Abstract: S139

Title: INTERIM ANALYSIS OF A REGISTRATION ENABLING STUDY OF PIVEKIMAB SUNIRINE (PVEK, IMGN632) A CD123-TARGETING ANTIBODY-DRUG CONJUGATE, IN PATIENTS WITH BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM (BPDCN)

Abstract Type: Oral Presentation

Session Title: AML clinical studies and risk stratification

Background:

BPDCN is a rare, aggressive hematologic malignancy with skin, lymph node, blood, CNS, and bone marrow (BM) involvement. Overexpression of CD123 (IL-3Rα) is observed on BPDCN blasts but has limited expression on normal tissues. BPDCN currently has 1 approved therapy, tagraxofusp (TAG), with a median age of 68, CR/CRc rate of 57% and mOS of 15.8 mos (n=65; Pemmaraju JCO 2022). Pivekimab sunirine (PVEK, IMGN632) is a first-in-class antibody-drug conjugate (ADC) comprising a high-affinity CD123 antibody, cleavable linker and an indolinobenzodiazepine pseudodimer (IGN) payload. This payload alkylates DNA and causes single strand breaks without crosslinking.

Aims:

To report an interim analysis of safety and anti-tumor activity data in frontline BPDCN pts and updated data on R/R BPDCN pts.

Methods:

In this phase 1b/2 study, adults with frontline or R/R BPDCN received PVEK 0.045 mg/kg IV on D1 of a 21-day cycle, as a <30-min outpatient infusion.

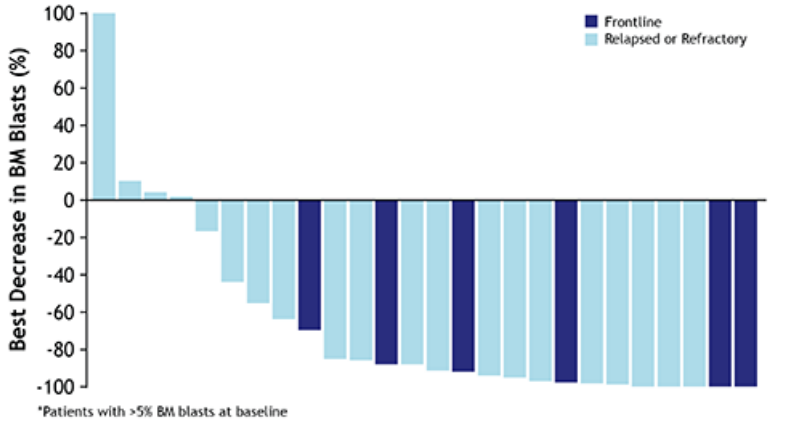
Results:

As of Sep 14, 2022, anti-tumor activity and safety data are available for 58 BPDCN pts (16 frontline, 42 R/R). Median age was 74y (range, 60-80y) for frontline and 69y (range, 19-83y) for R/R pts, with 88% of frontline pts ≥65y. At screening, 76% of pts had skin involvement, 50% had BM involvement and 43% had nodal/visceral disease per PET/CT scan. Half of the frontline BPDCN pts had a prior or concomitant hematologic malignancy, e.g. MDS, CMML. Of the 42 R/R BPDCN pts, 33% had received a SCT and 45% received prior TAG. Median number of PVEK doses received overall was 3 (range 1-19); frontline pts received a median of 5 doses (range 2-19). Response data were available for 16 frontline BPDCN pts. Objective response rate (ORR [CR, CRc, CRh, CRi, PR]) was 81% (13/16) with a composite complete remission (CCR [CR, CRc, CRh, CRi]) of 75% (12/16), with an additional pt achieving a CR post-transplant. BM remissions were reported in 6/6 frontline pts with baseline BM involvement. Four (25%) frontline pts were bridged to alloSCT. Median time to first response was 1.5 mos (0.5-3.7 mos). Median duration of response (DOR) in frontline pts was 10.7 mos (up to 13.3 mos without transplant); 7 pts remain on PVEK. For R/R BPDCN pts, ORR was 31% (13/42), with a CCR of 19% (8/42), including pts who failed intensive chemotherapy and transplant. In pts who received prior TAG, ORR was 26% (5/19) and CCR rate was 16% (3/19). Median DOR in R/R BPDCN pts was 3.1 mos (up to 9.2 mos); 10 pts remain on PVEK. The most common treatment-emergent adverse events (TEAEs) (all Gr [Gr 3+]) in >20% of all pts were peripheral edema (53% [12%]), thrombocytopenia (31% [26%]), infusion-related reactions (26% [5%]), constipation (24% [0%]), fatigue (22% [5%]), nausea (22% [0%]) and neutropenia (22% [21%]). Of pts with peripheral edema, 24 (77%) had Gr 1 or 2 events and none were Gr 4; Gr 3 hypoalbuminemia was reported in 3% of pts. No CLS or CRS events were reported. One frontline pt (6%) experienced Gr 2 infusion-related reaction (IRR). Grade ≥3 ALT/AST/TBILI laboratory elevations were recorded in 5%/2%/0% of pts; 1 pt experienced a DLT (Gr 3 ALT increase). The reported 30-day mortality was 2% (1 pt died due to disease progression) and no treatment-related deaths. One (2%) treatment-related AE (TRAE) led to dose reduction and 2 pts (3%) discontinued PVEK due to a TRAE.

Summary/Conclusion:

PVEK demonstrates compelling activity in frontline and R/R BPDCN pts, including durable responses in the R/R setting for pts who received prior TAG. PVEK safety was manageable with primarily low-grade IRRs and edema and no new safety signals were observed. Enrollment continues in the pivotal de novo frontline BPDCN cohort (NCT03386513)

Figure 1. Best Decrease in BM Blast (%) for Patients with Frontline and R/R BPDCN treated with PVEK*



Keywords: Antibody targeting, Monoclonal antibody, Myeloid malignancies