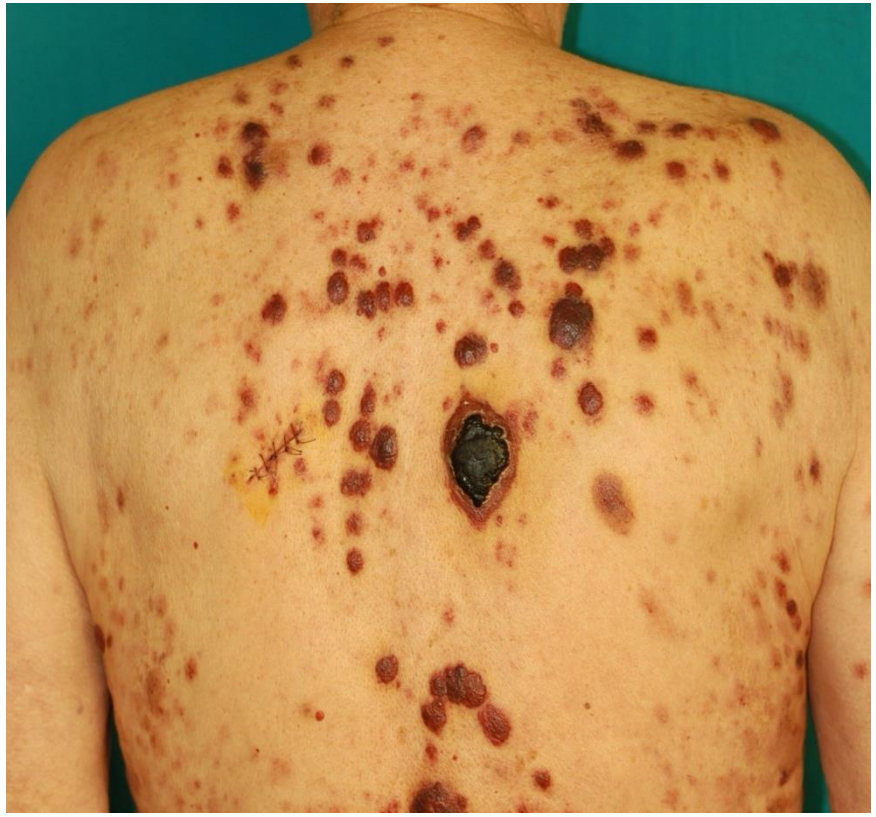
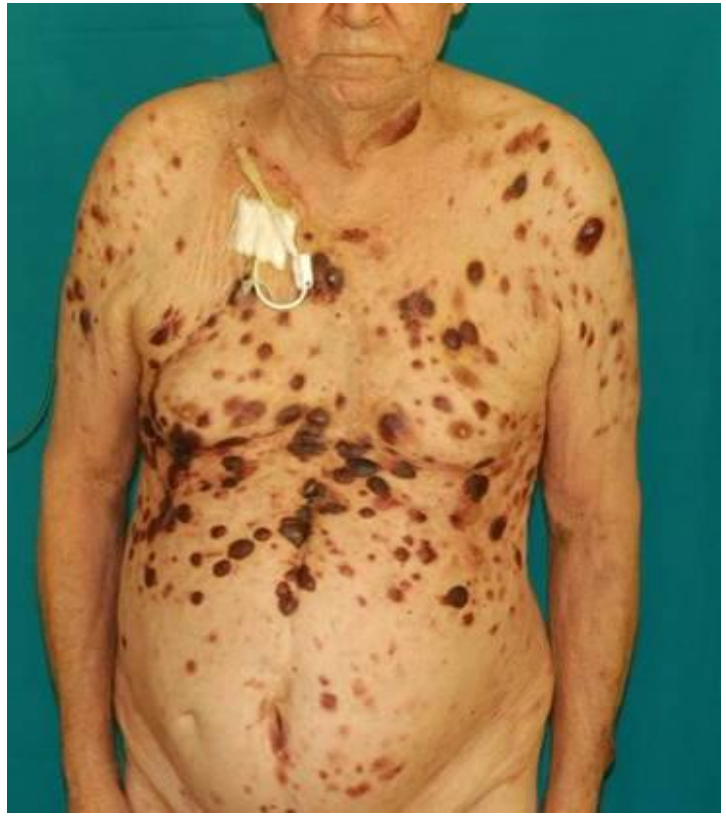
Raccomandazioni terapeutiche per pazienti “anziani e unfit”

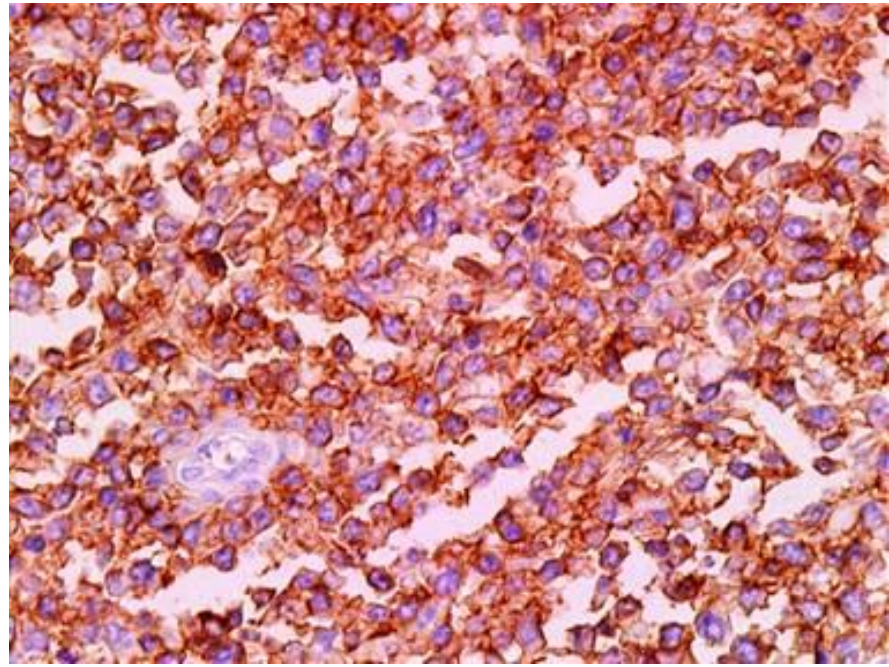
P. Quaglino, Torino

Precursor haematologic neoplasms

CD4+CD56+ hematodermic neoplasm
Blastic cell lymphoma
BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM, BPDCN)







CD56

BACKGROUND

- There are several guiding principles in the treatment of older/unfit patients with BPDCN that differ from the younger/fit patient approach.
- Most, if not all, in this category will not be able to go for curative alloSCT.
- Subset of patients might be considered for autologous stem cell transplant (autoSCT)
- Not all patients with BPDCN will be eligible for CD123-targeted therapy as in the setting of baseline severe hypoalbuminemia, cardiac co-morbidities, or renal insufficiency.

REGULAR ARTICLE

blood advances

Blastic plasmacytoid dendritic cell neoplasms: results of an international survey on 398 adult patients

Kamel Laribi,[1] Alix Baugier de Materre,[2] Mohamad Sobh,[3] Lorenzo Cerroni,[4] Caterina Giovanna Valentini,[5] Tomohiro Aoki,[6] Ritsuro Suzuki,[7] Kengo Takeuchi,[8] Arthur E. Frankel,[9] Carlo Cota,[10] David Ghez,[11] Ronan Le Calloch,[12] Livio Pagano,[5] and Tony Petrella[13]

[1]Department of Hematology, Centre Hospitalier Le Mans, Le Mans, France; [2]Geriatric Department, Assistance Publique–Hôpitaux de Paris, Hôpital Broca, Paris, France; [3]Hematology, BMT Program, The Ottawa Hospital, Ottawa, ON, Canada; [4]Department of Dermatology, Medical University of Graz, Graz, Austria; [5]Fondazione Policlinico Universitario A. Gemelli, IRCCS–Università Cattolica del Sacro Cuore, Rome, Italy; [6]Department of Hematology and Oncology, Nagoya University Graduate School of Medicine, Nagoya, Japan; [7]Department of Oncology/Hematology, Shimane University Hospital, Izumo, Japan; [8]Pathology Project for Molecular Targets and Division of Pathology, The Cancer Institute, Japanese Foundation for Cancer Research, Tokyo, Japan; [9]University of South Alabama Mitchell Cancer Institute, Mobile, AL; [10]Department of Dermatology, IRCCS INRCA, Ancona, Italy; [11]Department of Hematology, Institut Gustave Roussy, Villejuif, France; [12]Service de Médecine Interne-Maladies du Sang-Maladies Infectieuses, Centre Hospitalier de Cornouaille, Quimper, France; and [13]Department of Pathology, University of Montréal, Hospital Maisonneuve-Rosemont, Montreal, QC, Canada

Table 3. Patient characteristics according to treatment

	Chemotherapy+ allo-HSCT (n = 61)	Chemotherapy+ auto-HSCT (n = 16)	Chemotherapy without consolidation (n = 222)
Age, median (range), y	50 (18-70)	63 (19-68)	68 (18-87)
Disseminated with cutaneous involvement	37 (60)	12 (75)	133 (60)
Disseminated noncutaneous	12 (20)	1 (6)	20 (9)
Cutaneous isolated	12 (20)	3 (19)	69 (31)
ALL-type	33 (53)	6 (38)	57 (26)
AML-type	16 (27)	1 (6)	36 (16)
NHL-type	12 (20)	9 (56)	129 (58)
Response to treatment			
CR	57 (94)	16 (100)	153 (69)
PR	2 (3)	0	31 (14)
PD	2 (3)	0	38 (17)
Relapse	16/60 (27)	5/16 (31)	131/168 (78)

Unless otherwise noted, data are n (%). Patients treated with new drugs (n = 6), radiotherapy (n = 27), or palliative approaches (n = 62) were excluded.

HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Guideline Article - Expert opinion

Open Access

Unmet Clinical Needs and Management Recommendations for Blastic Plasmacytoid Dendritic Cell Neoplasm: A Consensus-based Position Paper From an Ad Hoc International Expert Panel

Livio Pagano[1,2], Pier Luigi Zinzani[3,4], Stefano Pileri[5], Pietro Quaglino[6], Branko Cuglievan[7], Emilio Berti[8,9], Naveen Pemmaraju[10], Francesco Onida[11,12], Rein Willemze[13], Alberto Orfao[14,15], Giovanni Barosi[16]

Correspondence: Livio Pagano (livio.pagano@unicatt.it).

No worldwide consensus on guiding principles for the treatment of older/unfit patients with BPDCN has been yet reached.

RECOMMENDATIONS AND PROPOSALS

- No worldwide consensus on guiding principles for the treatment of older/unfit patients with BPDCN has been yet reached.
- Several active programs were put forward by the Panel for consideration:
- (a) clinical trials, if available;

RECOMMENDATIONS AND PROPOSALS

- No worldwide consensus on guiding principles for the treatment of older/unfit patients with BPDCN has been yet reached.
- Several active programs were put forward by the Panel for consideration:
- (a) clinical trials, if available;
- (b) CD123-targeted agents, if available;

Long-Term Benefits of Tagraxofusp for Patients With Blastic Plasmacytoid Dendritic Cell Neoplasm

Naveen Pemmaraju, MD[1]; Kendra L. Sweet, MD[2]; Anthony S. Stein, MD[3]; Eunice S. Wang, MD[4]; David A. Rizzieri, MD[5]; Sumithira Vasu, MD, MBBS[6]; Todd L. Rosenblat, MD[7]; Christopher L. Brooks, PhD[8]; Nassir Habboubi, PhD[8]; Tariq I. Mughal, MD[8,9]; Hagop Kantarjian, MD[1]; Marina Konopleva, MD, PhD[1]; and Andrew A. Lane, MD, PhD[10]

Demographic and Baseline Disease Characteristics

TABLE 1. Baseline Characteristics of Patients Treated Once Daily With Tagraxofusp 12 μg/kg

Parameter	1L BPDCN (n = 65)	R/R BPDCN (n = 19)
Sex, No. (%)		
Male	52 (80)	16 (84)
Female	13 (20)	3 (16)
Race, No. (%)		
White	57 (88)	17 (90)
Others	8 (12)	2 (11)
Age, years, median (range [minimum-maximum])	68 (22-84)	72 (44-87)
ECOG, No. (%)		
0	31 (48)	7 (37)
1	31 (48)	12 (63)
2	2 (3)	0
BPDCN at baseline, No. (%)		
Skin	60 (92)	15 (79)
BM	32 (49)	12 (63)
Peripheral blood	17 (26)	1 (5)
Lymph nodes	33 (51)	9 (47)
Visceral	9 (14)	4 (21)
Prior therapies,[a] No. (%)		
1	—	11 (58)
2	—	3 (16)
3	—	2 (11)
≥ 4	—	2 (11)

Abbreviations: 1L, first-line; BM, bone marrow; BPDCN, blastic plasmacytoid dendritic cell neoplasm; ECOG, Eastern Cooperative Oncology Group; R/R, relapsed/refractory.

[a]Prior therapy data from one patient are missing.

Pemmaraju N, et al: J Clin Oncol. 2022 July 12

RECOMMENDATIONS AND PROPOSALS

- No worldwide consensus on guiding principles for the treatment of older/unfit patients with BPDCN has been yet reached.
- Several active programs were put forward by the Panel for consideration:
- (a) clinical trials, if available;
- (b) CD123-targeted agents, if available;
- (c) strong consideration for venetoclax in combination with hypomethylating agents approach;

VEN +/- CT

- Ven and HMA in 10 patients (median age; 70 years; 22–82) with BPDCN treated at the Mayo Clinic (n=5) and MDAnderson Cancer Center (n=5).
- 8 CR and 2 PR, 2 alloHSCT and 1 forthcoming
- Responses short lived (4 rapid relapses..)
- Safety profile more favourable

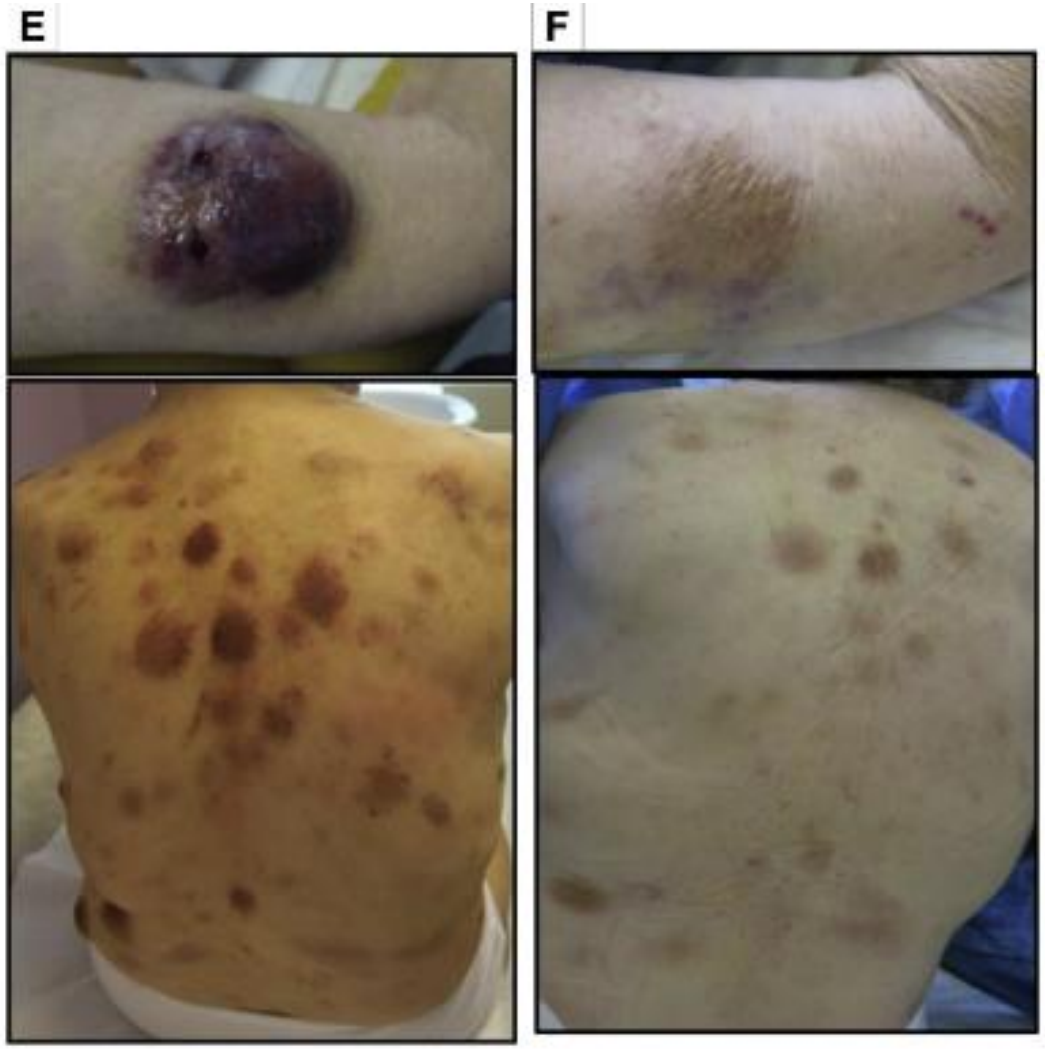
Gangat N, Konopleva M, Patnaik MM, et al. Venetoclax and hypomethylating agents in older/unfit patients with blastic plasmacytoid dendriticcell neoplasm. Am J Hematol. 2022;97:E62–E67.

Still a role for cytotoxic chemotherapy

The key is to use markedly reduced doses, omit highly toxic and/or myelosuppressive agents, watch renal, hepatic, and immune systemfunction carefully.

In older/unfit BPDCN

- mini-cyclophosphamide,vincristine, and prednisone (CVD) regimen (HCVAD minus the anthracycline; reduction of doses of all agents);
- cyclophosphamide, doxorubicin, vincristine and prednisolone(CHOP) lymphoma-based regimen;
- dose reduced AML-based regimens.



2 cases

Chahine C, Roos-Weil D, Saada V, et al. Bortezomib, lenalidomide, and dexamethasone in elderly patients with blastic plasmacytoid dendriticcell neoplasm. Clin Lymphoma Myeloma Leuk. 2020;20:e986–e989.

RECOMMENDATIONS AND PROPOSALS

- No worldwide consensus on guiding principles for the treatment of older/unfit patients with BPDCN has been yet reached.
- Several active programs were put forward by the Panel for consideration:
- (a) clinical trials, if available;
- (b) CD123-targeted agents, if available;
- (c) strong consideration for venetoclax in combination with hypomethylating agents approach;
- and (d)cytotoxic chemotherapy.

  The Panel agreed on recommending the use of markedly reduced doses of cytotoxic chemotherapy, omitting highly toxic and/or myelosuppressive agents, watch renal, hepatic, andimmune system function carefully.

blood® Special Report

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

Naveen Pemmaraju,[1] Hagop Kantarjian,[1] Kendra Sweet,[2] Eunice Wang,[3] Jayastu Senapati,[1] Nathaniel R. Wilson,[4] Marina Konopleva,[1] Arthur E. Frankel,[5] Vikas Gupta,[6] Ruben Mesa,[7] Matthew Ulrickson,[8] Edward Gorak,[9] Sumeet Bhatia,[10] Tulin Budak-Alpdogan,[11] James Mason,[12] Maria Teresa Garcia-Romero,[13] Norma Lopez-Santiago,[14] Gabriela Cesarman-Maus,[15] Pankit Vachhani,[16] Sangmin Lee,[17] Vijaya Raj Bhatt,[18] William Blum,[19] Roland B. Walter,[20] Dale Bixby,[21] Ivana Gojo,[22] Madeleine Duvic,[23] Raajit K. Rampal,[24] Marcos de Lima,[25] James Foran,[26] Amir T. Fathi,[27] Aric Cameron Hall,[28] Meagan A. Jacoby,[29] Jeffrey Lancet,[2] Gabriel Mannis,[30] Anthony S. Stein,[31] Alice Mims,[32] David Rizzieri,[33] Rebecca Olin,[34] Alexander Perl,[35] Gary Schiller,[36] Paul Shami,[37] Richard M. Stone,[38] Stephen Strickland,[39] Matthew J. Wieduwilt,[40] Naval Daver,[1] Farhad Ravandi,[1] Sumithira Vasu,[41] Monica Guzman,[42] Gail J. Roboz,[43] Joseph Khoury,[44] Muzaffar Qazilbash,[45] Phyu P. Aung,[46] Branko Cuglievan,[47] Yazan Madanat,[48] Mohamed A. Kharfan-Dabaja,[26] Anna Pawlowska,[49] Justin Taylor,[50] Martin Tallman,[51] Prajwal Dhakal,[52] and Andrew A. Lane[38]

[1]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Department of Malignant Hematology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY; [4]Department of Internal Medicine, The University of Texas School of Health Sciences at Houston, Houston, TX; [5]West Palm Beach VA Medical Center, West Palm Beach, FL; [6]MPN Program, Princess Margaret Cancer

tagraxofusp monotherapy or HMA + venetoclax combination in older/unfit patients are potential choices.

HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Guideline Article - Expert opinion

Open Access

Unmet Clinical Needs and Management Recommendations for Blastic Plasmacytoid Dendritic Cell Neoplasm: A Consensus-based Position Paper From an Ad Hoc International Expert Panel

Livio Pagano[1,2], Pier Luigi Zinzani[3,4], Stefano Pileri[5], Pietro Quaglino[6], Branko Cuglievan[7], Emilio Berti[8,9], Naveen Pemmaraju[10], Francesco Onida[11,12], Rein Willemze[13], Alberto Orfao[14,15], Giovanni Barosi[16]

Correspondence: Livio Pagano (livio.pagano@unicatt.it).