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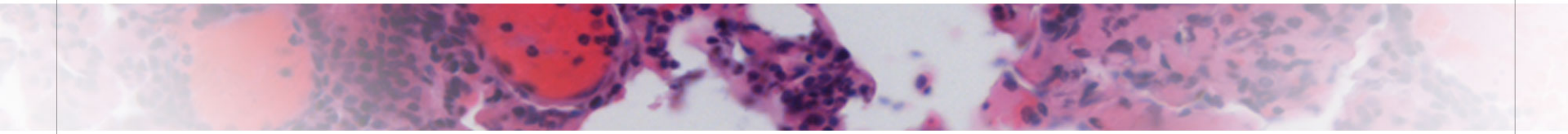

Clinical Profile of IMGN632, a Novel CD123-Targeting Antibody-Drug Conjugate (ADC), in Patients with Relapsed/Refractory (R/R) Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

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BPDCN Background

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- BPDCN is a rare, aggressive hematologic malignancy characterized by historically poor overall survival and limited therapeutic options
- Overexpression of CD123 (IL-3Rα) is present in all BPDCN cases, thereby establishing this surface marker as a rational target for therapeutic intervention
- Despite the recent approval of tagraxofusp-erzs, outcomes remain poor in the setting of relapsed and refractory (R/R) BPDCN and novel approaches are urgently needed

IMGN632: A Novel CD123-Targeting ADC

- Novel Anti-CD123 Antibody
  - High 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 greater stability in circulation
  - Efficient intracellular payload release

- IMGN632 demonstrated 22-40% ORR in R/R AML at the RP2D of 0.045 mg/kg every 3 weeks, in subgroups of de novo and relapsed patients (ASH 2019)

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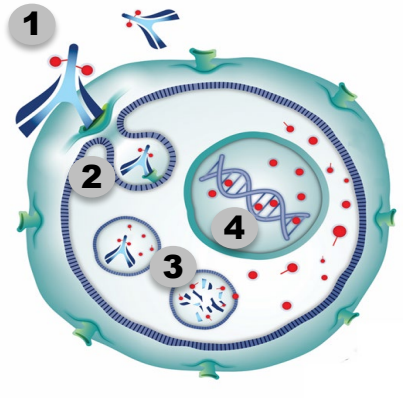

1 - ADC binds target
2 - ADC internalized
3 - Payload released
4 - Payload alkylates DNA

Efficacy in refractory BPDCN PDX models

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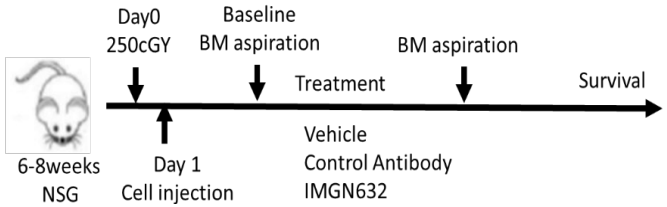

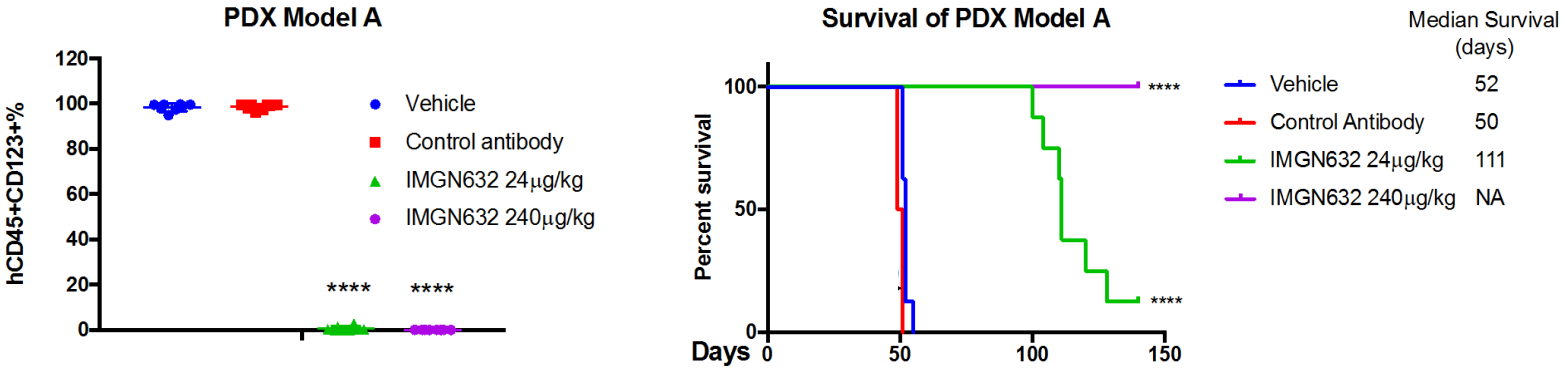

- IMGN632 rapidly cleared BPDCN in the bone marrow
- IMGN632 dramatically extended the lifespan of BPDCN tumor-bearing mice

Study Design and Objectives

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Study Design

- Patients ≥18 years old
- BPDCN, R/R or frontline
- Any CD123 positivity (flow cytometry or IHC)
- Up to 4 prior lines of therapy
- No minimum serum albumin requirement
- IMGN632 (0.045 mg/kg) is administered IV in under 30 minutes on day 1 of a 21-day cycle

Objectives

- Establish safety and tolerability and initial efficacy of IMGN632 in patients with BPDCN

Patient Characteristics (n=29)

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Age years, median (range)		**72y (19-82)**
Gender, % (n)	**Male**	**76% (22)**
	Female	**24% (7)**
Disease, % (n)	**Compartment involvement**	
	Skin	**69% (20)**
	Bone marrow	**62% (18)**
	Lymph node/visceral	**52% (15)**
	Prior/concurrent malignancy	**24% (7)**
Baseline status, % (n)	**First relapse**	**21% (6)**
	Primary refractory	**59% (17)**
	Relapsed	**17% (5)**
	Untreated	**3% (1)**
Prior therapy, % (n)	**Pts with ≥2 prior therapies**	**45% (13)**
	Intense (e.g. HyperCVAD, FLAG, CHOP)	**52% (15)**
	Prior exposure to tagraxofusp-erzs	**45% (13)**
	Prior allogeneic stem cell transplant	**24% (7)**

Favorable safety profile (TEAEs >15%) (n=29)

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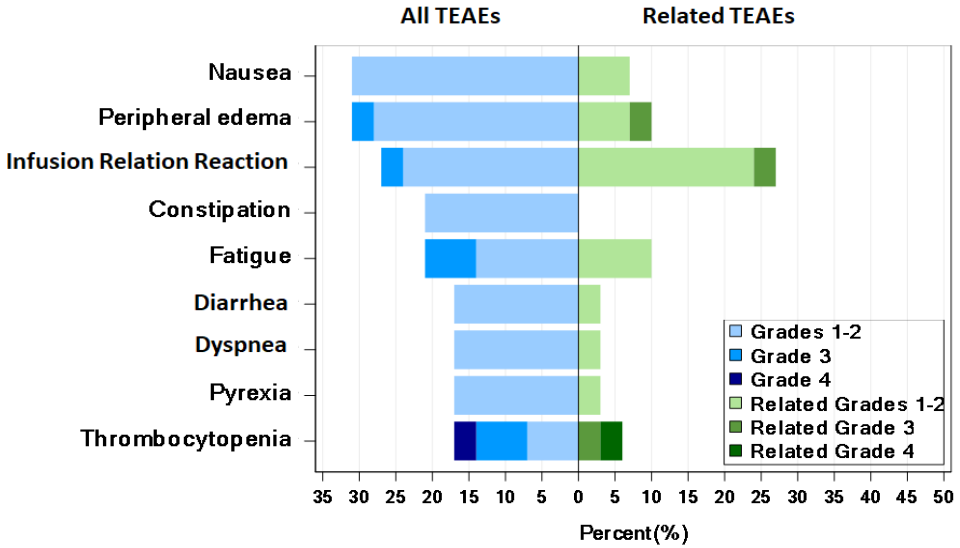
- No capillary leak syndrome (CLS)
- No drug related discontinuations
- No drug related deaths, 30-day mortality 0%
- The most common grade ≥3 AEs were thrombocytopenia, febrile neutropenia, and hyperglycemia (10% each)
- Rare liver-related AEs
  - One (3%) grade ≥3 LFT elevation: Gr3 ALT for >7 days (DLT), resolved
  - One (3%) grade 3 hyperbilirubinemia and weight gain: “Grade 2 clinical VOD” resolved and went to HSCT



Efficacy in R/R BPDCN

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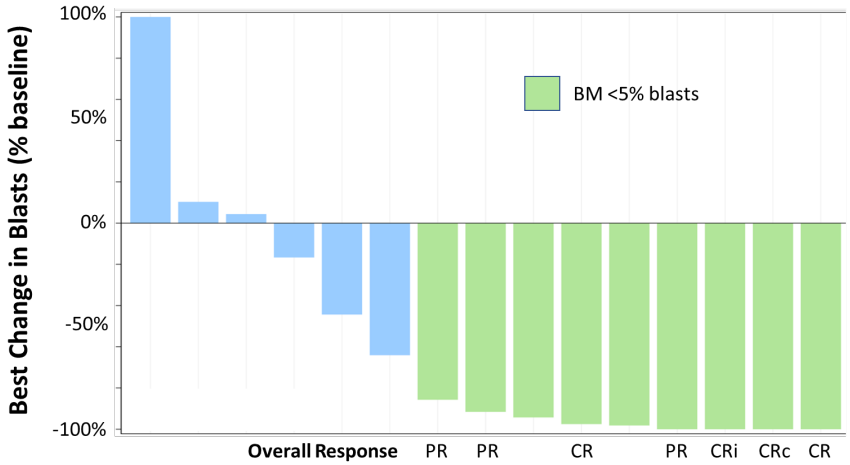
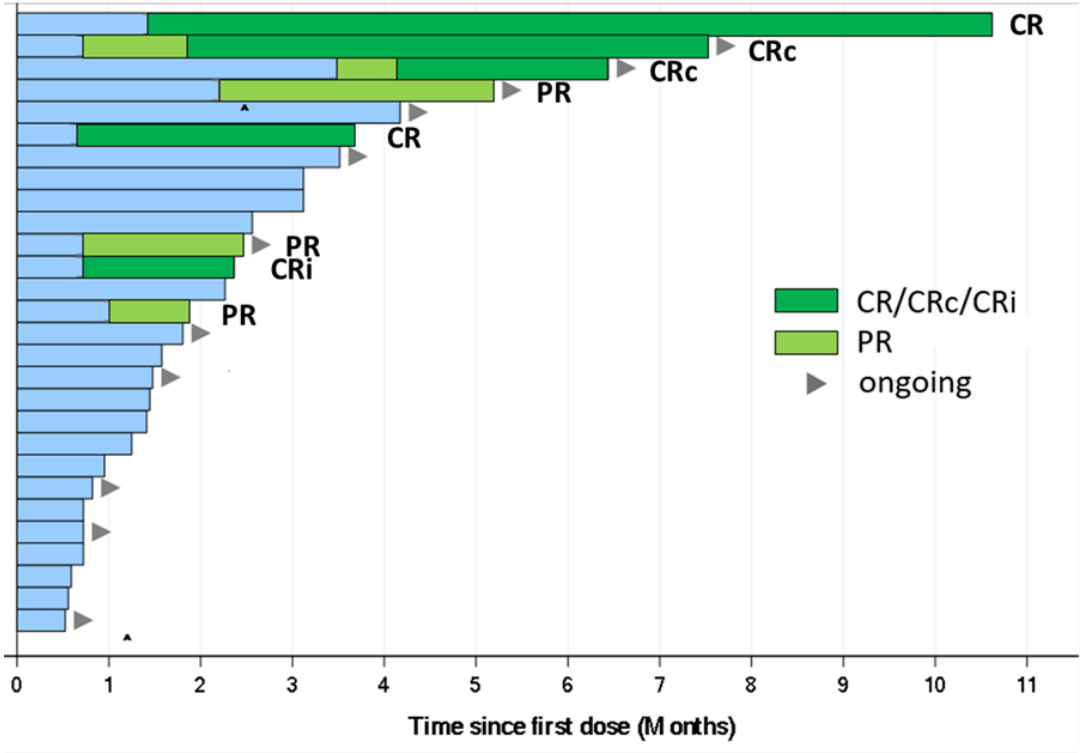
- In all R/R BPDCN patients:
  - Overall response rate (ORR) 29% (8/28, 2 CR, 2 CRc*, 1 CRi, 3 PR)
  - Composite complete remission rate (CCR#) of 18% (5/28)
- Importantly, in patients with prior tagraxofusp exposure:
  - ORR was 31% (4/13, 1 CR, 1CRi, 2 PR)
  - CCR of 15% (2/13)
- Among 15 patients with bone marrow response assessment to date, 60% (9/15) achieved a bone marrow complete remission (blasts <5%), most (78%, 7/9) also achieving an overall response



* = clinical CR: CR criteria EXCEPT limited residual skin disease “marked clearance of all skin lesions from baseline; residual hyperpigmentation or abnormality with BPDCN identified on biopsy (or no biopsy performed)”
# CCR = CR+CRc+CRi

Time on treatment and response



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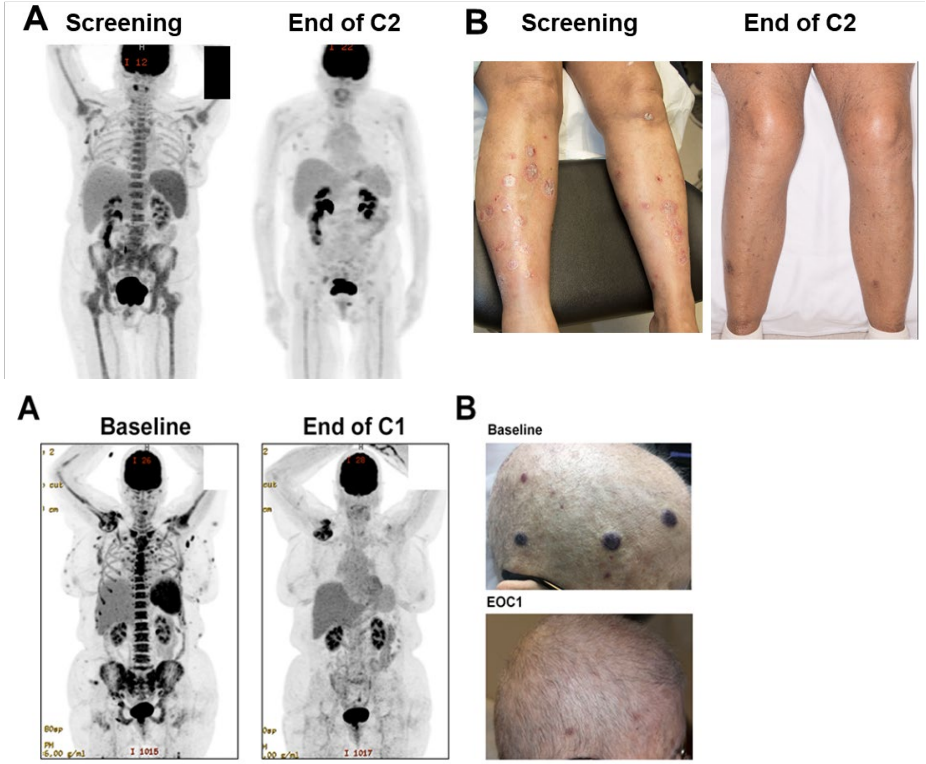
- 39% (11/28) remain on treatment
- Responses are often rapid: mean time to response 1.1 months (range 0.7-3.5)
- Durable responses seen (up to 9.2 months) without HSCT

Responses in refractory patients



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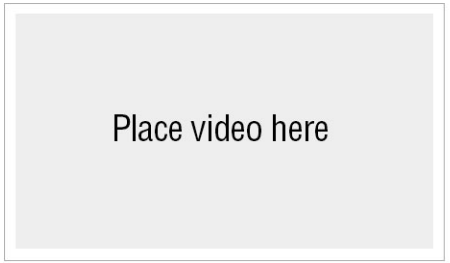
- 63yo female with BPDCN, refractory to tagraxofusp x2 presented with extensive marrow and skin involvement
- 69yo female with MDS/BPDCN, refractory to tagraxofusp, CLAG-M, CLAG and presented with extensive skin/PET/BM involvement.

Conclusions



- This clinical trial represents the largest-to-date prospective group of uniformly treated patients with R/R BPDCN
- Favorable safety profile with no cases of CLS, limited grade ≥3 TEAEs, no treatment-related discontinuations, 0% 30-day mortality, and no treatment-related deaths
  - IMGN632 administered every 3 wks, typically given in the outpatient setting
- IMGN632 demonstrated a 29% (8/28) ORR, with 5 complete responses, including patients who had failed prior tagraxofusp-erzs
  - Multiple durable responses observed in the absence of HSCT

- FDA Breakthrough Therapy Designation (BTD) granted in R/R BPDCN
- Enrollment is open for patients with R/R and frontline BPDCN