

## **Blastic Plasmacytoid Dendritic Cell Neoplasm**

Revised November 2014

*A critical research need exists for this challenging to diagnose, under-reported, and usually rapidly fatal disease*

### **Background**

Blastic plasmacytoid dendritic cell neoplasm (BPDCN), previously known as natural killer (NK) cell leukemia/lymphoma, is categorized by the World Health Organization (4th edition, 2008) under acute myeloid leukemia (AML). Typically, BPDCN presents with features of both lymphoma and leukemia. There are little data on the biology of BPDCN and there is no established standard of care. The skin is the most frequently involved site of disease (80 percent of cases). However, BPDCN usually progresses to a terminal leukemic phase with bone marrow involvement and pancytopenia; the lymph nodes and spleen may also be involved. The median age at presentation is 60 to 70 years, with a 3:1 male predominance.

### **Diagnosis and Incidence**

The diagnosis of BPDCN is challenging because of the lack of traditional lineage-specific markers, however CD4/CD56 co-expression is common. BPDCN blasts almost always express the interleukin-3 receptor (IL-3R), also known as CD123. The true incidence rate of BPDCN is unknown because this disease is frequently misdiagnosed and under-reported. BPDCN can be misdiagnosed as a variety of other malignant and non-malignant conditions, including non-Hodgkin lymphoma, AML, leukemia cutis, melanoma and lupus erythematosus. When BPDCN presents with involvement of both the skin and bone marrow, differentiating BPDCN from leukemia cutis or cutaneous lymphoma with bone marrow involvement may pose significant diagnostic challenges, and BPDCN should be considered in the differential diagnosis. In cases with skin manifestations, patients typically present with nonspecific and asymptomatic rashes; thus, BPDCN should be considered in the differential diagnosis of atypical rashes, especially when malignant cells are observed on histopathologic examination.

### **Current Treatment and Outcomes**

There are no prospective randomized clinical study data, or prospective trial data, to define the optimal frontline therapy for BPDCN patients. Standard care consists of AML-like or acute lymphoblastic leukemia-like regimens used for induction therapy, as well as lymphoma-like regimens. Response duration is typically brief. Median survival from diagnosis has been reported to range from 9 to 12 months. Second remissions with conventional chemotherapy are difficult to achieve. Allogeneic hematopoietic stem cell transplant (allo-HCT), especially if offered in first remission, may result in longer remissions. Although most data are limited to small case series or single case reports, current recommendations are to evaluate BPDCN patients for an allo-HCT as soon as possible and to initiate donor identification in appropriate cases. Allo-HCT should be considered in patients in first complete response (CR) if a suitable human leukocyte antigen compatible donor is identified.

### **Research and Evolving Novel Treatments**

In view of the unsatisfactory results of standard treatments for BPDCN patients, such as those described above, enrollment of patients in clinical trials of new therapies should be encouraged. Indeed, research efforts to identify an effective treatment for all presentations of this generally aggressive and fatal disease are crucial. SL-401 is one example of a potential new therapy. SL-401 is a novel biologic targeted therapy comprised of recombinant human IL-3 joined recombinantly to truncated diphtheria toxin. Preclinical and early clinical studies have suggested a role for SL-401, which targets the IL-3R, in treating BPDCN patients. The rationale for evaluating SL-401 is based on

*(over)*

the overexpression of the IL-3R on cancer stem cells (CSCs) and tumor bulk, relative to normal hematopoietic cells, in BPDCN and a range of other hematologic malignancies. SL-401 targets both leukemic blasts and CSCs; as a result, both significant antitumor effects and improvement in long-term outcomes are expected. Seven out of 9 evaluable BPDCN patients had major responses including 5 complete responses and 2 partial responses after a single cycle of the drug as a single agent in reported Phase I/II clinical trials. A new trial “SL-401 in Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm or Acute Myeloid Leukemia” is now open for enrollment (<http://clinicaltrials.gov/ct2/show/NCT02113982>). Participating sites include City of Hope National Medical Center in Duarte, California, H. Lee Moffitt Cancer Center & Research Institute in Tampa, Florida, Dana Farber Cancer Institute in Boston, Massachusetts, Roswell Park Cancer Institute in Buffalo, New York, Duke University Medical Center in Durham, North Carolina, Ohio State University in Columbus, Ohio, and MD Anderson Cancer Center in Houston, Texas.

*The Leukemia & Lymphoma Society gratefully acknowledges Elihu H. Estey, MD, Member and Director of AML Clinical Research, Clinical Research Division, Fred Hutchinson Cancer Research Center, and Jane Liesveld, MD, Clinical Director, Blood and Marrow Transplant Program, University of Rochester Medical Center, for their reviews of this report.*

## References

Bueno C, Almeida J, Lucio P, et al. Incidence and characteristics of CD4(+)/HLA DRhi dendritic cell malignancies. *Haematologica*. 2004;89(1):58–69. Available at: [www.ncbi.nlm.nih.gov/pubmed/14754607](http://www.ncbi.nlm.nih.gov/pubmed/14754607).

Chang HJ, Lee MD, Yi HG, et al. A case of blastic plasmacytoid dendritic cell neoplasm initially mimicking cutaneous lupus erythematosus. *Cancer Res. Treat*. 2010;42(4):239–43. Available at: [www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3021744&tool=pmcentrez&rendertype=abstract](http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3021744&tool=pmcentrez&rendertype=abstract).

FitzGerald DJ. Targeted diphtheria toxin to treat BPDCN *Blood* 2014;124(3):310-2. Available at <http://www.ncbi.nlm.nih.gov/pubmed/25035145>

Frankel AE, Konopleva M, Hogge D, Al E. Activity and tolerability of SL-401, a targeted therapy directed to the interleukin-3 receptor on cancer stem cells and tumor bulk, as a single agent in patients with advanced hematologic malignancies. *Clin. Oncol*. 2013. Available at: [www.stemline.com/ScientificPresDownloads/SL-401\\_ASCO\\_2013\\_AML\\_abst.pdf](http://www.stemline.com/ScientificPresDownloads/SL-401_ASCO_2013_AML_abst.pdf).

Frankel AE, Woo JH, Ahn, C. et al. Activity of SL-401, a targeted therapy directed to interleukin-3 receptor, in blastic plasmacytoid dendritic cell neoplasm patients. *Blood* 2014;124(3):385-92. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24859366>.

Julia F, Petrella T, Beylot-Barry M, et al. Blastic plasmacytoid dendritic cell neoplasm: clinical features in 90 patients. *Br. J. Dermatol*. 2013;169(3):579–86. Available at: [www.ncbi.nlm.nih.gov/pubmed/23646868](http://www.ncbi.nlm.nih.gov/pubmed/23646868).

Kharfan-Dabaja MA, Lazarus HM, Nishihori T, Mahfouz RA, Hamadani M. Diagnostic and therapeutic advances in blastic plasmacytoid dendritic cell neoplasm: a focus on hematopoietic cell transplantation. *Biol. Blood Marrow Transplant*. 2013;19(7):1006–12. Available at: [www.ncbi.nlm.nih.gov/pubmed/23396213](http://www.ncbi.nlm.nih.gov/pubmed/23396213).

León-Martínez G, Meillón-García L, Morales-Polanco M, Soler-Montecinos L, Ortiz-Hidalgo C. Unusual Morphologic Presentations of Blastic Plasmacytoid Dendritic Cell Neoplasm: Report of Two Cases Misdiagnosed as Melanoma and Leprosy. *Int. J. Surg. Pathol*. 2013. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23515558>.

Lucioni M, Novara F, Fiandrino G, et al. Twenty-one cases of blastic plasmacytoid dendritic cell neoplasm: focus on biallelic locus 9p21.3 deletion. *Blood*. 2011;118(17):4591–4. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21900200>.

Male HJ, Davis MB, McGuirk JP, et al. Blastic plasmacytoid dendritic cell neoplasm should be treated with acute leukemia type induction chemotherapy and allogeneic stem cell transplantation in first remission. *Int. J. Hematol*. 2010;92(2):398–400. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20697854>.

Pagano L, Valentini CG, Pulsoni A, et al. Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation: an Italian multicenter study. *Haematologica*. 2013;98(2):239–46. Available at: [www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3561431&tool=pmcentrez&rendertype=abstract](http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3561431&tool=pmcentrez&rendertype=abstract).

Rauh MJ, Rahman F, Good D, et al. Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation, lacking cutaneous involvement: Case series and literature review. *Leuk. Res*. 2012;36(1):81–6. Available at: [www.ncbi.nlm.nih.gov/pubmed/21890199](http://www.ncbi.nlm.nih.gov/pubmed/21890199).

Roos-Weil D, Dietrich S, Boumendil A, et al. Stem cell transplantation can provide durable disease control in blastic plasmacytoid dendritic cell neoplasm: a retrospective study from the European Group for Blood and Marrow Transplantation. *Blood*. 2013;121(3):440–6. Available at: [www.ncbi.nlm.nih.gov/pubmed/23203822](http://www.ncbi.nlm.nih.gov/pubmed/23203822).

*This publication is designed to provide accurate and authoritative information regarding the subject matter covered. It is distributed as a public service by The Leukemia & Lymphoma Society (LLS) with the understanding that LLS is not engaged in rendering medical or other professional services.*