A Phase 1b/2 Study of IMGN632 as Monotherapy or Combination with Venetoclax and/or Azacitidine for Patients with CD123-Positive Acute Myeloid Leukemia

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BACKGROUND

CD123, the alpha-subunit of interleukin-3 receptor (IL3RA), expression is elevated on Acute Myeloid Leukemia (AML) blasts and leukemic stem cell compared with normal hematopoietic stem and progenitor cells.1 CD123 is rapidly internalized making it well suited for antibody-drug conjugate (ADC)-based therapeutic strategies. IMGN632 is a CD123-targeting ADC, comprising a high affinity anti-CD123 antibody coupled to a DNA alkylating payload of the novel IGN (indolinobenzodiazepine pseudomodifier) class. Previously published data ASH 2018: (n=33) demonstrated clinical activity across multiple dose levels (0.015-0.45 mg/kg) with complete remission (CR)/complete remission without partial hematologic recovery (CRpH) in 26% of R/R AML and 1 prolonged neutropenia. Expansion cohorts enrolling at 0.045 and 0.09 mg/kg.2 Updates on Monday, December 9th at 3PM (Oral Abstract #734).

Pre-clinical data indicate IMGN632 combinations with azacitidine (AZA), venetoclax (VEN), and AZA with VEN result in increased survival in mouse models of AML (Abstract #1375).3

Study Design

- The IMGN632-0802 study is a multi-center Phase 1b/2 study to assess the safety and efficacy of IMGN632 when administered in monotherapy for patients in remission with minimal residual disease (MRD+) after induction or consolidation or in combination in adult patients with CD123-positive, relapsed/refractory (R/R) or treatment-naive AML
- IMGN632 administered in distinct regimens: IMGN632 + azacitidine IMGN632 + venetoclax IMGN632 + azacitidine + venetoclax (enrollment follows safety assessment of single agents)
- Patients who benefited from combination regimens may continue to receive IMGN632 monotherapy as maintenance
- IMGN632 dosing levels for combinations: 0.015, 0.045 and 0.09 mg/kg/dose

Trial Endpoints

Primary
- Combination cohorts: Evaluate safety and tolerability and Recommended Phase 2 Dose (RP2D) when IMGN632 is administered with AZA, VEN, or with AZA and VEN in patients with R/R AML
- Assess preliminary antileukemia activity when IMGN632 is administered in combination with AZA, VEN, or with AZA and VEN in patients with relapsed AML or untreated AML
- MRD- cohort: IMGN632 monotherapy
- Assess MRD conversion rate using central flow cytometry-based testing
- Relapse-free survival (RFS)

Eligibility

Key Inclusion
- CD123+ AML
- Relapsed/refractory AML (up to 2 prior lines) or treatment-naive
- Patients with prior bone marrow transplant are eligible (greater than 120 days)
- Washout period 14 days (except for checkpoint inhibitors 28 days)
- MRD- AML confirmed by central lab

Key Exclusion
- Patients with history of veno-occlusive disease


Registration

This study is registered at clinicaltrials.gov NCT04086264. For more information please contact medicalaffairs@immunogen.com.

REFERENCES

For more information please visit medicalaffairs@immunogen.com.

Abstract 2601

IMGN632: A Novel CD123-Targeting ADC

Novel Anti-CD123 Antibody
- High affinity binding to CD123
- Unique epitope in extracellular domain

Novel IGN Payload (DGNS549)
- DNA-alkylating activity, single strand DNA breaks (vs. double strand)
- Uniform drug:antibody ratio (GAR=2)

Novel Peptide Linker
- Confers stability in circulation, and efficient intracellular payload release

MECHANISM OF ACTION
1: ADC binds CD123
2: ADC internalized
3: Payload released
4: Payload alkytes DNA

Study Schema

Safety Run-in

R/R AML (Phase 1b)

Venetoclax

Relapsed and 1L AML

A: IMGN632 + AZA

AZA x7d, IMGN632 x1 on day 7 of 28 days

Relapsed 1L AML

3+3

B: IMGN632 + VEN

VEN x21d, IMGN632 x1 on day 7 of 21 days

Relapsed AML

3+3

C: IMGN632 + AZA + VEN

AZA x14d, VEN x7d, IMGN632 x1 on day 7 of 20 days

1L AML

3+3

D: IMGN632 monotherapy

0.045 mg/kg every 21 days

POC Cohorts (Phase 2)

n=35 patients each

Program Updates

- This trial is open and enrolling: ~35 centers in US and Europe plan to participate
- Continued Phase I trial of IMGN632 as a single agent, currently enrolling three expansion cohorts: Untreated or R/R BPDCN, AML and B- or T-ALL, will be presented Sunday, December 8th from 6-8PM (Abstract #1334)
- Clinical safety and efficacy updates to the Phase 1 trial will be presented on Monday, December 9th at 3PM (Oral Abstract #734)