Phase III Study of Vosaroxin and Decitabine in Older Patients (pts) with Acute Myeloid Leukemia (AML) and High Risk Myelodysplastic Syndrome (MDS)
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Abstract
Background: Vosaroxin (foremoxane), is a first-in-class anti-cancer quinoline derivative (AQD) DNA topoisomerase II inhibitor, which is not a substrate for P-gp or P-glycoprotein, has limited toxicity, and is currently under evaluation for the treatment of pts with AML and high-risk MDS. Methods: Pts were eligible if they had AML, or high-risk MDS (defined as having ≥10% blasts in the bone marrow), were 60 years of age or older, and had adequate performance status (ECOG ≤ 2) and organ function. Pts younger than 60 who were unsuitable for standard chemotherapy were also eligible. The treatment regimen included vosaroxin 90 mg/m² daily on days 1 and 4 with decitabine 20 mg/m² daily for 5 days. Vosaroxin dose was reduced to 70 mg/m² in pts with >10% blasts in the bone marrow. Pts were eligible if they had AML or high-risk MDS (defined as having ≥10% blasts in the bone marrow), were 60 years of age or older, and had adequate performance status (ECOG ≤ 2) and organ function. Pts younger than 60 who were unsuitable for standard chemotherapy were also eligible. The treatment regimen included vosaroxin 90 mg/m² daily on days 1 and 4 with decitabine 20 mg/m² daily for 5 days. Vosaroxin dose was reduced to 70 mg/m² in pts with >10% blasts in the bone marrow. Pts younger than 60 who were unsuitable for standard chemotherapy were also eligible.

The non-overlapping toxicology profile of vosaroxin and decitabine and their distinct anti-leukemic activities make them well suited for frontline combination therapy in elderly patients (≥60 years) with AML or high-risk MDS.

Objectives
Primary objectives (Phase II)
- To determine the overall response rate (ORR) of vosaroxin in combination with decitabine in patients with high-risk MDS or AML who are elderly (≥60) and/or insufficient hematological recovery (CRi).
- To determine the safety of vosaroxin in combination with decitabine in patients with high-risk MDS or AML who are elderly (≥60) and/or insufficient hematological recovery (CRi).

Secondary objectives (Phase II)
- To determine the safety of vosaroxin in combination with decitabine in patients with high-risk MDS or AML who are elderly (≥60) and/or insufficient hematological recovery (CRi).
- To determine the duration of response, disease-free survival (DFS), early mortality, and overall survival (OS) of pts with high-risk MDS or AML who are elderly (≥60).

Methods
- Pts were eligible if they had previously untreated AML or high-risk MDS (defined as having ≥10% blasts in the bone marrow), were 60 years of age or older, and had adequate performance status (ECOG ≤ 2) and organ function. Pts younger than 60 who were unsuitable for standard chemotherapy were also eligible.
- The treatment regimen included vosaroxin 90 mg/m² daily on days 1 and 4 with decitabine 20 mg/m² daily for 5 days.

Results:
- Pts were eligible if they had previously untreated AML or high-risk MDS (defined as having ≥10% blasts in the bone marrow), were 60 years of age or older, and had adequate performance status (ECOG ≤ 2) and organ function. Pts younger than 60 who were unsuitable for standard chemotherapy were also eligible.

Conclusions:
- Combination of vosaroxin and decitabine is effective and well tolerated in elderly patients with AML and high-risk MDS. Enrollment is ongoing.