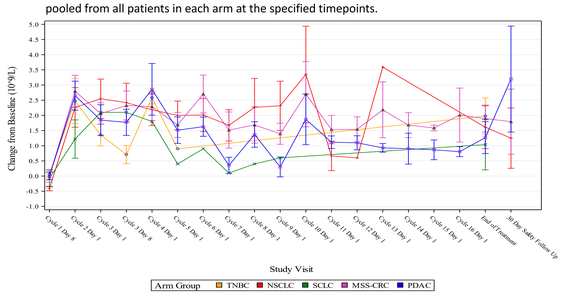
Table 2. Summary of NT-I7-related adverse events

n (%)		TNBC (n = 10)	NSCLC (n = 28)	SCLC (n = 7)	MSS-CRC (n = 29)	PDAC (n = 32)	Total (n = 106)
Any ADR related to NT-I7		6 (60.0)	23 (82.1)	3 (42.9)	23 (79.3)	24 (75.0)	79 (74.5)
ADR (related to NT-I7) ADR by severity	Grade 1	3 (30.0)	5 (17.9)	0	8 (27.6)	10 (31.3)	26 (24.5)
	Grade 2	1 (10.0)	12 (42.9)	3 (42.9)	9 (31.0)	9 (28.1)	34 (32.1)
	Grade 3	2 (20.0)	6 (21.4)	0	6 (20.7)	4 (12.5)	18 (17.0)
	Grade 4	0	0	0	0	1 (3.1)	1 (0.9)
	Grade 5	0	0	0	0	0	0
Most frequently reported ADR		2 (20.0)	2 (7.1)	1 (14.3)	8 (27.6)	5 (15.6)	18 (17.0)
Fatigue		3 (30.0)	-	-	5 (17.2)	9 (28.1)	17 (16.0)
Fever		-	2 (7.1)	-	7 (24.1)	7 (21.9)	16 (15.1)
Injection site reaction		2 (20.0)	3 (10.7)	-	5 (17.2)	2 (6.3)	12 (11.3)
Rash maculo-papular		2 (20.0)	1 (3.6)	-	7 (24.1)	1 (3.1)	11 (10.4)
Nausea							
ADR resulting in drug discontinuation		2 (20.0)	2 (7.1)	0	5 (17.2)	5 (15.6)	14 (13.2)

ADR: Adverse Drug Reaction

Absolute lymphocyte count

Figure 5. A sustained increase of mean absolute lymphocyte count change from baseline in all arms was observed, including CPI-naïve and CPI-pretreated. Data is pooled from all patients in each arm at the specified timepoints.



Efficacy

Table 3. Summary of efficacy results.

Efficacy Summary	TNBC (n = 7)	NSCLC (n = 18)	SCLC (n = 3)	MSS-CRC (n = 27)	PDAC (n = 26)	Total (n = 81)
ORR per RECIST 1.1, n (%)	0 (0.0)	1 (5.6)	1 (33.3)	1 (3.7)	1 (3.8)	4 (4.9)
ORR per iRECIST 1.1, n (%)	0 (0.0)	2 (11.1)	1 (33.3)	3 (11.1)	2 (7.7)	8 (9.9)
Disease control rate per RECIST 1.1, n (%)	1 (14.3)	6 (33.3)	1 (33.3)	10 (37.0)	8 (30.8)	26 (32.1)
Disease Control Rate per iRECIST 1.1, n (%)	2 (28.6)	12 (66.7)	1 (33.3)	11 (40.7)	9 (34.6)	35 (43.2)
Median duration of response per RECIST (months)	0	1.3	4.1	4.6	8.7	4.4
Median duration of response per iRECIST (months)	0	3.1	4.1	4.6	6.1	4.4
Median time to response per RECIST (months)	0	3.6	1.2	2.8	2.8	2.8
Median time to response per iRECIST (months)	0	3.3	1.2	4.1	3.4	3.3
Median treatment duration (weeks)	6.14	9.14	6.14	12.14	6.14	6.14
Median follow up (months)	6.08	4.85	6.08	5.13	3.53	5.13

Figure 1. Best percentage change in target lesions from baseline (* indicates immune partial response [iPR]).

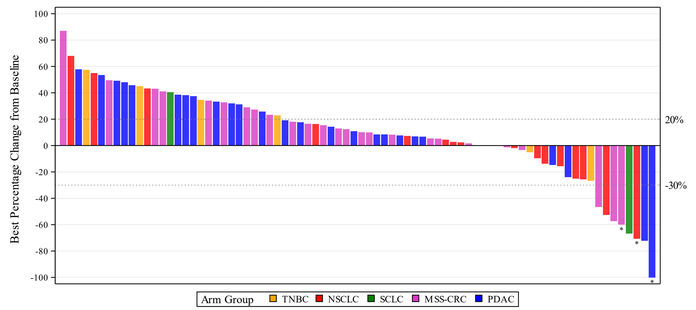


Figure 2. Individual percentage change in target lesions from baseline over time.

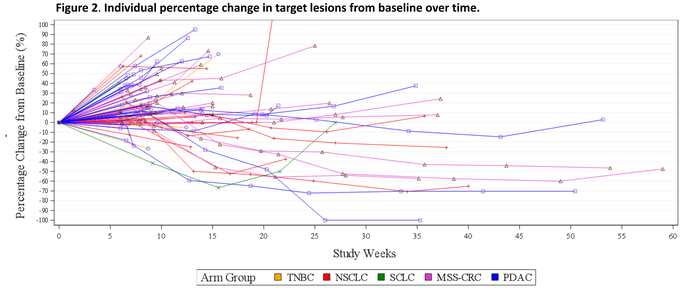


Figure 3. Treatment duration and response.

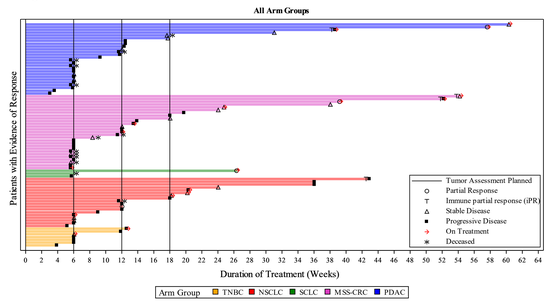
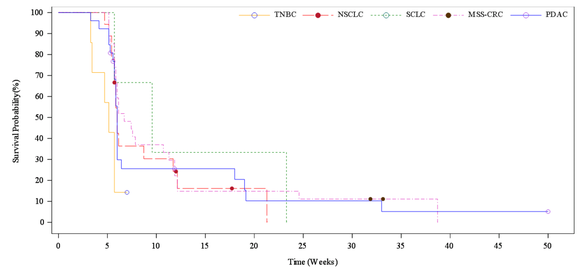


Figure 4. Kaplan-Meier curve for progression-free survival (PFS). Median PFS (in weeks) for each cohort: TNBC: 5.1, NSCLC: 6.0, SCLC: 9.6, MSS-CRC: 6.7, PDAC: 6.0



CONCLUSIONS

- The combination of NT-I7 and pembro showed preliminary anticancer activity and a manageable toxicity profile in heavily pretreated subjects with immunologically cold CPI-naïve MSS-CRC and PDAC tumors, as well as CPI-treated TNBC, NSCLC, and SCLC.
- Per iRECIST, DCR for the TNBC cohort was 28.6%; ORR for the NSCLC cohort was 11.1%, with a DCR of 66.67% DCR and 3.1 months DoR; ORR for the SCLC cohort was 33.3%, with a 33.3% DCR and 4.1 months DoR; ORR for the MSS-CRC cohort was 11.1% with 40.7% DCR and 4.6 months DoR; and the PDAC cohort had an ORR of 7.7% with 34.6% DCR, and 6.1 months DoR.
- NT-I7 plus pembro led to an increase in change of mean absolute lymphocyte count from baseline in all cohorts, including CPI-treated and CPI-naïve subjects.

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For more information, please contact **Aung Naing, MD, at aung.naing@mdanderson.org**