Abstract
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A Phase I 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

CD123, the alpha-subunit of interleukin-3 receptor (IL3RA), is expressed in the majority of acute myeloid leukemia (AML) and B- and T-cell acute lymphoblastic leukemia (ALL) cases, and nearly all blastic plasmacytoid dendritic cell neoplasm (BPDCN) with the highest CD123 levels in the latter.\textsuperscript{1,2} IL3R/CD123 is a clinically validated target in BPDCN. CD123 expression is elevated on AML blasts and leukemic stem cells compared with normal hematopoietic stem and progenitor cells. Recent studies indicate that CD123 may contribute to the proliferative advantage of leukemic cells.\textsuperscript{3} CD123 is rapidly internalized making it well suited for antibody-drug conjugate (ADC)-based therapeutic strategies.\textsuperscript{4}

IMGN632 is a CD123-targeting ADC, comprising a high affinity anti-CD123 antibody coupled to a DNA alkylation payload of the novel IGD (indolinoindolizinepeptide)-sodiumistheter. Previous published data ASH 2018: (n=13) demonstrated clinical activity across multiple dose levels (0.015-0.45 mg/kg) with complete remission/CR/complete remission without complete hematological recovery (CRI) in 26% of R/R AML and 2 of 3 relapsed BPDCN patients. DLTs seen only at higher dose levels ≥ 0.18 mg/kg. IMGN632 administered as a 1 hour IV infusion on Day 1 of a 21 day cycle.

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-CD123 activity of IMGN632 when administered as monotherapy to patients with CD123+ hematologic malignancies.

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 Antbody (ADA)

Eligibility
Key Inclusion
- CD123+ AML, ALL or BPDCN
- Relapsed/refractory (R/R) AML up to 3 prior lines
- R/R B- and T-ALL (up to 4 prior lines)*

- Selected untreated patients with BPDCN (i.e., those who are inappropriate for available therapies) or R/R BPDCN
- Patients with prior bone marrow transplant are eligible (greater than 120 days)

- Washout period 14 days (except for checkpoint inhibitors 28 days)

Key Exclusion
- History of veno-occlusive disease, Grade 4 capillary leash syndrome, or non-cardiac grade 4 edema

*Amendment pending to include selected untreated BPDCN and to increase number of prior lines from 3 to 4

For additional information please contact medicalcall@immunogen.com.

REFERENCES

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