Abstract 1284

Experience with IMGN632, a Novel CD123-Targeting Antibody-Drug Conjugate (ADC), in Frontline Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

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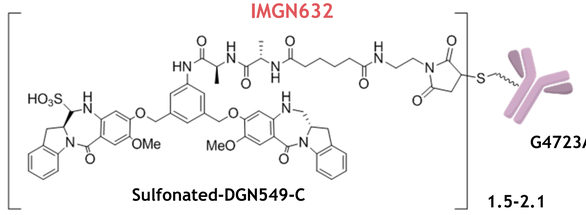
Introduction

- BPDCN is a rare, aggressive hematologic malignancy characterized by historically poor overall survival and limited therapeutic options
- Despite the recent approval of tagraxofusp-erzs for BPDCN, outcomes remain suboptimal for many patients
- Overexpression of CD123 (IL-3Rα) is present in all BPDCN cases, thereby establishing this surface marker as a target for therapeutic intervention[1]
- IMGN632 is a CD123-targeting antibody-drug conjugate (ADC) comprised of a high-affinity antibody coupled to a DNA-alkylating payload of the novel IGN (indolinobenzodiazepine pseudodimer) class
- IGN payloads alkylate DNA and cause single strand breaks without crosslinking. IGNs are designed to have high potency against tumor cells, while demonstrating less toxicity to normal marrow progenitors than other DNA-targeting payloads
- IMGN632 has demonstrated favorable safety and promising clinical activity in relapsed/refractory (R/R) BPDCN, including patients who had failed prior tagraxofusp-erzs[2]
- IMGN632 was granted FDA Breakthrough Therapy Designation (BTD) for R/R BPDCN (Oct 2020)
- Here we present data on frontline BPDCN patients who received IMGN632 prior to opening of the pivotal cohort in frontline BPDCN patients that is currently enrolling

IMGN632



Study Design and Trial Endpoints

- The IMGN632-0801 study is a multi-center Phase 1b/2 study to assess the safety and efficacy of IMGN632 when administered in frontline and R/R BPDCN patients

Primary Endpoint

- Composite CR rate (CR+CRc*)

Select Secondary Endpoints

- Duration of composite complete response (DOCR) and Overall response rate (ORR)

Efficacy was assessed using modified Severity Weighted Assessment Tool (mSWAT) for skin lesions, PET/CT, and blast percentage in bone marrow aspirates[3]

*CRc - CR (clinical) with minimal residual skin abnormality (marked clearance of all skin lesions from baseline; residual hyperpigmentation or abnormality with BPDCN identified on biopsy [or no biopsy performed])

Frontline and Relapsed/Refractory Cohorts Enrolling in BPDCN

Patients with BPDCN

Cohort 1: Patients with R/R BPDCN who have received 1-3 prior systemic therapies (n = up to 50)

Cohort 6: Patients with frontline BPDCN who have not received prior systemic therapy (n = up to 20)

All patients receive 0.045 mg/kg IMGN632 IV on Day 1 of a 21-day cycle (< 30-minute outpatient infusion)

Key Inclusion

- Patients ≥18 years old
- BPDCN, frontline or R/R
- CD123 positivity (flow cytometry or IHC)
- Frontline patients may have received local therapy
- No minimum serum albumin requirement

Key Exclusion

- Patients with history of veno-occlusive disease or active CNS involvement

Initial three frontline patients achieved a clinical complete response (CRc)

Patient 1 - A 79-year-old woman initially diagnosed with isolated skin involvement and was treated with skin irradiation with no effect. Due to her age and comorbidities, she was not considered appropriate for intensive therapies and presented for frontline treatment with IMGN632 with widely disseminated BPDCN (bone marrow, skin, and nodal lesions)

- She cleared her bone marrow (80% to 0%) after one dose of IMGN632 and her nodal lesions after 2 cycles of therapy, at which point she was deemed a PR. Following her third cycle, her skin lesions completely resolved (mSWAT 14 to 0), and she was determined to be a CRc (no skin biopsy performed)
- Due to her age and a pulmonary embolism, treatment with IMGN632 was suspended after 3 cycles, and she had a DOCR of 9.6 months (DOR of 10.7 months) without further therapy, until disease progression

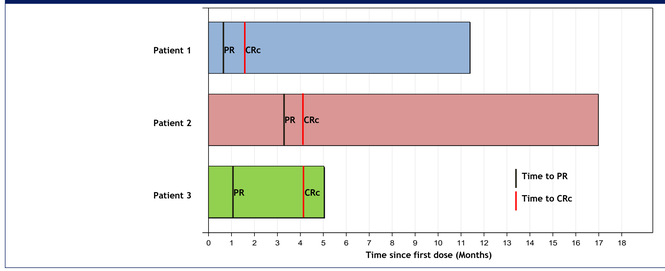
Patient 2 - A 67-year-old man received localized radiation for his skin-only presentation and, due to comorbidities, was not considered appropriate for available systemic therapies. He presented for frontline treatment with IMGN632 with a high burden of skin disease (mSWAT 50), reflecting extensive skin infiltration

- During initial cycles of IMGN632 treatment, he was noted to have a steady improvement in the skin areas involved and the nature of the skin plaques until Cycle 5, when he was assessed as a PR (mSWAT 23)
- He achieved a CRc (mSWAT 3) at the end of Cycle 6 and went on to receive an allogeneic SCT. The patient had a DOCR of 12.8 months (DOR of 13.5 months) when he died from disease progression post stem cell transplant

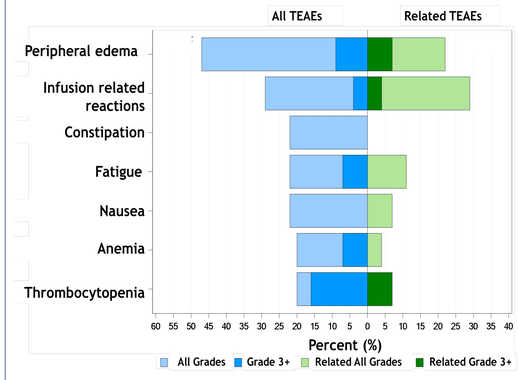
Patient 3 - A 66-year-old woman was diagnosed with skin and nodal BPDCN. She presented for frontline systemic treatment with IMGN632 with a high burden of skin disease (mSWAT 26)

- She was noted to have a steady improvement in the skin areas involved. By the end of Cycle 2, the patient was deemed PR (mSWAT 8) and by the end of cycle 4 achieved CRc (cleared nodes and mSWAT 3)
- The patient had a DOCR of 1.0 month (DOR of 3.7 months) at the time of her death from COVID-19 pneumonia

Swimmer Plot of Frontline Responders



Safety Profile in R/R and Frontline BPDCN (TEAEs ≥ 20%, n = 45)



- No capillary leak syndrome (CLS)
- The most common grade ≥ 3 AEs were thrombocytopenia (16%), peripheral edema and neutropenia (9% each)
- Infusion related reactions were mostly low grade and manageable
- 2% 30-day mortality (one patient died from disease progression)

Summary

- IMGN632 in frontline BPDCN patients resulted in durable clinical complete responses
- IMGN632 can be administered as a brief outpatient infusion
- Favorable safety profile with no cases of CLS and limited grade ≥3 TEAEs
- Enrollment continues in the pivotal frontline and R/R cohorts (BPDCNtrial.com; NCT03386513)

References:

[1]Pemmaraju, *Blood* (2019) 134 (Supplement_1): 2723.; [2]Daver, *Blood* (2019) 134 (Supplement_1): 734.; [3]Pemmaraju, *N Engl J Med* 2019;380:1628-1637.