Background:
EZN-2208 is a water soluble, polymeric SN38 conjugate, EZN-2208 showed marked antitumor activity in mice that failed treatment with irinotecan.

Objectives
- Phase 2, multicenter, multiple-dose, open-label, multicenter, parallel-arm, cohort study to determine the safety and efficacy of EZN-2208 in combination with cetuximab in patients with mCRC whose tumors had K-RAS and / or NRAS mutations.
- Efficacy: Primary outcome measure: 2-year survival.
- Secondary outcome measures: 18-month survival, median duration of progression-free survival, time to progression, safety, and tolerability.

Methods:
Patients with metastatic colorectal cancer who are refractory to irinotecan treatment with irinotecan, oxaliplatin, and fluoropyrimidine (as above) were treated with single agent EZN-2208 (1 dose weekly for 3 weeks in 4 week cycles + 2208 (PEG 20K)) or combination with cetuximab.

Key eligibility criteria:
- Patients with any RECIST-defined measurable lesion not amenable to surgery or radiotherapy
- Life expectancy of at least 12 weeks
- No prior chemotherapy
- No prior irinotecan
- No prior cetuximab

Provision of SN38 increases its stability and half-life, yielding higher SN38 exposure in patients with mCRC.

Primary Objectives
- Defer the line of therapy (PO) of EZN-2208 for phase II patients in combination with cetuximab.
- Patients with irinotecan-refractory CRC whose tumors have K-RAS and/or NRAS mutations were treated with single agent EZN-2208 (Arm A) and EZN-2208 in combination with cetuximab (Arm B).

Secondary Objectives
- Evaluate d'orioni of doxorubicin (DOR) for each treatment arm
- Evaluate DOSS and safety for each treatment arm
- Evaluate primary and secondary endpoints in Arm B with those seen in Arm A.
- Safety parameters were assessed.

Conclusions
The primary objective was to defer the line of therapy (PO) of EZN-2208 for phase II patients in combination with cetuximab.

References