**Phase 1/2 Study of IMGN632, a Novel CD123-Targeting Antibody-Drug Conjugate, in Patients with Relapsed/Refractory Acute Myeloid Leukemia, Blastic Plasmacytoid Dendritic Cell Neoplasm, and Other CD123-Positive Hematologic Malignancies**

**AUTHORS:** Naval Gustad Daver1, Pau Montesinos2, Daniel J. DeAngelis1, Eunice S. Wang1, Elisabetta Todisco1, Corrado Tarella1, Giovanni Martinelli, Harry Paul Erba2, Eric Deconinck3, Kendra L. Sweet4, Roland B. Walter5, Moshe Yair Levy5, Naveen Pemmaraju1, Andrew A. Lane6, David Rizzieri12, Marina Konopleva14, Callum Mortimer Sloss15, Jizhou Wang15, Kari A. Malcolm15, Patrick A. Zweidler-Mckay15

1University of Texas MD Anderson Cancer Center, Houston, TX; 2Hospital Universitario de Politécnico LaFe, Valencia, Spain; 3Dana-Farber Cancer Institute, Boston, MA; 4Novell Park Comprehensive Cancer Center, Buffalo, NY; 5Istituto Europeo di Oncologia, Milan, Italy; 6European Institute of Oncology (IEO), Milan, Italy; 7Istituto Scientifico Romagnolo per lo Studio e la Cura del Tumore (IRCCS) IRCCS, Milano, Italy; 8Duke University, Durham, NC; 9University Hospital Brussels, Brussels, Belgium; 10University Hospital Ixelles, Brussels, Belgium; 11Clinical Research Division; Fred Hutchinson Cancer Research Center, Seattle, WA; 12Texas Oncology-Barclay Charles A. Sammons Cancer Center, US Oncology, Dallas, TX; 13Duke University School of Medicine, Durham, NC; 14Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX; 15ImmunoGen, Inc., Waltham, MA

**BACKGROUND**

Overexpression of CD123 occurs in multiple hematologic malignancies, including acute myeloid leukemia (AML), blastic plasmacytoid dendritic cell neoplasm (BPDCN), acute lymphoblastic leukemia (ALL) and others, thus making this antigen an attractive target for the development of new therapeutics.

**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 and efficient intracellular payload release

**Expansion Cohorts are enrolling in BPDCN and ALL**

**TRIAL ENDPOINTS**

- Primary: Maximum Tolerated Dose (MTD) and RP2D
- Secondary: Treatment emergent adverse events
- Objective Response Rate (ORR)
- Pharmacokinetic parameters
  - Maximum plasma concentration (Cmax) of IMGN632
  - Area under the time-concentration curve (AUC) of IMGN632
- Terminal half-life (t1/2) of IMGN632
- Immunogenicity
- Presence of Antibody-Drug Antibody (ADA)

**FUTURE DIRECTIONS FOR RESEARCH**

The trial is open and enrolling at 11 centers in the US and Europe; 2 additional centers in Europe are planning to participate. See clinicaltrials.gov: NCT03386513

**REFERENCES**

- Testa U, Pelosi E, and Frankel A. Biomarker Research; 2-4, 2014
- Angelova E, Audette C, Kavun Y et al. Haematologica; 104:749-755, 2018
- Su R and Chen M. American Journal of Clinical Pathology; 144:2, 2015

**STUDY DESIGN**

The IMGN632-0801 study is a multi-center, Phase 1 study to determine the recommended Phase 2 Dose (RP2D) and assess the safety, tolerability, PK, immunogenicity, and preliminary anti-leukemia activity of IMGN632 when administered as monotherapy to patients with CD123+ hematologic malignancies.

The study is enrolling eligible adults with CD123-positive BPDCN and ALL. Any detectable level by flow or IHC by local assessment.

IMGN632 administered as a ≤1 hour IV infusion on Day 1 of a 21-day cycle.

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**Dose Escalation COMPLETED**

| RP2D | 0.045 mg/kg Q3W | R/R B- and T- ALL | Untreated or R/R BPDCN |

**Key Inclusion**

- CD123 positive BPDCN or ALL
- Selected untreated patients with BPDCN (i.e. those who are inappropriate for available therapies)
- R/R BPDCN (up to 4 prior lines)
- R/R B- and T- ALL (up to 4 prior lines)
- Patients with prior bone marrow transplant are eligible (greater than 120 days)
- Washout period 14 days (except for checkpoint inhibitors 28 days)

**Key Exclusion**

- Active CNS disease
- History of veno-occlusive disease, Grade 4 capillary leak syndrome, or non-cardiac grade 4 edema

**REFERENCES**

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