Adaptive Design of VALOR, A Phase 3 Trial of Vosaroxin or Placebo in Combination with Cytarabine for Patients With First Relapsed or Refractory Acute Myeloid Leukemia

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**Adaptive Design: VALOR, A Phase 3 Trial of Vosaroxin or Placebo in Combination with Cytarabine for Patients With First Relapsed or Refractory Acute Myeloid Leukemia**

**Abstract**

Background: Standard treatments for patients with relapsed or refractory AML have not changed significantly to offer consistent overall survival benefit over the past 30 years, with expected median overall survival limited to 6 months, a significant unmet need that was the basis for the Phase 1b/2a study of vosaroxin. Previous studies in combination with concomitant chemotherapy as an initial salvage strategy was associated with prolonged overall survival with possible very high response rates but with a high rate of toxicity. In the Phase 1b/2a study, vosaroxin in combination with cytarabine in relapsed AML patients with a median of three prior regimens and a median time from last prior chemotherapy of 0.9 months was associated with a 28% overall response rate and improved overall survival (OS). Median OS was 6 months (95% CI: 2.3-7.3 months). In the Phase 1b/2a study, vosaroxin demonstrated similar activity in newly diagnosed AML patients with a high rate of lower-grade toxicity. The current study is a Phase 3 trial designed to confirm these findings and to evaluate the impact of an adaptive design, a strategy that allows for ongoing change in the study design based on accumulating data and early results.

**Adaptive Design of VALOR Trial**

The VALOR trial is a Phase 3 randomized study comparing vosaroxin plus cytarabine to placebo plus cytarabine in patients with first relapsed or refractory AML. The primary endpoint is 3 year overall survival (OS) and secondary endpoints include progression-free survival (PFS), response rate, and safety. The study incorporates an adaptive design feature, which allows for ongoing change in the study design based on accumulating data and early results. The study is designed to enroll 540 patients, who will be randomized 1:1 to either the experimental arm (vosaroxin plus cytarabine) or the control arm (placebo plus cytarabine). The study will be conducted in 150 centers with at least 10 patients per center. The study is planned to be completed in 4 years, with an anticipated median follow-up of 3 years.

**Results**

The adaptive design of the VALOR trial allows for flexibility in the study design based on accumulating data and early results. The primary endpoint is 3 year OS, and secondary endpoints include PFS, response rate, and safety. The study is designed to enroll 540 patients, who will be randomized 1:1 to either the experimental arm (vosaroxin plus cytarabine) or the control arm (placebo plus cytarabine). The study will be conducted in 150 centers with at least 10 patients per center. The study is planned to be completed in 4 years, with an anticipated median follow-up of 3 years.

**Conclusion**

The adaptive design of the VALOR trial allows for flexibility in the study design based on accumulating data and early results. The primary endpoint is 3 year OS, and secondary endpoints include PFS, response rate, and safety. The study is designed to enroll 540 patients, who will be randomized 1:1 to either the experimental arm (vosaroxin plus cytarabine) or the control arm (placebo plus cytarabine). The study will be conducted in 150 centers with at least 10 patients per center. The study is planned to be completed in 4 years, with an anticipated median follow-up of 3 years.

**Appendix**

The Appendix provides additional information and details related to the study design, including inclusion and exclusion criteria, study endpoints, and data analysis. This information is crucial for understanding the study's objectives and methodology, and for interpreting the results. It also includes a section on data safety and monitoring, which is essential for ensuring the ethical conduct of the trial and protecting the well-being of the participants.

**Author Contributions**

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**Disclosure**

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