Abstract: PB2454

Title: VICEROY: A PHASE I/II STUDY OF GILTERITINIB, VENETOCLAX AND AZACITIDINE COMBINATION IN PATIENTS WITH NEWLY DIAGNOSED FLT3-MUTATED ACUTE MYELOID LEUKEMIA INELIGIBLE FOR INTENSIVE INDUCTION CHEMOTHERAPY

Abstract Type: Publication Only

Topic: Acute myeloid leukemia - Clinical

Background:

Owing to poor outcomes with high relapse rates and limited survival, additional treatment options are needed for patients with FMS-like tyrosine kinase (FLT3)-mutated (mut+) acute myeloid leukemia (AML), including those with newly diagnosed (ND) disease who are not eligible for intensive induction chemotherapy due to older age or comorbidities. The complete remission (CR) rates and overall survival (OS) with azacitidine plus venetoclax in patients with ND FLT3mut+ AML remain poor at 38.1% and 12.5 months, respectively.

Aims:

The phase I/II VICEROY trial (NCT05520567) will evaluate the efficacy and safety of the combination of gilteritinib, venetoclax and azacitidine in adults with ND FLT3mut+ AML not eligible for intensive induction chemotherapy.

Methods:

This multicenter, open-label, randomized, two-phase, dose-ranging and expansion study will enroll ~70 patients aged ≥18 years with untreated FLT3mut+ AML ineligible for intensive induction chemotherapy at centers in North America. Patients will be excluded if they have acute promyelocytic leukemia, clinically active central nervous system leukemia, history of myeloproliferative neoplasms, or history of long QT syndrome or Fridericia-corrected QT interval >450 msec. Following screening, eligible patients will be randomized 1:1 to one of two venetoclax doses and evaluated for dose-limiting toxicities (DLTs) during the first 28 days of the phase I dose-ranging part (Figure 1). Primary objectives are to determine the optimized dose for the triple combination, and its safety, tolerability, efficacy and pharmacological activity. Phase II dose expansion phase will be initiated upon establishment of the optimized dose from phase I, provided that DLT rate is not above 0.238, safety event rate <0.2 and CR rate by the end of 3 cycles (or sooner) from either dose-ranging cohorts is >44%. Secondary objectives are to evaluate anti-leukemic activity of the triple combination, characterize the pharmacokinetics of gilteritinib, and evaluate depth of molecular response by measurable residual disease centrally assessed by a FLT3-ITD next generation sequencing assay with a sensitivity of 10-5. In both phases, ≥6 treatment cycles are recommended in the triplet regimen, but patients may continue treatment with the triplet if tolerated for up to 12 cycles, at the discretion of the investigator. Dose modifications are allowed. Based on response and tolerability, patients may transition to long-term maintenance treatment of azacitidine and gilteritinib (increased to 120 mg daily in maintenance) for up to 24 cycles or until they meet a discontinuation criterion. Patients who have an identified donor and achieve either CR, CR with incomplete platelet recovery or CR with incomplete hematologic recovery are eligible to undergo hematopoietic stem cell transplantation (HSCT) at any time, as per institutional standards, without having to come off the study if they have completed ≥1 cycle of the triplet regimen. However, the triplet regimen or the long-term maintenance treatment should be stopped and a pre-HSCT visit should be performed prior to starting the conditioning regimen for HSCT. Patients can resume gilteritinib monotherapy 120 mg daily at 30 to 90 days post-HSCT for up to 24 cycles if they meet all resumption conditions. The first patient was enrolled in January 2023

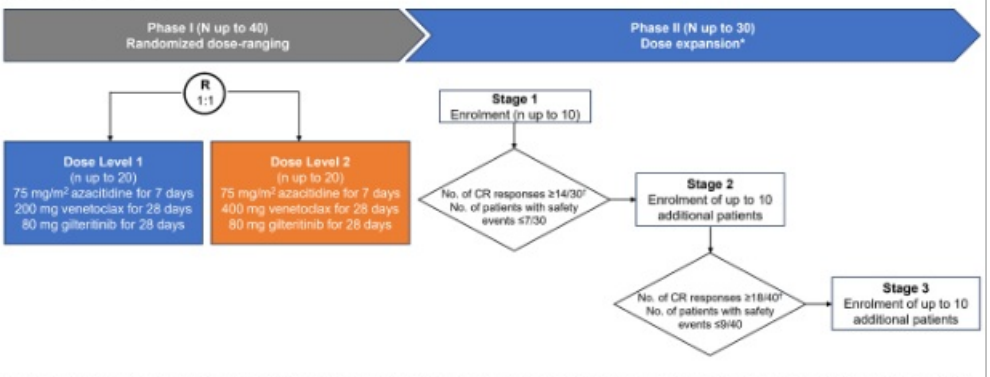
Results:

The randomized dose-ranging phase I of the trial is in progress.

Summary/Conclusion:

The ongoing VICEROY study will assess response to gilteritinib, venetoclax and azacitidine combination in adults with ND *FLT3*mut+ AML, who are ineligible for intensive induction chemotherapy.

Figure 1. Study design



* Dose expansion phase will evaluate the optimal dose (Dose Level 1 or Dose Level 2) as determined in the randomized dose-ranging Phase I. Phase II may not open if the CR rate after 3 cycles from either dose-ranging cohort does not exceed 44%. One cycle is 28 days. Safety events are any ≥ Grade 3 non-hematologic AEs considered at least possibly related to the study treatment regimen, and AEs of any grade leading to treatment discontinuation or death considered at least possibly related to the study treatment regimen.
† Dosed participants who have been enrolled for at least 3 cycles.
AE, adverse event; CR, complete remission; R, randomization

Keywords: Randomized, flt3 inhibitor, Acute myeloid leukemia, Phase I/II