ONGOING

NUTIDE:303 - MODULE 1/NUC-3373 + pembrolizumab

SOLID TUMOR - MODULAR PHASE 1b/2 STUDY

Designed to assess the safety of NUC-3373 in combination with pembrolizumab

Key Eligibility Criteria

- Advanced solid tumors
- RECIST v1.1 measurable disease
- ECOG PS 0-1

Phase 1b
NUC-3373
(1875 mg/m²)
Q1W
+
pembrolizumab
(200 mg/m²)
Q3W

Objectives	▪ Determine safety & tolerability of NUC-3373 in combination with pembrolizumab
Key endpoints	▪ Safety ▪ Anti-tumor activity
Patient population	▪ Progressed on ≤2 prior lines of therapy, may include a PD-(L)1 inhibitor

NUC-3373 + pembrolizumab

Number of patients	Age (median)	Prior chemotherapy regimens (median)*
13	68 (range 49-75)	1 (range 0-2)

Sex	Male Female	11 (85%) 2 (15%)
ECOG PS	0 1	4 (31%) 9 (69%)
Metastatic sites, n	≤3 ≥4	11 (85%) 2 (15%)

Middleton *et al* (2024) medRxiv doi: 10.1101/2024.11.07.24316829. Data cut-off: October 8, 2024

*for metastatic disease

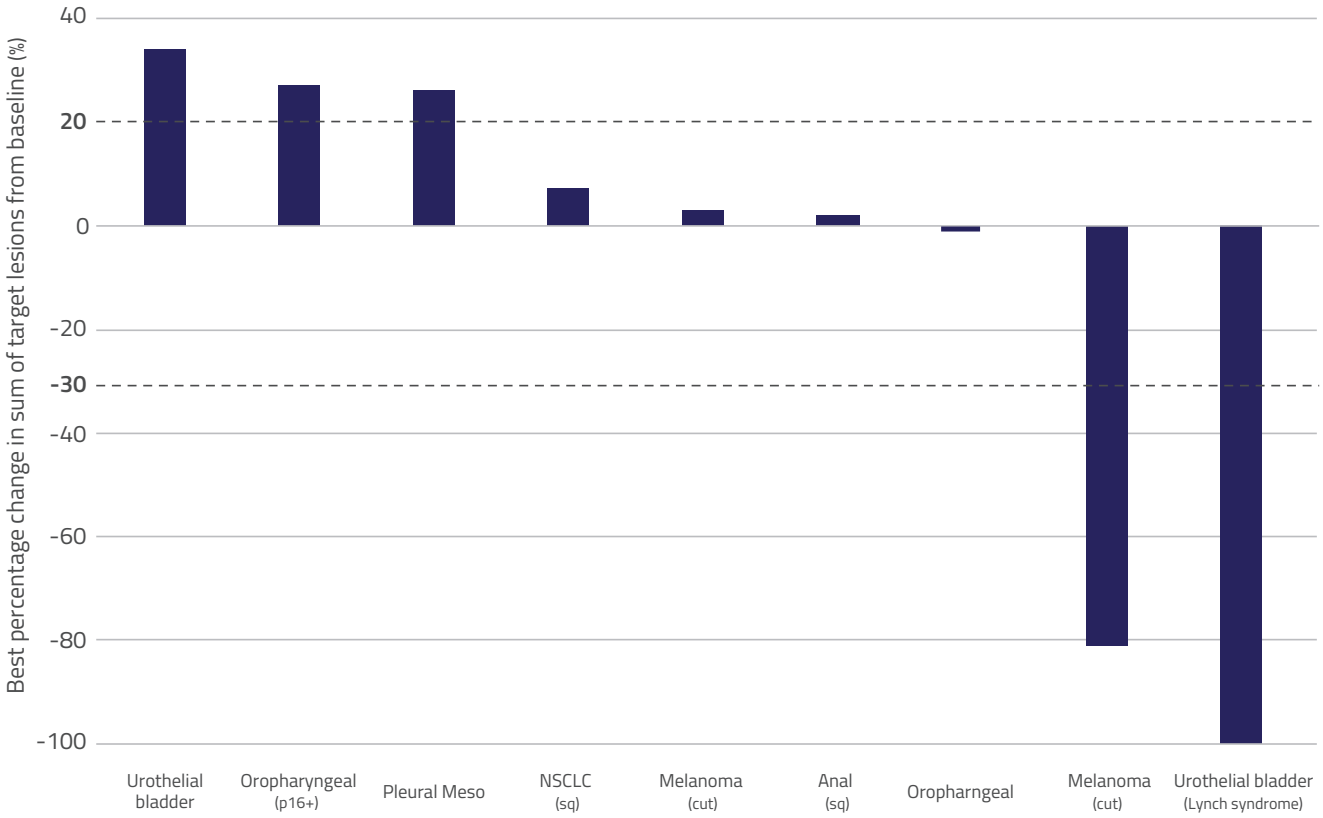
NUC-3373 + pembrolizumab has been well tolerated

	NUC-3373 + pembrolizumab (n=13)		
	All Grades, n(%)	**Grade 3, n(%)**	**Grade 4, n(%)**
Nausea	9 (69)	0	0
Vomiting	9 (69)	0	0
Diarrhea	6 (46)	0	0
Fatigue	5 (38)	0	0
AST increased	4 (31)	0	0
Infusion related reaction	4 (31)	0	0
Anemia	3 (23)	0	0
Constipation	3 (23)	0	0
ALT increased	3 (23)	0	0
Hot flush	3 (23)	0	0
Abdominal pain	2 (15)	0	0
Flushing	2 (15)	0	0

All Grade TRAEs with prevalence ≥15% patients related to NUC-3373, pembrolizumab or both
1 patient experienced Grade 3 hyponatremia

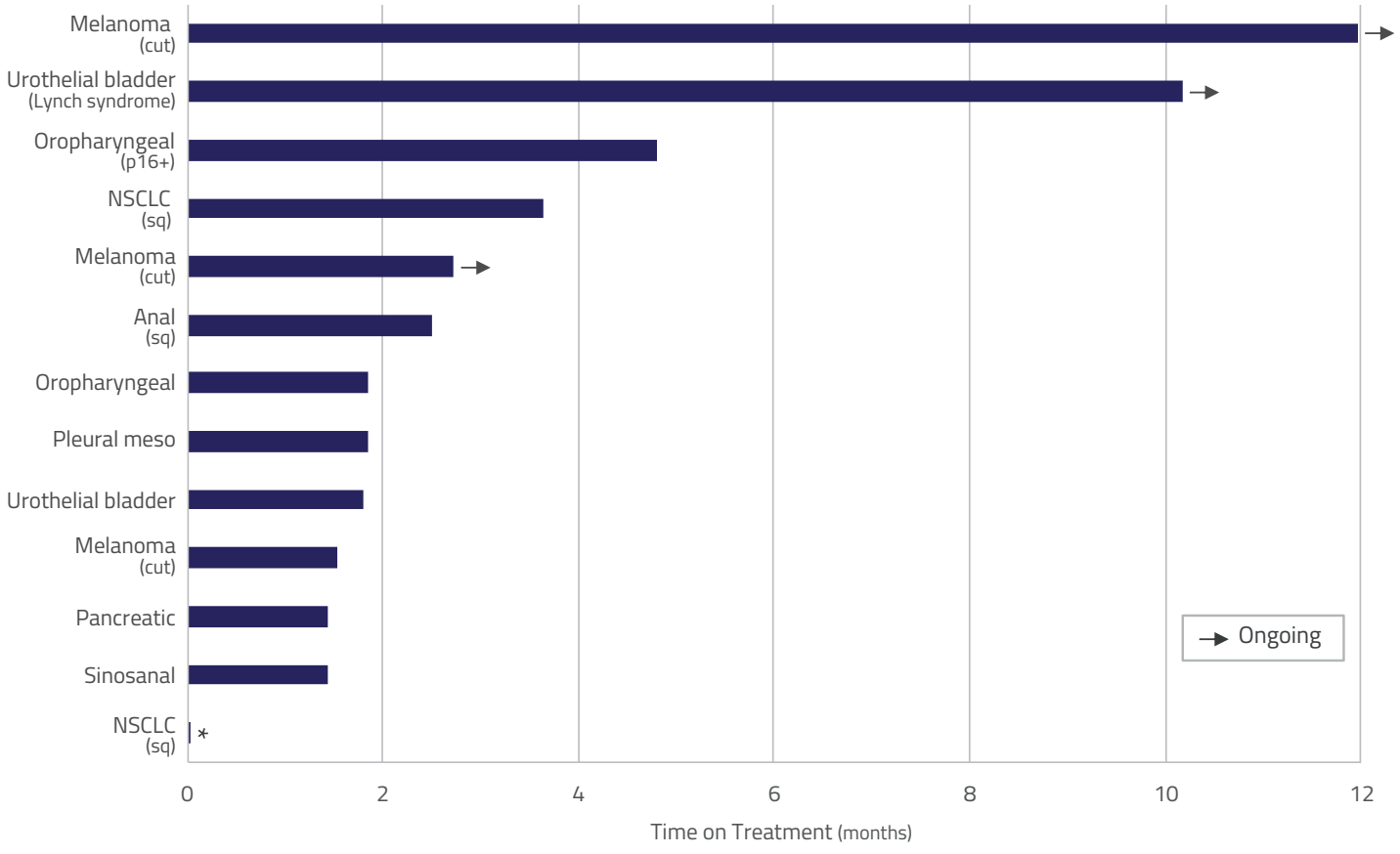
- 1 patient experienced Grade 3 hyponatremia
- No Grade 4 toxicities

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



- Patient who had previously received PD-L1 inhibitor (atezolizumab) had 100% reduction in sum of target lesions
- Patient with resistance to PD-1 inhibition (pembrolizumab) had 81% reduction

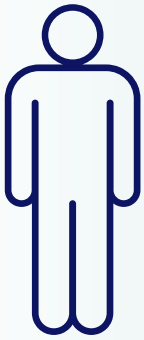
Encouraging time on treatment



*Patient only received 1 dose of study treatment and was not DLT-evaluable

Partial Response in PD-(L)1 inhibitor experienced patients

75 YRS
BRAF mt



Cutaneous Melanoma

Prior lines of therapy

1) pembrolizumab:
progressive disease within **5 months**

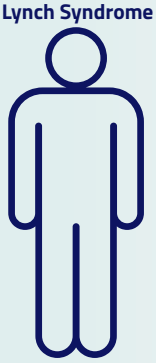
2) trametinib + dabrafenib:
trametinib discontinued after **1 month** (toxicity) dabrafenib for 7 years (progressive disease)

NUC-3373 1875 mg/m² + pembrolizumab 200 mg
- 1 target lesion (bilateral lymph node)

Partial Response (confirmed): 81% reduction in tumor volume

Treatment duration: 12+ months (ongoing)
- No dose reductions

72 YRS
Lynch Syndrome



Bladder Cancer

Prior lines of therapy

1) gemcitabine + cisplatin (adjuvant):
discontinued due to myelosuppression **2 months**

2) atezolizumab (metastatic):
best response SD, discontinued after **23 months**

NUC-3373 1875 mg/m² + pembrolizumab 200 mg
- 1 target lesion (lung)

100% reduction in sum of target lesions

Partial Response (confirmed): due to presence of non-target lesions

Treatment duration: 10+ months (ongoing)
- No dose reductions

Key takeaways

NUC-3373 + pembrolizumab has shown tumor reductions and prolonged disease control in PD-(L)1 inhibitor experienced patients

NUC-3373 + pembrolizumab has a favorable safety profile

Combination RP2D: 1875 mg/m² NUC-3373 (Q1W) + 200 mg pembrolizumab (Q3W)