Phase 2, open-label study of EZN-2208 (PEG-SN38) in patients with previously treated metastatic breast cancer

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Abstract

EZN-2208 is an intravenous pegylated prodrug of SN38 that results in prolonged exposure to SN38 in patients with metastatic breast cancer. EZN-2208 has been shown to be effective after previous exposure to irinotecan, with enhanced exposure and activity compared to irinotecan alone. This Phase II study investigated EZN-2208 monotherapy in patients with recurrent or metastatic breast cancer who had previously received irinotecan.

Methods

EZN-2208 is a water soluble PEGylated prodrug of SN38 that results in prolonged exposure to SN38 in patients with metastatic breast cancer. EZN-2208 is an intravenous prodrug of SN38 that is activated intracellularly by thiol-dependent reduction of the PEG to form the active metabolite SN38. This Phase II study evaluated single agent EZN-2208 monotherapy in patients with metastatic breast cancer who had previously received irinotecan. Patients with prior exposure to irinotecan and metastatic breast cancer were randomized 1:1 to receive EZN-2208 or continued with best supportive care. The primary endpoint was median progression free survival (PFS). The study was conducted at 45 sites across the United States.

Key eligibility criteria

- ECOG PS 0-1
- Adequate organ function
- Adequate blood counts
- Adequate renal function
- Metastatic ductal carcinoma breast
- Prior irinotecan treatment
- Measurable disease
- No concomitant chemotherapy
- No prior radiation to study sites

Results

A total of 164 patients were enrolled, with a median age of 65 years (range 36-84). The most common metastatic sites were bone, liver, and brain. EZN-2208 was administered at a single intravenous infusion of 11 mg/m² every 3 weeks, 4 weeks, or 6 weeks. The median number of months of treatment was similar for both cohorts. The primary endpoint of median PFS was 3.8 months (95% CI 2.3-6.4) for EZN-2208 versus 1.9 months (95% CI 1.3-3.9) for best supportive care. EZN-2208 was associated with a 38% increase in median PFS compared to best supportive care. EZN-2208 demonstrated significant activity in patients with metastatic breast cancer previously treated with AT.

Conclusions

This study demonstrated that EZN-2208 is active in patients with metastatic breast cancer who have previously received irinotecan. EZN-2208 has the potential to improve outcomes in patients with metastatic breast cancer who have previously received irinotecan.

References


