



MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

BOLOGNA, ROYAL HOTEL CARLTON
12 OTTOBRE 2026

BPDCN: panoramica oggi

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Istituto di Ematologia «Seràgnoli»*

MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

Disclosures of CRISTINA PAPAYANNIDIS

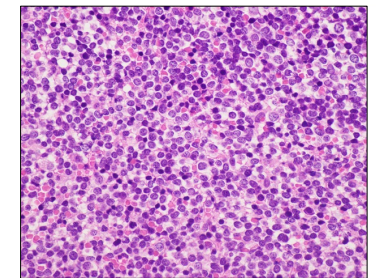
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Abbvie							X
Astellas							X
Servier						X	X
Menarini							X
BMS							X
Pfizer							X
Amgen						X	X
Janssen						X	
GSK						X	
Blueprint							X
Incyte							X
Imcheck						X	
AZD						X	
Kura Oncology						X	
Jazz pharmaceuticals							X
MSD						X	
Otsuka						X	
Syndax						X	

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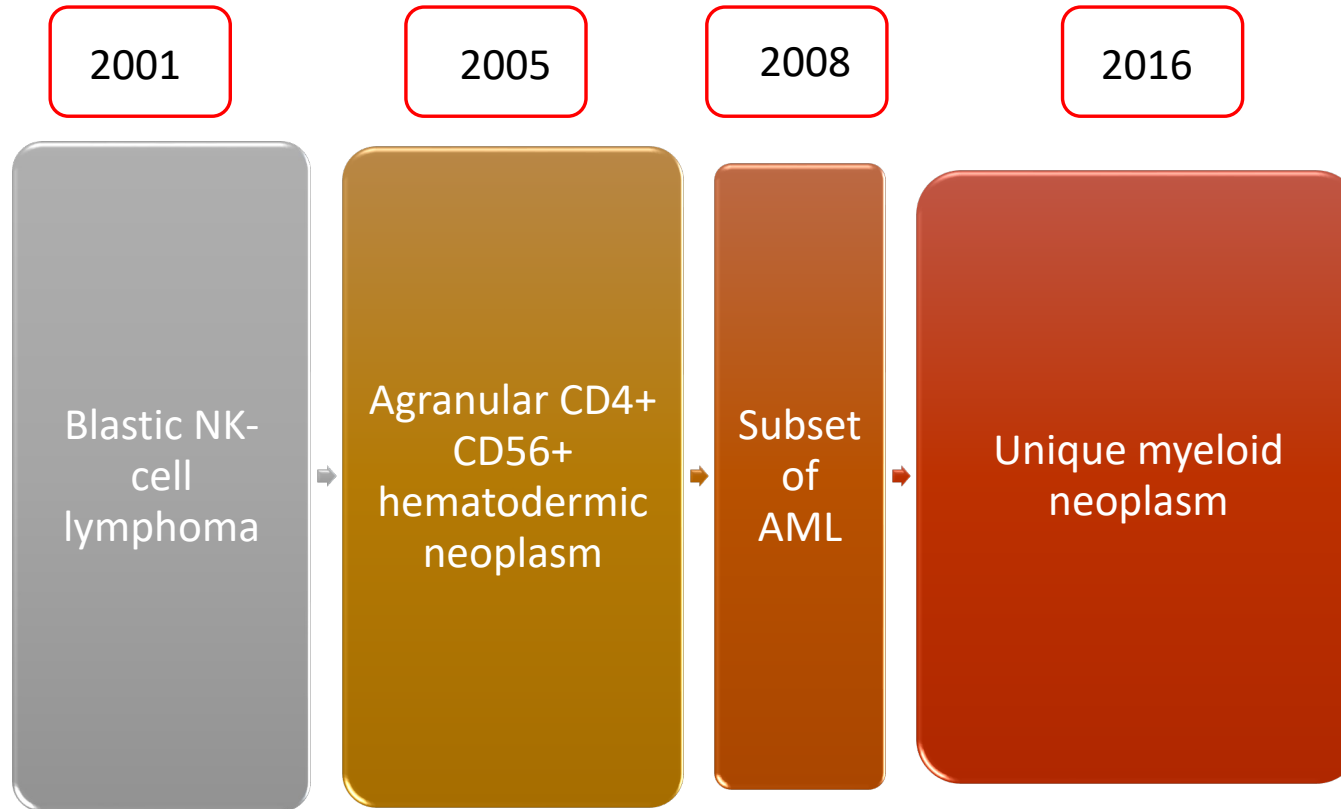
Background and epidemiology

- BPDCN is a **highly aggressive malignancy** accounting for **0.44%** of all hematological malignancies
- Exact incidence of BPDCN is **difficult to estimate** due to its rarity, evolving terminology and likely underdiagnosis
- An estimated **1000 to 1400 cases** annually in the US and Europe combined is reported
- BPDCN is typically a disease of the **middle-aged** and elderly, with a median age at diagnosis in the mid-60s
- **Males** are disproportionately affected, with a sex ratio of 2.5:1
- **Pediatric cases** have also been described in children as young as 8 months of age



Sullivan JM et al, Hematology Am Soc Hematol Educ Program 2016; Falcone U et al, Crit Rev Oncol Hematol 2016; Shapiro R et al, J Cell Sci Ther 2015; Nguyen CM et al, Am J Dermatopathol 2015; Jagalian AG et al, Haematologica 2010; Pemmaraju N et al, NEJM 2019

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Frequent reclassification and renaming has contributed to **under recognition**

Vardiman JW et al. Blood, 2009; Arber DA et al. Blood, 2016; Arber et al. Blood 2022; Khoumry et al. Leukaemia 2022

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2022 WHO Classification

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

Khoury JD et al. Leukemia 2022

ICC

Table 1. Major ICC categories of myeloid neoplasms and acute leukemias

- Myeloproliferative neoplasms
- Myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions
- Mastocytosis
- Myelodysplastic/myeloproliferative neoplasms
- Pre-malignant clonal cytopenias and myelodysplastic syndromes
- Pediatric and/or germline mutation-associated disorders
- Acute myeloid leukemias
- Myeloid proliferations associated with Down Syndrome
- Blastic plasmacytoid dendritic cell neoplasm
- Acute leukemia of ambiguous lineage
- B-lymphoblastic leukemia/lymphoma
- T-lymphoblastic leukemia/lymphoma

Arber DA et al, Blood 2022

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Variability of presentation of BPDCN

- Approximately **80%-90%** of patients diagnosed with BPDCN present with **skin lesions**
- A significant percentage (**40%-60%**) of patients initially present with involvement of the **bone marrow and lymph nodes**.
- Other extracutaneous sites may include: spleen, liver, tonsils and **CNS**
- In few cases BPDCN patients may present with bone marrow disease without skin involvement

N=398

Characteristic	Data
Males/females	294 (74)/104 (26)
ECOG score 0-1	207 (65)
Age, median (range), y	67 (18-96)
Localization	
Skin	353 (89)
BM	243 (62)
Peripheral blood	36 (15)
Lymph nodes	152 (39)
Forms	
Cutaneous isolated	121 (30)
Disseminated with cutaneous localization	200 (50)
Disseminated with cutaneous and extranodal localization	26 (7)
Disseminated noncutaneous	43 (11)
Disseminated noncutaneous with extranodal localization	8 (2)

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Skin involvement

- Cutaneous lesions **vary** in size, shape, color and distribution and **can be confused** with other benign and malignant skin lesions
- They can appear as bruise-like or erythematous papules, plaques or tumors, commonly on the face, trunk and extremities, although they **can occur anywhere**
- These lesions may appear to be **indolent initially**, but **progression invariably occurs** with involvement of multiple sites including bone marrow, peripheral blood, lymphnodes, liver, spleen and, in some cases, CNS



Pagano. Br J Haematol. 2016; Sullivan. Hematology Am Soc Hematol Educ Program. 2016; Julia F et al, Br J Dermatol 2013; Shapiro R et al, J Cell Sci Ther 2015

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Clinical scenario 1

GENERAL
PRACTITIONER??

Atypical skin
lesion



Dermatologist



Biopsy

Often mistaken for other, more familiar hematologic malignancies (AML, leukemia cutis, NHL, ALL, CMML, MDS, cutaneous lymphoma), leading to **frequent misdiagnosis or underdiagnosis of BPDCN**

Mean time between the **onset** of lesions and the pathologic **diagnosis** of BPDCN is **6.2 mos** based on a retrospective analysis

Expertise is required:
Differential diagnosis

Julia F et al, Br J Dermatol 2013

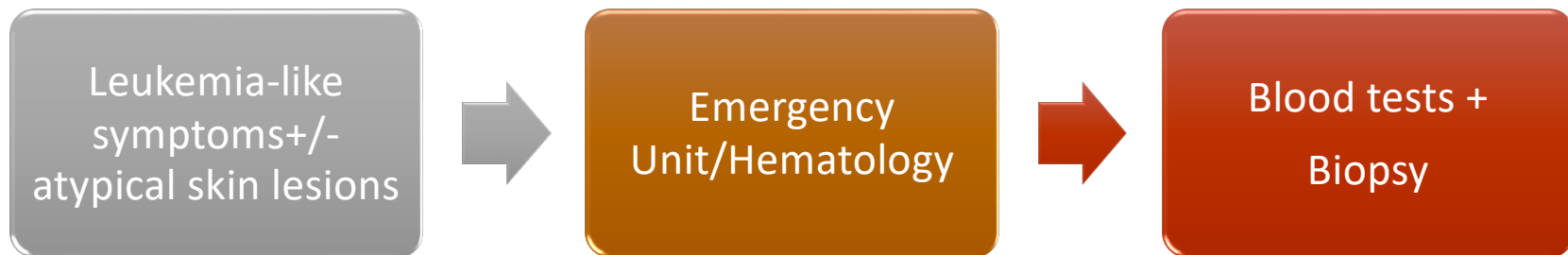


Speaker's opinion

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Clinical scenario 2

Often mistaken for other, more familiar hematologic malignancies (AML, leukemia cutis, NHL, ALL, CMML, MDS, cutaneous lymphoma), leading to **frequent misdiagnosis or underdiagnosis of BPDCN**



GENERAL
PRACTITIONER????

Expertise is required:
Differential diagnosis

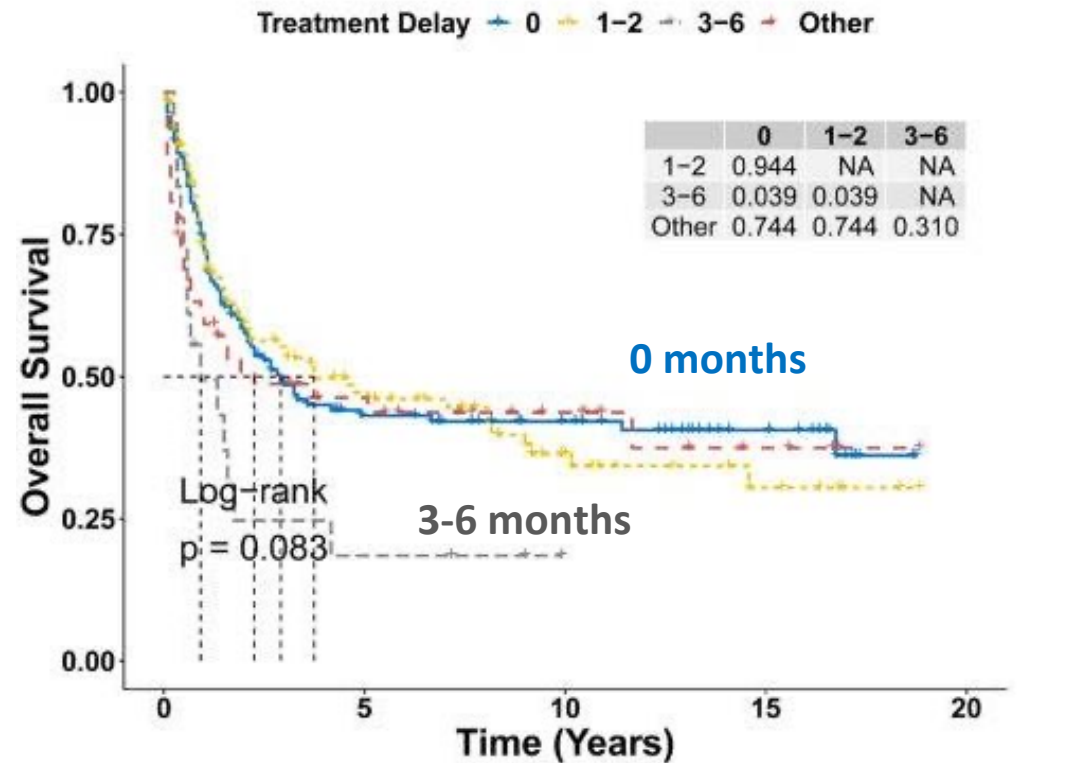


Speaker's opinion

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Impact of treatment delay

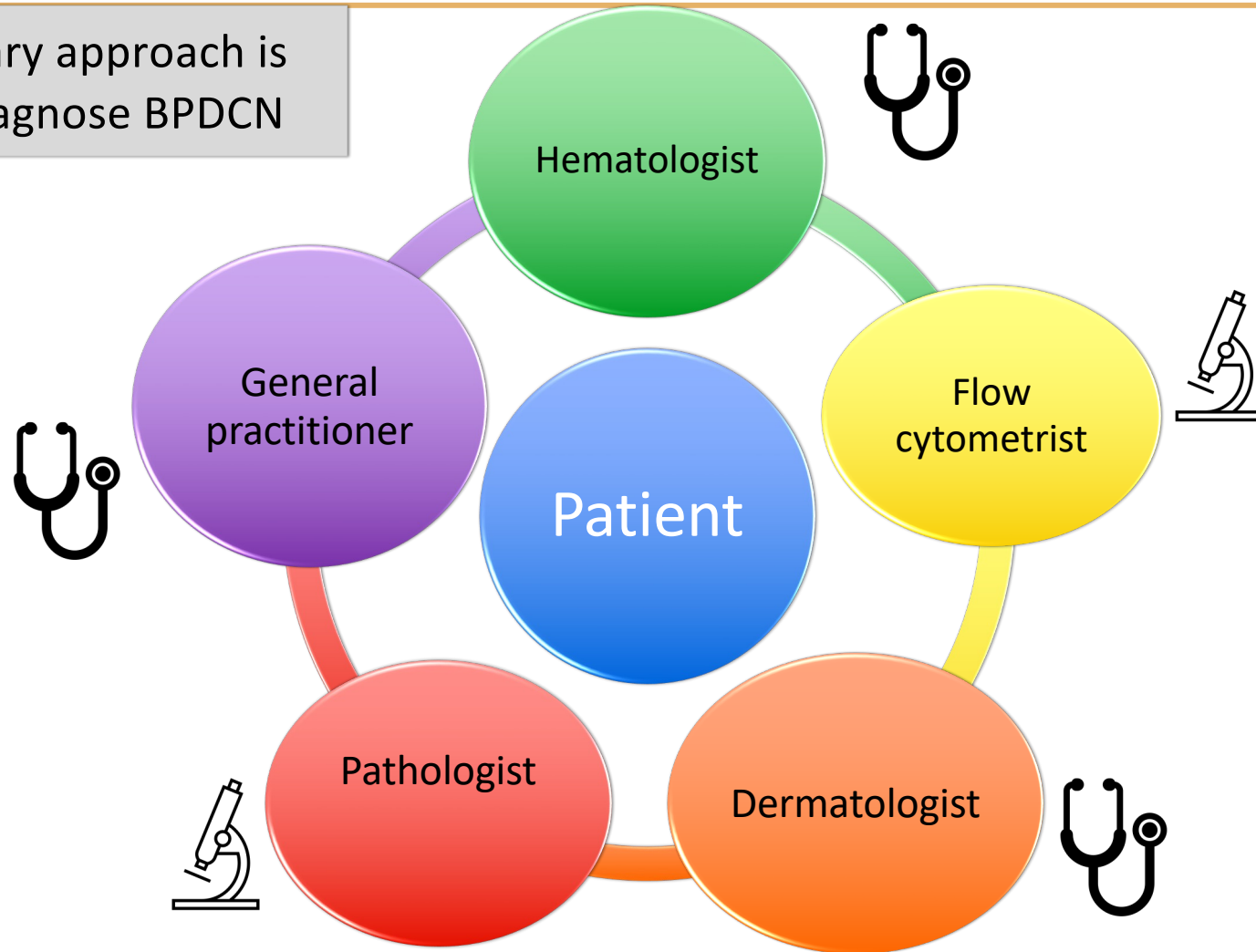
Treatment delay =
time from diagnosis to
treatment
✓ Consider also time to
diagnosis



*other: includes unknown/> 6 months

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Multidisciplinary approach is required to diagnose BPDCN



Speaker's opinion

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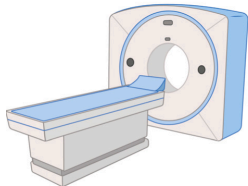
Diagnostic work-up

Cutaneous and systemic evaluation



Violaceous skin lesions on inspection

- Skin biopsy and baseline photography

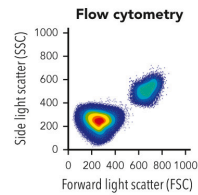
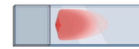


- PET-CT or CT scan for assessment of lymph nodes and/or other extra-medullary disease

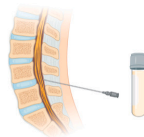
Cytomorphological evaluation



- Bone marrow aspirate and biopsy

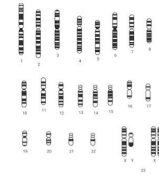


- Flow cytometry evaluation
- 1. CD123, CD4, D56
- 2. CD303
- 3. TCL1
- 4. TCF4

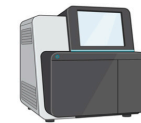


- CSF evaluation for assessment of CNS disease

Adjunct tests



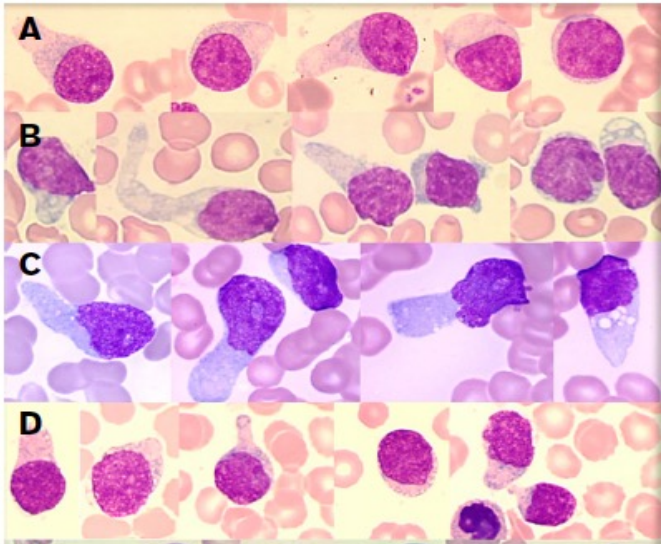
- Cytogenetics



- NGS for myeloid mutation assessment

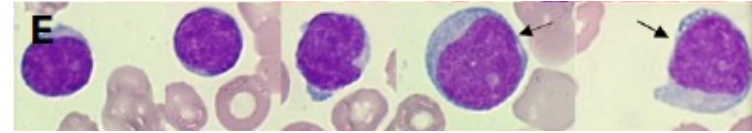
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Morphology

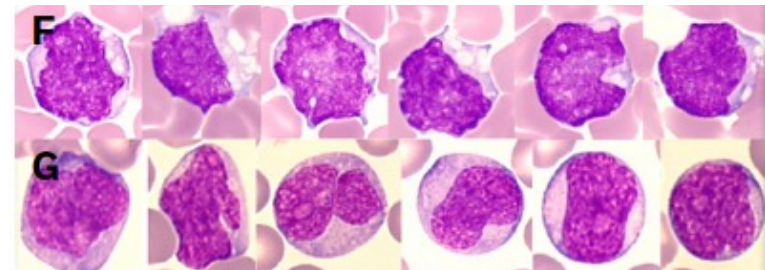


Typical morphology with large pseudopodia, microvacuoles, an eccentrically located nucleus, heterogeneous coloration of the cytoplasm

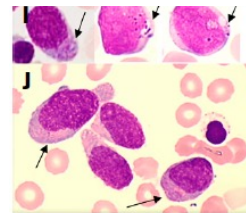
Garnache-Ottou F et al, Blood Adv 2019



Lymphoid-like morphology



Monoblast-like morphology



Presence of granules in the cytoplasm

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Flow-cytometry

CD123, CD4, and CD56, completes a signature marker triad that can differentiate BPDCN from other hematologic malignancies^{4,5§}

ANTIGENS THAT HELP CONFIRM THE DIAGNOSIS OF BPDCN^{1-4*§}

CD123+
CD4+
CD56+
TCL1+
TCF4+
CD303+ (BDCA2+)

CD3-
CD19-
TIA1-
Granzyme B-
Myeloperoxidase-

BPDCN is characterized by the expression of the pDC-associated marker, CD123^{3§}

ANTIGENS THAT EXCLUDE THE DIAGNOSIS OF BPDCN¹

Pan T-cell markers
CD3

Pan B-cell markers
CD20
CD79a

Myeloid markers
CD11c
CD34
Lysozyme
Myeloperoxidase

*One or more of these markers may be negative in some cases of BPDCN. Negativity does not

Immunophenotypic diagnostic criteria:

Expression of CD123 and one other pDC marker (TCF4, TCL1, CD303) in addition to CD4 and/or CD56, or,
Expression of any three pDC markers and absent expression of all expected negative markers

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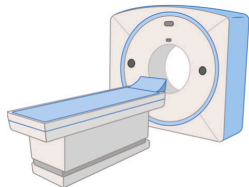
Diagnostic work-up

Cutaneous and systemic evaluation



Violaceous skin lesions on inspection

- Skin biopsy and baseline photography

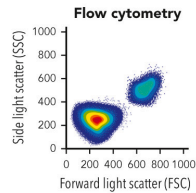
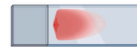


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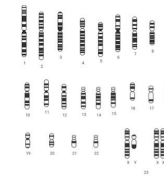


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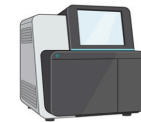


- CSF evaluation for assessment of CNS disease

Adjunct tests



- Cytogenetics



- NGS for myeloid mutation assessment

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CNS involvement in BPDCN

Table 2

Incidence of CNS Involvement in BPDCN Patients

References	BPDCN Cases	CNS Involvement		
		At Diagnosis	At Relapse	Overall
Pagano et al ⁴¹	43	4 (9%)	3 (7%)	7 (16%)
Julia et al ⁵²	90	nr	nr	9 (10%)
Martín-Martín et al ⁵³	13	6 (46%)	3 (23%)	9 (69%)
Yun et al ²⁷	49	0	0	0
Cernan et al ⁵⁴	14	1	1	1 (7%)
Laribi et al ²²	398	NR	NR	10 (2.5%)
Ozdemir et al ⁵⁵	9	2	0	2 (22%)
Pemmaraju et al ⁴⁴	103	13 (13%)	10 (10%)	23 (22%)
Valentini et al ¹¹	68	4	2	6 (12.5%)

- **Medicated lumbar punctures should be performed during the induction phase** (at least 6-8) by combining methotrexate, cytarabine and steroids
- A diagnostic and medicated lumbar puncture should be **mandatory** performed in patients with leukemic presentation **at diagnosis** and in all patients at relapse

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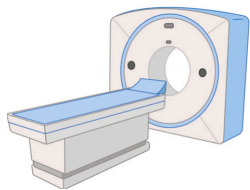
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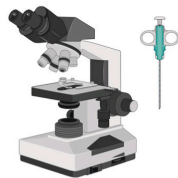
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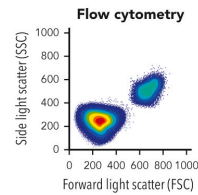
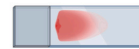


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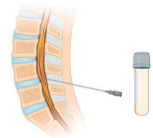
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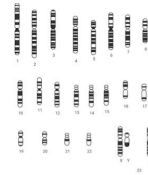


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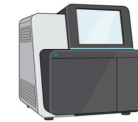


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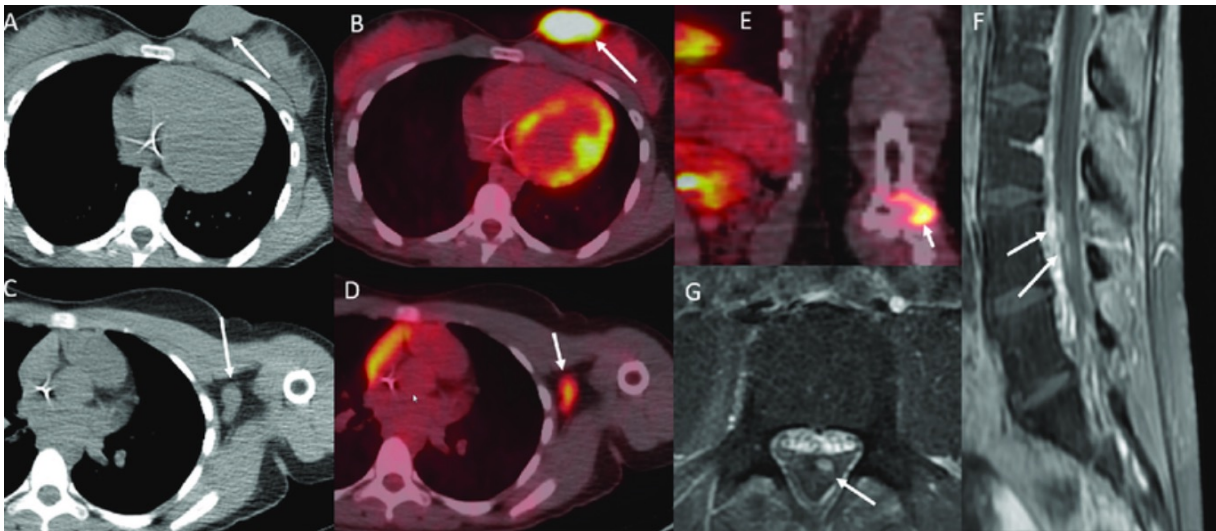
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FDG PET/CT in BPDCN



- FDG PET/CT may revealed, in addition to already detected skin lesions, mild FDG-avid uptake on other sites, apparently not clinically involved by the disease
- This may be useful not only for **staging**, but also for disease **monitoring overtime**

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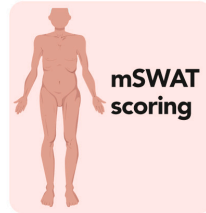
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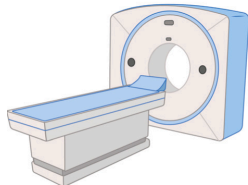


Violaceous skin lesions on inspection

- Skin biopsy and baseline photography



mSWAT scoring

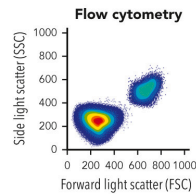


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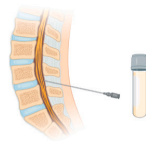
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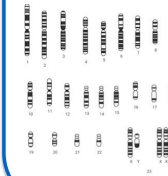


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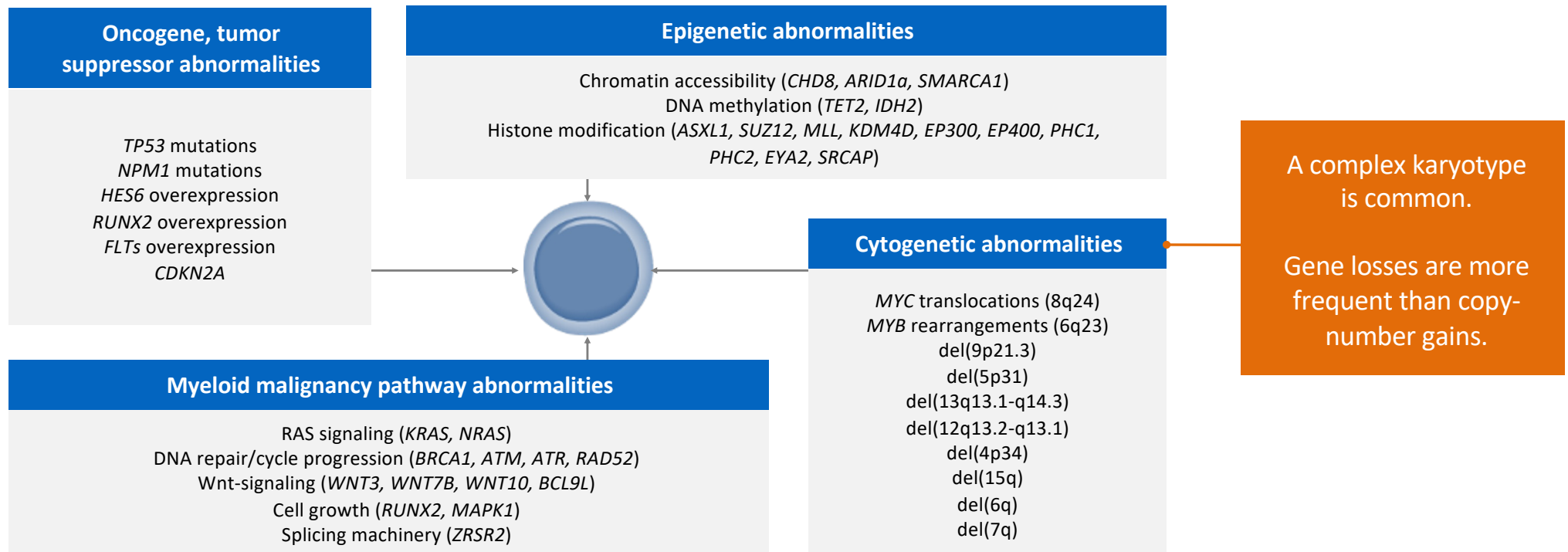
- Cytogenetics



- NGS for myeloid mutation assessment

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Genomic abnormalities in BPDCN



Lezama L, et al. Haematologica. 2019; Sapienza MR, et al. Haematologica. 2019

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NCCN Clinical Practice Guidelines: treatment induction



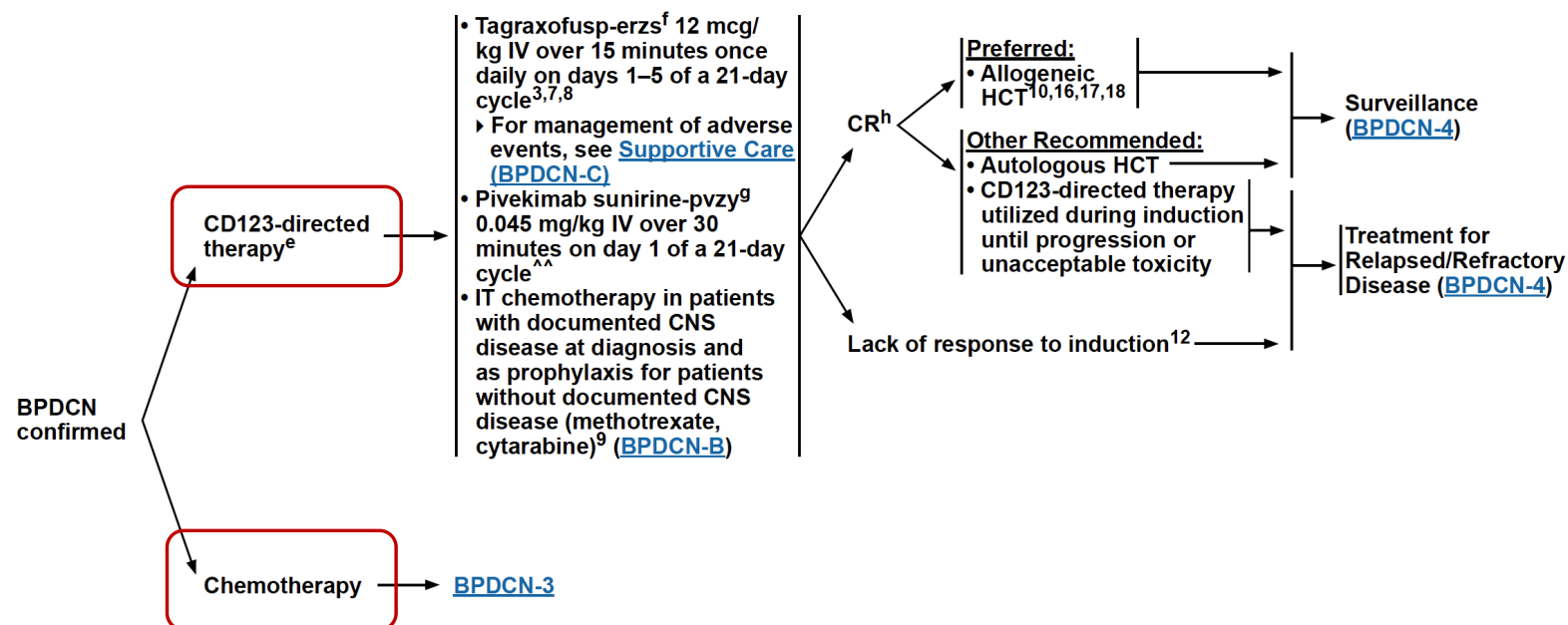
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NCCN Guidelines Version 5.2026 Blastic Plasmacytoid Dendritic Cell Neoplasm (Age ≥18 years)

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TREATMENT OF BPDCN^d

TREATMENT INDUCTION⁶

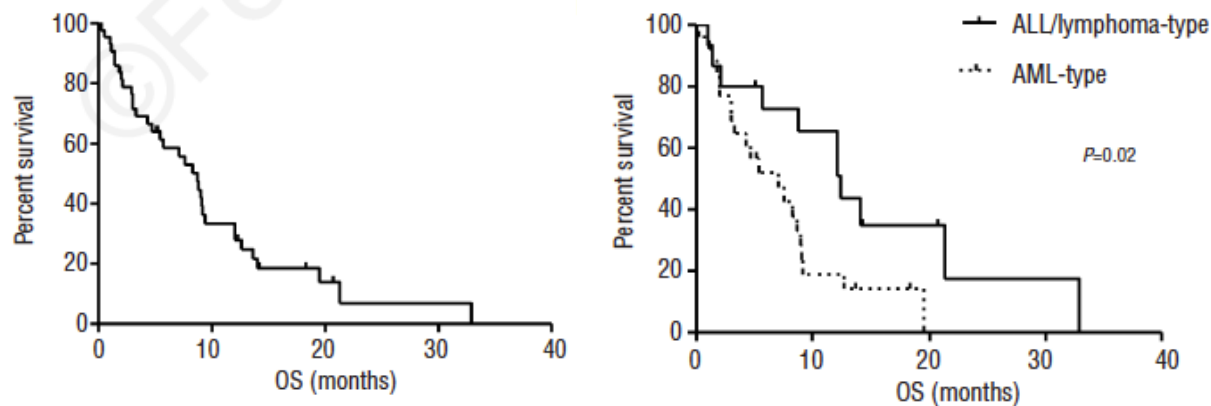


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Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation: an Italian multicenter study

Livio Pagano,¹ Caterina Giovanna Valentini,¹ Alessandro Pulsoni,² Simona Fisogni,³ Paola Carluccio,⁴ Francesco Mannelli,⁵ Monia Lunghi,⁶ Gianmatteo Pica,⁷ Francesco Onida,⁸ Chiara Cattaneo,⁹ Pier Paolo Piccaluga,¹⁰ Eros Di Bona,¹¹ Elisabetta Todisco,¹² Pellegrino Musto,¹³ Antonio Spadea,¹⁴ Alfonso D'Arco,¹⁵ Stefano Pileri,¹⁰ Giuseppe Leone,¹ Sergio Amadori,¹⁶ and Fabio Facchetti³ for GIMEMA-ALWP* (*Gruppo Italiano Malattie EMatologiche dell'Adulto, Acute Leukemia Working Party*)

*See Appendix for other co-authors.



Response (outcome)	All patients (n=41)	AML-type (n=26)	ALL/lymphoma-type (n=15)	P value
Complete remission	17 (41%)	7*	10	0.02
Partial remission*	6	5	1	0.63
Resistant	11	10	1	0.03
Death in induction	7	4	3	0.69
Relapse	6/17 (35%)	0/7	6/10	0.03

*Two patients, partial responders, achieved complete remission after consolidation.

Death in induction rate: 17%

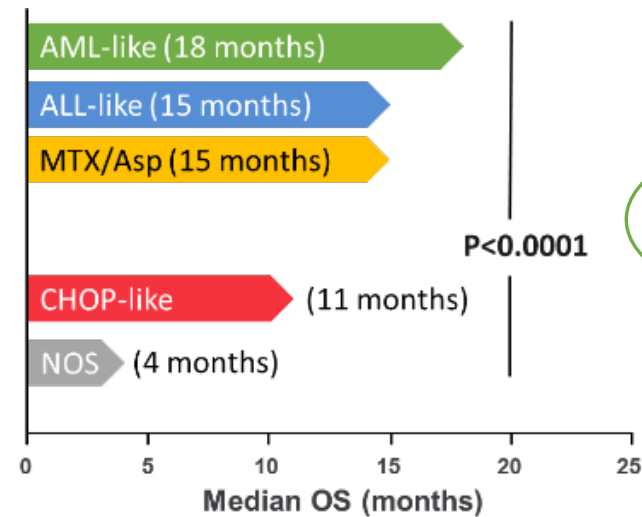
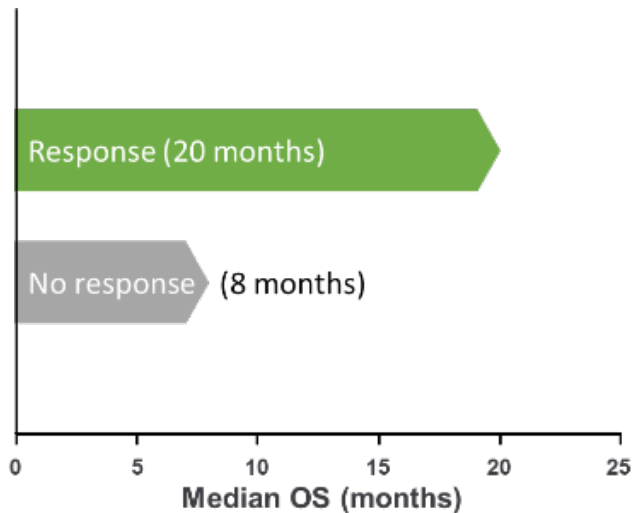
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Chemotherapy in BPDCN

- High rate of response
- Lack of durable response
- Low OS

Treatment group	Complete remission, n (%)	Median remission duration (range), months	HCT, n (%) of CR patients
AML-like (n=19)	13 (68.4)	68 (4–399)*	7 (2 auto) (36.8–53.8)
ALL-like (n=19)	15 (78.9)	47 (6–224)	7 (46.7)
Asp-MTX (n=16)	12 (75.0)	26 (5–166)	6 (37.5–50)
CHOP-like (n=16)	6 (37.5)	17 (4–22)*	2 (12.5–33.3)
NOS (n=10)	1	35	0

N=86



New approaches are required!

*Data are missing for one patient.
Garnache-Ottou F et al. *Blood Adv* 2019;3:4238–4251.

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Allo-SCT is strongly recommended in young/fit patients

- Younger age and allo-HCT in CR1 predicted for improved survival
- MAC with TBI predicted for improved DFS and less relapse

Multivariate analysis

	N	HR (95% CI)	P value
OS			
Age at HCT, years			
< 60	92	-	-
≥60	72	2.16 (1.35, 3.46)	0.001
Disease status			
CR1	121	-	-
PIF/CR2/relapse	43	1.87 (1.14, 3.06)	0.01
DFS			
Conditioning intensity/TBI usage			
MAC/TBI	43	-	-
MAC/no TBI	41	2.89 (1.41, 5.94)	0.004
RIC/NMA	79	3.09 (1.59, 5.98)	0.001
RIC/NMA vs MAC/no TBI	-	1.07 (0.66, 1.73)	0.79
Relapse			
Conditioning intensity/TBI usage			
MAC/TBI	43	-	-
MAC/no TBI	41	3.28 (1.27-8.5)	0.01
RIC/NMA	79	3.13 (1.29-7.61)	0.01
RIC/NMA vs MAC/no TBI	-	0.95 (0.51-1.80)	0.88

allo, allogeneic; CR1/2, first/second complete remission; DFS, disease-free survival; HCT, haematopoietic cell transplantation; MAC, myeloablative conditioning; SCT, stem cell transplantation; TBI, total body irradiation.
Murthy HS et al. *Blood Adv* 2023;7:7007–7016.

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NCCN Clinical Practice Guidelines: treatment induction



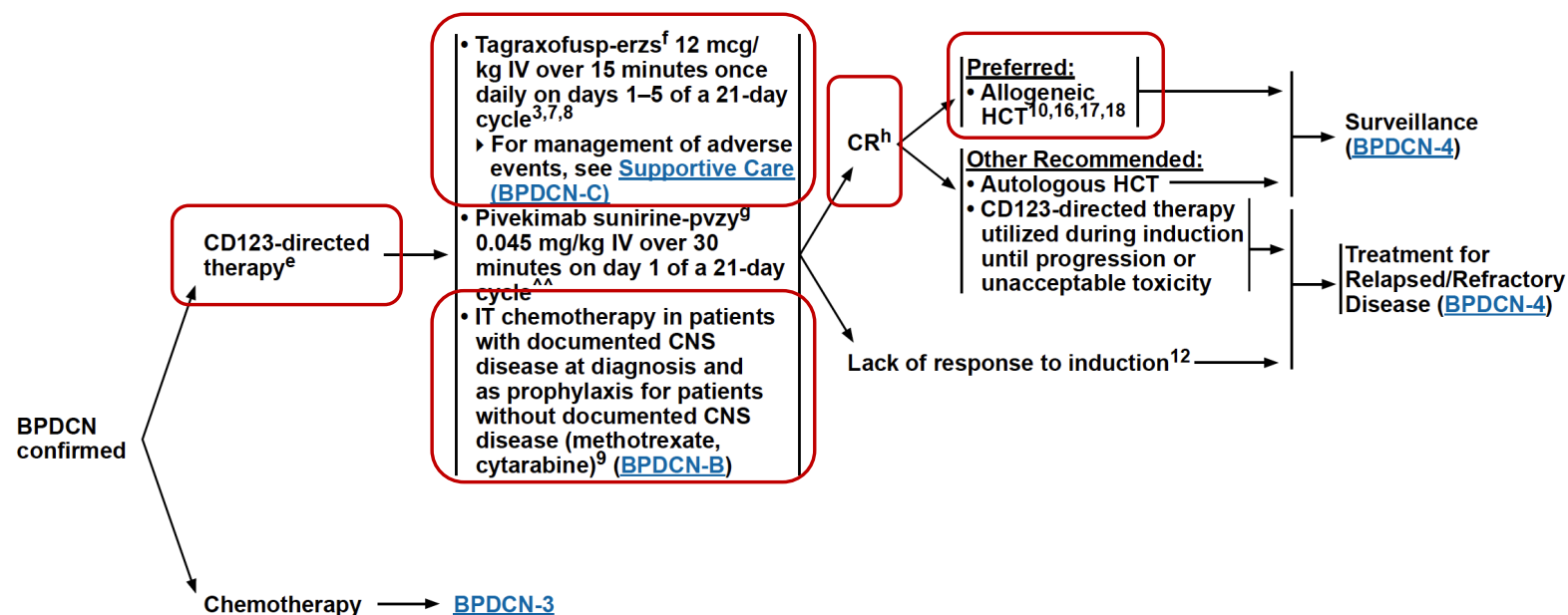
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TREATMENT
OF BPDCN^d

TREATMENT INDUCTION⁶

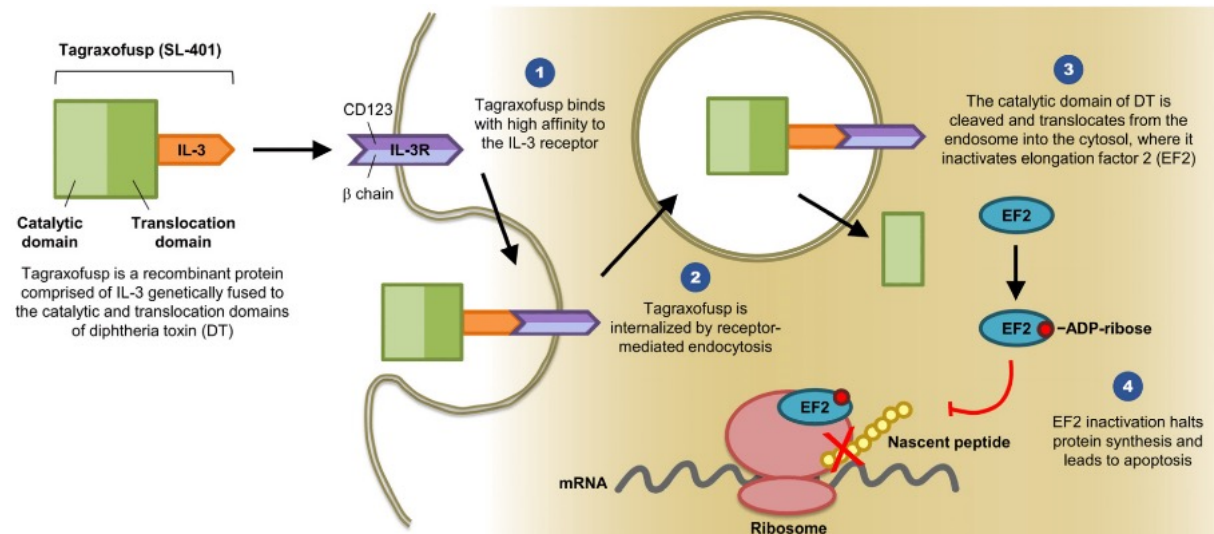


MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

Tagraxofusp

Tagraxofusp is an IL-3 diphtheria toxin conjugate targeting CD123 (IL-3R α) evaluated in the first prospective, multicentre trial in BPDCN^{1,2}

Tagraxofusp was **approved** by the FDA for BPDCN in 2018, by the EMA in 2020 and by the AIFA in 2023



AIFA, Italian Medicines Agency; BPDCN, blastic plasmacytoid dendritic cell neoplasm; EMA, European Medicines Agency; FDA, US Food and Drug Administration.

1. Pemmaraju N et al. *N Engl J Med* 2019;380:1628–1637; 2. Alkharabsheh O and Frankel AE. *Biomedicine* 2019;7:6.

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STML-401-0114
Phase 1/2 trial

- Multicentre, multicohort, open-label, **non-randomised Phase 1/2 trial** of tagraxofusp monotherapy in untreated (n=32) and pretreated (n=15) patients with BPDCN

Patients with BPDCN with ECOG PS ≤ 2 , adequate organ function and no CT or investigative therapy in the prior 14 days
(N=47)

Tagraxofusp

7 or 12 $\mu\text{g/kg/day}$ IV infusion
on Days 1–5 of each 21-day cycle*



Characteristic	Treatment-naïve patients with BPDCN (n=32)
Male, n (%)	26 (81)
Median age (range), years	68 (22–84)
ECOG PS, n (%)	
0	17 (53)
1	15 (47)
BPDCN at BL, n (%)	
Skin	31 (97)
Bone marrow	15 (47)
Peripheral blood	7 (22)
Lymph nodes	13 (41)

*Cycles were repeated until PD or unacceptable toxicity. Nine patients received tagraxofusp 7 $\mu\text{g/kg/day}$ dose in initial dose-escalation phase; all other patients received 12 $\mu\text{g/kg/day}$ dose.

BPDCN, blastic plasmacytoid dendritic cell neoplasm; BL, baseline; CR, complete response; CRc, CR with residual skin abnormality not indicative of active disease; CT, chemotherapy;

ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; PD, progressive disease; ORR, overall response rate; OS, overall survival.

Pemmaraju N et al. *N Engl J Med* 2019;380:1628–1637.

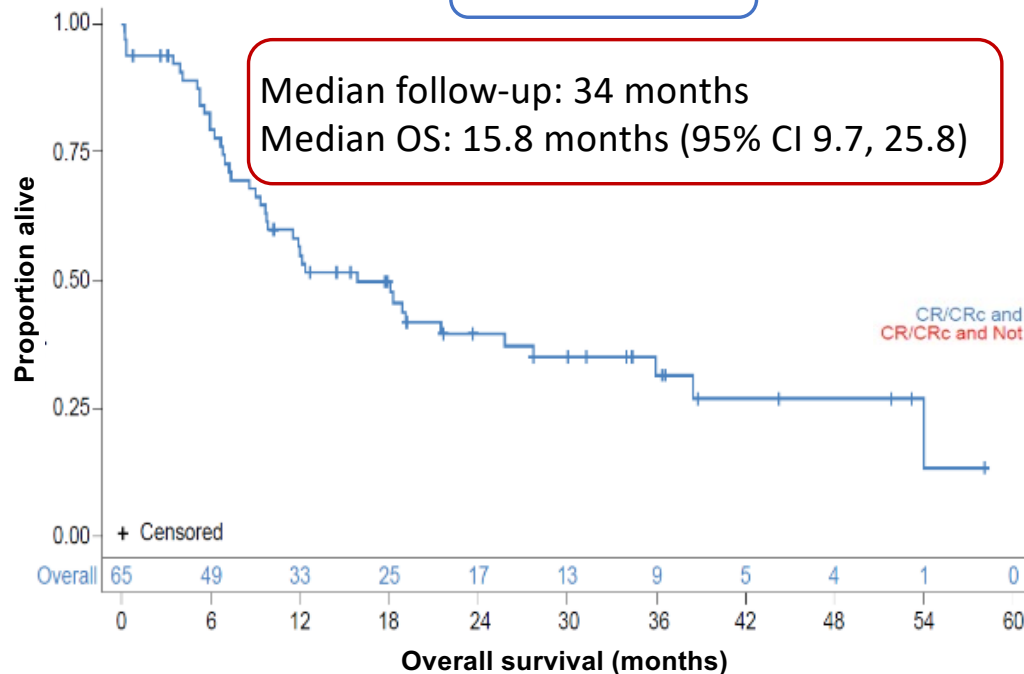
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Long-term outcome

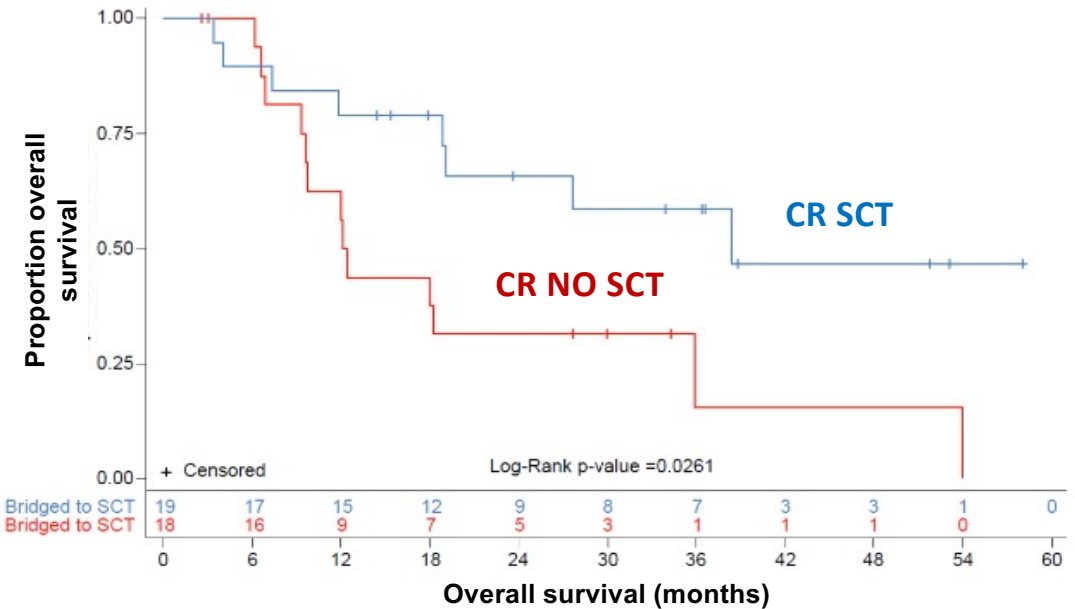
ORR 75%

Median follow-up: 34 months
Median OS: 15.8 months (95% CI 9.7, 25.8)



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CI, confidence interval; CR, complete response; CRc, CR with residual skin abnormality not indicative of active disease; ORR, overall response rate; OS, overall survival; SCT, stem cell transplantation.
Pemmaraju N et al. *J Clin Oncol* 2022;40:3032–3036.

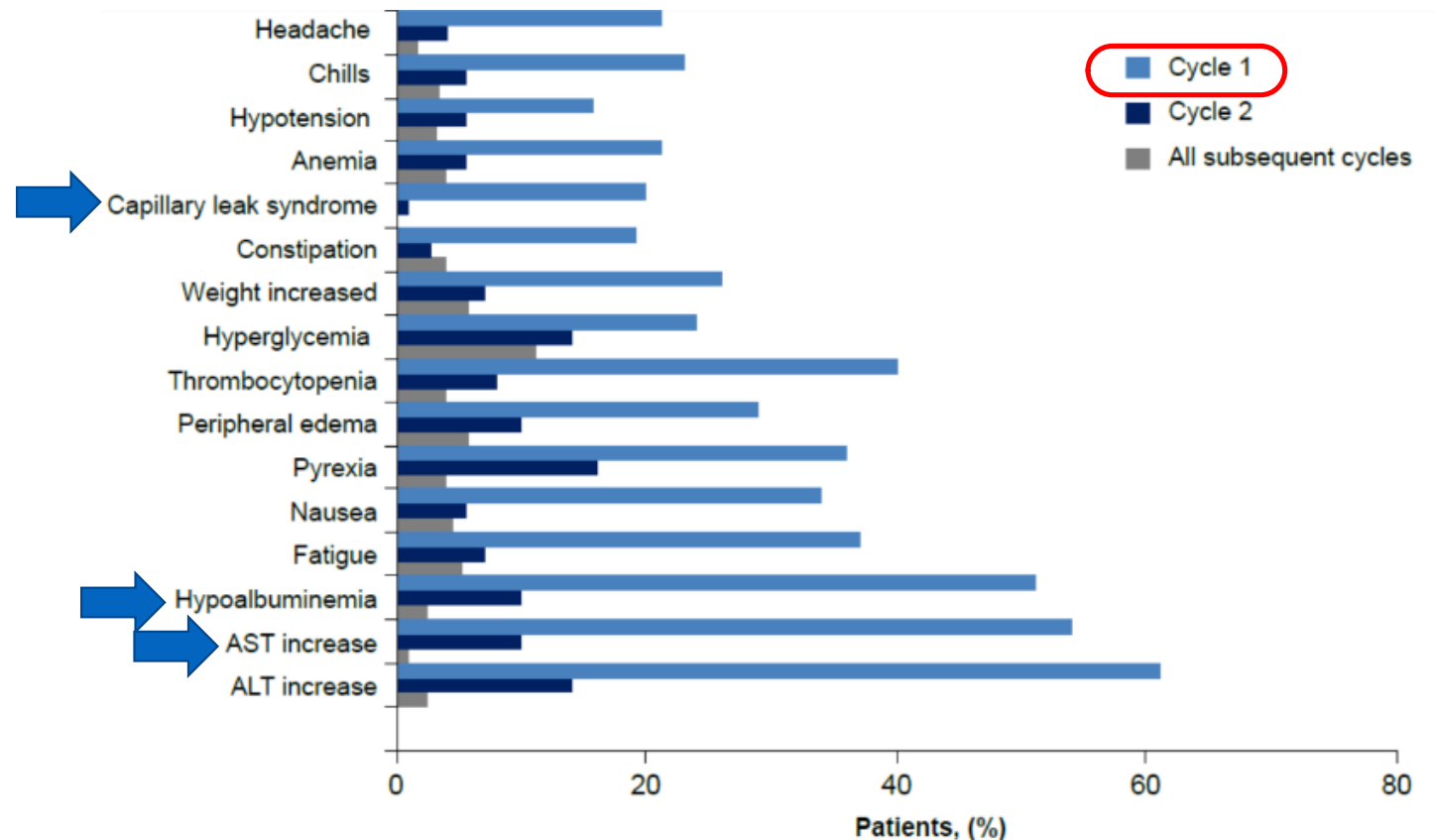


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Of patients who achieved CR + CRc and underwent transplant, the median OS was 38.4 months (range, 3.4-58.1)

Which adverse events may occur with tagraxofusp? And when?

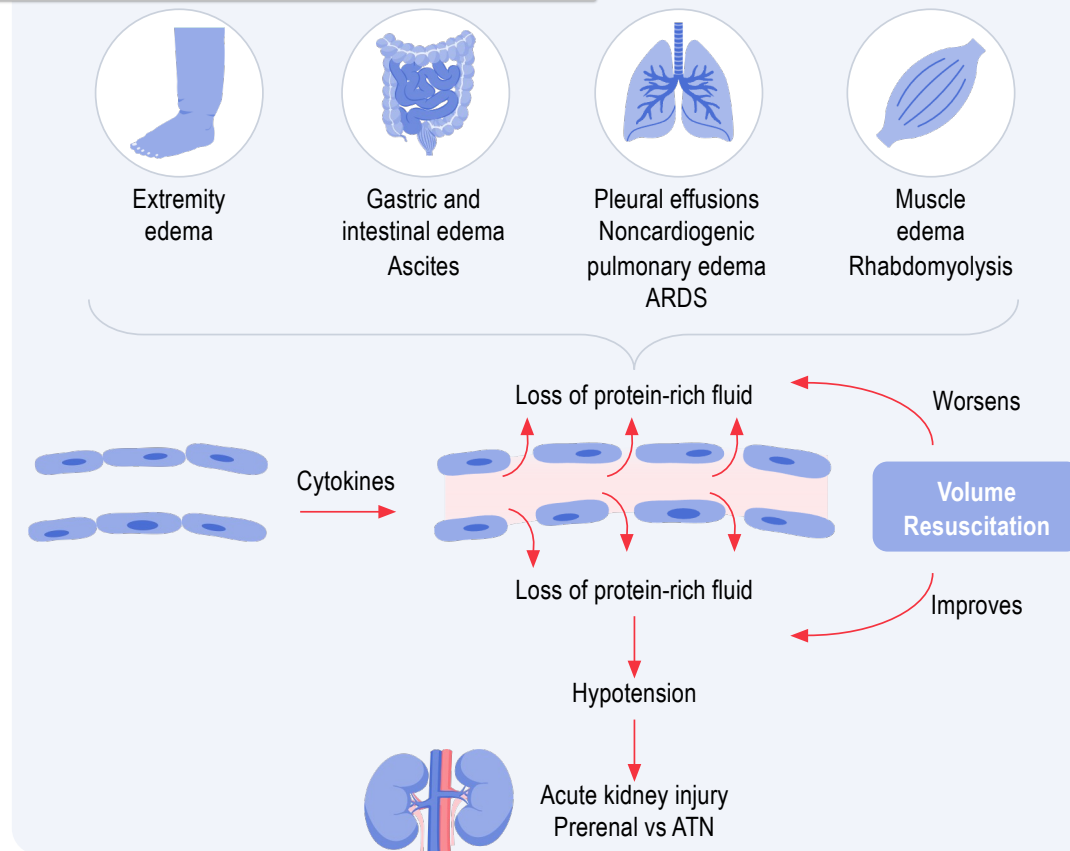
AE	Total (N = 89), No. (%)
AE leading to discontinuations	6 (7)
AE leading to dose interruption	61 (69)
Weight increased	24 (27)
AST increased	17 (19)
ALT increased	15 (17)
Hypoalbuminemia	14 (16)
AEs of any grade that occurred in at least 20% of patients	
ALT increased	57 (64)
AST increased	53 (60)
Hypoalbuminemia	45 (51)
Fatigue	39 (44)
Pyrexia	39 (44)
Thrombocytopenia	38 (43)
Nausea	37 (42)
Edema peripheral	37 (42)
Weight increased	31 (35)
Hyperglycemia	27 (30)
Chills	24 (27)
Headache	22 (25)
Constipation	22 (25)
Anemia	21 (24)
Hypotension	21 (24)
CLS	19 (21)
Hypokalemia	18 (20)
Hypocalcemia	18 (20)
At least one grade $\geq$ 3 TEAE	75 (84)
Thrombocytopenia	29 (33)
ALT increased	28 (32)
AST increased	27 (30)



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Capillary leak syndrome



Typical signs:

- Hypoalbuminemia
- Edema, including pulmonary edema
- Weight gain
- Hypotension
- Hemodynamic instability



The best way to treat CLS is to prevent it!

- Occurs early, during the first cycle
- Monitor patients daily for CLS signs/symptoms
- Monitor serum albumin levels

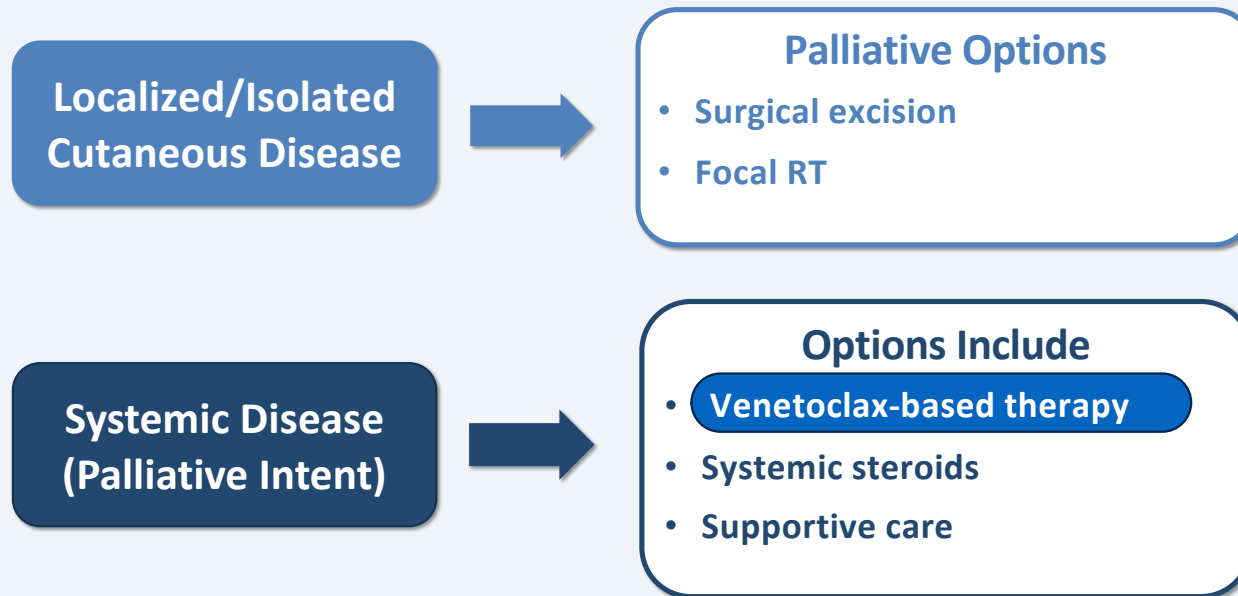
ARDS, acute respiratory distress syndrome; ATN, acute tubular necrosis; CLS, capillary leak syndrome.

MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

NCCN Clinical Practice Guidelines: treatment induction of unfit patients

Patients with low performance and/or nutritional status

(i.e. serum albumin <3.2 g/dL; not a candidate for intensive remission induction therapy or tagraxofusp-erzs)

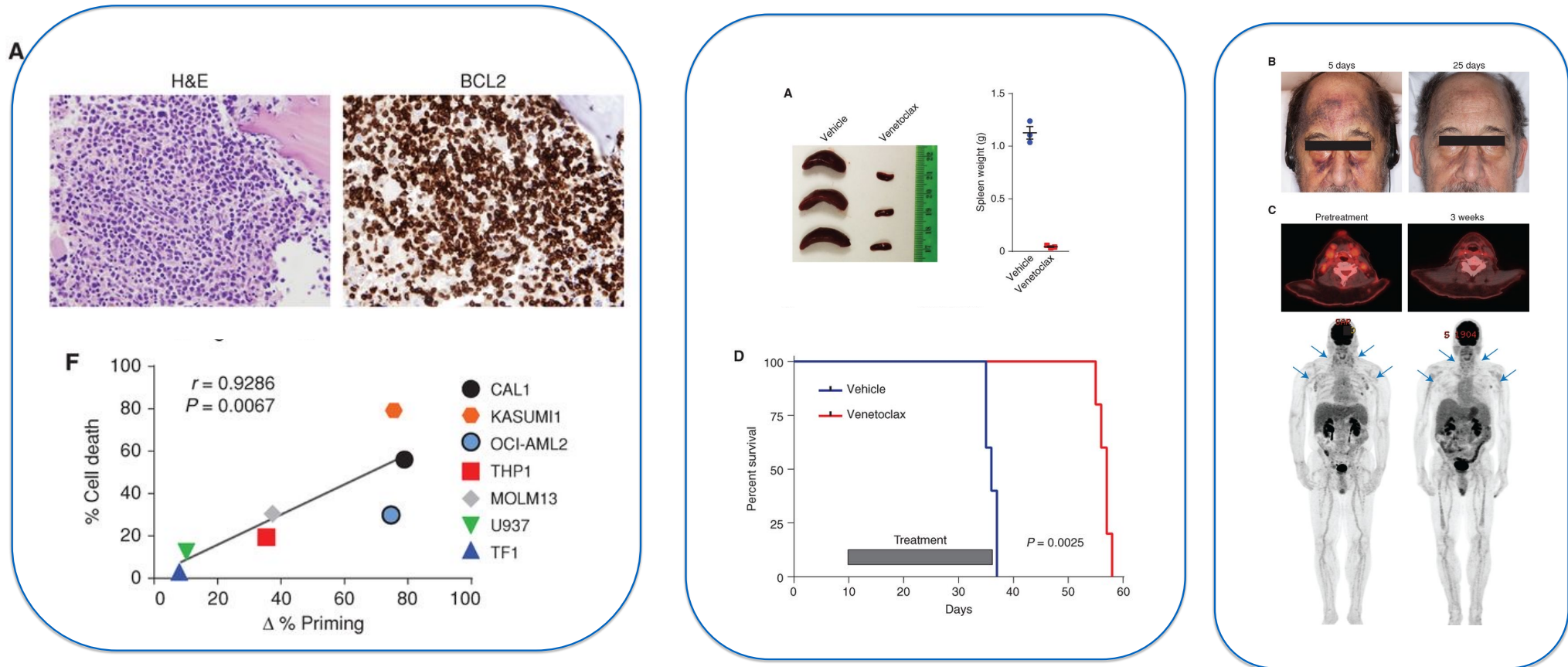


RT, radiation therapy.

Referenced without permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Lymphoma V.3.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed May 21, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org.

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BPDCN is dependent on BCL-2 and sensitive to Venetoclax



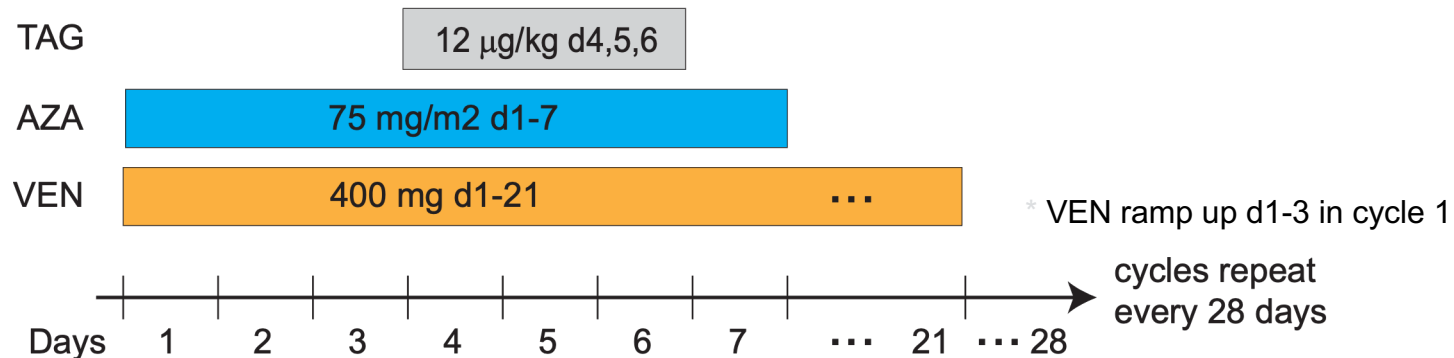
Montero J et al, Cancer Discovery 2017

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MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

Combined approach: AZA+VEN+TAG in 1L and R/R BPDCN patients

- **Key Eligibility:**
 - Adults age > 18 with BPDCN, previously untreated or relapsed/refractory (separate cohorts)
 - Albumin > 3.2 g/dl, ALT/AST < 2.5x ULN, bilirubin < 1.5x ULN, creatinine < 1.5x ULN
 - ECOG < 2, normal cardiac ejection fraction
 - Screening lumbar puncture required. Asymptomatic CNS positivity allowed to enroll and receive IT chemotherapy. IT prophylaxis allowed and encouraged for all.
- **Objectives:**
 - **Primary:** Determine safety of the regimen
 - **Secondary:** Determine response rate; estimate PFS, OS
 - Response evaluation: marrow, skin (mSWAT), extramedullary (CT or PET/CT)
- **Treatment:**
 - Hospitalization required in cycle 1 until completion of TAG to monitor for capillary leak syndrome
 - Cycle 2+ outpatient allowed



ALT, alanine aminotransferase; AST, aspartate aminotransferase; CNS, central nervous system; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; IT, intrathecal; kg, kilogram; mg, milligram; µg, microgram; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; ULN, upper limit of normal.

Lane A et al, Blood 2026

MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

Demographics

	Overall (n=27)	1L (n=16)	R/R (n=11)
Age, median (range)	70 (21, 81)	71 (29, 81)	65 (21, 81)
Sex, n (%)			
Female	2 (7)	2 (13)	0 (0)
Male	25 (93)	14 (88)	11 (100)
Race, n (%)			
White	25 (93)	16 (100)	9 (82)
Other	2 (7)	0 (0)	2 (18)
Ethnicity, n (%)			
Non-Hispanic	21 (78)	13 (81)	8 (73)
Hispanic or Latino	4 (15)	3 (19)	1 (9)
Not known	2 (7)	0 (0)	2 (18)
ECOG PS, n (%)			
1	17 (63)	10 (63)	7 (64)
0	10 (37)	6 (38)	4 (36)
"Skin only", n (%)	8 (30)	5 (31)	3 (27)
CNS involvement, n (%)	6 (22)	3 (19)	3 (27)

Prior or Concomitant Heme Malignancy (PCHM)	Overall (n=27)	Details
	10 (37%)	CMML x4, MDS x4, MPN x3
Prior treatment	R/R cohort (n=11)	
TAG	7 (64%)	
Pivekimab	4 (36%)	
Venetoclax	3 (27%), 2 were with HMA	
Stem cell transplant	4 (36%) Allogeneic SCT: 3 Autologous SCT: 1	
Median prior therapies (range) = 2 (1-3)		
Gene mutations	Overall (n=27)	
TET2	10 (37%)	
ASXL1	7 (26%)	
RNA splicing factor	5 (19%)	
NRAS, KRAS, FLT3	4 (15%)	
TP53	2 (7%)	

1L, first-line; CMML, chronic myelomonocytic leukemia; HMA, hypomethylating agent; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasm; n, number; PS, performance status; R/R, relapsed/refractory; RNA, ribonucleic acid.

Lane A et al, Blood 2026

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Safety

Grade 3 or higher treatment-related adverse events (TRAEs) Overall (n=27)

Thrombocytopenia, n (%)	17 (63)
WBC decrease, n (%)	16 (59)
Neutropenia, n (%)	13 (48)
Anemia, n (%)	5 (19)
Hypoxia, n (%)	3 (11)
ALT increase, n (%)	1 (4)
AST increase, n (%)	1 (4)
Atrial fibrillation, n (%)	1 (4)
Febrile neutropenia, n (%)	1 (4)
Hyperglycemia, n (%)	1 (4)
Hypophosphatemia, n (%)	1 (4)
Multi-organ failure, n (%)	1 (4)
Sinus tachycardia, n (%)	1 (4)
Syncope, n (%)	1 (4)

Median cycle 1 start to cycle 2 start = 33 days

Capillary Leak Syndrome (CLS) n (%)

Overall	4 (14.8)
Grade 2	3 (11.1)
Grade 3	1 (3.7)
Grade 4	0
Grade 5	0

All CLS was in cycle 1 and manageable with albumin, diuresis

There were no cases of veno-occlusive disease (VOD)

Mortality, all cause n (%)	Overall (n=27)	1L (n=16)	R/R (n=11)
30 day	1 (3.7%)	1 (6%)	0
60 day	2 (7.4%)	1 (6%)	1 (9%)

One 1L death (TRAE) in cycle 1 of multi-organ failure

One R/R death after cycle 1 of disease progression

ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cell.

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Efficacy

Best response, n (%)	1L (n=16)	R/R (n=11)
CR	8 (50)	1 (9)
CRi	6 (38)	4 (36)
CRc	0 (0)	2 (18)
Composite CR CR + CRi + CRc	14/16 (88%)	7/11 (64%)
PR	1 (6)	0 (0)
ORR	15/16 (94%)	7/11 (64%)
SD	0 (0)	3 (27)
PD	0 (0)	1 (9)
Not evaluable	1 (6), early death	0 (0)

• Median number of cycles received

- 1L = 2.5 cycles (range 1-14)
- R/R = 2 cycles (range 1-5)

• Median follow up

- 1L = 16.7 months
- R/R = all but one had relapse or death; remaining patient follow up 42.4 months

• Median duration of response (DOR)

- 1L = not reached
- R/R = 7.2 months

• Proceeded directly to allogeneic SCT

- 1L = 10 of 16 (63%), including 10 of 11 age ≤75
- R/R = 6 of 11 (55%)

CR, complete remission; CRc, CR in all organ sites except minimal skin abnormality without evidence of active disease; CRi, CR with incomplete count recovery; ORR, overall response rate; PR, partial response; PD, progressive disease; SCT, stem cell transplant; SD, stable disease.

Lane A et al, Blood 2026

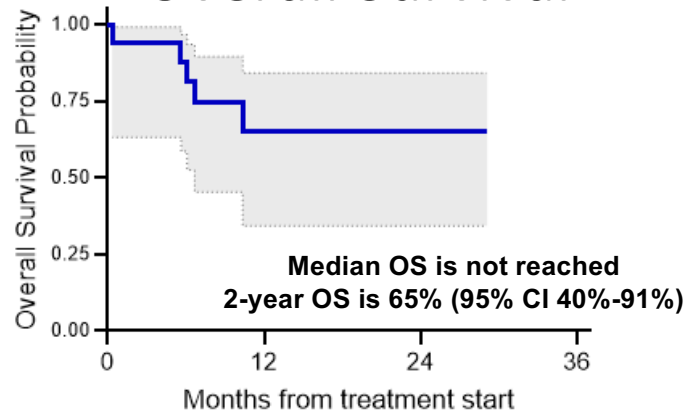
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Survival Data

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1L

Overall Survival



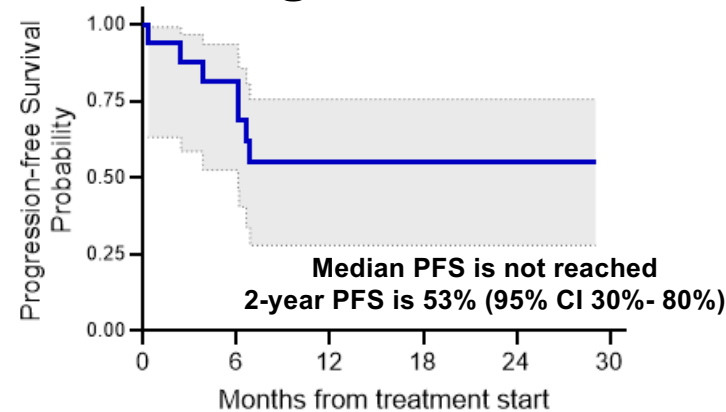
At risk 16

6

4

0

Progression-Free Survival



At risk 16

13

6

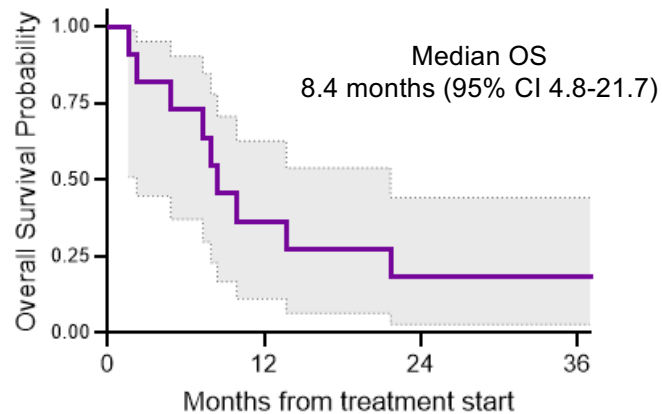
5

4

0

Median Duration of Response (DOR) is not reached

R/R

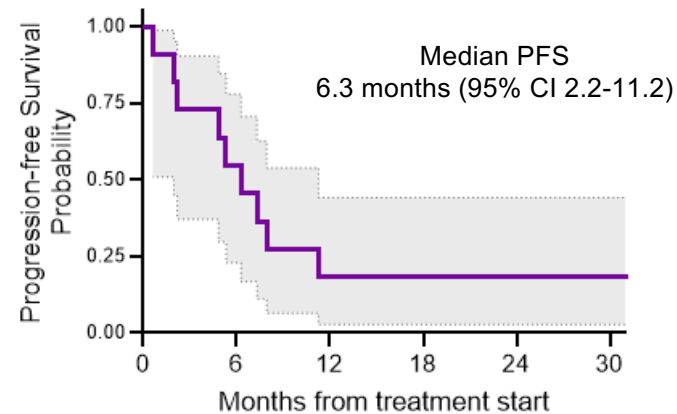


At risk 11

4

2

2



At risk 11

6

2

2

2

2

Median DOR is 7.2 months (95% CI 5.5-36.4)

Lane A et al, Blood 2026

MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

Comparison with historical TAG single agent data

	1L TAG-AZA-VEN (n=16)	1L TAG alone* (n=65)	R/R TAG-AZA-VEN (n=11)	R/R TAG alone* (n=19)	CLS	TAG (x3d) AZA-VEN (n=27)	TAG (x5d) (n=86)
Composite CR rate (CR + CRi + CRc)	88%	57%	64%	16%	Overall	14.8%	20.9%
ORR (composite CR + PR)	94%	75%	64%	58%	Grade 3+	3.7%	7%
Proceeded to SCT	63%	32%	55%	5%			
OS (median)	Not reached	15.8 months	8.4 months	8.2 months			
OS (2-year)	65%	40%	18%	-			

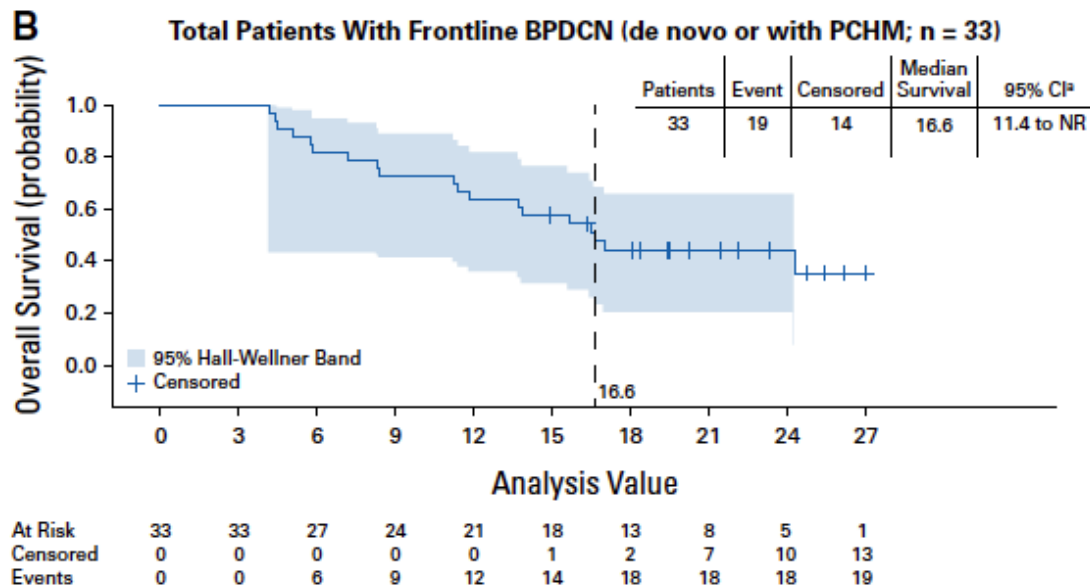
median f/u: 16.7 vs. 34 months

No direct, head-to-head clinical trials have been conducted between single agent tagraxofusp-erzs (TAG) and the combination treatment of TAG-AZA-VEN, therefore, no direct efficacy or safety comparisons can be made between the two treatments.

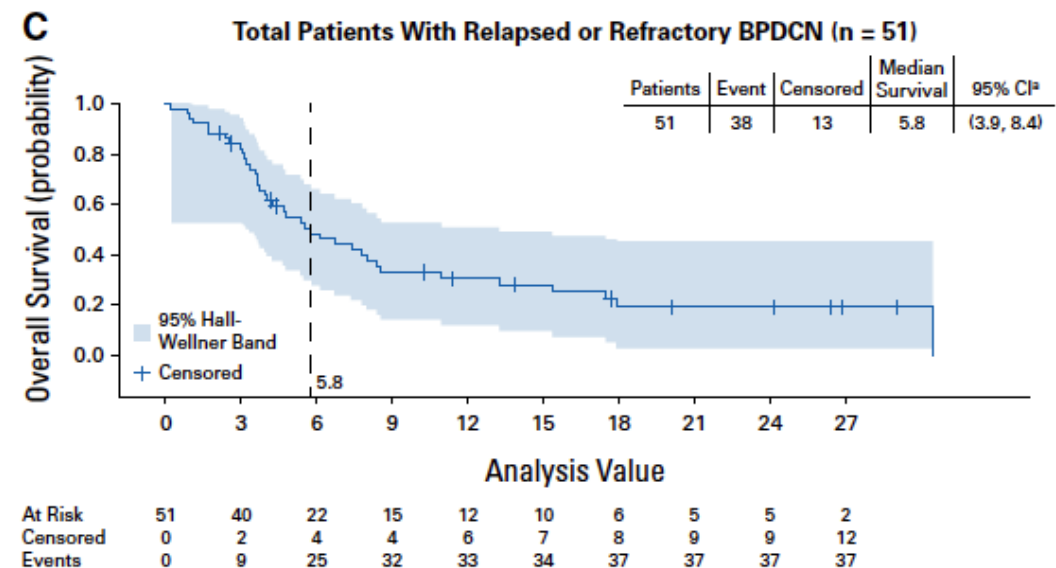
*TAG single-agent data from: Pemmaraju N, et al., *J Clin Oncol.* 2022;40(26):3032-3036

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New agents: Pivekimab Sunirine



ORR 85%
No CLS



ORR 35%
No CLS

Pemmaraju N et al, JCO 2026

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MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

Ongoing clinical trials

Clinicaltrials.gov	Phase	Agent(s)	Mechanism of action	Eligible patients
NCT04318678	I	CD123 CART	Anti-CD123 CAR T cell	R/R BPDCN
NCT07007052	II	Venetoclax, Tagraxofusp	Anti-Bcl2, Anti CD123	BPDCN
NCT05476770	I	Tagraxofusp	Anti-CD123	pediatric BPDCN
NCT03113643	I	Tagraxofusp, Azacitidine, Venetoclax	Anti-CD123, HMA, anti-Bcl2	BPDCN
NCT04216524	II	Tagraxofusp, Venetoclax, chemotherapy	Anti-CD123, anti-Bcl2	BPDCN
NCT07523555	I/II	CD33/CD123 dual-target CAR-T module	Anti-CD123/CD33 CAR T cell	BPDCN
NCT06690827	I/II	CD123 CAR-NK	Anti-CD123 CAR-NK cell	BPDCN

www.clinicaltrials.gov

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Take home messages and open issues

- **Early, accurate diagnosis is essential**; any delays in the time before BPDCN is recognized can mean that disease progression may have already occurred
- **AlloSCT** must be considered in first CR for all young/fit patients
- **Tagraxofusp is approved** in US and EU for the first line therapy in BPDCN patients, and represents the **best option to induce a CR**
- How should BPDCN with **associated hematologic malignancy** be managed? Role for combinations?
- What is the role of **measurable residual disease** monitoring? What about anti-CD123 therapies as relapse prevention after HSCT?
- **Immunotherapy** (CAR-T cells) approaches are ongoing

MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

Thank you!

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