How We Treat Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

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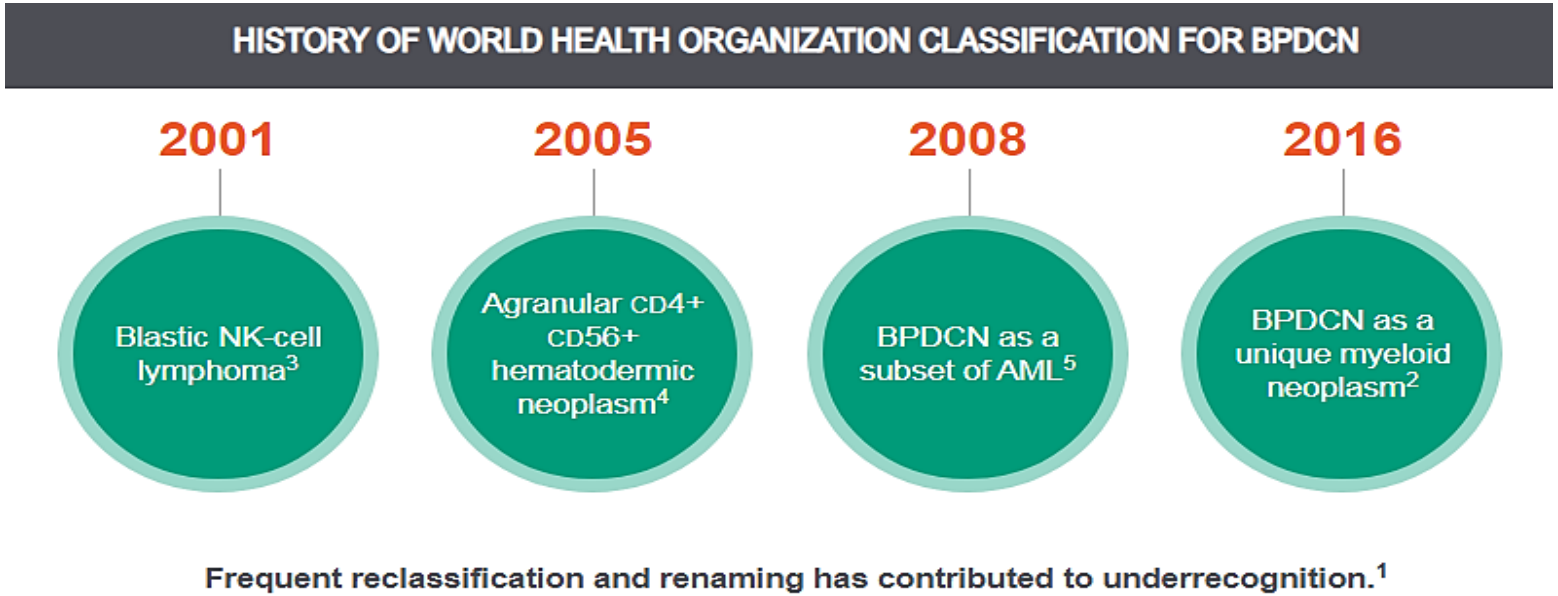
Disclosures

- Amgen: Honoraria, Speakers Bureau
- Debio Pharma: Consultancy, Honoraria
- Sanofi and Daiichi Sankyo: Consultancy
- Syndex Bio: Honoraria, Consultancy

BPDCN: Nomenclature & Classification Changes Over Time



Frequent reclassification and renaming has contributed to underrecognition.[1]

2022 Update: 5th edition WHO classification of Haematolymphoid Tumours: Myeloid/Histiocytic/Dendritic Neoplasms:

-Dendritic cell and histiocytic neoplasms (Table 14):

-Plasmacytoid dendritic cell neoplasms

-Blastic plasmacytoid dendritic cell neoplasm

Table 14. Dendritic cell and histiocytic neoplasms.

Plasmacytoid dendritic cell neoplasms
Mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm
Blastic plasmacytoid dendritic cell neoplasm
Langerhans cell and other dendritic cell neoplasms
Langerhans cells neoplasms
Langerhans cell histiocytosis
Langerhans cell sarcoma
Other dendritic cell neoplasms
Indeterminate dendritic cell tumour
Interdigitating dendritic cell sarcoma
Histiocytic neoplasms
Juvenile xanthogranuloma
Erdheim-Chester disease
Rosai-Dorfman disease
ALK-positive histiocytosis
Histiocytic sarcoma

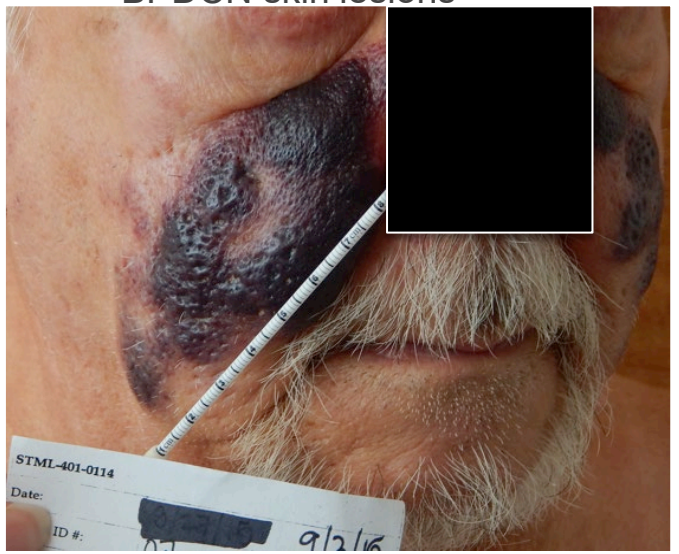
Arber et al. Blood (2016) 127 (20): 2391-2405; slide modified Prof Eric Deconinck;

Khoury J et al, Leukemia 2022; Jul;36(7):1703-1719. epub 2022 Jun 22

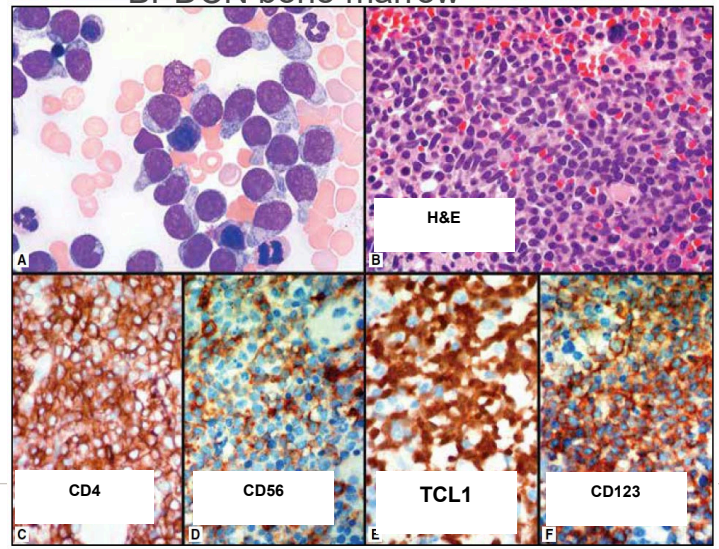
BPDCN: Aggressive Hematologic Malignancy with Poor Clinical Outcomes

- Incidence 500-1000 patients per year in USA
- Common sites involved are skin, bone marrow, lymph node and CNS
- Hallmark: **Overexpression → CD123 (IL3Rα)**
- Classic Triad: CD123+, CD4+, CD56+ “Think 123456”
- TCL-1, TCF-4, CD303
- *TET2, ASXL1, RAS, ZRSR2, TP53*

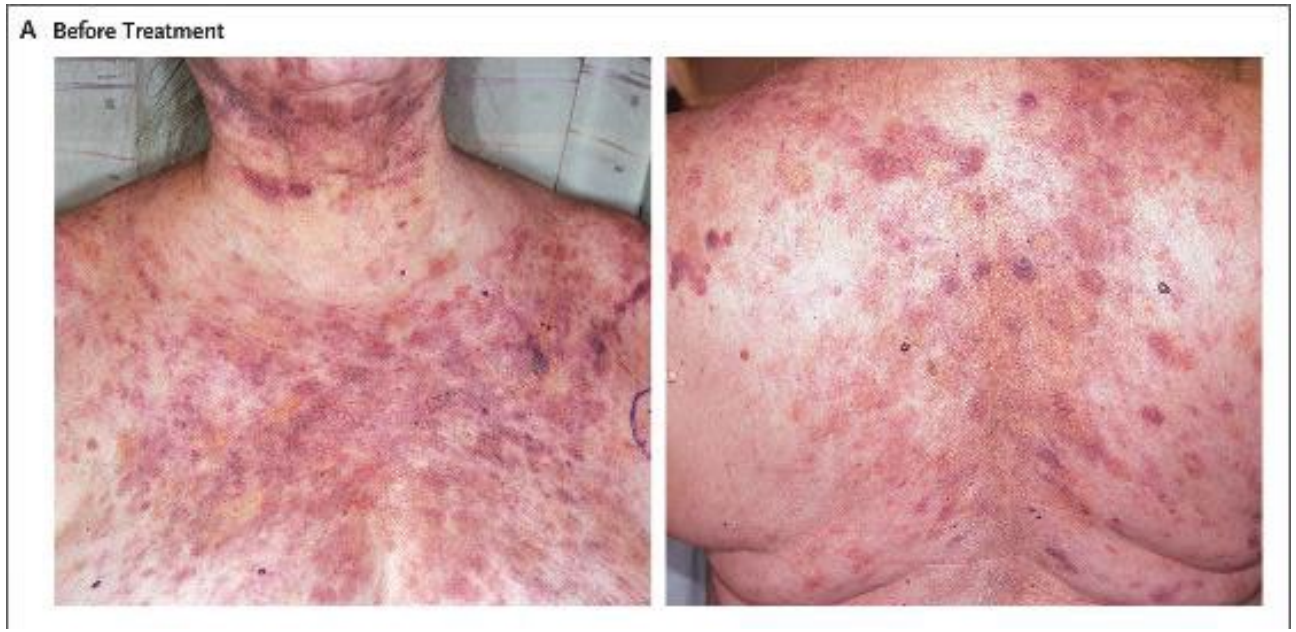
BPDCN skin lesions

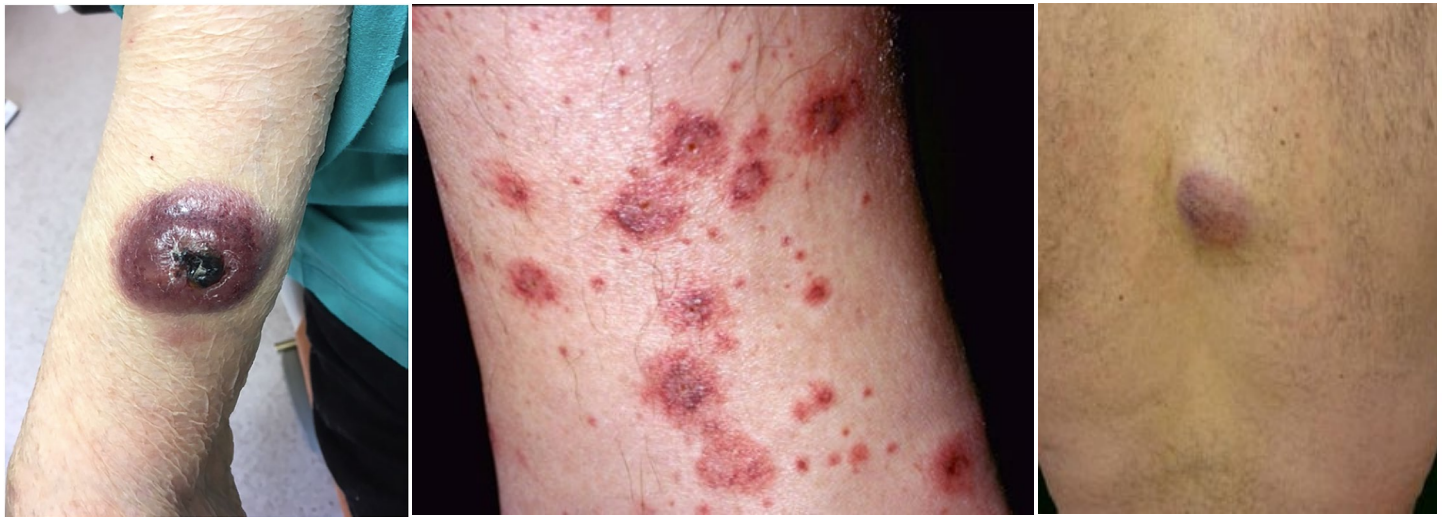


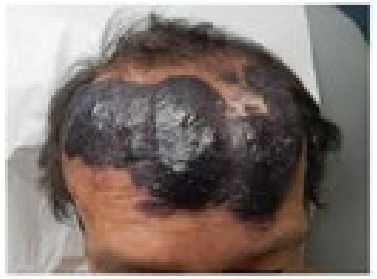
BPDCN bone marrow

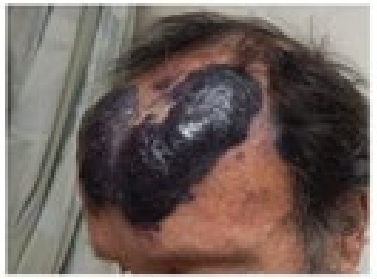


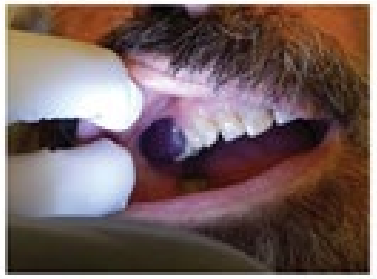
Feuillard J, Jacob M-C, Valensi F, et al. Blood 2002;99 (5):1556-63 | Murthy G, Pemmaraju N, et al. Leuk Res. 2018 Oct:73:21-23
Sapienza M, Pileri S. Hematol Oncol Clin North Am 2020 Jun;34(3):511-521

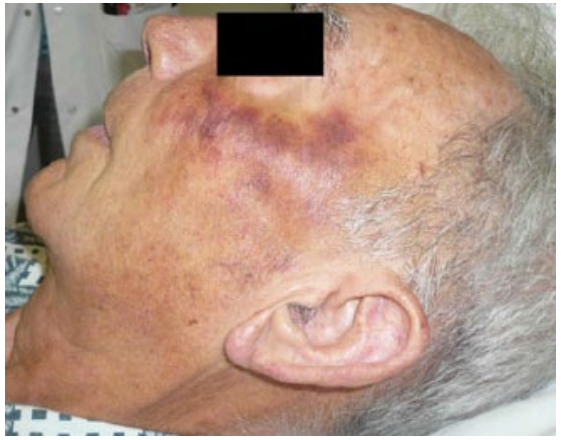


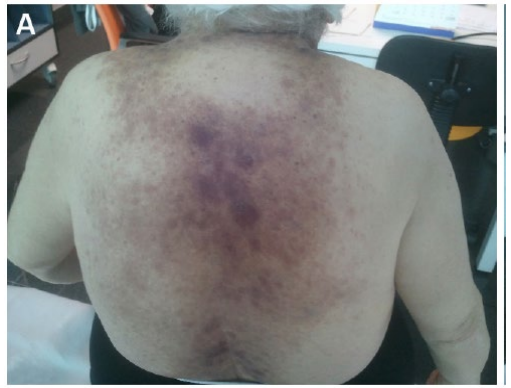


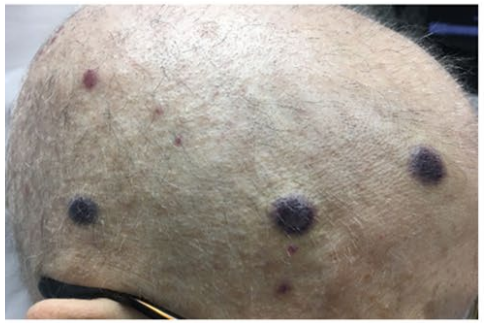










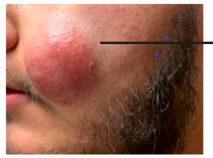


N Pemmaraju N Engl J Med 2019;380:1628-1637, *IMGN632 In R/R AML And BPDCN, Abstract #27.*
Garcia-recio Oncotargets And Therapy 2016:9 5507–551, Marmouset.Hemato Oncol. 2019 Oct;37(4):487-489
Slide: Andy Lane, Naveen Pemmarjau, Prof Eric Deconinck

North American Blastic Plasmacytoid Dendritic Cell Neoplasm Consortium: position on standards of care and areas of need

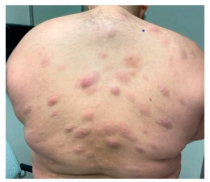
Outline of diagnostic evaluation for BPDCN

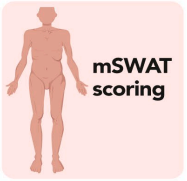
Cutaneous and systemic evaluation

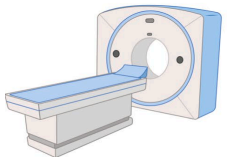


Violaceous skin lesions on inspection

- Skin biopsy and baseline photography

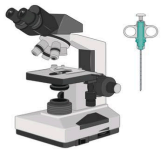




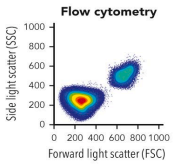


- PET-CT or CT scan for assessment of lymph nodes and/or other extra-medullary disease

Cytomorphological evaluation

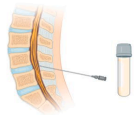


- Bone marrow aspirate and biopsy



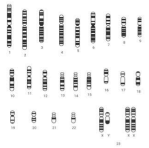
- Flow cytometry evaluation

1. CD123, CD4, D56
2. CD303
3. TCL1
4. TCF4



- CSF evaluation for assessment of CNS disease

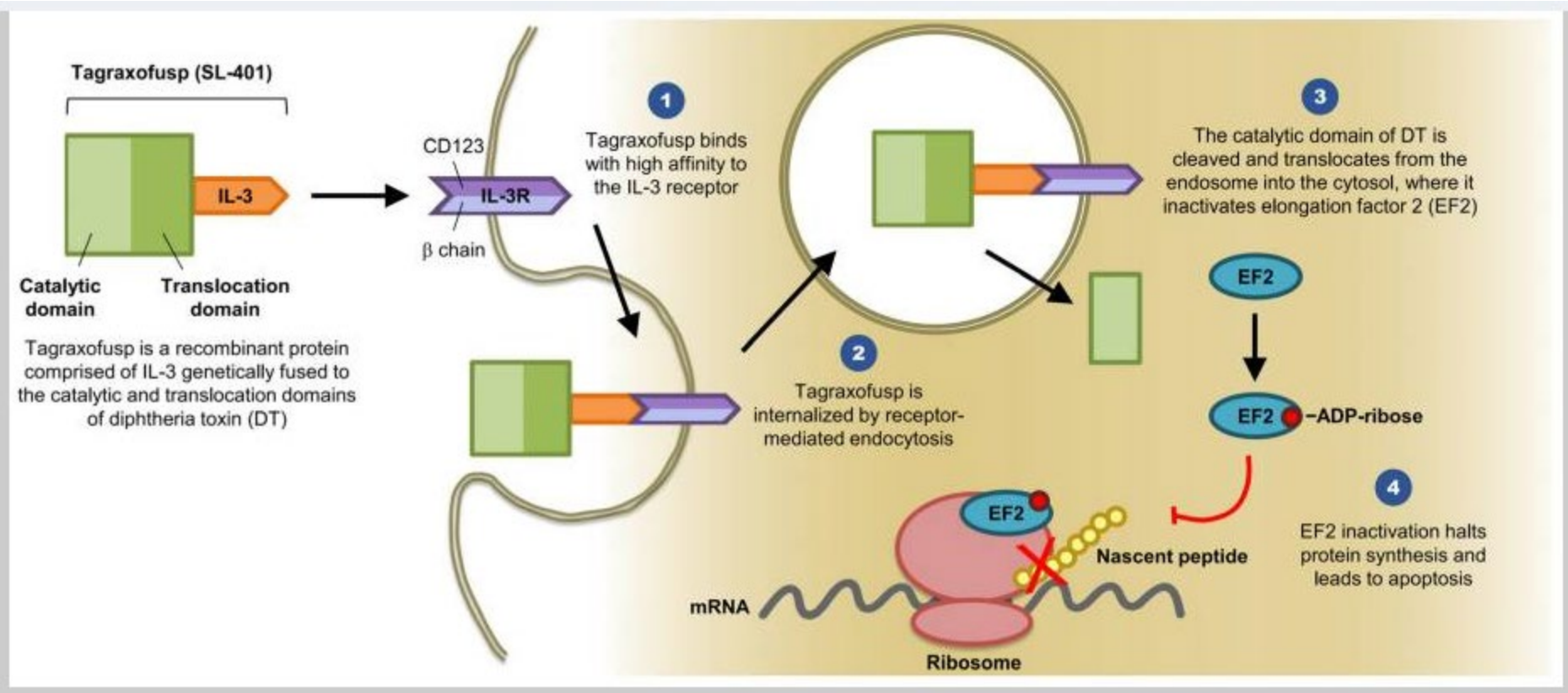
Adjunct tests



- Cytogenetics

- NGS for myeloid mutation assessment

Blood. 2023 Feb 9; 141(6):567-578 | Pemmaraju N, Kantarjian H, Sweet K, et al.



Clinical Activity and Tolerability of SL-401 (Tagraxofusp): Recombinant Diphtheria Toxin and Interleukin-3 in Hematologic Malignancies. Alkharabsheh O, Frankel A. Biomedicines. 2019 Mar; 7(1): 6.

Tagraxofusp in Blastic Plasmacytoid Dendritic-Cell Neoplasm

Characteristic	No Previous Treatment (N=32)	Previous Treatment (N=15)	All Patients (N=47)
Median age (range) — yr	68 (22–84)	72 (44–80)	70 (22–84)
Male sex — no. (%)	26 (81)	13 (87)	39 (83)
White race — no. (%)†	30 (94)	13 (87)	43 (91)
ECOG performance-status score — no. (%)‡			
0	17 (53)	5 (33)	22 (47)
1	15 (47)	10 (67)	25 (53)
BPDCN manifestation — no. (%)			
Bone marrow	15 (47)	9 (60)	24 (51)
Peripheral blood	7 (22)	1 (7)	8 (17)
Skin	31 (97)	13 (87)	44 (94)
Lymph nodes	13 (41)	8 (53)	21 (45)
Previous lines of therapy — no. (%)			
1	NA	9 (60)	NA
2–4	NA	4 (27)	NA
>4	NA	2 (13)	NA

* BPDCN denotes blastic plasmacytoid dendritic-cell neoplasm, and NA not applicable.

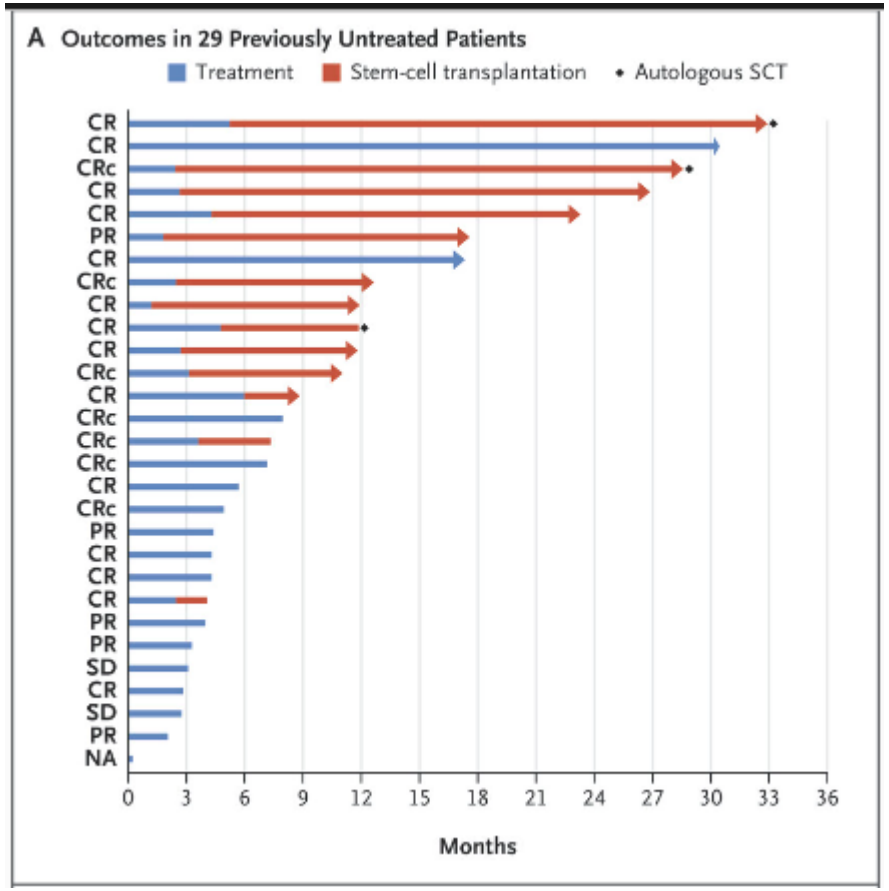
† Race was reported by the patients.

‡ Performance-status scores on the Eastern Cooperative Oncology Group (ECOG) scale range from 0 to 5, with 0 indicating no symptoms and higher scores indicating an increasing severity of symptoms.

N Engl J Med. 2019 Apr 25;380(17):1628-1637 | Pemmaraju N, Lane A, Sweet A, et al

Tagraxofusp in Blastic Plasmacytoid Dendritic-Cell Neoplasm

Clinical Activity



Untreated Patients [24]
- CR + CRc = 72%
- Medium time to response 43 days [14-131]
- 45% of patients bridged to transplant while in remission

Previously Treated Patients [15]
- Overall response rate 67%
- Median time to response 24 days [17-48]
- Median duration of response= 2.8 months [0.7-14]

N Engl J Med. 2019 Apr 25;380(17):1628-1637 | Pemmaraju N, Lane A, Sweet A, et al

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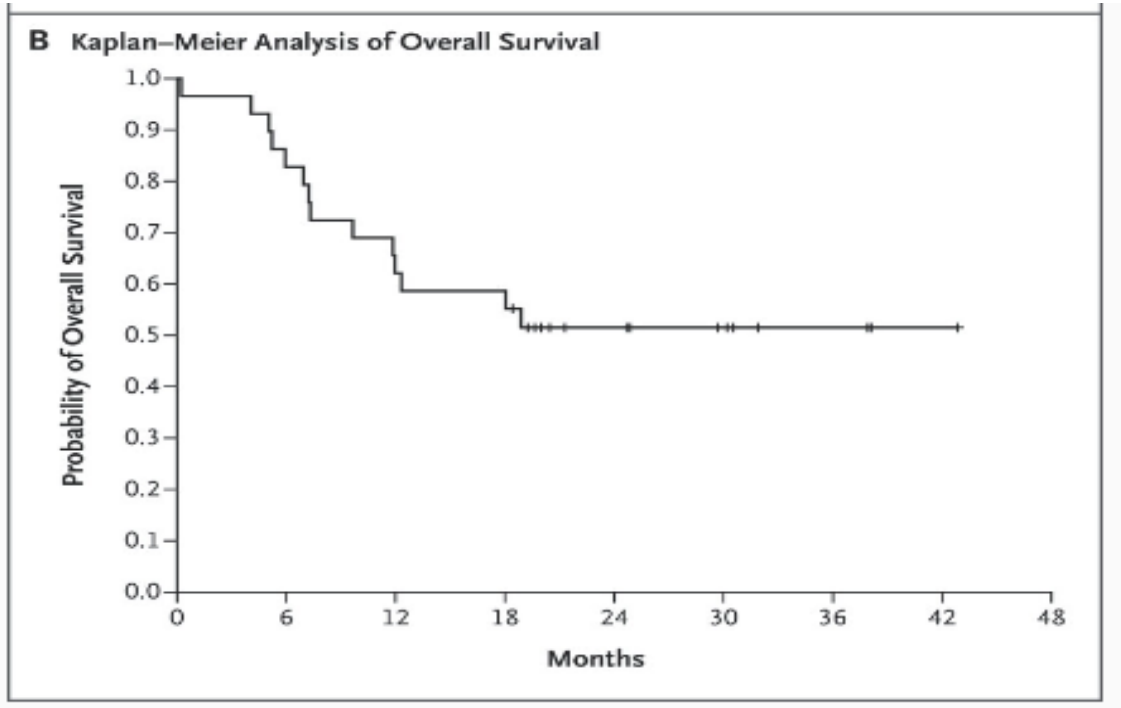


Outcomes in 29 Previously Untreated Patients and Overall Survival

N Engl J Med. 2019 Apr 25;380(17):1628-1637 | Pemmaraju N, Lane A, Sweet A, et al

Real-world Tagraxofusp treatment in R/R BPDCN for patients with very Poor Prognosis

Population with a very poor prognosis was independently and retrospectively analyzed data from patients enrolled in the European Named Patient Program (NPP)

Key Inclusion Criteria

- BPDCN diagnosis by immunophenotyping with established panels inclusive of conventional myeloid and lymphatic lineage markers as well as CD123, CD4, and CD56
- Adults with r/r BPDCN

Endpoints

Primary:

- Complete response (CR) after 2-3 cycles
- Incidence and grade of capillary leak syndrome (CLS)

Secondary:

- Number of patients bridged to stem cell transplantation (SCT)
- Progression-free survival (PFS)
- Overall survival (OS)
- Best overall response rate (ORR)
- Duration of response (DOR)
- Adverse events (AEs)

Real World NPP Treatment

- Patients treated via European NPP at discretion of treating physician:
  - TAG 12 mcg/kg as a daily intravenous infusion on days 1-5 (or by day 10) of each 21-day cycle
  - Hospitalization required for first cycle
  - Subsequent cycles allowed in outpatient setting
  - Clinicians received training on CLS monitoring and management guidelines[4-5]

Herling et al, ASCO 2024

Data Analysis from 18 adults (median age, 66 years) with R/R BPDCN enrolled in the European NPP

Characteristic	Patients (N=18)
Median age, years (range)	66 (29-83)
Gender, no. (%)	
Male	16 (89)
Female	2 (11)
Disease assessment prior to TAG start, no. (%)	n=14*
Bone marrow involvement	12 (86)
Skin involvement	10 (71)
Lymph node involvement	8 (57)
Blood	7 (50)
CNS involvement	4 (29)
Spleen involvement	3 (21)
Median albumin level prior to TAG start, g/L (range)	37 (32-46)
Median time from diagnosis to TAG start, months (range)	7.4 (1-27)
Number of prior lines of therapy	
Median (range)	1 (1-3)
1	12 (67)
2	5 (28)
3	1 (6)
4	0
Allogeneic SCT prior to TAG start, no. (%)	
Yes	4 (22)
No	14 (78)
Status regarding last line of treatment, n (%)	
Refractory	6 (33)
Relapsed	6 (33)
Unknown	3 (17)
Missing	3 (17)

*Assessment available in 14 patients. CNS, central nervous system; SCT, stem cell transplant; TAG, tagraxofusp.

– 3 most common sites of disease involvement prior to TAG start: bone marrow
(86%), skin (71%), and lymph nodes (57%)

- The majority of patients had multiple initial skin lesions

– Median time from initial diagnosis to TAG start: 7.4 mo (range, 1–27)

– Median number of prior lines of therapies was 1

– At a median follow-up of 8 months, patients received a median of 2 (range, 1–5)
cycles of TAG

Herling et al, ASCO 2024

Most CLS events occurred in cycle 1 and were mild

Incidence and Management of CLS Events (All Cycles)

Patients with ≥ 1 observed CLS event, no. (%)	11 (61)
CLS grade*, n (%)	
2	8 (62)
3	4 (31)
4	1 (8)
5	0
Action taken on TAG, no. of events (%)	
No modification	4 (31)
Dose reduced	0
Drug interrupted	5 (39)
Drug withdrawn	4 (31)
Median duration of CLS events, days (range)	4 (2-11)

†As reported by the investigator, symptoms associated with CLS events were edema (n=11 patients), weight gain (n=11), hypotension (n=7), hypoalbuminemia (n=1), and other (n=5).
*As reported for 13 events (12 in cycle 1 and 1 in cycle 2).

How I Manage Capillary Leak Syndrome [CLS]

How to recognize CLS:

- Decrease Albumin
- Gain in Weight
- Edema

How to Manage:

- Stop TAG
- Albumin replacement
- Diuretics
- Steroids

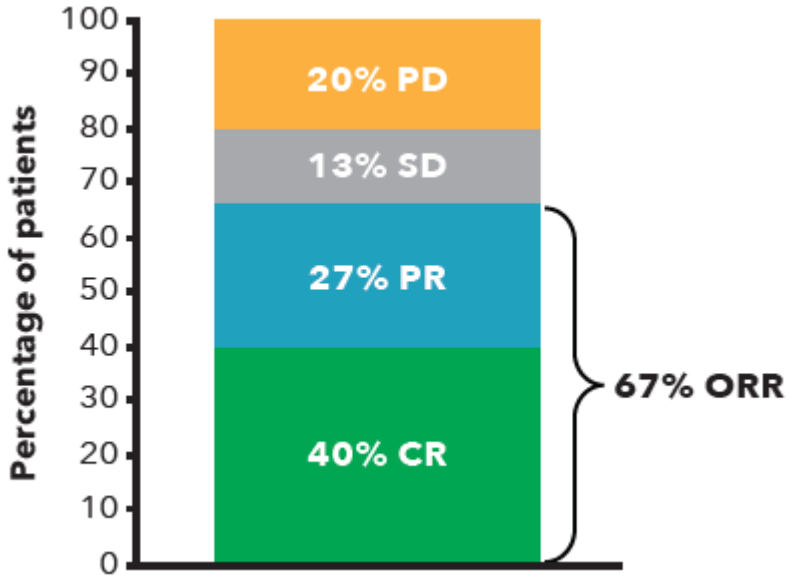
Majority of grade 3-4 AEs occurred during cycle 1 and were transient

AEs Related to TAG (Excluding CLS) in ≥2 Patients

	Pts, no. (%)	Time to resolution, median days (range)
Grade 3-4 Hematologic AEs†		
Thrombocytopenia	2 (11)	18 (7-28)
Pancytopenia	2 (11)	9 (7-10)
Grade 3-4 and SAE Non-hematologic		
Tumor lysis syndrome	2 (11)	4 (1-7)
Hepatic cytolysis	2 (11)	7 (7-7)
Pneumonia	2 (11)	8 (5-11)

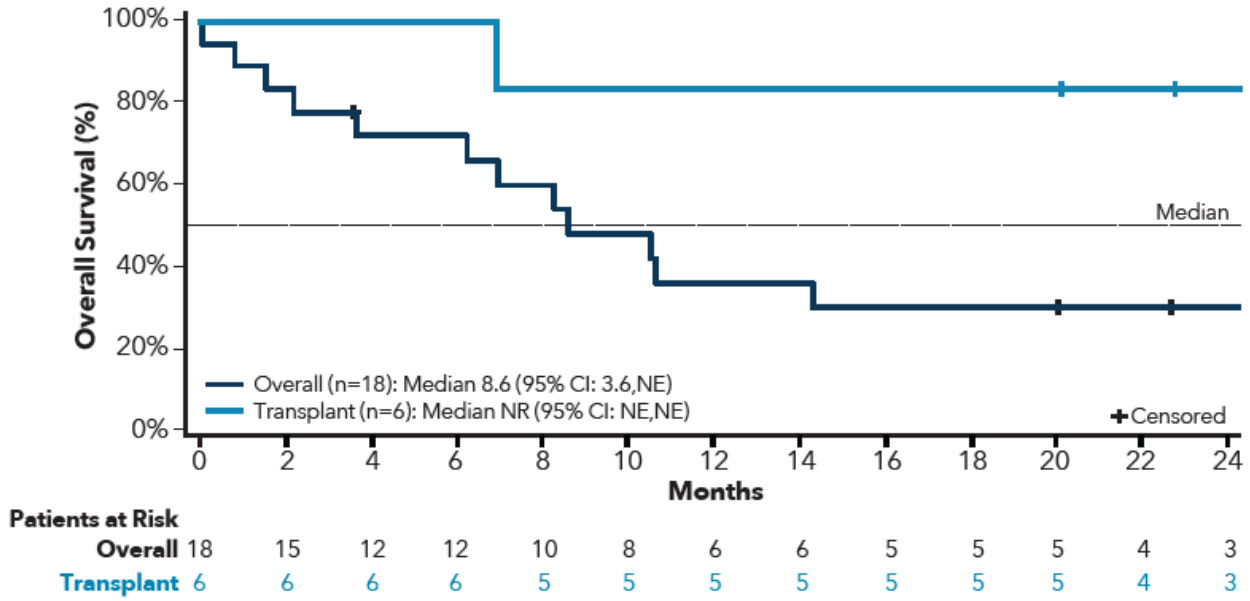
†Serious adverse events (SAEs) were not collected for hematologic AEs.

Patients with R/R BPDCN achieved durable outcomes with Tagraxofusp treatment
ORR: 67% included 40% CRs and 27% PRs; Median DOR: 5.0 months



Real-world Tagraxofusp treatment for patients with R/R BPDCN led to prolonged survival

OS Curves Overall and for Transplanted Patients



*Overall survival is defined as time from start of TAG to death. NR, not reached.

Patients with CNS involvement

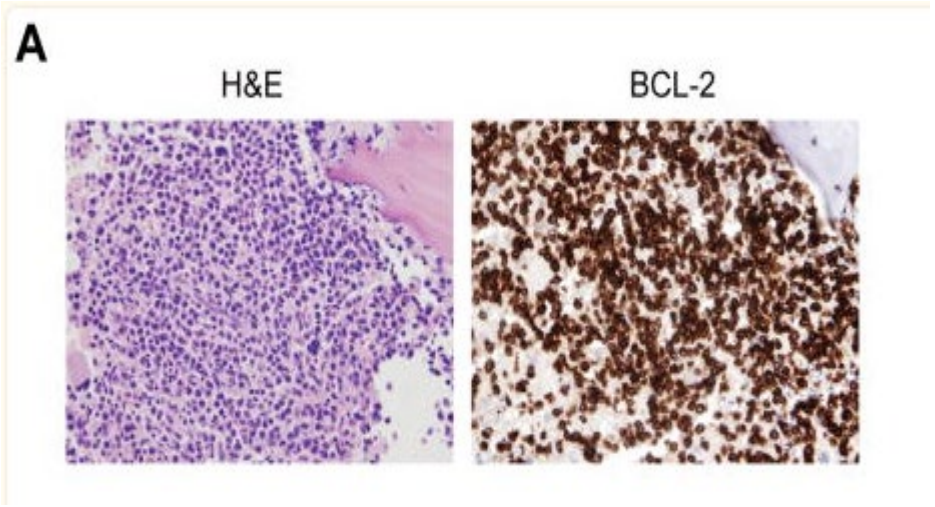
- 4 patients had documented CNS involvement at initial diagnosis and TAG start, 3 of which received intrathecal chemotherapy before initiating TAG
- Of the 3 responders, 2 achieved CR in marrow and one achieved a PR
  - One patient in CR bridged to SCT

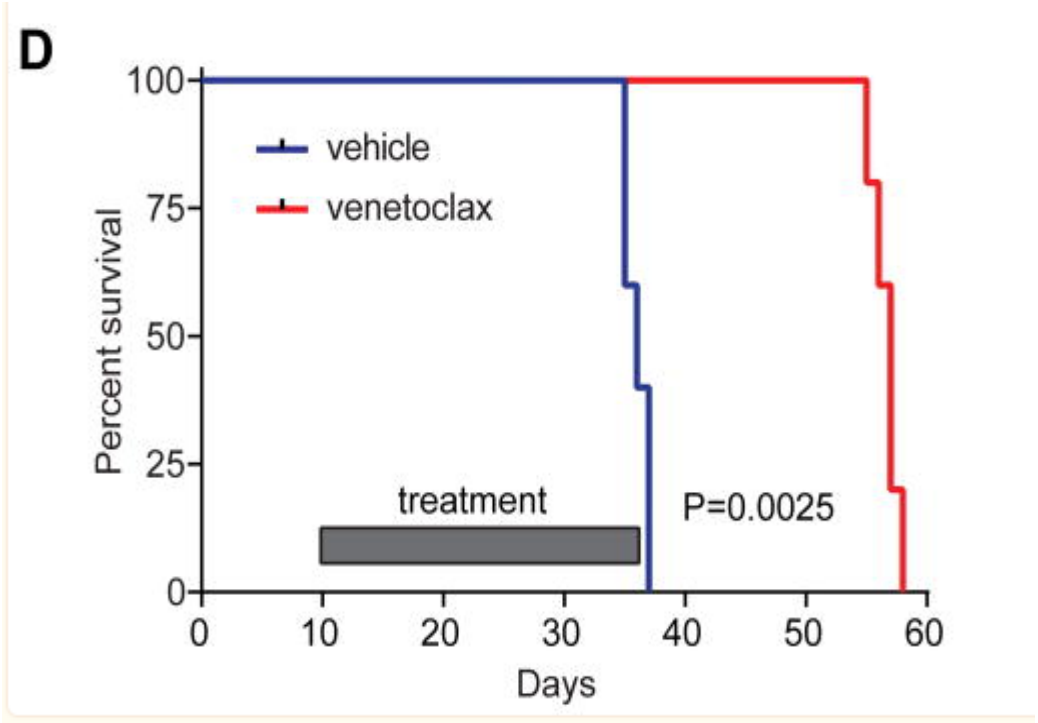
Resistance Mechanisms

- TAG resistance not due to loss of CD123
- Mediated by DNA methylation and down regulation of dipthamide genes which eliminates the diphtheria toxin
- TAG resistance reversed with AZA which increases DPHI expression and restores DT target
- Cell escaping TAG therapy had an altered mitochondrial apoptosis threshold and increased propensity to undergo cell death in setting of BCL-2 inhibition by venetoclax

J Clin Invest. 2019 | Togami K, Pastika T, Stephansky J, et al.

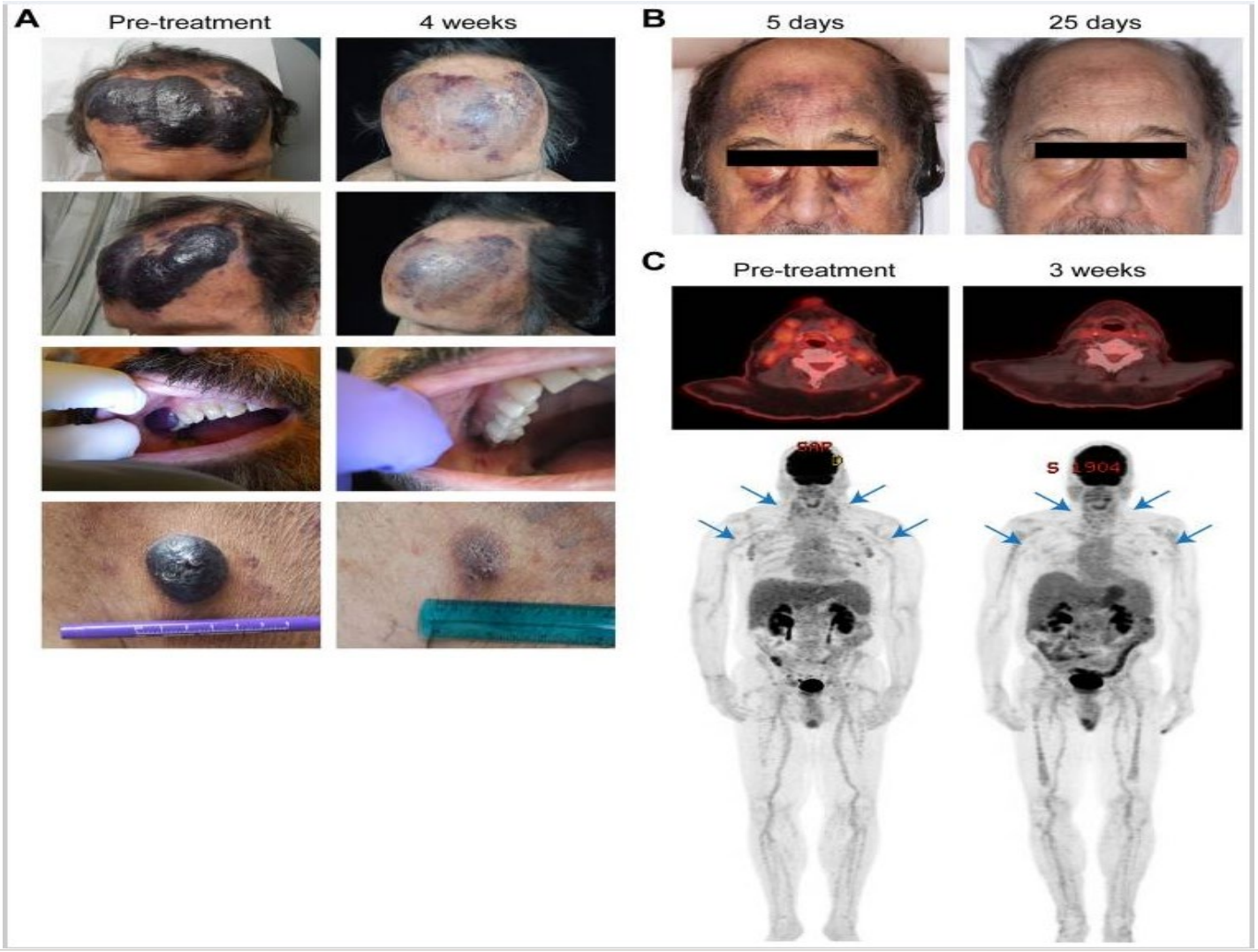
Blastic plasmacytoid dendritic cell neoplasm is dependent on BCL-2 and sensitive to venetoclax





Montero J, Stephansky J, Cai T, et al. Cancer Discov. 2017 Feb;7(2):156-164

Blastic plasmacytoid dendritic cell neoplasm is dependent on BCL-2 and sensitive to venetoclax



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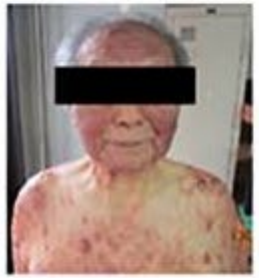
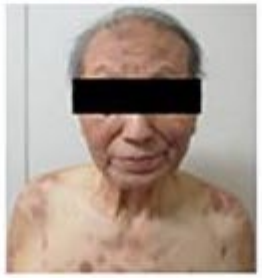
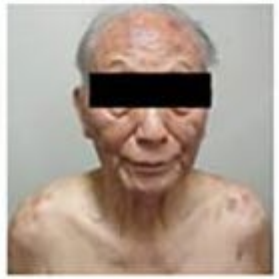
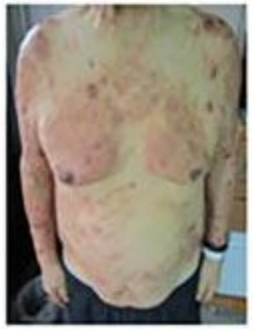
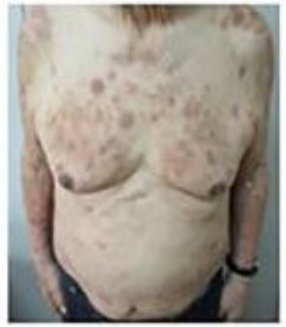
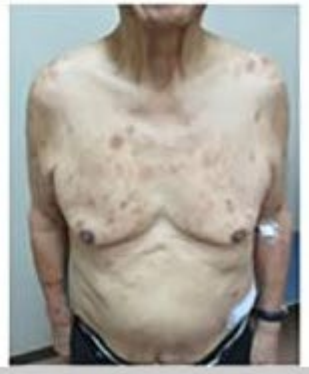
Venetoclax Combined with Azacytidine Can Be a First-line Treatment Option for Elderly Blastic Plasmacytoid Dendritic Cell Neoplasm

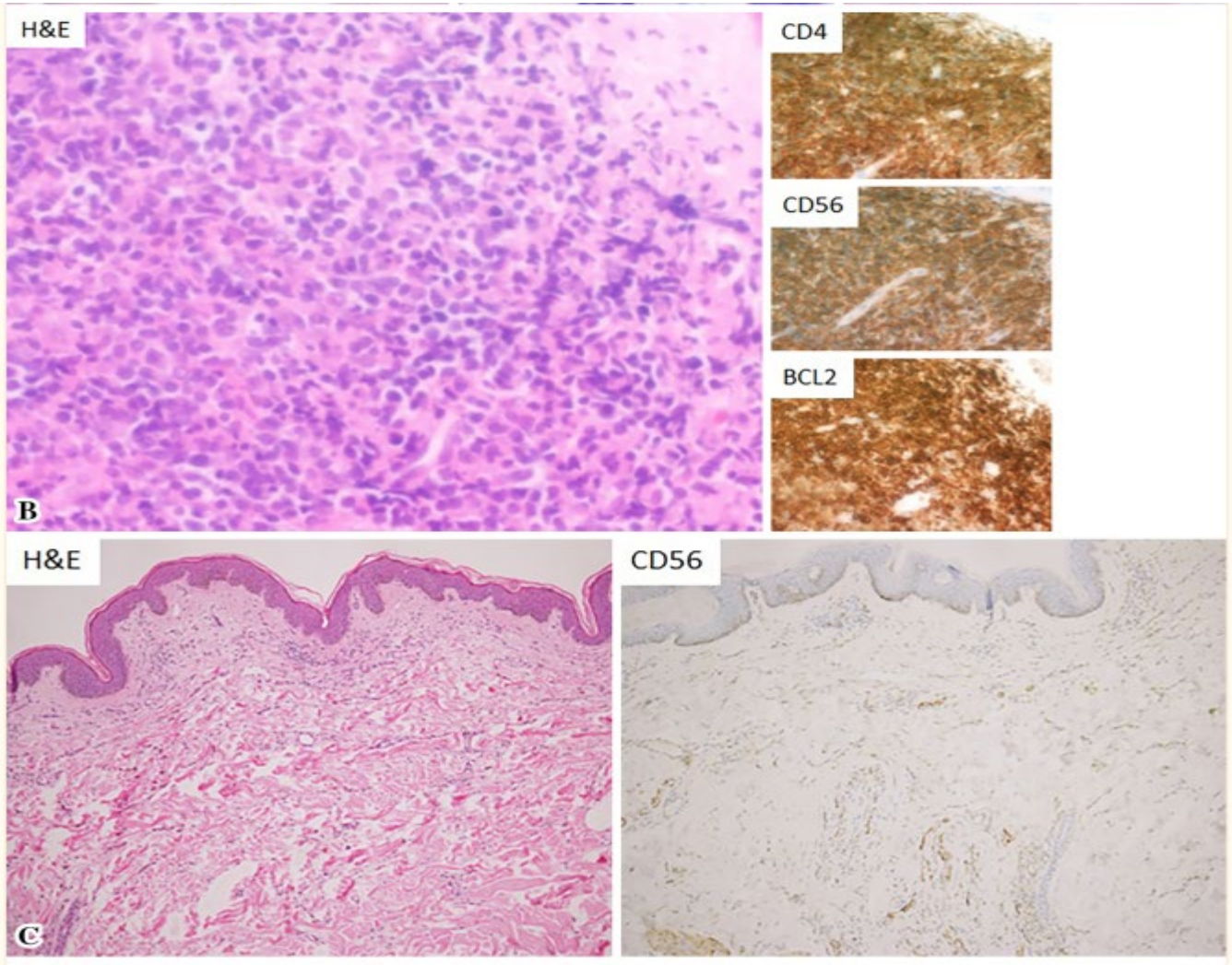
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
	VEN 200mg (day3-28)* AZA 75mg/m^2 (day1-7)	VEN 100mg (day1-21) AZA 75mg/m^2 (day1-7)	VEN 100mg (day1-21) AZA 75mg/m^2 (day1-7)	VEN 100mg (day1-21) AZA 75mg/m^2 (day1-7)	VEN 100mg (day1-21) AZA 75mg/m^2 (day1-7)	VEN 100mg (day1-21) AZA 75mg/m^2 (day1-7)
Adverse Events						
neutropenia	G4	G4	G4	G4	G4	G4
thrombocytopenia	G2	G2	G2	G2	G2	G2
stomatitis	G3	G3	G3	G3	G3	G3
G-CSF		✓	✓	✓	✓	✓



Nagate Y, Nakaya A, et al. Intern Med. 2023 Sep 1; 62(17): 2547-2551

Venetoclax Combined with Azacytidine Can Be a First-line Treatment Option for Elderly Blastic Plasmacytoid Dendritic Cell Neoplasm



Nagate Y, Nakaya A, et al. Intern Med. 2023 Sep 1; 62(17): 2547-2551

VEN+HMA combinations in BPDCN

MDACC-Mayo experience (n=10)

Older/unfit patients with multiple co-morbidities treated off-protocol HMA+VEN approach for BPDCN: med age 70 [20-88 years]

- **AZA+VEN (n=3)**
- **DEC5d+VEN (n=3)**
- **DEC10d+VEN (n=4)**

All 10 patients had some form of response, although some transient,

Including n=2 ultimately bridged to alloSCT

Gangat N- Pemmaraju N. AJH 2022 Feb 1;97(2):E62-E67; epub 2021 Nov 29

Phase 1b trial of tagraxofusp in combination with azacitidine with or without venetoclax in acute myeloid leukemia

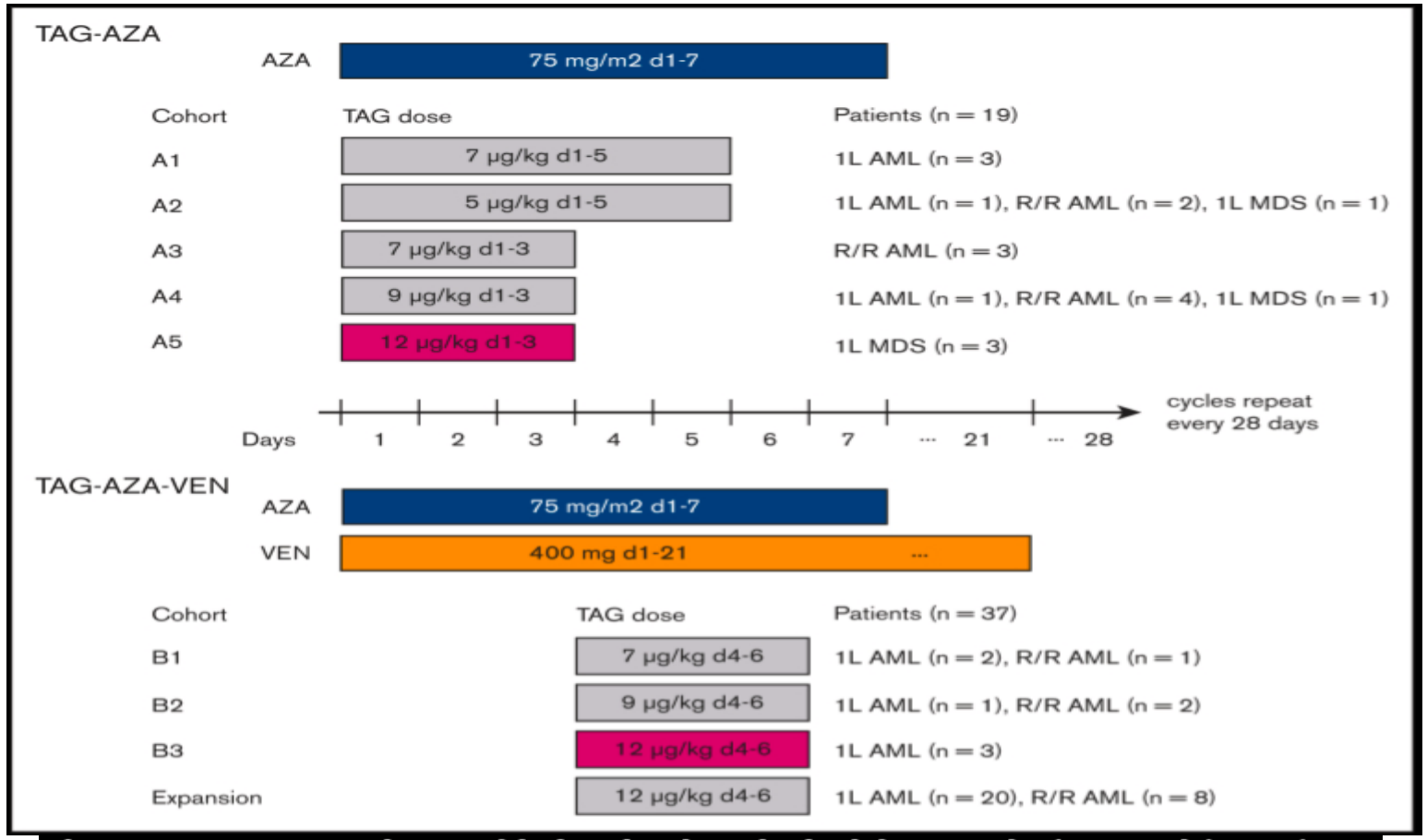


Figure 1. Treatment schema with dose levels and schedules tested. Diagram of the study design and participants. (Top) TAG and AZA were first tested as a doublet combination at 5 different doses/schedules of TAG with 7-day dosing of AZA. The RP2D of TAG was determined to be 12 µg/kg daily for 3 days (d1, 2, 3; in magenta) in combination with AZA. Patients with

Blood Adv. 2024 Feb 13;8(3):591-602 | Lane A, Garcia J, Raulston E, et al.

Triplet TAG-AZA-VEN (n = 37)					
Event term	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	**Total, grade 2+**
Platelet count decreased	2 (5.4)	2 (5.4)	17 (45.9)		21 (56.8)
White blood cell decreased		1 (2.7)	17 (45.9)		18 (48.6)
Neutrophil count decreased			14 (37.8)		14 (37.8)
Anemia	1 (2.7)	10 (27)	1 (2.7)		12 (32.4)
Febrile neutropenia	1 (2.7)	9 (24.3)	1 (2.7)		11 (29.7)
Infections and infestations - other	2 (5.4)	6 (16.2)			8 (21.7)
CLS	5 (13.5)	1 (2.7)	1 (2.7)		7 (18.9)
Lymphocyte count decreased			5 (13.5)		5 (13.5)
Tumor lysis syndrome	1 (2.7)	4 (10.8)			5 (13.5)
Sepsis		1 (2.7)	1 (2.7)	2 (5.4)	4 (10.8)

Blood Adv. Lane A, Garcia J, Raulston E, Garzon J, et al.

Tagraxofusp, a first-in-class CD123-targeted agent: Five-year post approval comprehensive review of the literature

TABLE 2. Novel CD123-directed therapies.

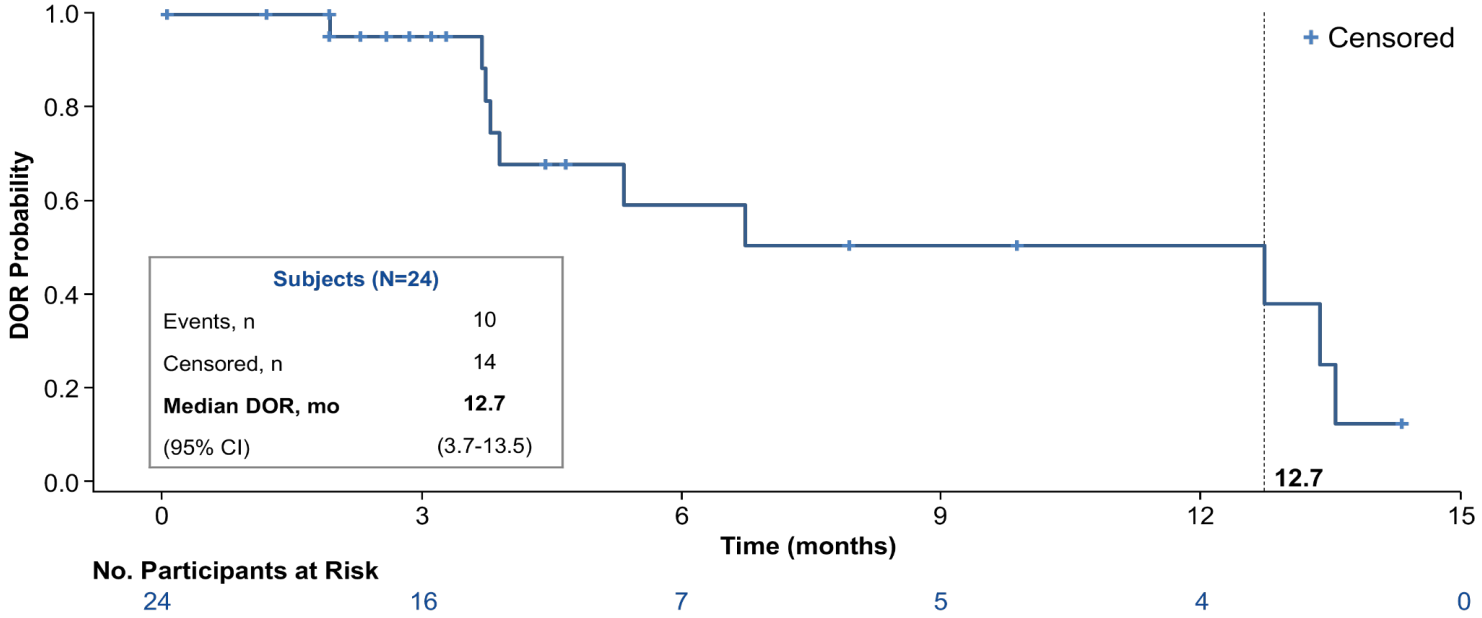
Therapy	Class	NCT ID	Data supporting use
Pivekimab sunirine	ADC	NCT03386513	BPDCN: ORR 81% (26% in tagraxofusp exposed)[108]
		NCT04086264	AML: ORR 21% (monotherapy)[109]
			AML: CRc 66% (with HMA-VEN)[110]
CD123 CAR T cells	CAR-T	NCT02159495	BPDCN: case report of CR after infusion[111]
Flotetuzumab	DART	NCT02152956	AML: ORR 30%[112]
		NCT04681105	
Vibecotamab	BiTE	NCT02730312	AML: ORR 9%[113]
		NCT05285813	MDS/CMML: ORR 64%[114]
APV0436	BiTE	NCT03647800	AML: ORR 20%–40% (monotherapy or in combination)[115]
SAR443579	NKCE	NCT05086315	AML: CRc 13%[116]

Jen W-Y, Konopleva M, et al. Cancer. Vol 130, Issue 13. July 1 2024

Response Data in Frontline BPDCN

ORR= CR+CRc+CRh+CRi+PR
Composite CR=CR+CRc+CRh+CRi

Frontline patients (N=30)		
	ORR	**Composite CR**
Response rate	**80% (24/30)**	**73% (22/30)**
Time to first response		
Median (range), months	1.3 (0.5-3.5)	1.5 (0.5-4.6)



- The safety profile was manageable with mostly low-grade peripheral edema and infusion-related reactions
- PVEK monotherapy leads to high composite CR rates (73%) in frontline BPDCN (median DOR 12.7 months (95% CI 3.7-13.5), as well as durable responses in R/R patients (DOR 7.1 months), including those treated with prior tagraxofusp

Pemmaraju N, et al, EHA 2023 Abstract S139

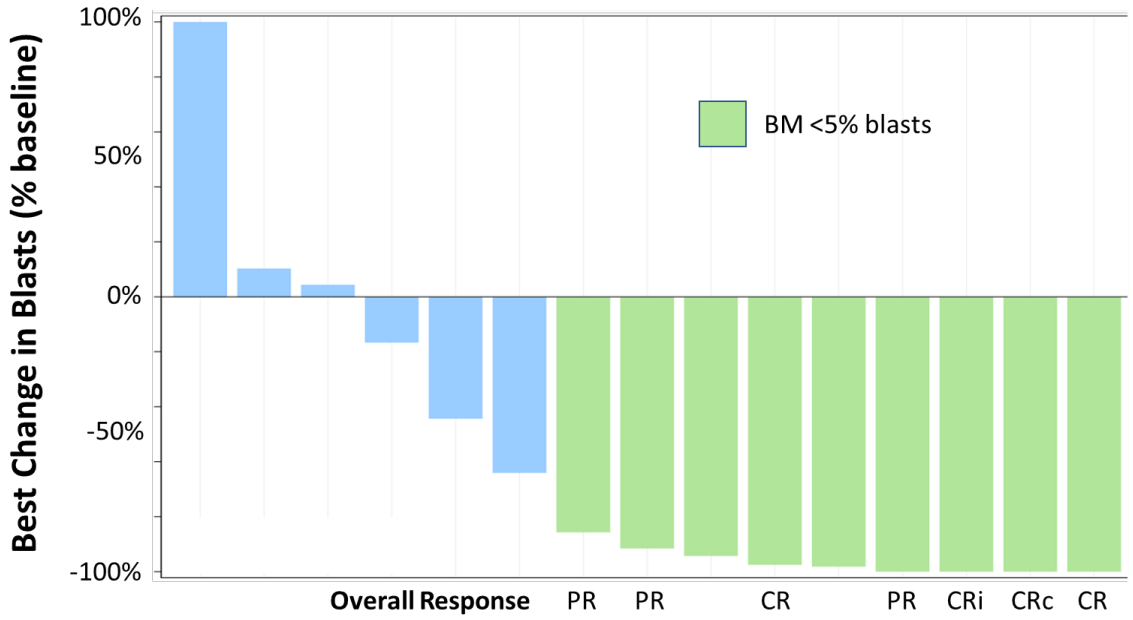
IMGN632 in R/R BPDCN: Efficacy

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

Pemmaraju et all IMGN632 in BPDCN, Abstract #167: 2023

Targeting CD123 in BPDCN using Allo Anti-CD123 CAR-T Cells

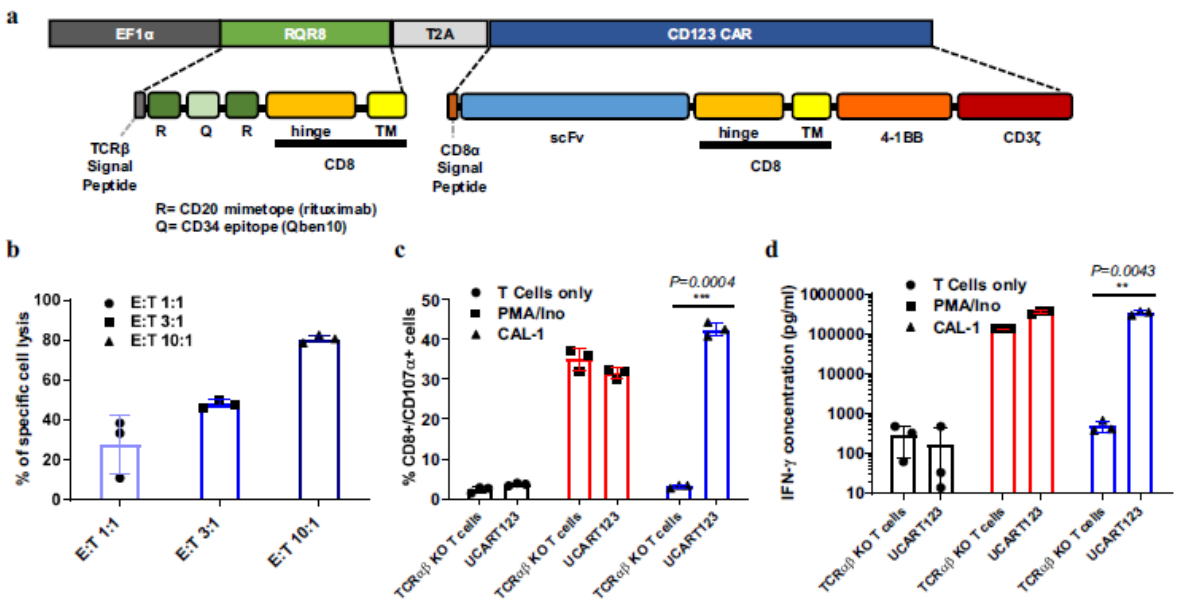


Fig. 1 Cytotoxicity of UCART123 against CAL-1 BPDCN cells in vitro. a UCART123 cells express (i) a second-generation chimeric antigen receptor (CAR;

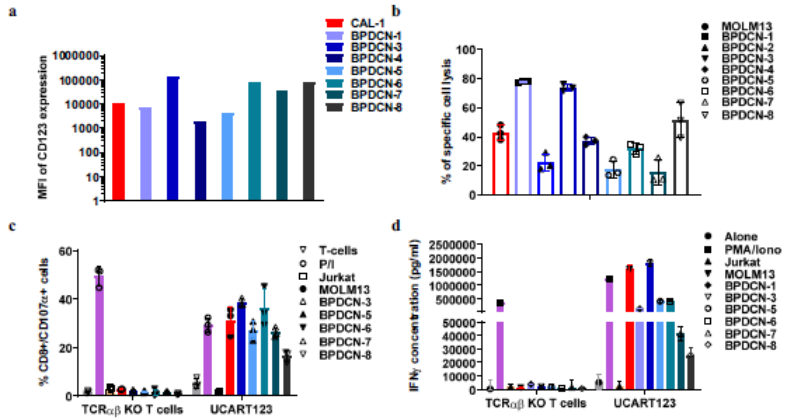


Fig. 2 Antitumor activity of UCART123 against primary BPDCN samples in vitro. a Expression of CD123 in CAL-1 cells and BPDCN patient samples was

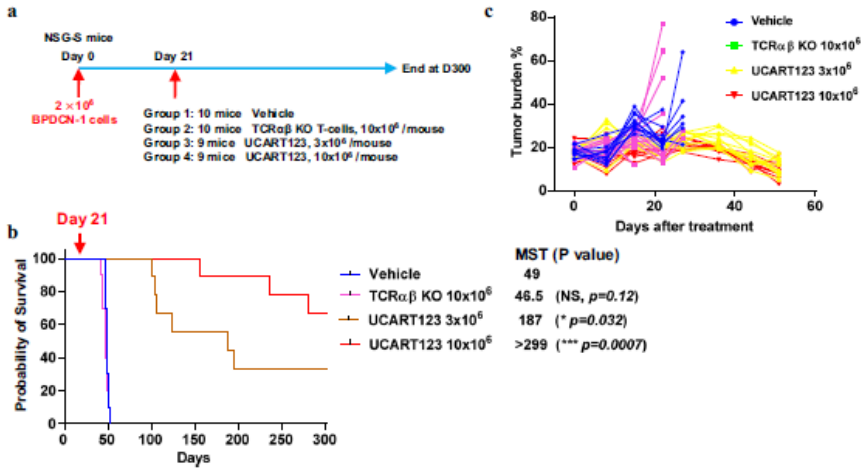


Fig. 3 UCART123 treatment results in long-term survival of primary BPDCN PDX. a Experimental design. NSGS mice were injected intravenously with

Cai, T / Konopleva M et al *Nat Commun* 2022 Apr 28;13(1):2228

Allogeneic Hematopoietic Cell Transplantation for Blastic Plasmacytoid Dendritic Cell Neoplasm: A CIBMTR Analysis

Patient Characteristics [164 patients between 2007-2018]

	MAC	RIC (NMA)
Age	49 (18-70)	65 (20-78)
Sex		
Male	60 (71)	66 (83)
Female	24 (27)	14 (18)
HCT-CI		
0	27 (32)	16 (20)
1-2	24 (29)	26 (33)
≥3	32 (38)	36 (45)
Not Reported	1 (1)	2 (3)
Disease Status		
Primary Induction Failure	10 (12)	10 (13)
CR1	62 (74)	59 (74)
CR2	10 (12)	7 (9)
Relapse	2 (2)	4 (5)

Blood Adv. 2023 Nov 28;7(22):7007-7016

Allogeneic Hematopoietic Cell Transplantation for Blastic Plasmacytoid Dendritic Cell Neoplasm: A CIBMTR Analysis

Patient Characteristics [164 patients between 2007-2018]

	MAC	RIC (NMA)
Time from Diagnosis to HCT		
<6 months	50 (60)	32 (40)
6-12 months	29 (35)	37 (46)
>12	5 (6)	11 (14)
GRAFT Type		
BM	9 (11)	9 (11)
Peripheral Blood	68 (81)	67 (84)
Cord Blood	7 (8)	4 (5)
TBI Usage		
No	40 (48)	47 (59)
Yes	44 (52)	33 (41)

Blood Adv. 2023 Nov 28;7(22):7007-7016

Allogeneic Hematopoietic Cell Transplantation for Blastic Plasmacytoid Dendritic Cell Neoplasm: A CIBMTR Analysis

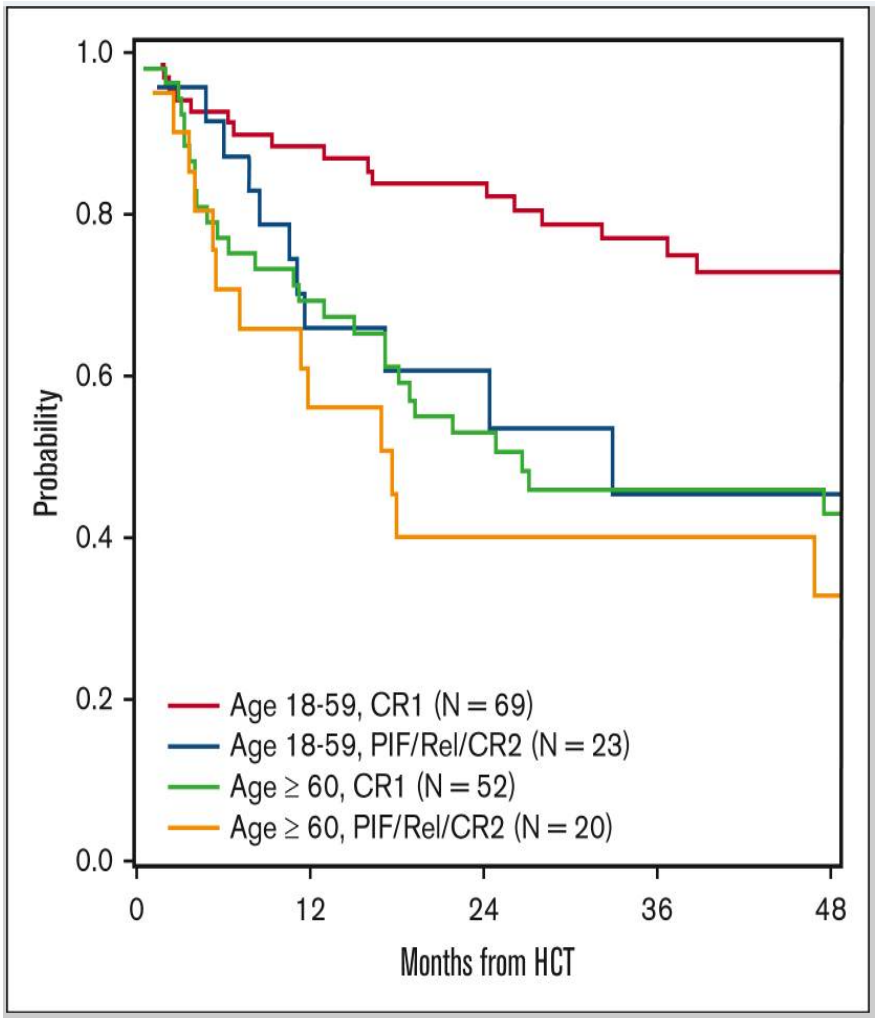
Table 2.

Multivariate analysis results

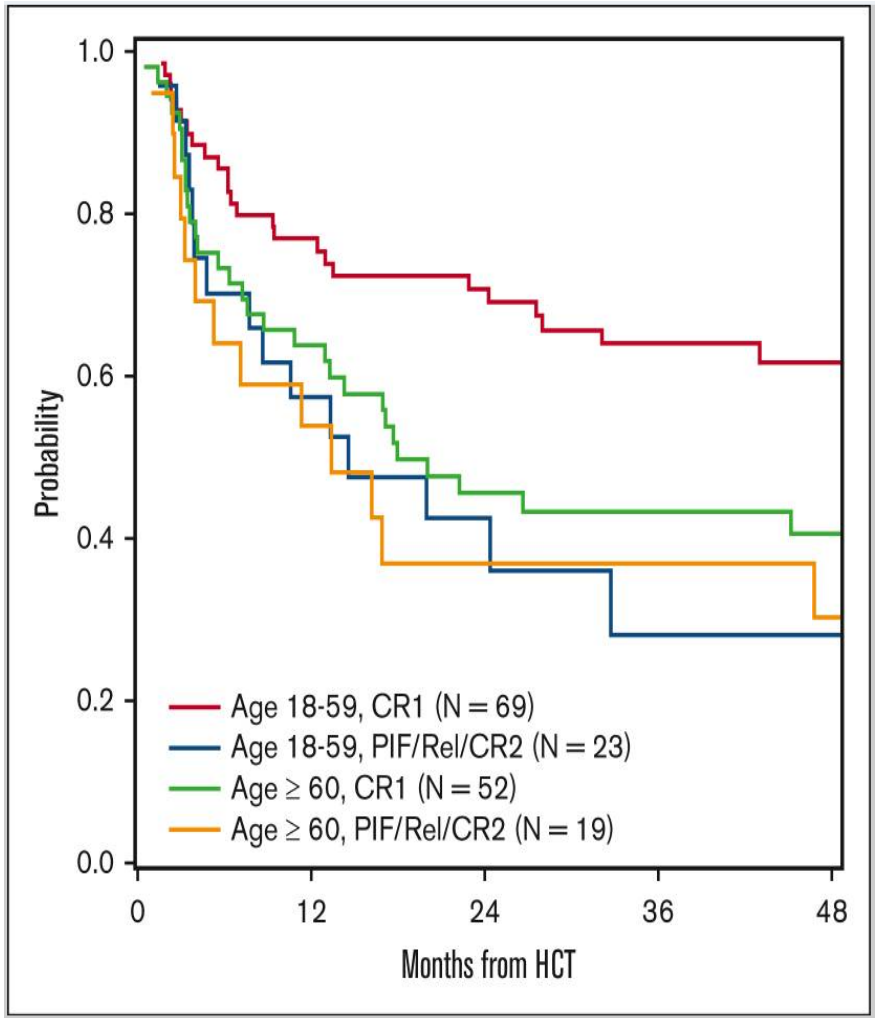
≥60	72	2.16 (1.35-3.46)	.001
Disease status			
CR1	121	Reference	
PIF/CR2/relapse	43	1.87 (1.14-3.06)	.01
DFS			
Disease status			
CR1	121	Reference	
PIF/CR2/relapse	42	1.75 (1.11-2.76)	.02
Conditioning intensity/TBI usage			.003
MAC/TBI	43	Reference	
MAC/no TBI	41	2.89 (1.41-5.94)	.004
RIC/NMA	79	3.09 (1.59-5.98)	.001
RIC/NMA vs MAC/no TBI		1.07 (0.66-1.73)	.79
Relapse			
Conditioning intensity/TBI usage			.03
MAC/TBI	43	Reference	
MAC/no TBI	41	3.28 (1.27-8.5)	.01
RIC/NMA	79	3.13 (1.29-7.61)	.01
RIC/NMA vs MAC/no TBI		0.95 (0.51-1.80)	.88
NRM			
Age (y) at HCT			
<60	92	Reference	
≥60	71	2.19 (1.13-4.22)	.02

PIF, primary induction failure.

Blood Adv. 2023 Nov 28;7(22):7007-7016



OS by age and remission status. Rel, relapse; PIF, primary induction failure.



DFS by age and remission status. Rel, relapse; PIF, primary induction failure.

HCVAD in BPDCN: Still a key role in Modern Treatment Era

- Among N=100; n=35 →HCVAD-based frontline
- CR 80%
- Med OS = 28 months
- 2 LPs per cycle , alternating IT MTX with ARA-C (as in ALL paradigm) x 4 cycles

Pemmaraju N, Wilson NR, Garcia-Manero G et al. Blood Advances Jan 21, 2022

General Treatment Schema: Frontline SL-401 (TAG) + HCVAD/mini-CVD + VEN in BPDCN: Triple/Total Therapy

Induction Cycle 1 =TAG <u>single-agent induction</u>

Induction: SL-401, at 12 ug/kg/IV per day (Days 1-5, 10-day window)

Cycle 2, 4, 6, 8 = <u>TAG (Days 1 – 5) [10-day window] + VEN (Cycle 2 Days 1 – 14, Cycles 4, 6, 8 Days 1-7)</u>

Cycles 3, 5, 7 = <u>VEN & HCVAD/ mini-CVD regimen</u>

HCVAD/mini-CVD (age-adjusted) regimen + VEN (Days 1-7)

<u>Maintenance:</u>

POMP x 24 months, in addition to Venetoclax Days 1-7;

With 3 more consolidative cycles of TAG+VEN to be given Maint Month: 6, 12, and 18

<u>Cycle 3, 5, 7 = Intrathecal chemotherapy (IT chemo):</u>

Lumbar Puncture (LP) IT chemo: 2 LP /IT chemo per cycle, during Cycles 3, 5, 7, alternating ARA-C and MTX, as in ALL chemotherapy regimens (total 6 IT).

→

In-House Correlatives on each patient enrolled:

APOLLO TEAM: Selected for Rare Disease Initiative (RDI)

ClinicalTrials.gov ID NCT04216524

CSF+ in BPDCN: A Frequent Occurrence even in Modern Treatment Era

Among n=103 patients BPDCN: MDACC series (Pemmaraju/Kantarjian)

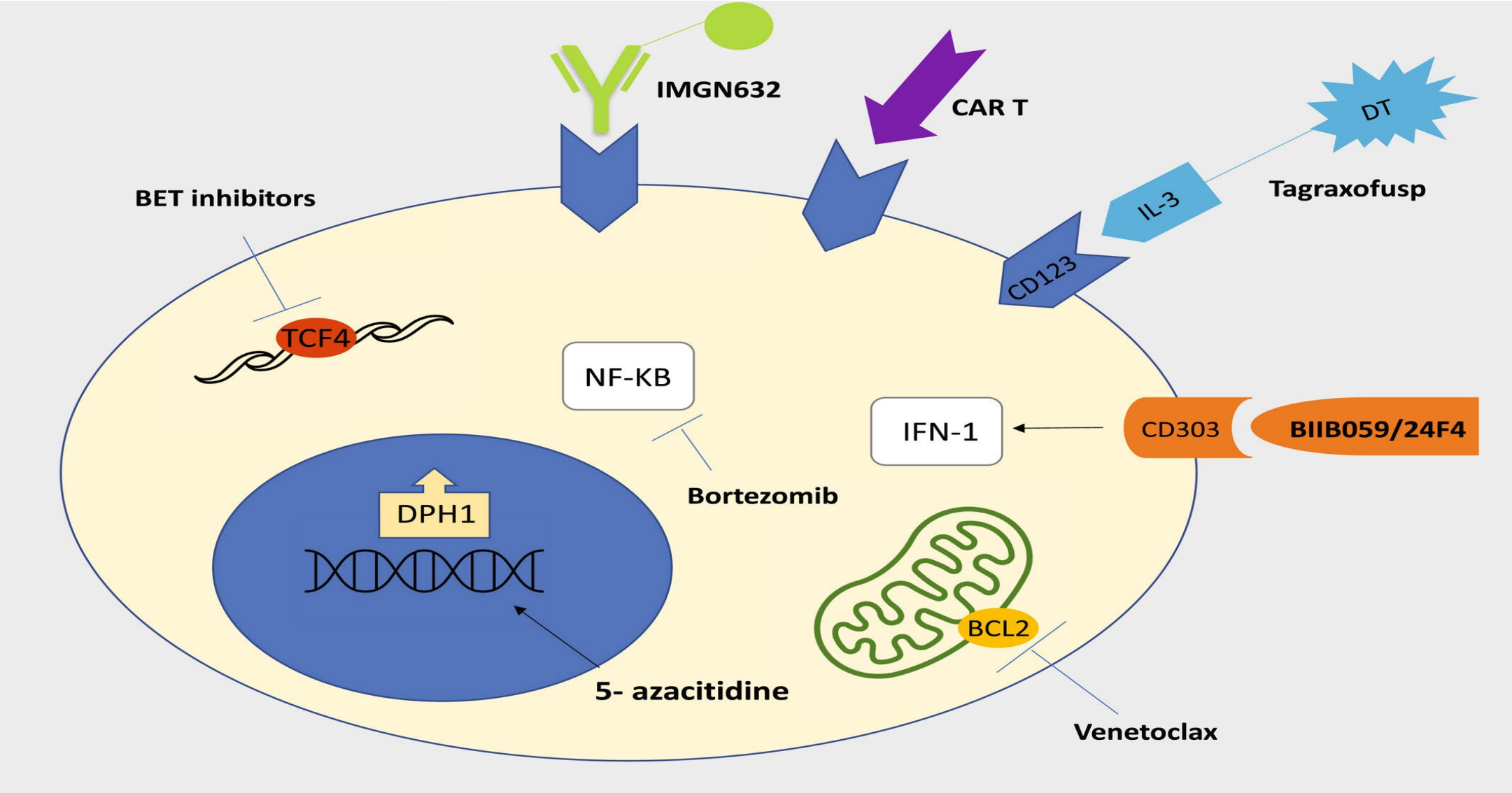
22% were CSF+ at anytime during BPDCN disease course

- **Among these n=23 patients:**
  - **57% = frontline setting, most occult/asymptomatic**

CSF+ cohort : significant p-values for:

- **Lower median baseline Hb**
- **Higher frequency of *TET2* mutations/variants**
- **Higher rate of bone marrow involvement (96% of patients with CSF+ had BM involvement)**

Action plan: Implement systematic use of LP's with IT chemo as we do in ALL/Burkitt's



Cancer. Vol 128, Issue 16. Aug 15, 2022, pages 3019-3026

Current & Future Treatment Approaches for BPDCN: FRONTLINE

Frontline BPDCN: SOC: CD123 or chemo/VEN, chemo-directed +alloSCT in CR1

- Historical: cytotoxic chemo: ALL-based HCVAD: ORR ~80% +/- VEN
- SL401: ORR 75% frontline; CLS
- IMGN 632 clinical trial –frontline enrolling (recent EHA dataset)
- HMA+VEN older/unfit
- CNS-directed IT chemo (CSF+ 22%)
- AlloSCT in CR1 (autoSCT is used, but unclear in modern era of BPDCN)

Frontline BPDCN: Recommended & FUTURE Triplets →CD123/BCL2/Chemo with CNS-directed: CLINICAL Trials

- SL401/VEN/HCVAD : younger/fit
- SL401/VEN/AZA : older/unfit
- CNS-directed IT chemo: 2x/cycle x8 alternating IT ARAC and MTX for all patients with BPDCN
- Eliminate need for SCT if CR/MRD negative?