Abstract: P1794

Title: A PHASE 1B/2 STUDY OF PIVEKIMAB SUNIRINE (PVEK, IMGN632) IN COMBINATION WITH VENETOCLAX/AZACITIDINE FOR PATIENTS WITH NEWLY DIAGNOSED CD123-POSITIVE ACUTE MYELOID LEUKEMIA

Abstract Type: e-Poster Presentation

Topic: Acute myeloid leukemia - Clinical

Background:

Despite improved outcomes with azacitidine (AZA) and venetoclax (VEN) in newly diagnosed (ND) unfit acute myeloid leukemia (AML), only a subset of patients (pts) respond (CR 37%; CR/CRi 66%) and long-term survival remains inadequate (mOS <15m, DiNardo NEJM 2020). The measurable residual disease (MRD)-negative rate was 41% in AZA-VEN treated pts in VIALE-A which was associated with improved survival (Pratz JCO 2022). CD123 is expressed on the majority of AML blasts and leukemic stem cells while minimally expressed on normal hematopoietic stem cells (Kovtun Blood Adv 2018). Pivekimab sunirine (PVEK, IMGN632) is an antibody-drug conjugate comprising a high-affinity CD123 antibody, cleavable linker, and an indolinobenzodiazepine pseudodimer (IGN) payload. The IGN payload alkylates DNA and causes single strand breaks without crosslinking. IGNs are designed to have high potency against tumor cells, while demonstrating less toxicity to normal marrow progenitors than other DNA-targeting payloads. Clinical data from the first 50 pts in the dose expansion cohorts 1 and 2 with ND AML demonstrated a 76% (22/29) MRD negativity rate (by flow cytometry, negativity threshold <0.1%) (Daver ASH 2023), supporting the continued enrollment of the PVEK+AZA+VEN triplet and further evaluation of the regimen's antileukemia activity and safety in consideration of potential registration-enabling trials.

Aims:

To evaluate antileukemia activity and MRD levels in the combination of PVEK+AZA+VEN in pts with newly diagnosed AML.

Methods:

This is an open-label, multicenter, Phase 1b/2 study of PVEK administered in a combination with AZA+VEN in pts with ND CD123-positive (CD123+ by flow cytometry or IHC) AML, with no prior treatment with hypomethylating agents (HMA). Pts will receive the recommended phase 2 dose of PVEK 0.045 mg/kg IV as a < 30-minute outpatient infusion on day 7, AZA 75 mg/m2 SC or IV daily on days 1 to 7, and VEN 400 mg PO daily for up to 28 days in a 28-day cycle. During cycle 1, a bone marrow evaluation at or around day 21 is required to inform VEN dose duration. Current eligibility criteria for continued enrollment of AML patients unfit for intensive chemotherapy include age ≥ 75 years old, or age < 75 years old with ECOG 2-3, or at least one defined comorbidity. The primary study objectives are to assess antileukemia clinical activity (composite CR [complete remission] rate, overall response rate, duration of remission) and MRD-negativity rates. Key secondary objectives are safety and tolerability, pharmacokinetics and immunogenicity.

Results:

Trial in progress

Summary/Conclusion:

The PVEK+AZA+VEN triplet in pts with ND unfit AML is currently enrolling across sites in France, Germany, Italy, Spain, UK and USA. Clinical trial information: NCT04086264.

Keywords: Clinical trial, Acute myeloid leukemia