COMPLETE

NUTIDE:701 - PART 1

SOLID TUMOR - PHASE 1 STUDY (MONOTHERAPY)

Designed to establish the RP2D of NUC-7738

Key Eligibility Criteria

- Advanced solid tumors
- Exhausted all treatment options
- RECIST v1.1 measurable disease
- ECOG PS 0-1

Phase 1

NUC-7738

(14 mg/m² - 2000 mg/m²)

Q1W

Objective
- Establish RP2D

Key endpoints
- Safety & tolerability
- Anti-tumor activity
- PK

Patient population
- Exhausted all therapeutic options

Number of patients	Age (median)	Prior lines of therapy (median)*
38	67 (range 39-84)	2 (range 0-7)

* for advanced disease

NUC-7738 is well tolerated in patients who have exhausted all other therapies

- No Grade 4 toxicities
- Low rates of Grade 3 toxicities

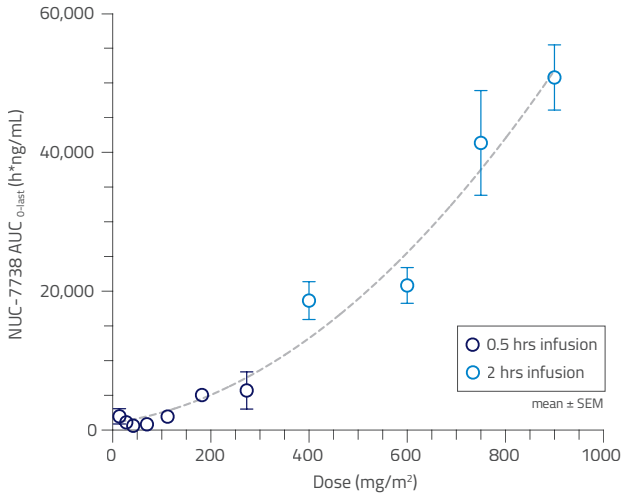
Dose AE occurred (mg/m²)	14 n=2	28 n=3	42 n=2	70 n=3	112 n=4	182 n=4	273 n=5	400 n=6	600 n=9	750 n=5	900 n=8	MTD 1350 n=11	2000 n=2	Total* n=38
All Grade Treatment-Related Adverse Events (≥10%)														
Nausea	0	1 (33%)	0	0	0	0	1 (20%)	0	3 (33%)	2 (40%)	3 (38%)	5 (45%)	1 (50%)	16 (42%)
Fatigue	0	1 (33%)	0	0	0	0	0	1 (17%)	3 (33%)	1 (20%)	3 (38%)	7 (64%)	2 (100%)	14 (37%)
Anemia	0	0	0	0	0	0	0	0	0	0	2 (25%)	4 (36%)	2 (100%)	7 (18%)
Diarrhea	0	0	0	0	0	0	1 (20%)	0	0	1 (20%)	1 (13%)	4 (36%)	0	6 (16%)
Vomiting	0	0	0	0	0	0	0	0	0	1 (20%)	1 (13%)	3 (27%)	1 (50%)	6 (16%)
Mucosal inflammation	0	0	0	0	0	0	0	0	1 (11%)	1 (20%)	0	1 (9%)	1 (50%)	4 (11%)
Decreased appetite	0	0	0	1 (33%)	0	1 (25%)	1 (20%)	0	0	0	1 (13%)	0	0	4 (11%)
Grade 3 Treatment-Related Adverse Events (ALL)														
Fatigue	0	0	0	0	0	0	0	0	0	0	0	3 (27%)	2 (100%)	4 (11%)
Anemia	0	0	0	0	0	0	0	0	0	0	1 (13%)	0	0	1 (3%)
Neutropenia	0	0	0	0	0	0	0	0	1 (11%)	0	0	0	0	1 (3%)
Vomiting	0	0	0	0	0	0	0	0	0	0	0	0	1 (50%)	1 (3%)

MTD: maximum tolerated dose

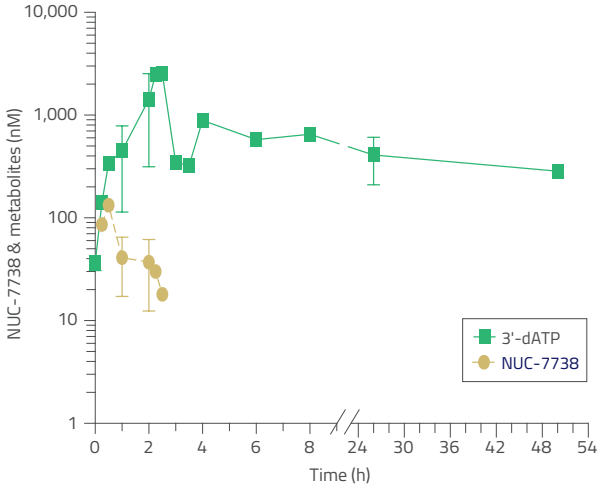
n: number of patients receiving each dose level at any time during the study *total number of patients who experienced TRAE

Attractive pharmacokinetic profile

Plasma



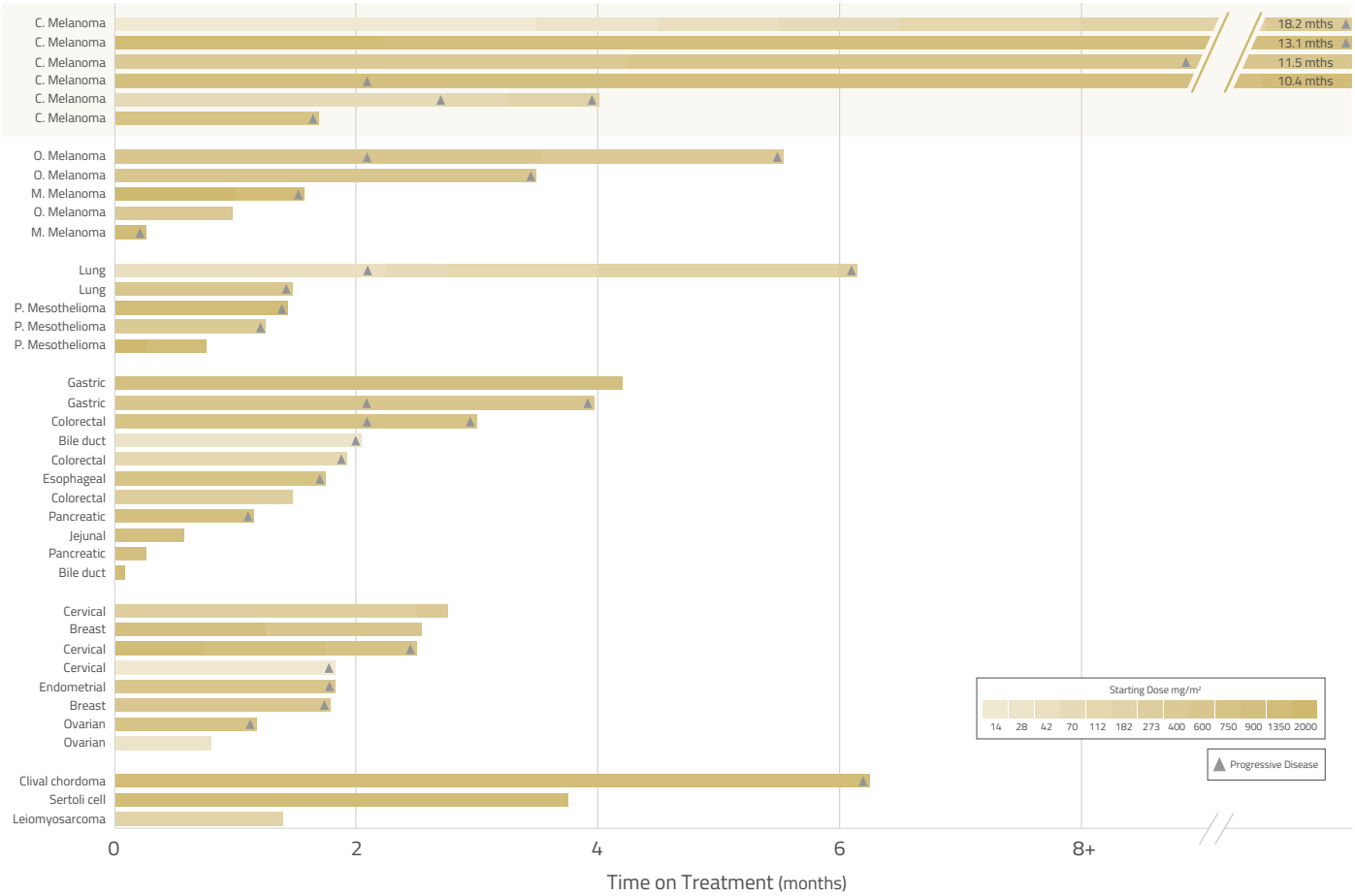
Intracellular



- Favorable pharmacokinetic profile
- Efficiently generates the active anti-cancer metabolite 3'-dATP intracellularly
- Intracellular 3'-dATP persists (half-life 42 hours)

Encouraging activity across a broad range of tumors and doses

- Promising efficacy observed, despite >75% of patients treated below MTD
- Notable clinical activity observed in patients with cutaneous melanoma



Case Studies

Encouraging signs of efficacy in patients who had exhausted all other therapies

62 YRS

Metastatic Cutaneous Melanoma

Prior lines of therapy

1. nivolumab + ipilimumab: discontinued within **1 month**
2. CK7 inhibitor: progressed at **1 month**

NUC-7738
starting dose 14 mg/m^2
(8 dose escalations)

18 months treatment duration
(Stable Disease 12 months)

14% reduction in tumor volume

65 YRS

Metastatic Cutaneous Melanoma

Prior line of therapy

1. nivolumab + ipilimumab: discontinued within **1 month**

NUC-7738
starting dose 400 mg/m^2
(1 dose escalation)

11 months treatment duration
(Stable Disease 9 months)

NUC-7738 enabled complete resection. Patient had diffuse disease that was inoperable prior to NUC-7738

72 YRS

Metastatic Clival Chordoma

Prior line of therapy

1. imatinib: progressed at **19 months**

NUC-7738
dose 1350 mg/m^2

Stable Disease 6 months

Bleeding from nasal lesion resolved

Complete disappearance of lip lesion

45% reduction in mandibular lesion

65 YRS

Metastatic Lung Adenocarcinoma

Prior lines of therapy

1. carboplatin + pemetrexed: progressed at **6 months**
2. docetaxel: progressed at **4 months**

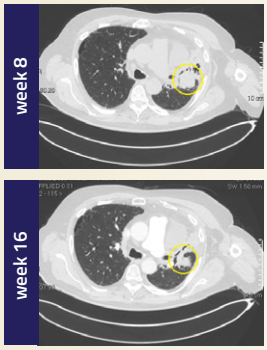
NUC-7738
starting dose 42 mg/m^2
(4 dose escalations)

6 months treatment duration

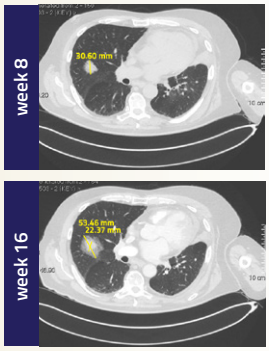
46% reduction in lung lesion 1

Change in character in lung lesion 2

Target Lesion 1:
Encouraging signs of anti-tumour activity with a **46% reduction** in lesion between Week 8 and Week 16 (41mm to 22mm).



Target Lesion 2:
"Small dense core surrounded by a larger diffuse ground-glass periphery". This may be indicative of lymphocyte infiltration into the tumor and/or other changes to the TME.



Symeonides *et al* (2022) Ann Oncol: 33: Suppl 7 Abstract ID 455MO (ESMO oral September 2022). Data cut-off: July 7, 2022

Key takeaways

NUC-7738 demonstrates encouraging signs of anti-cancer activity, particularly in cutaneous melanoma

NUC-7738 has a favorable safety profile

NUC-7738 has an attractive PK profile