Discover Oncology

Research

Blastic plasmacytoid dendritic cell neoplasm (BPDCN): international, multi-center collaboration and global registry program

Astghik Voskanyan[1,2] · Maria Badikyan[1,2] · Marina Konopleva[3,4] · Alvaro Alencar[5] · Arusyak Ivanyan[2] · Carolyn Owen[6] · Consolato M. Sergi[7] · Ching-Tien Peng[8] · Dickran Kazandjian[5] · Justin Taylor[5] · Funda Tekkesin[9] · Hasanein Ghali[10] · Karen Bedirian[1,2] · Maria Paola Martelli[11] · Enrico Attardi[12] · Maria Teresa Voso[12] · Mariam Abramashvili[13] · Mazin Faisal Al-Jadiry[10] · Michalis Michael[14] · Min-Yu Su[8] · Nare Martirosyan[2] · Nerses Ghahramanyan[2] · Nino Totogashvili[13] · Pavel P. Kotoucek[15] · Rejin Kebudi[16] · Robin Ohannessian[17] · Ruzanna Papyan[1,2,18,19] · Shushan Hovsepyan[1,2,18] · Salma Elashwah[20] · Sameer Bakhshi[21] · Samvel Bardakhchyan[1,2] · Samvel Danelyan[2] · Shaimaa El-Ashwah[20] · Tezer Kutluk[22] · Deniz Tuğcu[16] · Ahmad Alhuraiji[23] · Vassilios Lazaris[24] · Gevorg Tamamyan[1,2,18,19] · Naveen Pemmaraju[4]

Received: 29 September 2024 / Accepted: 18 April 2025
Published online: 21 December 2025

✉ Shushan Hovsepyan, Shushan.hovsepyan@oncodailyjournal.com; Astghik Voskanyan, astghikvos@gmail.com; Maria Badikyan, badikyanmaria@gmail.com; Marina Konopleva, marina.Konopleva@einsteinmed.edu; Alvaro Alencar, aalencar@med.miami.edu; Arusyak Ivanyan, ivanyan.arusyak@gmail.com; Carolyn Owen, carolyn.owen@ahs.ca; Consolato M. Sergi, CSergi@cheo.on.ca; Ching-Tien Peng, penect@gmail.com; Dickran Kazandjian, dkazandjian@miami.edu; Justin Taylor, jxt1091@miami.edu; Funda Tekkesin, tekkesinfunda@gmail.com; Hasanein Ghali, hasaneinghali@gmail.com; Karen Bedirian, karenbedirian@gmail.com; Maria Paola Martelli, maria.martelli@unipg.it; Enrico Attardi, enricoattardi@gmail.com; Maria Teresa Voso, voso@med.uniroma2.it; Mariam Abramashvili, m.abramishvili@evex.ge; Mazin Faisal Al-Jadiry, mazinaljadiry@yahoo.com; Michalis Michael, Michalis.D.Michael@bococ.org.cy; Min-Yu Su, 035515@tool.caaumed.org.tw; Nare Martirosyan, narehmartirosyan@gmail.com; Nerses Ghahramanyan, nersesghahramanyan@gmail.com; Nino Totogashvili, nino_totogashvili@yahoo.com; Pavel P. Kotoucek, pavel.kotoucek@nhs.net; Rejin Kebudi, rejinkebudi@yahoo.com; Robin Ohannessian, robin@telemonica.com; Ruzanna Papyan, ruzannapapyan92@gmail.com; Salma Elashwah, salmasaber@mans.edu.eg; Sameer Bakhshi, sambakh@hotmail.com; Samvel Bardakhchyan, bardakchyan-5samvel@yandex.ru; Samvel Danelyan, danielsamvel@yahoo.com; Shaimaa El-Ashwah, shaimaasaber@mans.edu.eg; Tezer Kutluk, tezerkutluk@gmail.com; Deniz Tuğcu, tugcudeniz@gmail.com; Ahmad Alhuraiji, aalhuraiji@moh.gov.kw; Vassilios Lazaris, vlazaris@gmail.com; Gevorg Tamamyan, gevorgtamamyan@gmail.com; Naveen Pemmaraju, NPemmaraju@mdanderson.org | [1]Immune Oncology Research Institute, 7 Nersisyan, 0014 Yerevan, Armenia. [2]Yeolyan Hematology and Oncology Center, Yerevan, Armenia. [3]Albert Einstein College of Medicine, Montefiore Einstein Cancer Center, Bronx, NY, USA. [4]University of Texas MD Anderson Cancer Center, Houston, TX, USA. [5]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA. [6]University of Calgary, Calgary, AB, Canada. [7]Children's Hospital of Eastern Ontario (CHEO), University of Ottawa, Ottawa, ON, Canada. [8]China Medical University Children's Hospital, Taichung, Taiwan. [9] Pediatric Bone Marrow Transplantation Unit, Pediatric Hematology and Oncology Department, Umraniye Research and Education Hospital, University of Health Sciences, Istanbul, Turkey. [10]Pediatric Hematology Oncology, Children's Welfare Teaching Hospital Medical City, College of Medicine, University of Baghdad, Baghdad, Iraq. [11]University of Perugia - Azienda Ospedaliera Perugia, Perugia, Italy. [12]Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy. [13]M. Iashvili Children's Central Hospital, Tbilisi, Georgia. [14]Cyprus Society of Haematology, Nicosia, Cyprus. [15]Broomfield Hospital, Haematology Mid and South Essex University Hospitals Group, Chelmsford, Essex, UK. [16]Istanbul University, Oncology Institute, Istanbul, Turkey. [17]Telemedicine 360 By Telemonica, Paris, France. [18]Pediatric Cancer and Blood Disorders Center of Armenia, Hematology Center After Prof. R. H. Yeolyan, Yerevan, Armenia. [19]Department of Pediatric Oncology and Hematology, Yerevan State Medical University, Yerevan, Armenia. [20]Oncology Center, Mansoura University, Mansoura, Egypt. [21]Department of Medical Oncology, Dr. B.R. A Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India. [22]Turkish Pediatric Cancer Registry, Ankara, Turkey. [23]Kuwait Cancer Centre, Sabah Medical Region, 1031 Shuwaikh, Kuwait. [24]Nicosia General Hospital, Lemesou, Cyprus.

Abstract

Background Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare and aggressive hematologic malignancy originating from plasmacytoid dendritic cell precursors. BPDCN shares common diagnostic and clinical features with other hematologic malignancies and various dermatological disorders. Differential diagnosis and treatment are challenging and require awareness by the dermatologist, hemato-oncologist, pathologist for detailed diagnostic and therapeutic workup. The outcomes remain poor, and the optimal treatment for the disease is yet to be established, emphasizing the need for a more comprehensive and globally inclusive approach.

Methods In response to these challenges, we initiated an international, multi-center collaboration and established a global registry program for BPDCN patients. The registry collected both retrospective and prospective data on demographics, clinical presentations, diagnostic criteria, treatment regimens, and outcomes for cases diagnosed after Jan 2010. Data for this report was obtained from 36 patients across 16 centers in 12 countries, with ongoing contributions from additional centers.

Results Preliminary analysis revealed a male predominance (78%), with a median age at diagnosis of 63 years, involving all age groups. The immunophenotype (CD123 + , CD4 + , CD56 +) was consistently observed in a majority of patients (88.8%), validating its diagnostic utility and paramount significance in the BPDCN diagnosis. Treatment responses varied based on initial regimens, with ALL-like approaches demonstrating more favorable outcomes compared to AML-like strategies, which were given to younger patients. Notably, relapse rates remained high.

Conclusion The BPDCN International Registry Program provides a valuable tool in consolidating global data and fostering collaboration among researchers and clinicians. This collaborative effort involving multiple countries on several continents not only aims to advance our comprehension of BPDCN but also lays the groundwork for standardized treatment protocols for improving outcomes for BPDCN patients worldwide.

Key points

1. Global Collaboration and Data Collection: The BPDCN International Registry Program collected data from 36 patients across 16 centers in 12 countries, highlighting a robust global collaboration effort. This initiative aims to consolidate comprehensive data on demographics, clinical presentations, treatments, and outcomes, providing a valuable resource for researchers and clinicians worldwide.
2. Clinical Implications and Future Directions: The registry's preliminary analysis underscores the need for standardized treatment protocols for BPDCN. Despite varied initial treatment responses, the high relapse rates suggest a critical need for further research into more effective therapeutic strategies. This collaborative effort sets the stage for advancing understanding and improving outcomes for BPDCN patients globally.

1 Introduction

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare and clinically aggressive hematologic malignancy originating from the precursors of plasmacytoid dendritic cells. BPDCN typically presents with cutaneous dissemination and bone marrow (BM) involvement, as well as extramedullary sites, including the central nervous system (CNS) in 20–30% of cases. (3:1 up to 5:1) [1, 2]. Estimating the true incidence of the disease is challenging; however, it is suggested that BPDCN constitutes 0.44% of all hematologic malignancies and 0.7% of all cutaneous leukemia/lymphoma cases [3]. While typically diagnosed around the age of 65, BPDCN has been observed across all age groups, including children [4] and exhibits a male predominance. In 2008, the World Health Organization (WHO) recognized BPDCN as a distinct entity, previously, it was known as agranular CD4 +/CD56 + hematodermic neoplasm or blastic natural-killer lymphoma. In the 2022 5 th edition update of the WHO Classification [5], it is now recognised under the Myeloid/Histiocytic/Dendritic neoplasms category [6–8]. The diagnosis requires at least 4 of the 6 BPDCN antigens: CD123, CD4, CD56, CD303/BDCA-2, TCL-1, CD2 AP, and lack of expression of myeloid markers (myeloperoxidase (MPO), lysozyme, CD14, CD34, CD116, and CD163), T and B lineage markers [3, 9]. Although antigens of disease as diagnostic criteria are well defined, the heterogeneity of clinical course of BPDCN can lead to misdiagnosis. To avoid diagnostic gaps, awareness of specialists should be enhanced and decisions should involve multidisciplinary discussions between hemato-oncologists, dermatologists and pathologists. Retrospective studies indicate that the majority of patients received multi-agent chemotherapy with acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), or lymphoma-based treatment regimens, with relatively high response rates including complete remission rates of 53–89% [9] but short frequent and rapid relapses and

subsequent mortality, with a median survival of 12–18 months. ALL-based treatment regimens were reported to be more effective than AML regimens in these retrospective series; however, patient numbers were small with significant inter-patient variability [10].

The rarity and diagnostic challenges of BPDCN contribute to the absence of a worldwide consensus on disease management. In North American, the NABC sought to better understand and discuss BPDCN in the United States, Canada, and Mexico, and a recent Italian consensus paper convened a group of primarily European investigators for BPDCN guidelines and future directions. While these efforts have greatly added to the worldwide BPDCN literature, there still are many more areas of the world for further BPDCN research, investigation, and outcomes research and therefore we convened the current global initiative [3, 11].

The extreme rarity renders prospective clinical trials not feasible leading to a lack of standardized treatment approaches. These issues emphasize the need for collaborative research efforts and international cooperation to advance understanding and improve patient outcomes.

To address these challenges regarding diagnostic and treatment gaps, the Immune-Oncology Research Institute launched an international registry on Jul 1 st, 2022, aiming to foster multi-center collaboration and build a comprehensive database of BPDCN patients, thereby facilitating data-driven diagnostic and treatment recommendations. The registry collects retrospective and prospective data on the clinical presentation, diagnostics, treatment regimens, and outcomes of patients diagnosed with BPDCN after Jan 1 st, 2010.

This manuscript aims to present and analyze the data of 36 patients diagnosed with BPDCN, drawing insights from the BPDCN International Registry.

2 Methods

This is a retrospective and prospective review of patients diagnosed with BPDCN, utilizing data extracted from the BPDCN International Registry. The registry is a global data collection platform via electronic Case Report Forms (eCRF) and Excel forms. Through the questionaries the data on patients characteristics (including demographics and clinical manifestations), disease characteristics (laboratory and imaging data including cytogenetics, immunophenotyping and/or immunochemistry), details on treatment regimens, outcomes, death causes. As of Jan 1 st, 2024, retrospective data were collected from a total of 17 centers from 13 countries, including Armenia, Canada, Cyprus, Egypt, Georgia, India, Italy, Taiwan, Turkey, the UK, the USA, Kuwait and Iraq, which actively contributed to the registry (Fig. 1). For prospectively enrolled cases, ongoing data collection includes regular follow-ups to capture dynamic information on treatment responses, disease progression, and survival outcomes.

This registry adheres to ethical standards, having received approval from the Ethical Committee of Yerevan State Medical University, complemented with center-specific Institutional Review Board (IRB) approvals as required by local regulations. Informed consent has been obtained from all patients participating in the prospective arm of the study, ensuring ethical compliance and prioritizing patient confidentiality throughout the research process.

Statistical analyses will employ descriptive methods, presenting demographic and clinical characteristics and treatment outcomes. The anonymization of patient data is maintained, aligning with privacy regulations and ethical considerations. The BPDCN International Registry is registered on ClinicalTrials.gov under the identifier NCT05430971.

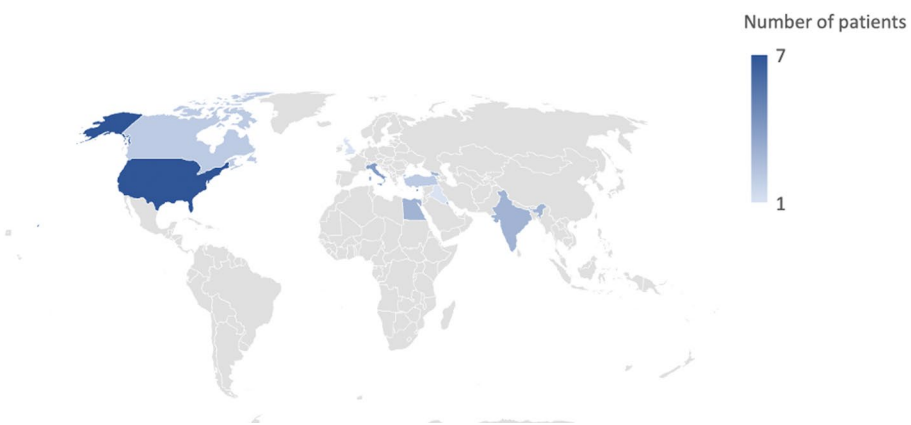

Fig. 1 International Distribution of BPDCN Patients Across Countries and Centers

Table 1 Clinical and biological characteristics of patients

Characteristics	N (%) or Mean [Range]
Site(s)	
Skin	32
Lymph Nodes	21
Splenomegaly (over 14 cm)	10
CNS	1
Complete blood count and bone marrow blast cells	
Hgb g/dL	10.7 [6.3–17.1]
WBC 10^9/L	5.3 [2.0–29.2]
PLT 10^9/L	83.0 [17.0–238.0]
Blast cells % in peripheral blood	7 [0–90]
Bone marrow blast cells%	55 [20–95]
Expression of BPDCN markers	Positive cases N (%)
CD123 (n = 32)	32 (100%)
CD4 (n = 33)	33 (100%)
CD 56 (n 34)	34 (100%)
TCL (n = 5)	5 (100%)
CD303 (n = 2)	2 (100%)
CD2 AP (n = 3)	3 (100%)

Table 2 Response to first-line treatment

Treatment regimen	Complete response, n	Partial response, n%	Response duration, median range), mo	Relapse rate, n (%) of CR patients	Allo-SCT, n (%) of CR and PR patients
ALL-like (n = 25)	20 (80%)	3 (12%)	5	9 (45%)	6(24%)
AML-like (n = 6)	3 (50%)	2(3%)	7	3 (100%)	1(20%)
Lymphoma-like (n = 2)	0	0	0	0	0
Clinical trial (n = 1)	1	1	9	1	1
Tagraxofusp (n = 2)	0	2	3	0	0

The map illustrates the distribution of BPDCN patients across various countries. Darker shades represent a higher number of patients, lighter shades correspond to fewer patients. The scale starts with a minimum of 1 patient (light purple) and increases to the maximum number (bright yellow).

3 Results

3.1 Patient characteristics

Data from 36 patients (33 retrospective and 3 prospective) were analyzed based on our registry. 78% of patients were male, in keeping with the historical expectation of BPDCN. The median age at diagnosis was 63 years (range 4–97 years). Cutaneous lesions were present in 32 patients (89%), and CNS involvement was documented in only 1 patient (3%) (Table 1). Splenomegaly (> 14 cm) was detected in 10% of cases wither with ultrasound or CT scan.

3.2 Complete blood count, bone marrow blast count, immunophenotyping, and/or immunohistochemistry

The complete blood count revealed that, at diagnosis, 67% of patients had anemia, 53% had thrombocytopenia, and 28% had leukopenia. Leukocytosis was observed in 14% of patients, with 42% having circulating blast cells in peripheral blood. Fifty-three percent had over 5% of blast cells in the bone marrow (Table 2). Immunophenotyping showed consistent

positive expression for CD123 (100%) evaluated in 32 cases, CD4 (100%) in 33 patients, CD56 (100%) in 34 patients, TCL1 (100%) in 5 patients, CD303 (100%) in 2 patients, and CD2 AP (100%) in 3 patients (Table 2).

The immunophenotyping results demonstrated the following findings: CD123 expression was examined in 32 cases, all of which were positive. CD123 expression was not evaluated for three patients, and data for one patient was unavailable. CD4 expression was assessed in 33 patients, all of whom tested positive. However, CD4 expression was not checked for three patients. CD56 expression was investigated in 34 patients, all of whom were positive, with no assessment for two patients. TCL1 expression was studied in only 5 patients, all of whom were positive. CD303 expression was assessed in two patients, both of whom tested positive, while CD2 AP expression was studied in three patients, all of whom showed positive results (Table 1).

3.3 Conventional cytogenetic and molecular analysis

Karyotypes were obtained for six patients, revealing trisomy (n = 2), 46, XX, der, and (X; 5) (q28; p13) (n = 1) (Do you have the cytogenetics photo to add to the manuscript?), while the remaining three had normal karyotypes. Molecular analysis with PCR method was conducted in 6 patients. In 4 patients mutations were revealed in *JAK 2 V617 F plus ASXL1 and TET2* (n = 1), *SRSF2*(n = 2) and *TET2*(n = 1) genes. As the molecular analysis was performed in 6 patients and only 4 of them had mutations, we could not find out any relevance of these mutations to disease course and treatment results.

3.4 Treatment response

In 25 patients (23 retrospective), the initial treatment involved an ALL-like regimen, resulting in 20 complete responses (CR), three partial responses (PR), and two with an unknown response, with overall response rates of 92%. Among the six patients (5 in CR, 1 in PR) who underwent allo-HSCT, three were alive in CR at the last contact, two died from non-relapse mortality following HSCT, and one was lost to follow-up. The median duration of response was 5 months. Within the ALL-based treatment group, 3 patients died from unknown causes (without disease progression) within 3–6 months, 9 patients experienced relapse and received varied treatments, including AML-like regimen (n = 4) including azacytidine and venetoclax HAM (High Dose-Ara-C and mitoxantrone) (n = 1), palliative irradiation (n = 1), gemcitabine + docetaxel followed by allo-HSCT (n = 1), and CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) (n = 1). All patients died from disease progression except for one patient treated with HAM who experienced CR and was alive after 38 months at the last follow-up. The duration of the second response was evaluated in 5 patients, with a median of 11 months. In 6 patients (5 retrospective), initial treatment was based on an AML-like regimen, resulting in 3 CR, 2 PR, and one unknown response. The median duration of response was 6.5 months. The patient in PR underwent allo-HSCT and was alive at the last follow-up, six years after diagnosis.

Within the AML-based treatment group, 4 patients experienced relapse and received various treatments, including an ALL-like regimen (n = 1), tagraxofusp (TAG) (n = 1), and an AML-like regimen (n = 2). All patients died within 2 months after diagnosis from the progression of the disease. One patient was initially involved in a clinical trial and achieved PR with a duration of response of 9 months. After progression, the patient received six cycles of HyperCVAD (cyclophosphamide, vincristine, adriamycin, methotrexate, cytarabine, and dexamethasone) and underwent allo-HSCT. At the last follow-up (10 years after diagnosis) patient was alive in CR. In two patients, diagnosed after 2018, initial treatment was performed with tagraxofusp. One patient experienced PR for 2 months. Subsequently, treatment continued with an AML-like regimen, resulting in CR. Unfortunately, the patient died from disease progression, and the duration of CR is unknown. The second patient experienced stable disease for 3 months, due to disease progression, the treatment was continued with AML-like regimen with partial response. The duration of response is unknown, with the patient lost to follow-up. (Table 2).

3.5 Survival

At the last documented follow-up, ten patients from the retrospective cohort were alive. The median duration from the initial diagnosis to the last follow-up was 5 years, spanning from one to ten years. Five patients among this cohort were under the age of 18. Eight patients received treatment with an ALL-like regimen, one with AML-like regimen, and another was initially enrolled in a clinical trial. Five patients underwent allo-HSCT. Among the three prospective patients, one is currently in CR, while the data for the other two patients is unknown.

3.6 Adolescents and young adults with BPDCN

Studies showed that adolescents and young adults (AYA) often achieve better treatment outcomes compared to adults, particularly when pediatric treatment protocols are utilized. However, AYA patients frequently face distinct challenges, both in terms of psychosocial aspects and treatment-related side effects(12). In our cohort the number of AYA patients was nine, the median age was 11 years old, with a range from 3 to 19 years. Among them, there were four females, all exhibiting skin involvement, with four showing bone marrow infiltration and one affecting the CNS. Treatment was administered using ALL-based regimens. Of the nine patients, seven experienced complete responses to treatment, while one exhibited a partial response, and another had stable disease. Four patients underwent transplantation as part of their treatment strategy. Unfortunately, one patient passed away due to complications following transplantation, while another relapsed within nine months. Subsequently, treatment was continued with Azacitidine, but the patient died from the disease progression. The exact date of death for this patient is unknown. At the latest follow-up, seven patients were still alive, with a median follow-up duration of five years, ranging from one to seven years.

4 Discussion

This comprehensive analysis of a 36-patient global cohort of BPDCN conducted by the Immune Oncology Research Institute sheds light on the heterogeneous nature of treatment regimens and the challenges associated with this rare and aggressive hematologic malignancy. Immunophenotyping results confirmed the triple-positive immunophenotype (CD123 + CD4 +, CD56 +), of the majority of assessed patients, validating the utility of these markers in diagnosis. Additionally, conventional cytogenetic and molecular analyses revealed mutations in *JAK2 V617 F*, *ASXL1*, and *TET2* genes, underlining the genetic complexity of BPDCN. Treatment responses varied based on initial regimens, emphasizing ALL-like and AML-like approaches. Notably, Within the limits of this small series with a broad range of patient ages, intensive ALL-therapies appeared to result in better response rates and more durable responses.69% of patients were treated with ALL-like regimens and only 17% patients were treated with AML-like, due to small sample size it is difficult to evaluate the priority of ALL-like therapy, further research of more patients is needed to confirm this statement. However, a high relapse rate was observed, indicating the persistent challenges in achieving long-term remissions. Efforts to improve outcomes include exploring allogeneic hematopoietic stem cell transplantation (allo-HSCT), particularly for those in first complete remission. However, given the median age of BPDCN patients (65–70 years), many are ineligible for allo-HSCT. The role of auto-HSCT is a subject of debate with no cases of auto-HSCT noted within our retrospective series [10, 11].

In recent years, various novel and innovative therapies targeting surface molecules in BPDCN cells have been developed. These agents are either in clinical trials or in pre-clinical stages. In 2018, tagraxofusp became the first FDA-approved drug for patients with previously untreated or relapsed/refractory BPDCN(15). Tagraxofusp is an interleukin 3-diphtheria toxin recombinant fusion protein that targets CD 123, highly expressed on the surface of BPDCN cells (16). The first prospective multi-institutional study using tagraxofusp in BPDCN was conducted by Pemmaraju et al. The trial included 47 patients with BPDCN, 32 receiving tagraxofusp as a first-line therapy, while 15 received previous therapy. Among the 29 previously untreated patients, the overall response rate was 90%; 45% underwent stem-cell transplantation. Survival rates at 18 and 24 months were 59% and 52%, respectively. Among the 15 previously treated patients, the response rate was 67%, and the median overall survival was 8.5 months [12].

This dataset is subject to limitations frequent within rare diseases, including small sample size and potential biases in retrospective data collection. Despite these limitations, it is noteworthy to mention that this represents the first global initiative dedicated to collecting and analyzing BPDCN data on a worldwide scale.

In conclusion, the BPDCN International Registry Program serves as a critical initiative to consolidate data from various regions, fostering collaboration among researchers and clinicians globally. This study underscores the need for ongoing research efforts to confront the complexities of BPDCN, to improve diagnostic accuracy, and create uniform therapeutic strategies that can better be examined for efficacy. In addition to our ongoing effort with the registry, we have launched the BPDCN Global Network. It was initiated with the first lecture by the renowned Dr. N. Pemmaraju, who provided an in-depth review of BPDCN (https://oncodaily.com/blog/15713.html). Our agenda includes

the development of monthly meetings with case discussions and lectures by experts. Furthermore, we are actively planning to expand our registry to include the collection of specimens facilitating essential genetic and molecular testing to advance our understanding of the biology and development of therapeutic strategies for BPDCN.

Author contributions Astghik Voskanyan, MD: Conceptualization, Methodology, Data curation, Writing—Original Draft, Writing—Review and Editing, Supervision Maria Badikyan, MD: Data Collection, Writing—Review and Editing, Marina Konopleva, MD: Data Collection, Writing—Review and Editing, Data Curation, Alvaro Alencar, MD: Data Collection, Writing—Review and Editing, Data Curation, Arusyak Ivanyan, MD: Data Collection, Writing—Review and Editing, Data Curation, Carolyn Owen, MD: Data Collection, Writing—Review and Editing, Data Curation, Consolato M. Sergi, MD: Data Collection, Writing—Review and Editing, Data Curation, Ching-Tien Peng, MD: Data Collection, Writing—Review and Editing, Data Curation, Dickran Kazandjian, MD: Data Collection, Writing—Review and Editing, Data Curation, Justin Taylor, MD: Data Collection, Writing—Review and Editing, Data Curation, VisualizationFunda Tekkesin, MD: Data Collection, Writing—Review and Editing, Data Curation, Hasanein Ghali, MD: Data Collection, Writing—Review and Editing, Data Curation, Karen Bedirian, MPH: Writing—Review and Editing Maria Paola Martelli, MD: Data Collection, Writing—Review and Editing, Data Curation, Enrico Attardi, MD: Data Collection, Writing—Review and Editing, Data Curation, Maria Teresa Voso, MD: Data Collection, Writing—Review and Editing, Data Curation, Mariam Abramashvili, MD: Data Collection, Writing—Review and Editing, Data Curation, Mazin Faisal Al-Jadiry, MD: Data Collection, Writing—Review and Editing, Data Curation, Michalis Michael, MD: Data Collection, Writing—Review and Editing, Data Curation, Min-Yu Su, MD: Data Collection, Writing—Review and Editing, Data Curation, Nare Martirosyan, MD: Data Collection, Writing—Review and Editing. Nerses Ghahramanyan MD: Writing—Review and Editing. Nino Totogashvili, MD: Data Collection, Writing—Review and Editing, Data Curation. Pavel P Kotoucek, MD: Data Collection, Writing—Review and Editing, Data Curation. Rejin Kebudi, MD: Data Collection, Writing—Review and Editing, Data Curation. Robin Ohannessian, MD: Data Collection, Writing—Review and Editing. Ruzanna Papyan, MD: Writing—Review and Editing. Shushan Hovsepyan MD*: Writing—Original Draft Preparation, Writing—Review and Editing, Salma Elashwah, MD: Data Collection, Writing—Review and Editing, Data Curation. Sameer Bakhshi, MD: Data Collection, Writing—Review and Editing, Data Curation. Samvel Bardakhchyan, MD, PhD: Writing—Review and Editing, Supervision. Samvel Danelyan, MD, PhD: Writing—Review and Editing, Supervision. Shaimaa El-Ashwah, MD: Data Collection, Writing—Review and Editing, Data Curation. Tezer Kutluk, MD: Data Collection, Writing—Review and Editing, Data Curation. Deniz Tuğcu, MD: Data Collection, Writing—Review and Editing, Data Curation. Ahmad Alhuraiji, MD: Data Collection, Writing—Review and Editing, Data Curation. Vassilios Lazaris: Data Collection, Writing—Review and Editing, Data Curation. Gevorg Tamamyan MD, PhD: Conceptualization, Writing—Review and Editing, Supervision. Naveen Pemmaraju, MD: Data Collection, Writing—Review and Editing, Data Curation,

Data availability The data supporting the findings of this study are part of the BPDCN International Registry Program and include clinical, diagnostic, treatment, and outcome data from different countries. Due to patient confidentiality and compliance with ethical standards, the raw data are not publicly available. However, summarized and anonymized datasets can be accessed upon reasonable request. Requests for data should be directed to Dr. Astghik Voskanyan (astghikvos@gmail.com). Access to detailed data may require completion of a Data Use Agreement (DUA) and approval from relevant ethical review boards. For original data, please contact astghikvos@gmail.com.

Declarations

Competing interests Maria Paola Martelli declares honoraria/consultancy at scientific advisory boards for AbbVie, Amgen, BMS, Delbert, Janssen, Novartis, Pfizer, and Jazz Pharmaceuticals. Maria Teresa Voso declares: research support from Celgene/BMS and Novartis; speakers'bureau participation for Celgene/BMS, Astellas, Jazz, AbbVie, Novartis, and AstraZeneca; advisory board membership for Celgene/BMS, Jazz, and Syros. Alencar Alvaro declares research funding from Incyte, BeiGene, and LOXO/Lilly; honoraria from Dr. Reddy; and advisory board membership for ADC Therapeutics, BeiGene, AbbVie, Lilly, Genentech, Amgen, Incyte, and Janssen. Naveen Pemmaraju declares: Board of Directors/Management: Dan's House of Hope. Consulting/Scientific Advisory Board/Speaking: AbbVie, Aplastic Anemia & MDS International Foundation, Aptitude Health, Astellas Pharma US, Blueprint Medicines, Bristol-Myers Squibb Pharmaceuticals, CancerNet, CareDx, Celgene, Cimeio Therapeutics AG, ClearView Healthcare Partners, CTI BioPharma, Curio Science, Dava Oncology, EUSA Pharma, Harborside Press, Imedex, Immunogen, Intellisphere, Karyopharm, Magdalen Medical Publishing, Medscape, Menarini Group, Morphosys, Neopharm, Novartis Pharmaceuticals, OncLive, Pacylex, Patient Power, PeerView Institute for Medical Education, Pharma Essentia, Physician Education Resource (PER). Leadership: ASH Committee on Communications, ASCO Cancer.Net Editorial Board. Licenses: Karger Publishers. Research (Grant): United States Department of Defense (DOD), National Institute of Health/National Cancer Institute (NIH/NCI). Uncompensated: HemOnc Times/Oncology Times. Marina Konopleva declares research funding and consulting fees from AbbVie, Allogene, AstraZeneca, Auxenion, Bakx, Boehringer, Dark Blue Therapeutics, F. Hoffman-La Roche, Genentech, Gilead, ImmunoGen, Janssen, Legend, MEI Pharma, Precision, Rafael, Redona, Sanofi, Sellas, Stemline, and Vincerx. All other authors declare no conflicts of interest. Author Consolato M. Sergi MD has aposition on the editorial board of Discover Oncology, and was not involved in the review or decisionsrelated to this article.

References

1. Pemmaraju N, Wilson NR, Garcia-Manero G, et al. Characteristics and outcomes of patients with blastic plasmacytoid dendritic cell neoplasm treated with frontline HCVAD. Blood Adv. 2022;6(10):3027–35. https://doi.org/10.1182/bloodadvances.2021006645.
2. Sapienza MR, Pileri A, Derenzini E, et al. Blastic plasmacytoid dendritic cell neoplasm: state of the art and prospects. Cancers. 2019;11(5):595. https://doi.org/10.3390/cancers11050595.
3. Garnache-Ottou F, Feuillard J, Saas P. Plasmacytoid dendritic cell leukaemia/lymphoma: towards a well-defined entity? Br J Haematol. 2007;136(4):539–48. https://doi.org/10.1111/j.1365-2141.2006.06458.x.
4. Garnache-Ottou F, Feuillard J, Ferrand C, et al. Extended diagnostic criteria for plasmacytoid dendritic cell leukaemia. Br J Haematol. 2009;145(5):624–36. https://doi.org/10.1111/j.1365-2141.2009.07679.x.
5. Li W. The 5th Edition of the World Health Organization classification of hematolymphoid tumors. In: Li W, ed. Leukemia. Brisbane (AU): Exon Publications; October 16, 2022.
6. Pemmaraju N, Kantarjian H, Sweet K, et al. North American blastic plasmacytoid dendritic cell neoplasm consortium: position on standards of care and areas of need. Blood. 2023;141(6):567–78. https://doi.org/10.1182/blood.2022017865.
7. Cuglievan B, Connors J, He J, et al. Blastic plasmacytoid dendritic cell neoplasm: a comprehensive review in pediatrics, adolescents, and young adults (AYA) and an update of novel therapies. Leukemia. 2023;37(9):1767–78. https://doi.org/10.1038/s41375-023-01968-z.
8. Wang Y, Xiao L, Yin L, Zhou L, Deng Y, Deng H. Diagnosis, treatment, and genetic characteristics of blastic plasmacytoid dendritic cell neoplasm: a review. Medicine. 2023;102(7): e32904. https://doi.org/10.1097/MD.0000000000032904.
9. Aoki T, Suzuki R, Kuwatsuka Y, et al. Long-term survival following autologous and allogeneic stem cell transplantation for blastic plasmacytoid dendritic cell neoplasm. Blood. 2015;125(23):3559–62. https://doi.org/10.1182/blood-2015-01-621268.
10. Pagano L, Valentini CG, Grammatico S, Pulsoni A. Blastic plasmacytoid dendritic cell neoplasm: diagnostic criteria and therapeutical approaches. Br J Haematol. 2016;174(2):188–202. https://doi.org/10.1111/bjh.14146.
11. Pemmaraju N, Lane AA, Sweet KL, et al. Tagraxofusp in blastic plasmacytoid dendritic-cell neoplasm. N Engl J Med. 2019;380(17):1628–37. https://doi.org/10.1056/NEJMoa1815105.