Survival Benefit in Salvage Patients With Intratumoral Ultra-High Concentration Nitric Oxide Gas Injection in Cutaneous and Subcutaneous Solid Tumors in a Phase 1 Study

Poster #304

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Background

- High volume, ultra-high concentration nitric oxide (UNO) administered intratumorally has shown survival benefits in mouse colon and breast cancer models.
- UNO influences the immune system in the murine model, altering M1 macrophage, Treg, and CD8⁺ T cell levels.
- UNO also upregulates PD-L1 and thus its combination with immune checkpoint inhibitors (ICIs) has demonstrated improved tumor inhibition and ICI efficacy.
- UNO monotherapy was found to be more efficacious than murine anti-PD-1 therapy in 4T1 breast tumor-bearing mice.

Methods

- This first-in-human, phase 1a trial (NCT05351502) evaluated the safety, maximum tolerated dose (MTD), and recommended phase 1b dose of a single intratumoral UNO injection in patients administered as monotherapy.
- Patients ≥ 18 years old had unresectable cutaneous or subcutaneous solid tumors (superficial axis 4.5–30 mm) and had exhausted all standard treatment options.
- Patients were washed out of all other cancer therapies for 30 days prior to UNO treatment, and no other cancer therapies were allowed for at least 30 days after UNO treatment.
- UNO (0.2 L/min for 5 minutes) was administered at 25,000 or 50,000 ppm using a 23-gauge needle inserted horizontally through the tumor to create an exit portal, then retracted to the lesion center for treatment.

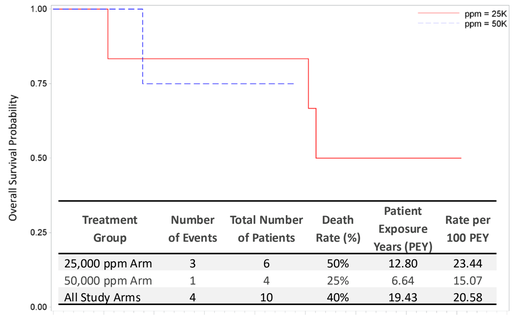
Results

Patient Demographics and Baseline Clinical Characteristics

Characteristic	25,000 ppm Arm *(n=6)*	50,000 ppm Arm *(n=4)*	All Study Arms *(n=10)*
Age (years)			
Mean (SD)	60 (18.4)	61.5 (15.9)	60.6 (16.5)
Median (range)	62 (34-82)	63.5 (41-78)	62 (34-82)
Sex, *n* (%)			
Male	2 (33)	1 (25)	3 (30)
Female	4 (67)	3 (75)	7 (70)
Race, *n* (%)			
White	6 (100)	4 (100)	10 (100)
Ethnicity, n (%)			
Hispanic or Latino	0	1 (25)	1 (10)
Not Hispanic or Latino	6 (100)	3 (75)	9 (90)
Weight (kg)			
Median (range)	64.2 (55-97)	56 (53-68)	61.2 (53-97)
ECOG PS, n (%)			
0	5 (83)	1 (25)	6 (60)
1	1 (17)	3 (75)	4 (40)
Disease Under Study, n (%)			
Breast cancer	3 (50)	3 (75)	6 (60)
Melanoma	1 (17)	1 (25)	2 (20)
Squamous cell carcinoma	2 (33)	0	2 (20)
Disease Stage, n (%)			
Stage III - locally advanced, late stages	2 (33)	0	2 (20)
Stage IV - metastatic	4 (67)	4 (100)	8 (80)
Type of Treated Lesion, n (%)			
Cutaneous	6 (100)	1 (25)	7 (70)
Subcutaneous	0	3 (75)	3 (30)
Origin of Treated Lesion, n (%)			
Primary	3 (50)	2 (50)	5 (50)
Metastatic	3 (50)	2 (50)	5 (50)
Location(s) of Treated Lesion, n (%)			
Back	2 (33)	0	2 (20)
Breast	3 (50)	3 (75)	6 (60)
Finger	1 (17)	0	1 (10)
Elbow (right)	0	1 (25)	1 (10)
Prior Treatments, Median (range)			
Lines of systemic treatments	4 (2-11)	4 (2-14)	4 (2-14)
Total no. of treatments: medication/surgery/radiation	12 (7-14)	7 (4-18)	11 (4-18)

ECOG PS: Eastern Cooperative Oncology Group performance status. Grade 0 represents fully active, no restrictions; Grade 1 represents restricted in strenuous activity, ambulatory/light work.

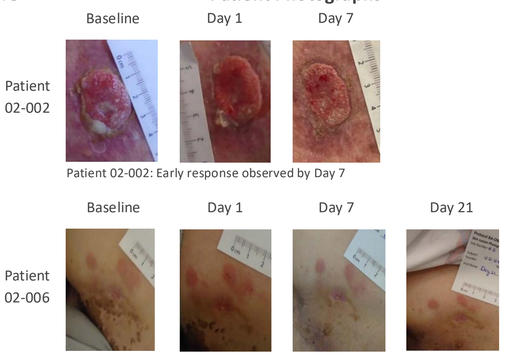
Kaplan-Meier Survival Analysis of Patients Receiving 25,000 ppm or 50,000 ppm UNO



Treatment Group	Number of Events	Total Number of Patients	Death Rate (%)	Patient Exposure Years (PEY)	Rate per 100 PEY
25,000 ppm Arm	3	6	50%	12.80	23.44
50,000 ppm Arm	1	4	25%	6.64	15.07
All Study Arms	4	10	40%	19.43	20.58

Median survival not estimable since survival plot over time does not dip below 50%

Patient Photographs



Patient 02-002: Early response observed by Day 7

Patient 02-006: Improvement of radiation dermatitis as early as Day 1. Prior surgical scar is noticeably smaller by Day 21.

Treatment-Emergent Adverse Events

System organ class	Preferred term, *n* (%)	Grade ≥3 Y/N	Serious AE Y/N	Relation to study drug (UNO)	25,000 ppm Arm *(n=6)* Events = 8	50,000 ppm Arm *(n=4)* Events = 9	All Study Arms *(n=10)* Events = 17
Gastrointestinal Disorders	Nausea	N	N	Possibly related	1 (16.7)	1 (25)	2 (20)
General Disorders & Administration Site Conditions	Fatigue	N	N	Possibly related	0	1 (25)	1 (10)
	Pain	N	N	Unrelated	0	1 (25)	1 (10)
Nervous System Disorders	Dizziness	N	N	Probably related	0	1 (25)	1 (10)
	Vasovagal syncope	Y	N	Possibly related	0	1 (25)	1 (10)
	Vocal cord paralysis	N	N	Unrelated	1 (16.7)	0	1 (10)
Respiratory, Thoracic & Mediastinal Disorders	Dyspnea	N	N	Certainly related	1 (16.7)	0	1 (10)
	Dyspnea	N	N	Unrelated	1 (16.7)	0	1 (10)
	Pleural effusion	N	Y	Unrelated	1 (16.7)	0	1 (10)
	Hypoxia	Y	Y	Certainly related	1 (16.7)	0	1 (10)
	Hypoxia	N	N	Certainly related	0	1 (25)	1 (10)
Skin & Subcutaneous Tissue Disorders	Palmar-plantar erythrodysaesthesia syndrome	N	N	Certainly related	1 (16.7)	0	1 (10)
	Subcutaneous emphysema	N	N	Certainly related	1 (16.7)	2 (50)	3 (30)
Vascular Disorders	Hypotension	N	N	Probably related	0	1 (25)	1 (10)

Conclusions

- Intratumoral administration of UNO monotherapy was generally safe and well tolerated in salvage patients with unresectable solid tumors.
- As of 2-Feb-2026, six of 10 patients remain alive 22-40 months post-single UNO injection, including two triple negative breast cancer patients with no evidence of disease, based on all available testing and examinations performed.
- The observed survival in this heavily pretreated population supports further evaluation of UNO, including in a study with either 25,000 or 50,000 ppm UNO in combination with ICIs.