ONGOING

NUTIDE:701 - PART 2

SOLID TUMOR - PHASE 2 STUDY (COMBINATION)

Designed to assess NUC-7738 in combination with pembrolizumab in patients with melanoma who had failed prior PD-1 inhibitor based therapy

Key Eligibility Criteria

- Cutaneous melanoma
- Immunotherapy experienced
- ECOG 0-1
- Exhausted all treatment options

Phase 2

NUC-7738
(1125 mg/m²)*
Q1W
+
pembrolizumab
(200 mg)
Q3W

Objective	▪ Establish RP2D
Key endpoints	▪ Safety & tolerability ▪ Anti-tumor activity ▪ PK
Patient population	▪ PD-1 inhibitor resistant patients

*Starting dose was 1125 mg/m² which was escalated to 1350 mg/m² if well tolerated

Number of patients	Age (median)	Prior lines of therapy (median)*
12	64 (range 18-67)	2 (range 1-3)

Prior Therapy: median (range)	2 (1-3)
PD-1 inhibitor	12
PD-1 inhibitor (adjuvant)	8
PD-1 inhibitor (non-adjuvant)	8
CTLA-4 inhibitor	11
PD-1 + CTLA inhibitor	9
BRAF + MEK inhibitor	1

*Including adjuvant

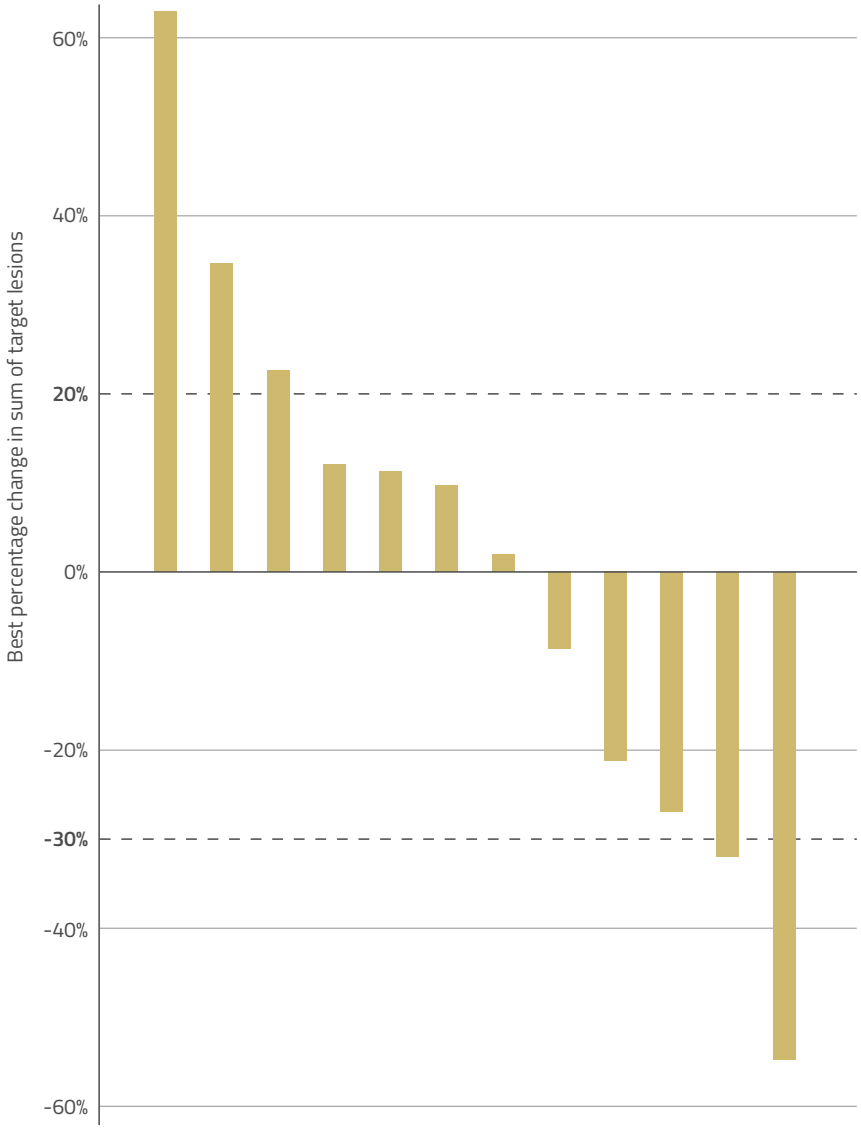
NUC-7738 plus pembrolizumab has been well tolerated

	NUC-7738 + pembrolizumab (n=12)		
	All Grades, n(%)	Grade 3, n(%)	Grade 4, n(%)
Nausea	9 (75)	0	0
ALT increased	6 (50)	1 (8)	1 (8)
Diarrhea	6 (50)	1 (8)	0
Vomiting	6 (50)	1 (8)	0
Anemia	5 (42)	0	0
AST increased	4 (33)	1 (8)	1 (8)
ALP increased	2 (17)	0	0
Blood magnesium decreased	2 (17)	0	0
Blood sodium decreased	2 (17)	0	0
Decreased appetite	2 (17)	0	0
Fatigue	2 (17)	1 (8)	0
GGT increased	2 (17)	1 (8)	0
Hypophosphatemia	2 (17)	0	0
Rash	2 (17)	0	0

- Low rates of Grade ≥3 toxicities
- 1 patient experienced Grade 4 transaminitis (ALT/AST increased)

All Grade TRAEs with prevalence ≥10% patients related to NUC-7738, pembrolizumab or both
Additional Grade 3 TRAEs ≤10%: abdominal pain (1 pt); immune-mediated hepatitis (1 pt); adrenal insufficiency, hypercalcemia and hypotension (1 pt).
No additional Grade 4 TRAEs

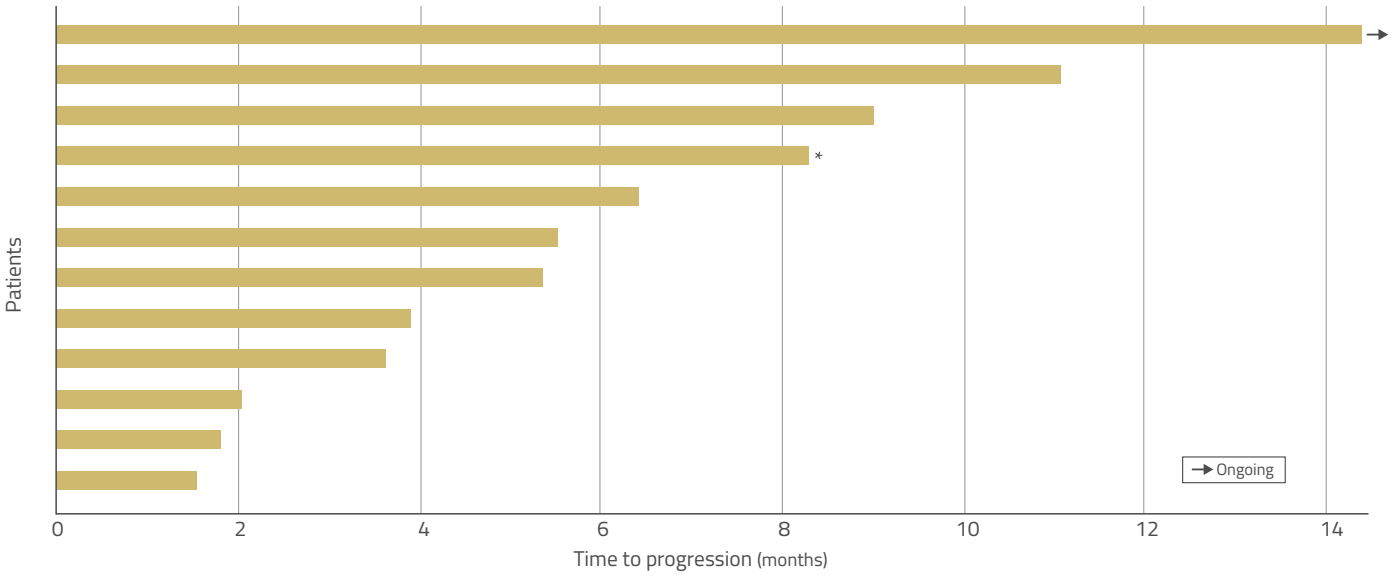
Encouraging anti-tumor activity in PD-1 inhibitor resistant patients



- Patient previously refractory to PD-1 inhibitor (nivolumab) + CTLA-4 inhibitor (ipilimumab) had 55% reduction
- Patient with resistance to PD-1 inhibition (pembrolizumab) had 32% reduction

Durable PFS in PD-1 inhibitor resistant patients

- PD-1 inhibitor rechallenge typically achieves PFS of 2-3 months in this patient population

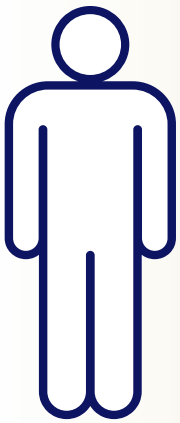


*Patient had mixed response with almost all sub-cutaneous lesions resolved and just two lymph nodes that required RT with resection intended. Patient remains on therapy.

Case Study 1

Partial Response in patient refractory to PD-1 inhibition

63 YRS



Metastatic Cutaneous Melanoma

Recieved 2 prior PD-1 inhibitor containing regimens

1. Nivolumab ± relatlimab (adjuvant):
   3.5 months until progression
2. Ipilimumab + nivolumab:
   1.5 months until progression

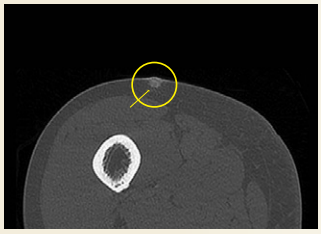
2 target lesions (skin)
BRAF wt

NUC-7738 (1125 mg/m² Q1W)
+ pembrolizumab (200 mg Q3W)

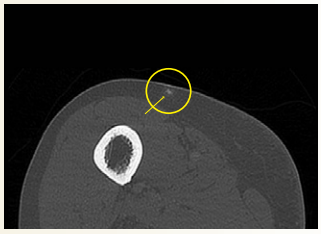
NUC-7738 + pembrolizumab

Partial Response (confirmed): 55% reduction in sum of target lesions
- 42% reduction in target lesion 1
- 70% reduction in target lesion 2 (see scans)

Time to progression 9 months
- 5 months treatment, discontinued due to unrelated SAE
- No further therapy, PR sustained for additional 4 months



Baseline: 1.0cm

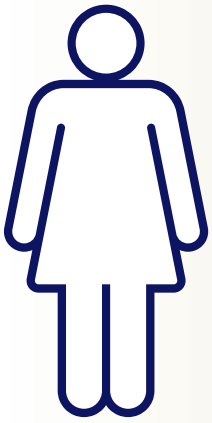


Week 17: 0.3cm

Case Study 2

Evidence of anti-cancer immune response in TME

67 YRS



Metastatic Cutaneous Melanoma

Recieved 3 prior PD-1 inhibitor containing regimens

1. Pembrolizumab (adjuvant):
   7 months until progression
2. Ipilimumab + nivolumab:
   3 months, stopped due to colitis, and progressed
3. IMM60 + pembrolizumab:
   5 months until progression

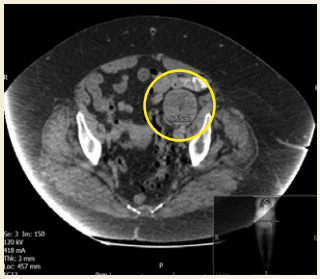
2 target lesions (lymph node)
BRAF wt

Starting dose: NUC-7738 (1125 mg/m² Q1W)
+ pembrolizumab (200 mg Q3W)
C8D1 onwards: NUC-7738 (900 mg/m² Q3W)
+ pembrolizumab (200 mg Q3W)

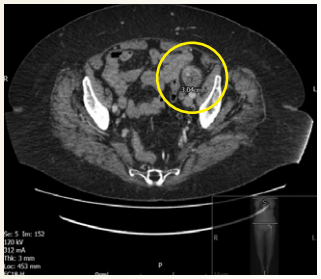
NUC-7738 + pembrolizumab

Partial Response (unconfirmed): 32% reduction in sum of target lesions
- 22% reduction in target lesion 1
- 45% reduction in target lesion 2 (see scans)

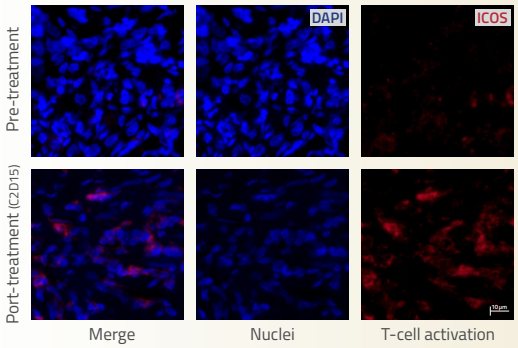
Time to progression 8 months
- Remains on treatment at 10 months due to clinical benefit (mixed response to oligometastatic disease; palliative radiotherapy to progressive lesions)



Baseline: 5.53cm



Week 24: 3.04cm



T-cell activation post-treatment
- Increased expression of ICOS (red) post-treatment indicates T-cell activation

Blagden *et al* (2024) ESMO September 2024. Data cut-off: August 1, 2024

Key takeaways

NUC-7738 + pembrolizumab has shown tumor reductions and prolonged disease control in PD-1 inhibitor resistant patients

NUC-7738 + pembrolizumab has a favorable safety profile

Combination RP2D: 1125 mg/m² NUC-7738 (Q1W) + 200 mg pembrolizumab (Q3W)