



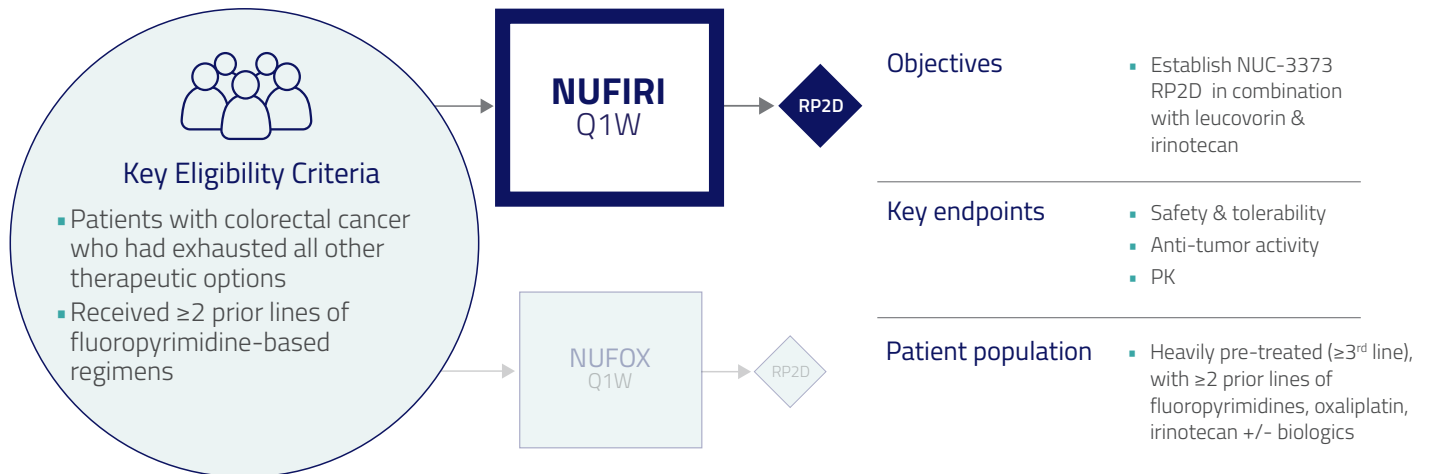
COMPLETE



NUTIDE:302 - PART 2 / NUFIRI

COLORECTAL CANCER - PHASE 1b STUDY

Designed to establish the RP2D of NUC-3373 + leucovorin in combination with irinotecan



NUFIRI

Number of patients

23

Age (median)

56

(range 36-74)

Prior chemotherapy regimens (median)

4

(range 2-10)

Sex	Male Female	8 (35%) 15 (65%)
ECOG PS	0 1	12 (52%) 11 (48%)
Metastatic sites, n	1-3 ≥ 4	12 (52%) 11 (48%)
KRAS mutated	Yes No	17 (74%) 5 (22%)
Prior bev exposure	Yes No	14 (61%) 9 (39%)

Coveler *et al* (2022) Ann Oncol; 33: Suppl 7 Abstract ID 354P (ESMO September 2022). Data cut-off: August 5, 2022

NUC-3373 is well tolerated in combination with leucovorin + irinotecan

	NUFIRI (n=23)		
	All Grades, n(%)	Grade 3, n(%)	Grade 4, n(%)
Nausea	10 (43%)	1 (4%)	0
Diarrhea	7 (30%)	2 (9%)	0
Vomiting	6 (26%)	0	0
Colitis	2 (9%)	1 (4%)	0
ALT increased	5 (22%)	2 (9%)	0
AST increased	3 (13%)	0	0
ALP increased	1 (4%)	1 (4%)	0
Appetite decreased	5 (22%)	0	0
Hypomagnesemia	3 (13%)	0	0
Anemia	5 (22%)	0	0
Fatigue	7 (30%)	2 (9%)	0
Proteinuria	1 (4%)	1 (4%)	0

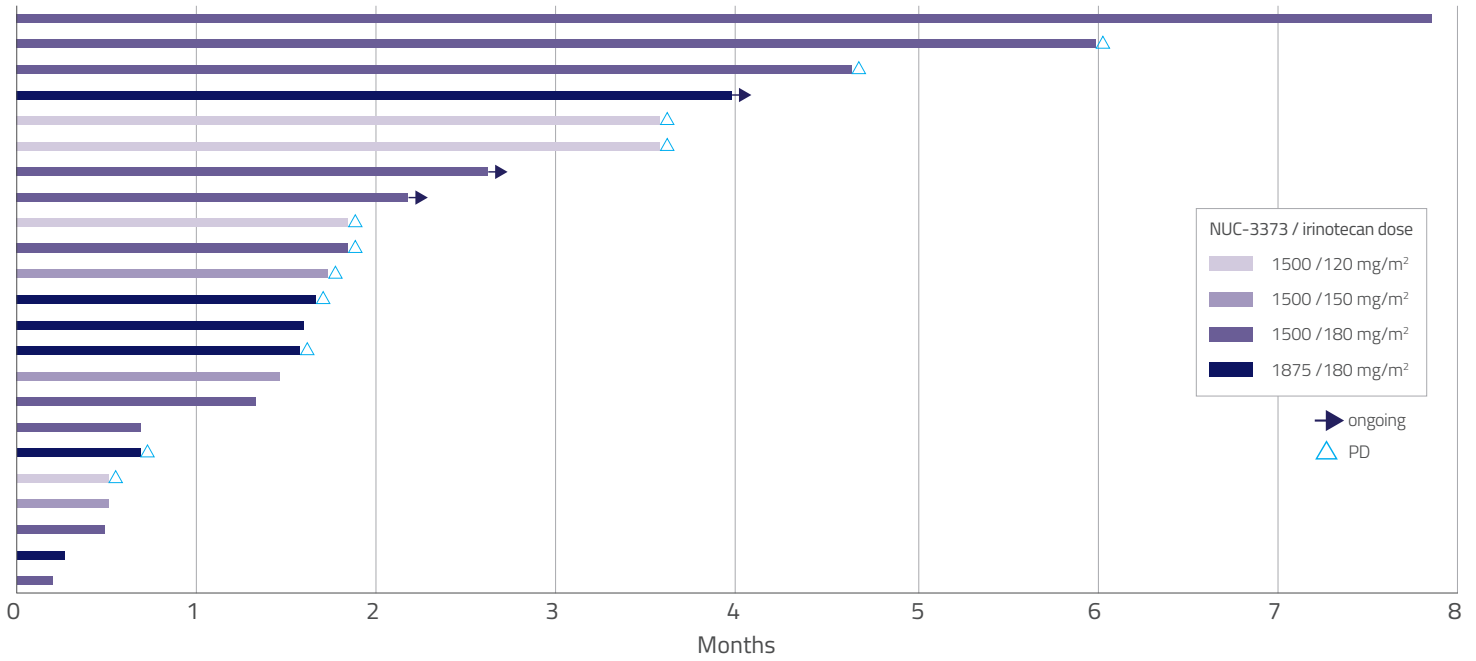
- No Grade 4 toxicities
- Low rates of Grade 3 toxicities
- DLTs in 3 patients
 - Grade 3 ALT/ALP increased (1 pt at NUC-3373 1500 mg/m² + irinotecan 180 mg/m²)
 - Grade 3 colitis (1 pt at NUC-3373 1875 mg/m² + irinotecan 180 mg/m²)
 - Grade 3 fatigue (1 pt at NUC-3373 1875 mg/m² + irinotecan 180 mg/m²)
- MTD: NUC-3373 1500 mg/m² + LV 400 mg/m² (Q1W) + irinotecan 180 mg/m² (Q2W)

TRAEs reported are related to NUC-3373 or NUC-3373 & irinotecan; All Grade TRAEs with incidence of $\geq 10\%$ in any dose cohort; All Grade 3 TRAEs reported.

NUC-3373 PK profile unchanged by irinotecan

- Irinotecan had no impact on NUC-3373 exposure

Encouraging treatment duration in a heavily pre-treated population



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Key takeaways

NUFIRI has shown encouraging signs of clinical activity in heavily pre-treated patients

NUFIRI has a favorable safety profile compared to FOLFIRI historical data

NUFIRI RP2D determined:
 NUC-3373: 1500 mg/m²
 LV: 400 mg/m²
 Irinotecan: 180 mg/m²