**IMGN779, A Next Generation CD33-Targeting ADC, Combines Effectively With Cytarabine in Acute Myeloid Leukemia (AML) Preclinical Models, Resulting in Increased DNA Damage Response, Cell Cycle Arrest and Apoptosis In Vitro, and Prolonged Survival In Vivo**

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**Abstract**

With improved patient outcomes in mind, we set out to evaluate the mechanism and antileukemia efficacy of the combination of IMGN779 and cytarabine using in vitro and in vivo human AML preclinical models.

**Methods**

**In vitro cytotoxicity** was assessed at 48 hours in MV4-11 and Molm-13 cell lines using a WST-8 based cell viability assay (GloMax Microplate Readers). IMGN779 data are shown. Molm-13 results were similar.

Apoptosis and DNA damage responses were measured at 48 hours by flow cytometry (Joel V. Thermo Fisher Scientific; Dallas, TX) and immunoblotting methods (Cell Signaling technology). MV4-11 data were shown. Molm-13 results were similar.

Cytarabine increases CD33 expression in AML cell lines in vitro.

**Combination of IMGN779 and cytarabine increases apoptosis and cell death in AML cell lines in vitro**

**Cytarabine increases CD33 expression in AML cell lines in vitro**

**Free payload of IMGN779, DGN462, displays strong synergism with MDM2 and CHK1/2 inhibitors**

**IMGN779 combines with cytarabine in vivo to increase survival in Molm-13 disseminated AML xenograft model**

**IMGN779 combines with cytarabine in vivo to increase survival in MV4-11 disseminated AML xenograft model**

**CONCLUSIONS**

- The combination of IMGN79 and cytarabine increased DNA damage response, cell cycle arrest and apoptosis in vitro, compared to single agents.
- Cytarabine increased cell surface CD33 levels on AML cells, indicating a potential novel mechanism for potentiating IMGN779 uptake and efficacy.
- The combination of IMGN79 and cytarabine leads to increased survival and greater numbers of complete responses in vivo preclinical AML models.
- These results support testing IMGN79 in combination with cytarabine and cytarabine containing regimens in clinical trials.

**IMGN779 Clinical Poster, #1312: IMGN79, a Next-Generation CD33-Targeting Antibody Drug Conjugate (ADC) Demonstrates Initial Antileukemia Activity in Patients with Relapsed or Refractory Acute Myeloid Leukemia; Saturday, December 9, 5:30-7:30 PM, Hall A2**

Clinical Testing: NCT02674631: Open-label Study of IMGN79 in Adult Patients With Relapsed/Refractory CD33-positive Acute Myeloid Leukemia.

ASH, Dec. 9 to 12, Atlanta, GA
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