**INTRODUCTION**

Etiroprone pegol (WPT-103) is a long-acting topoisomerase 1 inhibitor designed for prolonged tumor cell exposure.

- **In patients:** etiropone pegol leads to greatly prolonged plasma SN38 exposure compared to irinotecan (elimination half-life 50 days compared to 2 days), per maximal SN38 concentrations are at least 5- to 10-times higher.
- **In a Phase 3 trial:** patients with metastatic breast cancer whose disease had failed prior taxane-based treatment, etiropone pegol administered IV q14d or q21d. 21% of patients achieved a partial response, showing similar overall response rates.

**Objective Response Rate of Etiropone pegol in Patients with Metastatic Breast Cancer**

<table>
<thead>
<tr>
<th><strong>Treatment</strong></th>
<th><strong>Pts</strong></th>
<th><strong>PR or CR</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>IV q14d</td>
<td>100</td>
<td>21%</td>
</tr>
<tr>
<td>IV q21d</td>
<td>100</td>
<td>21%</td>
</tr>
</tbody>
</table>

**BEACON CTC SAMPLE FLOW**

- **Enrollment in BEACON:** A Phase 3, open-label, multi-country, multicenter trial in patients with metastatic breast cancer whose disease had failed prior taxane-based treatment.
- **Biomarkers:** Target-specific biomarkers of DNA damage/apoptosis were measured in CTCs isolated from patients participating in BEACON.

**BIOMARKER SELECTION**

- **CTCs** isolated from patients with breast cancer that had failed prior taxane-based treatment.
- **Biomarkers:** Target-specific DNA damage/apoptosis biomarkers were measured in CTCs isolated from patients participating in BEACON.

**Biomarkers**

- **Topoisomerase 2 (Top 2):** Increased levels of Top 2 are associated with resistance to SN38.
- **H2Ax:** Increased percentage of H2Ax-positive CTCs have been reported after treatment with Top 1 inhibitors.
- **Ki-67:** Increased Ki-67 index is a higher chemosensitivity and is a prognostic factor.
- **ABCG2:** Increased expression of ABCG2 is associated with lower chemosensitivity.
- **TdT:** Increased TdT activity is associated with DNA strand breaks.

**EXPRESSION OF BIOMARKER SIGNAL IN BASELINE SAMPLES**

- **CTCs detected in 97% of patients with high median number of CTCs**

**METHODS**

CTC samples were isolated using ApoStream CTC isolation system.

**BEACON CTC SAMPLING SCHEME AND PATIENT PARTICIPATION**

- **CTCs detected in 97% of patients with high median number of CTCs**

**CONCLUSIONS**

- **Blood sample collection for CTC analysis:** was successfully incorporated into the BEACON study with 80% patient participation.
- **Blood samples:** were successfully processed, with a low technical failure rate of 2%.
- **CTC detection rate:** using ApoStream was high (97% of patients; median # of CTCs: 472 CTCs/7.5 mL) and permitted evaluation of biomarkers at baseline and over time.
- **CTC detection rate:** was high in patients with breast cancer that had failed prior taxane-based treatment.
- **ETI-1604:** Etiropone pegol target-specific pharmacodynamic biomarkers can be measured in CTCs isolated from patients participating in BEACON.

**CTC Detection Rate**

- **CTCs detected in 97% of patients with high median number of CTCs**

**REFERENCES**