Pharmacokinetics of AC220 and its Active Metabolite AC886, a FLT-3 Inhibitor, Following Sequential Oral Dose Escalation to Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)

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Abstract

AC220, a FLT-3 inhibitor, is being investigated for the treatment of Acute Myeloid Leukemia (AML). The objective of this Phase I clinical trial is to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of AC220 and its active metabolite AC886 in patients with relapsed or refractory AML. The trial will be conducted in two phases: an initial dose-escalation phase followed by a dose-optimization phase. The goal is to determine the maximum tolerated dose (MTD) and to assess the drug's potential efficacy in this patient population.

Methods

The trial will be conducted at multiple sites in the United States. Eligible patients will be those with relapsed or refractory AML who have failed standard therapies. The study will follow a standard 3+3 design, starting with a low dose and escalating to higher doses based on safety and tolerability. Pharmacokinetic samples will be collected at baseline and after each dose escalation. The primary endpoint is to determine the MTD and assess the safety profile of AC220.

Results

Figure 1: Summary Mean Plasma AC220 Concentration in Human Subjects on Day 1 following a single dose of AC220.

Figure 2: Summary Mean Plasma AC886 Concentration in Human Subjects on Day 1 following a single dose of AC220.

Figure 3: Summary Mean Plasma AC886 to AC220 Ratio on Day 1 following a single dose of AC220.

Figure 4: Summary Mean Plasma AC220 and AC886 AUC on Day 1 following a single dose of AC220.

Figure 5: Summary Mean Plasma AC220 and AC886 AUC on Day 1 following a single dose of AC220.

Figure 6: Summary Mean Plasma AC220 and AC886 AUC on Day 1 following a single dose of AC220.

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Conclusions

AC220 demonstrates promising safety, tolerability, pharmacokinetic, and pharmacodynamic profiles in patients with relapsed or refractory AML. The trial will continue to evaluate the drug's potential efficacy and safety in this patient population.

References

