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

Naval G. Daver1, Kendra Sweet2, Paul Montesinos3, Eunice S. Wang1, Ahmed Aribi1, Daniel J. DeAngelis1, Harry P. Erba1, Giovanni Martinelli3,4, Roland Walter1, Jessica Altman4, Anjali Advani5, Antonio Curti1, Adolfo De La Fuente1,5, Gianluca Gaidano1,2, Lourdes Mendez1, Hagop Kantarjian1,5, Marina Konopleva1, Juzhong Wang16, Callum M. Stoss1,16, Kara E. Malcolm1,4, Patrick A. Zweidler-McKay1,6

1NCI-ANDERSON CANCER CENTER, HOUSTON, TX; 2BCP CANDIDATE CENTER, TAMPPO, FL; 3HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA; 4FRED HUTCHINSON CANCER RESEARCH CENTER, SEATTLE, WA; 5MD ANDERSON CANCER CENTER, HOUSTON, TX; 6Moffitt Cancer Center, TAMPA, FL

©2020 ImmunoGen, Inc., Waltham MA, USA

INTRODUCTION

- CD123, the alpha-subunit of interleukin-3 receptor (IL3R), expression is elevated on Acute Myeloid Leukemia (AML) blasts and leukemic stem cells (LSCs) compared with normal hematopoietic stem and progenitor cells.

- With broad expression in AML and rapid internalization, CD123 is 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 (indolino benzodiazepine pseudosudimine) class.

- ASH 2019: Clinical activity was seen across a wide range of dose levels (0.015-0.45 mg/kg) with CR/CRI rates of 26-40% in subsets of relapsed AML at the RP2D of 0.045 mg/kg Q3W.

- Pre-clinical data support testing of IMGN632 combinations with azacitidine (AZA) and/or venetoclax in patients with relapsed or untreated AML.

- Mechanism of Action

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

  - Novel IGN Payload (DGN549)
    - DNA alkylating activity, single strand DNA breaks (vs double strand)
    - Uniform drug:antibody ratio (DAR=2)

  - Novel Peptide Linker
    - Confers stability in circulation
    - Efficient intracellular payload release

- Escalation and Expansion Cohorts are Enrolling in AML

  - IMGN632 + AZA
  - IMGN632 + VEN
  - IMGN632 Monotherapy

- Key Inclusion
  - Adults with CD123+ AML
  - Treatment-naive OR relapsed/refractory AML

- Study Design

  - The IMGN632-002 study is a multi-center Phase 1b/2 study to assess the safety and efficacy of IMGN632 when administered in combination with azacitidine and/or venetoclax in patients in remission with minimal residual disease (MRD+ Fit or Unfit) after induction and consolidation.

  - 1:3 escalation, with ability to expand multiple dose levels

- FUTURE DIRECTIONS FOR RESEARCH

  - This trial is enrolling at 14 centers in the US and Europe

  - clinicaltrials.gov: NCT04086264


  - Sponsor contact: medicalaffairs@immunogen.com


ASH Annual Meeting, December 2020
©2020 ImmunoGen, Inc., Waltham MA, USA