A PHASE 2 DOSE REGIMENT OPTIMIZATION STUDY OF THREE SCHEDULES OF VORELOXIN AS SINGLE AGENT THERAPY FOR ELDERLY PATIENTS WITH NEWLY DIAGNOSED ACUTE MYELOID LEUKEMIA

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ABSTRACT - UPDATED

Background: Voreloxin is a novel, first-in-class, orally administered anticancer quinolone derivative (AQD), 5-ethyl-N-(3,4-dimethoxyphenyl)-3-fluoro-1-quinoline carboxamide, with potent and selective properties that include DNA damage analogous to quinolone antibacterials and inhibits topoisomerase II, inducing apoptosis. REVEAL-1, a Phase 2 dose regimen optimization study of 3 schedules of single agent voreloxin, was conducted in newly diagnosed acute myeloid leukemia (AML) patients aged ≥60 with 1 additional adverse risk factor. Median age was 75 ± 17 years, 67% of whom presented with ≥1 adverse risk factor as defined by NCCN guidelines; 59% had a history or recent myocardial infarction or thromboembolic events. Primary: Overall response rate (ORR) ≥CR - 72 mg/m2 qw x 2. Secondary: 30-day all-cause mortality, overall survival, leukemia-free survival, duration of response, and PK.

Study Design

- A randomized, open-label, multicenter Phase 2 study of 3 schedules of single agent voreloxin, in newly diagnosed AML patients aged ≥60 with 1 additional adverse risk factor as defined by NCCN guidelines.
- Evaluates the efficacy and safety of 3 dose regimens:
  - Sch A: 72 mg/m2 qw x 2, N=35
  - Sch B: 72 mg/m2 qw x 3, N=29
  - Sch C: 72 mg/m2 on D1,4, N=29

Population

- AML patients aged ≥60 with 1 adverse risk factor were enrolled from 21 centers in the U.S.
- Composition of adverse risk factors:
  - Performance status: ≤2
  - Age: ≥75
  - History or recent myocardial infarction or thromboembolic events
  - Additional risk factors: ≥1
- Exclusion Criteria:
  - Previously treated AML
  - Concurrent use of other investigational medicinal products

OUTCOME – OVERALL

Sch – Voreloxin Dose N (%)

<table>
<thead>
<tr>
<th>Sch A: 72 mg/m2 qw x 2</th>
<th>Sch B: 72 mg/m2 qw x 3</th>
<th>Sch C: 72 mg/m2 on D1,4</th>
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<tbody>
<tr>
<td>CR (CRp)</td>
<td>CR (CRp)</td>
<td>CR (CRp)</td>
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<td>7 (20%)</td>
<td>7 (20%)</td>
<td>4 (14%)</td>
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<tr>
<td>N/AN/A</td>
<td>9 (26%)</td>
<td>8 (28%)</td>
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Reinduction was performed in 35% of reinduced patients. 12 of 13 patients who achieved CR or CRp remain alive. 1 patient died of cardiovascular acute myocardial infarction. Acknowledgments: Ritva Torma, MDACC; Mary Cangany, Bobbie Frye, IU; Margaret Green, RMBMT; Jamal Jamal, St Francis Hospital; Francesco Rubini, MD, PhD, Arizona Cancer Center; Jonathan W. Licht, PhD, University of Pittsburgh; and Robert G. Anderson, MD, PhD, Duke University Medical Center.

http://www.sunesis.com/science/presentations_and_publications.php