Phase I Trial of Polyethylene Glycol (PEG) Conjugated SN38 in Children with Recurrent or Refractory Neuroblastoma (NB) and Other Solid Tumors

R Norris1, S Shusterman1, L Gore1, M Macy2, J Muscal2, E Fox1, Y Mosse1, N Berkowitz5, A Buchbinder1, R Bagatell1

1The Children’s Hospital of Philadelphia, Philadelphia PA; 2Dana-Farber Cancer Institute and Children’s Hospital Boston, Boston MA; 3University of Colorado and Children’s Hospital Colorado, Aurora CO; 4Baylor College of Medicine/Texas Children’s Hospital, Houston TX; 5Enzon Pharmaceuticals, Piscataway NJ

BACKGROUND
- Topoisomerase-1 inhibitors are used for treatment of children with NB and other solid tumors
- EZN-2208 is a water-soluble PEG conjugate of the topoisomerase-1 inhibitor SN38, the active metabolite of irinotecan
- EZN-2208 has a prolonged half-life, permitting extended exposure to SN38
- In preclinical NB models, antitumor activity of EZN-2208 is superior to that of irinotecan
- Febrile neutropenia is dose-limiting in adults
- EZN-2208 is a topoisomerase-1 inhibitor SN38, the active metabolite of irinotecan
- Topoisomerase-1 inhibitors are used for treatment of children with NB and other solid tumors

OBJECTIVE
- Diarrhea
  - Grade 3
    - Diarrhea (n=1)
    - Additional dose levels were: 16 mg/m²

PRIMARY OBJECTIVE
- To determine the MTD or recommended Phase 2 dose

STUDY DESIGN
- A Rolling 3 design was used; accrual was suspended when a cohort of 6 patients was enrolled
- The lowest dose level (12 mg/m²) was superior to that of irinotecan
- Objective responses lasting >10 months were seen in 2 out of 4 pts with NB and measurable disease
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RESPONSE
- Response was assessed using RECIST v1.1 after every 2 cycles
- Modified INRC criteria were used for assessment of bone and bone marrow disease
- MIBG scans were used for assessment of bone and bone marrow disease
- Tumor Type
  - Neuroblastoma
  - Sarcoma
  - Other

PATIENT CHARACTERISTICS

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Enrolled</th>
<th>Evaluable disease</th>
<th>Prior SCT</th>
<th>Prior Irinotecan</th>
<th>Prior Topotecan</th>
<th>Prior SN38</th>
<th>Prior Topoisomerase-1 inhibitor SN38</th>
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<td>Neuroblastoma</td>
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<td>11</td>
<td>30</td>
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<tr>
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Cycles 1-4

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<tr>
<th>Cycle</th>
<th>Dose Level</th>
<th>EZN-2208 (mg/m²)</th>
<th>DLT</th>
<th>Dose Level</th>
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<td>Baseline</td>
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<td>Diarrhea (n=1)</td>
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<td>5</td>
<td>Thrombocytopenia (n=2)</td>
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