DISCONTINUED

NUTIDE:323

COLORECTAL CANCER - PHASE 2 RANDOMIZED STUDY

Designed to assess the efficacy and safety of NUC-3373 in the second-line CRC setting

Key Eligibility Criteria

- Patients with metastatic colorectal cancer who have received 1 prior line of fluoropyrimidine and oxaliplatin-containing therapy
- RECIST v1.1 measurable disease
- ECOG PS 0-1

NUFIRI Q1W + **bevacizumab** (n=57)

NUFIRI Q2W + **bevacizumab** (n=65)

FOLFIRI Q2W + **bevacizumab** (n=60)

Objectives

- Compare PFS of NUFIRI + bev to FOLFIRI + bev
- Determine NUFIRI + bev dosing schedule

Key endpoints

- PFS
- Anti-tumor activity
- Safety & PK

Patient population

- Patients with previously treated unresectable metastatic colorectal cancer

NuTide:323 is a randomized, open-label, Phase 2, dose/schedule optimization study of NUC-3373 + LV + irinotecan + bevacizumab (NUFIRI + bev) versus 5-FU + LV + irinotecan + bevacizumab (FOLFIRI + bev) in patients with previously treated unresectable metastatic colorectal cancer (EudraCT 2022-001459-17; NCT05678257).

Patients must have previously received ≥2 months of a first-line fluoropyrimidine and oxaliplatin-containing regimen or have relapsed within 6 months of completing a fluoropyrimidine and oxaliplatin-containing neoadjuvant/adjuvant therapy. Patients must also have known RAS status and an ECOG performance status 0-1. Patients with MSI-H, dMMR or BRAF V600E mutations are not eligible.

A total of 182 patients have been randomized 1:1:1 to either NUFIRI + bev on a Q1W NUC-3373 + LV schedule (Arm A), NUFIRI + bev on a Q2W NUC-3373 + LV schedule (Arm B), or FOLFIRI + bev on a Q2W 5-FU + LV schedule (Arm C). In all arms, irinotecan and bevacizumab were administered on a Q2W schedule. Randomization was stratified by RAS status (wild-type vs KRAS mutant vs NRAS mutant), prior bevacizumab treatment (yes vs no) and duration of prior line of therapy (<6 months vs ≥6 months).

The primary objectives of this study are to compare PFS in the NUFIRI + bev arms to the FOLFIRI + bev arm and to determine the optimal NUFIRI + bev dosing schedule. The primary endpoint is PFS. Secondary endpoints include other anti-tumor activity, safety, and PK assessments.

The NuTide:323 study was discontinued in August 2024, following a pre-planned initial analysis and recommendation from the NuTide:323 Study Steering Committee. While there were prognostic imbalances favoring the control arm, the Steering Committee believed that the combination of NUC-3373 with leucovorin, irinotecan and bevacizumab (NUFIRI+bev) was unlikely to achieve the study's primary objective of superior Progression Free Survival (PFS) compared to the control arm of 5-FU, leucovorin, irinotecan and bevacizumab (FOLFIRI+bev) in the final analysis. In all three arms, the treatment regimens were observed to have a favorable safety profile and to be generally well tolerated, with only 12 of the 175 patients (four patients in each arm) discontinuing treatment due to adverse events.