A Phase 2a study of NT-I7 (efineptakin alfa), a long-acting IL-7, and pembrolizumab to evaluate efficacy, including overall survival, in hard to treat MSS-CRC and PDAC gastrointestinal tumors

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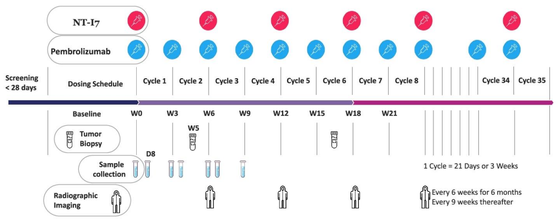
BACKGROUND

Microsatellite-stable colorectal (MSS-CRC) and pancreatic cancer (PDAC) are immunologically cold tumors with null response to checkpoint inhibitors (CPI). NT-I7, a long-acting IL-7, in combination with pembrolizumab (pembro) has shown to significantly increase intratumoral T cell infiltration and elicit some tumor control in these hard-to-treat gastrointestinal indications. The original MSS-CRC and PDAC cohorts, enrolling 25 subjects each, were expanded to 50 pts per indication. Here, we provide an updated analysis including the original and expansion cohorts.

STUDY DESIGN

Open-label Phase 2a study in subjects with relapsed/refractory CPI-naïve MSS-CRC and PDAC; NT-I7 1200 µg/kg IM every 6 weeks (Q6W), pembro 200 mg IV Q3W. Antitumor activity assessed by Response Evaluation Criteria in Solid Tumors 1.1 (RECIST 1.1) and immune Response Evaluation Criteria in Solid Tumors (iRECIST).



STUDY OBJECTIVES

- Primary Objectives: To assess the preliminary anti-tumor activity of NT-I7 in combination with pembrolizumab in subjects with CPI-naïve R/R tumors (MSS-CRC and PDAC) based on Objective Response Rate (ORR) as assessed by RECIST 1.1 and iRECIST.
- Secondary Objectives:
  - To further assess the 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 1.1 and iRECIST.
  - To evaluate immunogenicity of NT-I7 administered in combination with pembrolizumab in these patient populations.

CONCLUSIONS

- NT-I7 and pembrolizumab treatment was safe and well-tolerated.
- Median OS was 13.2 months in 50 MSS-CRC patients treated with NT-I7 and pembrolizumab (historical OS is 10.8 months[1]).
- Median OS was 11.1 months in 48 PDAC patients treated with NT-I7 and pembrolizumab (historical OS is 6.1 months[2]).

Identification of predictive biomarkers that may define subjects with higher likelihood of clinical benefit would be a promising step to maximizing potential of the NT-I7 + pembro treatment combination for patients with these indications. Research in this area is ongoing - visit the poster for abstract #2563 for more information.

ACKNOWLEDGMENTS

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RESULTS

Subject characteristics

- As of 02 Oct 2023, 119 subjects were enrolled and 98 subjects were efficacy-evaluable (50 MSS-CRC, 48 PDAC)
- All subjects had Eastern Cooperative Oncology Group (ECOG) status 0-1 at baseline
- 74.8% of subjects (89/119) were treated in the third line or beyond

Table 1. Subject characteristics

	MSS-CRC (N=55)	PDAC (N=64)	Total (N=119)
Age (years); median [min, max]	56.0 [35 – 81]	65.0 [31 – 81]	61.0 [31 – 81]
Sex (male); n (%)	30 (54.5%)	36 (56.3%)	66 (55.5%)
Race (white); n (%)	42 (76.4%)	50 (78.1%)	92 (77.3%)
Stage at diagnosis; n (%)			
1-3	19 (34.5%)	29 (45.3%)	48 (40.3%)
4	32 (58.2%)	30 (46.9%)	62 (52.1%)
Unknown	4 (7.3%)	5 (7.8%)	9 (7.6%)
ECOG status at baseline; n (%)			
0	15 (27.3%)	16 (25.0%)	31 (26.1%)
1	40 (72.7%)	48 (75.0%)	88 (73.9%)
Number of prior anti-cancer therapies; n (%)			
1	1 (1.8%)	5 (7.8%)	6 (5.0%)
2	6 (10.9%)	18 (28.1%)	24 (20.2%)
3	14 (25.5%)	18 (28.1%)	32 (26.9%)
4	10 (18.2%)	13 (20.3%)	23 (19.3%)
≥5	24 (43.6%)	10 (15.6%)	34 (28.6%)
Safety analysis set; n (%)	55 (100%)	64 (100%)	119 (100%)
Efficacy evaluable set; n (%)	50 (90.9%)	48 (75.0%)	98 (82.4%)
Treatment disposition; n (%)			
On treatment	3 (5.5%)	2 (3.1%)	5 (4.2%)
Completed the treatment	1 (1.8%)	1 (1.6%)	2 (1.7%)
Discontinued from treatment	51 (92.7%)	61 (95.3%)	112 (94.1%)
Reason for treatment discontinuation; n (%)			
Adverse event	12 (21.8%)	6 (9.4%)	18 (15.1%)
Death	1 (1.8%)	0	1 (0.8%)
Progressive disease	31 (56.4%)	45 (70.3%)	76 (63.9%)
Withdrawal by subject	3 (5.5%)	7 (10.9%)	10 (8.4%)
Other (including physician decision and non-compliance with study schedule)	4 (7.3%)	3 (4.7%)	7 (5.9%)

ECOG = Eastern Cooperative Oncology Group

Safety

- 80.7% (96/119) subjects experienced treatment-emergent adverse events (TEAEs) related to either NT-I7 or pembrolizumab.*
- The most common NT-I7-related TEAE was injection site reaction (30/119, 25.2%).
- One Grade 5 NT-I7-related TEAE was observed in the PDAC cohort (myocarditis).

Table 2. Overview of Adverse Drug Reactions (ADR)*

Preferred Term [n (%)]	MSS-CRC (N=55)	PDAC (N=64)	Total (N=119)
Any ADRs, n (%)	47 (85.5%)	49 (76.6%)	96 (80.7%)
Grade 1	9 (16.4%)	19 (29.7%)	28 (23.5%)
Grade 2	20 (36.4%)	19 (29.7%)	39 (32.8%)
≥Grade 3	18 (32.7%)	11 (17.2%)	29 (24.4%)
Grade 3	16 (29.1%)	9 (14.1%)	25 (21.0%)
Grade 4	2 (3.6%)	1 (1.6%)	3 (2.5%)
Grade 5	0	1 (1.6%)	1 (0.8%)
ADR observed in ≥10% subjects			
Injection site reaction	17 (30.9%)	13 (20.3%)	30 (25.2%)
Fatigue	17 (30.9%)	11 (17.2%)	28 (23.5%)
Pyrexia	13 (23.6%)	13 (20.3%)	26 (21.8%)
Rash maculo-popular	13 (23.6%)	13 (20.3%)	26 (21.8%)
Pruritus	13 (23.6%)	9 (14.1%)	22 (18.5%)
Nausea	12 (21.8%)	4 (6.3%)	16 (13.4%)
Rash	3 (5.5%)	12 (18.8%)	15 (12.6%)
Influenza-like illness	8(14.5%)	5 (7.8%)	13 (10.9%)

TEAE = treatment emergent adverse event
* ADRs listed here are related to either NT-I7 or pembrolizumab. Note that the safety data in the abstract only considered the relationship with NT-I7 and included the adverse drug reactions (ADRs) related to NT-I7.

Median overall survival was prolonged in MSS-CRC and PDAC cohorts treated with NT-I7 + pembro compared to historical data

- Median overall survival (mOS) was 13.2 months in MSS-CRC [95% CI 8.9 – 18.6 months] (Fig. 1A); historical mOS for standard of care is 10.8 months[1].
- mOS was 11.1 months in PDAC [95% CI 4.1-13.3 months] (Fig. 1B), compared to 6.1 months for historical standard of care[2].

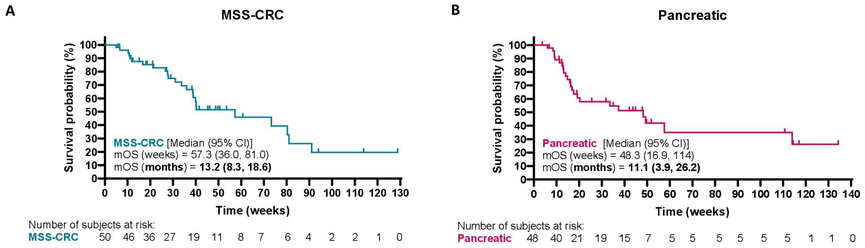

Figure 1. Median overall survival (mOS) in MSS-CRC and PDAC cohorts treated with NT-I7 + pembro. **A,** MSS-CRC mOS, including 50 efficacy-evaluable subjects; **B,** PDAC mOS, including 48 efficacy-evaluable subjects. Subjects were evaluable for efficacy if they received at least one dose of both study drugs with an evaluable baseline and at least one evaluable post-baseline assessment of tumor response.

Summary of objective response to NT-I7 + pembro treatment

- 3 subjects in each cohort achieved partial response (PR) by iRECIST, and 1 MSS-CRC subject and 2 PDAC subjects achieved PR by RECIST 1.1.
- 1 MSS-CRC responder per iRECIST and 2 PDAC responders per iRECIST were alive with no progression at data cutoff.
- Higher disease control rate by iRECIST (iDCR) was observed in MSS-CRC subjects with primary tumor in the rectum (66.7%, 6/9 subjects) than in MSS-CRC subjects with primary tumor in the colon (31.7%, 13/41 subjects).

Table 3. Summary of objective response to NT-I7 + pembro treatment

	MSS-CRC, N=50		PDAC, N=48	
	RECIST 1.1	iRECIST	RECIST 1.1	iRECIST
Best overall response [n, %]				
Complete response	0	0	0	0
Partial response	1 (2.0)	3 (6.0)	2 (4.2)	3 (6.3)
Stable disease	17 (34.0)	16 (32.0)	10 (20.8)	10 (20.8)
Progressive disease	31 (62.0)	30 (60.0)	36 (75.0)	35 (72.9)
Unknown	1 (2.0)	1 (2.0)	0	0
Objective response rate (%)	2.0	6.0	4.2	6.3
Disease control rate (%)	36.0	38.0	25.0	27.1
Duration of response in months (median)	13.1	13.0	NE	NE
Duration of response and stable disease in months (median)	4.2	14.5	2.9	11.1

Median progression-free survival by RECIST 1.1 and iRECIST (mPFS/miPFS)

- With 11 subjects on follow up in each cohort, PFS/iPFS was 1.5/3.8 months for MSS-CRC (Fig. 2A) and 1.4/2.1 months for PDAC (Fig 2B).

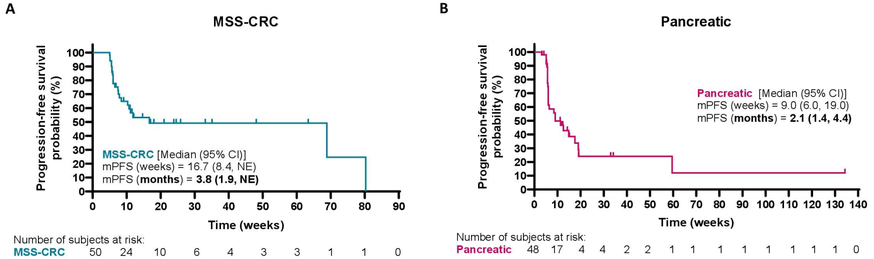

Figure 2. Median PFS by iRECIST. **A,** MSS-CRC mPFS by iRECIST, including 50 efficacy-evaluable subjects; **B,** PDAC mPFS by iRECIST, including 48 efficacy-evaluable subjects.

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