Data Supplement

Data Supplement to: Pivekimab Sunirine in Blastic Plasmacytoid Dendritic Cell Neoplasm

This Data Supplement has been provided by the authors to give readers additional information about the work.

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Methods

Table S1. Clinical Study Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
1. Disease characteristics: a. CD123 positivity by flow cytometry or immunohistochemistry performed in CLIA-certified laboratory. Patients who received prior CD123-targeting agents will be allowed as long as the blasts still have detectable CD123 expression. b. Dose Escalation: Relapsed or refractory AML (excluding acute promyelocytic leukemia) or BPDCN, based on World Health Organization classification. c. Dose Expansion: – Group 1 – Patients with relapsed or refractory BPDCN. – Group 2 – Patients will have relapsed AML. – Group 3 – Patients will have relapsed or refractory ALL (including any subtypes: B-cell, T-cell, Ph+, and Ph−). – Group 4 – Patients will have relapsed or refractory "other" hematologic malignancies not included in the cohorts above (e.g., high-risk/very high-risk MDS, MPN, CMML, BP-CML). Note: Blast-phase CML is defined as ≥30% blasts in blood, marrow, or both and the demonstration of extramedullary infiltrates of leukemic cells. – Group 5 – Patients will have relapsed or refractory (to non-intense therapies) CD123+ AML – Group 6 – Patients with frontline de novo BPDCN who have not received prior systemic therapy and patients with frontline BPDCN who have a PCHM and have not received prior systemic therapy Note: Patients in group 6 may have received local therapy (radiotherapy, surgical excision, photodynamic therapy). Eligible patients must have a recurrence or progression in the	1. Patients who, in the judgment of their treating physician, have appropriate standard-of-care therapies will be excluded from groups 1 through 5. 2. Frontline BPDCN patients with CNS disease will be excluded. A lumbar puncture must be performed during the 28-day screening period before drug administration. Relapsed or refractory BPDCN patients with a known history of CNS disease must have been treated locally, have at least one lumbar puncture with no evidence of CNS disease, and must be clinically stable before first dose. Concurrent therapy for CNS prophylaxis or continuation of therapy for controlled CNS disease is encouraged. 3. Patients with a history of veno-occlusive disease of the liver. 4. Patients with a history of grade 4 capillary leak syndrome, or non-cardiac grade 4 edema are ineligible, e.g., related to tagraxofusp-erzs or other etiology. 5. Corrected QT interval (QT interval corrected using Fridericia's formula) >480 msec. 6. Myocardial infarction within 6 months before enrollment or has New York Heart Association Class III or IV heart failure, uncontrolled angina, severe uncontrolled ventricular arrhythmias, or electrocardiographic evidence of acute ischemia or active conduction system abnormalities before study entry. 7. Interval from prior cancer therapy: a. For frontline BPDCN patients with prior local therapy (e.g., radiotherapy), patients must not have received treatment within 14 days before drug administration on this study. b. Relapsed or refractory BPDCN patients must not have received any anticancer therapy including chemotherapy, immunotherapy, radiotherapy, hormonal, biologic, or any

field of local therapy OR disease outside the field of local therapy. Patients identified as having concomitant malignancy whilon trial will continue to be identified as de novo BPDCN patients. 2. Patients in the BPDCN expansion phase group 1 may have received up to three prior lines of systemic therapy (regardless of tagraxofusp exposure). 3. Aged ≥18 years. 4. Eastern Cooperative Oncology Group performance status ≤1. If non-ambulatory due to a chronic disability, must be Karnofsky performance status >70. 5. Previous treatment-related toxicities must be resolved to grade 1 (excluding alopecia). 6. Liver enzymes (aspartate aminotransferase and alanine aminotransferase) ≤2.5 × ULN. Exceptions may be made for patients with elevated liver transaminases secondary to the underlying study disease. 7. Total bilirubin ≤1.5 × ULN; patients with Gilbert syndrome must have total bilirubin <3.0 × ULN with direct bilirubin <1.0 × ULN at the time of enrollment. 8. Estimated glomerular filtration rate of >30 mL/min/1.73 m^2 or creatinine clearance of >0 mL/min. 9. Left ventricular ejection fraction ≥45%. 10. Patients with a prior autologous or allogeneic bone marrow transplant are eligible for groups 1 to 5. Patients with an allogeneic transplant must meet the following conditions: The transplant must have been performed more than 120 days before the date of dosing on this study, the patient must not have active grade ≥2 acute GvHD, or extensive chronic GvHD of any severity, and must be off all immunosuppression for at least 2 weeks before first dose of pivekimab sunirine. 11. Patients or their legally authorized representative must voluntarily sign and date an informed consent, approved by an	investigational agents within 14 days before drug administration on this study. Patients must have recovered to baseline from all acute toxicity from this prior therapy. Note: Patients who have received a checkpoint inhibitor must not have received that therapy within 28 days before drug administration on this study. 8. Clinically relevant active infection including known active hepatitis B or C, human immunodeficiency virus infection, or cytomegalovirus or any other known concurrent infectious disease that, in the judgment of the Investigator, would make a patient inappropriate for enrollment into this study (testing not required). 9. Patients who have undergone major surgery within 4 weeks (or longer if not fully recovered) before study enrollment. 10. Serious or poorly controlled medical conditions that could be exacerbated by treatment or that would seriously compromise safety assessment or compliance with the protocol, in the judgment of the Investigator. 11. Patients who are pregnant or breastfeeding. 12. Patients who have a history of allergy to pivekimab sunirine or any of its excipients. 13. Patients who received a live vaccine 4 weeks or fewer prior to enrollment.

Independent Ethics Committee / Institutional Review Board, before performance of any study-related procedure not part of normal medical care. 12. Women of childbearing potential patients/partners, defined as a sexually mature woman who has not undergone surgical sterilization or who has not been naturally postmenopausal for at least 12 consecutive months (i.e., who has had menses any time in the preceding 12 consecutive months) must agree to use acceptable contraceptive methods while on study drug and for at least 7 months after the last dose of study drug. 13. Women of childbearing potential must have a negative pregnancy test before the first dose of study drug. 14. Male patients/partners who are able to father children must agree to use an effective method of contraception (e.g., condom), even if they have had a successful vasectomy, throughout the study and for at least 4 months after the last dose of pivekimab sunirine. 15. Patients with prior malignancy are eligible. Patients with a PCHM are eligible as long as no current therapy is required for the second malignancy (e.g., MDS, CMML). Patients with a nonhematologic prior malignancy must be in remission from the prior malignancy. Patients must have completed all chemotherapy and radiotherapy for prior malignancy at least 6 months before enrollment and all treatment-related toxicities must have resolved to Grade ≤1. Note: Patients with prostate cancer or breast cancer on adjuvant hormonal therapy are eligible. Note: Patients with tumors with a negligible risk for metastasis or death (e.g., adequately controlled basal cell carcinoma or squamous cell carcinoma of the skin, or carcinoma in situ of the cervix or breast) are eligible. 16. Patients must not be incarcerated and must be freely willing and able to provide informed consent. Examples of patients unable to freely provide informed consent may include some adults	

under legal protection measure (e.g., under guardianship/curatorship) or unable to express their consent and select adults under psychiatric care. Investigator's discretion should be applied.	

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BP-CML, blast phase of chronic myeloid leukemia; BPDCN, blastic plasmacytoid dendritic cell neoplasm; CLIA, Clinical Laboratory Improvement Amendments; CMML, chronic myelomonocytic leukemia; CNS, central nervous system; GvHD, graft-versus-host disease; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasms; PCHM, prior or concomitant hematologic malignancy.

Table S2. Response Criteria for Blastic Plasmacytoid Dendritic Cell Neoplasm

Response	Location	Criteria
CR	Marrow	Normalization of blast percentage (≤5%)
	Peripheral blood	Normalization of neutrophil count (≥1000/μL) and platelet count (≥100,000/μL) Absence of leukemic blasts
	Skin	100% clearance of all skin lesions from baseline; no new lesions in patients without lesions at baseline
	Nodal masses	Regression to normal size on computed tomography/positron emission tomography
	Spleen, liver	Not palpable, nodules disappeared
CR with CRc	Marrow	Normalization of blast percentage (≤5%)
	Peripheral blood	Normalization of neutrophil count (≥1000/μL) and platelet count (≥100,000/μL) Absence of leukemic blasts
	Skin	Marked clearance of all skin lesions from baseline; residual hyperpigmentation or abnormality with BPDCN identified on biopsy (or no biopsy performed)
	Nodal masses	Regression to normal size on computed tomography/positron emission tomography
	Spleen, liver	Not palpable, nodules disappeared
CR with CRh	Marrow	Normalization of blast percentage (≤5%)
	Peripheral blood	Normalization of neutrophil count (≥500/μL) AND platelet count (≥50,000/μL) Absence of leukemic blasts
	Skin	Marked clearance of all skin lesions from baseline; residual hyperpigmentation or abnormality with BPDCN identified on biopsy (or no biopsy performed)
	Nodal masses	Regression to normal size on computed tomography/positron emission tomography
	Spleen, liver	Not palpable, nodules disappeared
CR with CRi	Marrow	Normalization of blast percentage (≤5%)
	Peripheral blood	Normalization of neutrophil count (≥1000/μL) OR platelet count (≥100,000/μL) Absence of leukemic blasts
	Skin	Marked clearance of all skin lesions from baseline; residual hyperpigmentation or abnormality with BPDCN identified on biopsy (or no biopsy performed)
	Nodal masses	Regression to normal size on computed tomography/positron emission tomography
	Spleen, liver	Not palpable, nodules disappeared
PR	Marrow	Decreased by >50% in blast percentage to 5–25%
	Skin	50% to <100% clearance of all skin lesions from baseline; no new lesions in patients without lesions at baseline
	Nodal masses	≥50% decrease in the SPD of up to six largest dominant masses; no increase in size of other nodes

	Spleen, liver	≥50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen
SD		Failure to achieve at least a PR, but no evidence of progression for at least 8 weeks
Relapse after CR/CRi/CRc	Marrow	Blast percentage >5% (if no peripheral blasts, then confirmation aspirate required ≥1 week later)
	Peripheral blood	Presence of leukemic blasts
	Skin	Increase in skin score greater than the sum of nadir plus 50% baseline score
	Nodal masses	Appearance of a new lesion(s) >1.5 cm in any axis, ≥50% increase from nadir in SPD of more than 1 node, or ≥50% increase from nadir in longest diameter of a previously identified node >1 cm in short axis
	Spleen, liver	>50% increase from nadir in the SPD of any previous lesions
PD	Marrow	Any new lymph nodes or new skin lesions OR increase from nadir by >50% of SPD of any single previously involved lymph node or total assessed lymph node masses OR >50% increase in bone marrow blast percentage
	Nodal masses	
	Skin	

Hematologic parameters (i.e., neutrophil and platelet counts) could be assessed up to 14 days following bone marrow assessment to make formal response criteria assessment. Repeat computed tomography/positron emission tomography scans were to be performed on patients with nodal/visceral disease at baseline, or as indicated clinically.

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; CR, complete response; CRc, complete response with minimal residual skin abnormality; CRh, complete response with partial hematologic recovery; CRi, complete response with incomplete recovery; PD, progressive disease; PR, partial response; SD, stable disease; SPD, sum of the product of the diameters.

Table S3. Study Endpoints

Endpoints	Description
Pre-specified	
Primary	• Rate of composite complete response (CR + CRc) in frontline de novo BPDCN
Key secondary	• Duration of composite complete response in frontline de novo BPDCN
Other secondary	• Rate of composite complete response in all patients with frontline BPDCN and relapsed/refractory BPDCN, separately • Duration of composite complete response in all patients with frontline BPDCN and relapsed/refractory BPDCN, separately • Rate and duration of CR + CRc + CRh • Rate and duration of overall response (CR + CRc + CRh + CRi + PR) • Time to composite complete response • Time to CR + CRc + CRh • Time to overall response • Rate of overall survival • Percentage of patients able to bridge to SCT in patients with frontline BPDCN and relapsed/refractory BPDCN, separately • Duration of composite complete response by SCT in all patients with frontline BPDCN and relapsed/refractory BPDCN • Pharmacokinetic profile, total antibody, and active catabolite[a] • Immunogenicity via antidrug antibodies[a] • Transfusion independence conversion rate[a] • Frequency and severity of adverse events, including by prior tagraxofusp
Subgroup efficacy analyses for primary endpoint	• Post-treatment SCT for frontline and relapsed/refractory BPDCN, separately • Prior tagraxofusp treatment for relapsed/refractory BPDCN • Age group (18 to <65, 65 to <75, ≥65, ≥75 years) • Baseline renal status (normal, mild impairment, moderate impairment, severe impairment) • Baseline hepatic status (normal, mild impairment, moderate impairment, severe impairment) • Race and ethnicity
Post-hoc	
Exploratory	• Individual treatment response for individual efficacy components • Overall survival by post-treatment SCT status in patients with frontline BPDCN and relapsed/refractory BPDCN separately • Overall survival presented by PCHM in the frontline group

	• Subgroup analysis of secondary endpoints (e.g., overall response)
	• CD123 expression

[a]Outcomes not reported in this analysis.

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; CR, complete response; CRc, complete response with minimal residual skin abnormality; CRh, complete response with partial hematologic recovery; CRi, complete response with incomplete recovery; PCHM, prior or concomitant hematologic malignancy; PR, partial response; SCT, stem cell transplant.

Results

Table S4. Representativeness of the BPDCN Study Population

Category	Description
Special considerations related to:	
Age	BPDCN is more common in patients aged <20 years (33%) or ≥60 years (34%);[1] median age at diagnosis is mid 60s[2]
Sex	*(The overall incidence of BPDCN is 0.05 cases per 100,000 population)*[1] BPDCN affects men more than women (3:1)[3]
Race or ethnic group	BPDCN affects more White patients compared to Black patients (incidence rate ratio of 0.70)[1]
Geography	BPDCN affects people of all geographic regions[4]
Baseline disease involvement	Skin, bone marrow, and lymph nodes are the most common primary sites of disease involvement, present in approximately 90%, 60–90%, and 40–50%, respectively, in patients with BPDCN[5]
Other considerations	No definitive environmental, inherited, or acquired genetic factors have been identified as BPDCN risk factors;[2] however, research has implied that certain factors (e.g., cytogenetic abnormalities, ultraviolet radiation exposure) may be involved[6,7]
Overall representativeness of this trial	The baseline demographics and clinical characteristics of patients with BPDCN in this trial are consistent with what has been previously reported in published literature, described above. Median age of all patients with BPDCN was 72 years and majority were ≥65 years of age (71%). Majority of patients were male (82%) and White (82%). The most common sites of disease involvement were skin (77%), bone marrow (48%), and lymph nodes (36%). Previously, it has been reported that BPDCN does not appear to have any geographic predisposition;[4] however, this trial found that BPDCN was more prevalent in the United States than in Europe (61% vs 39%).

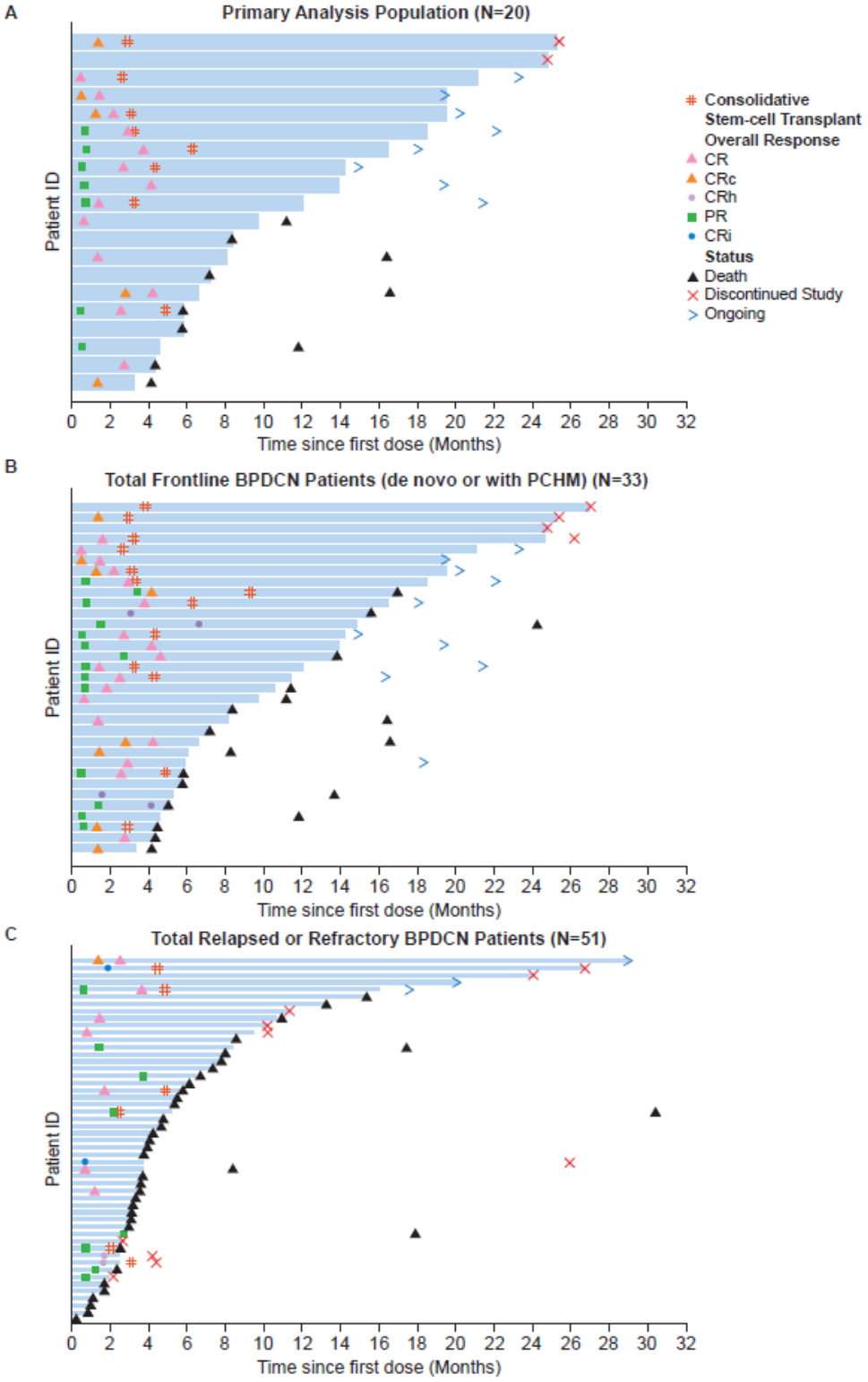
Abbreviation: BPDCN, blastic plasmacytoid dendritic-cell neoplasm.

Summary of Pivekimab Sunirine in Patients with Acute Myeloid Leukemia (AML)[8]:

Briefly, in the phase 1/2 study of pivekimab sunirine in relapsed or refractory AML, 6 doses of pivekimab sunirine every 3 weeks (Q3W) (0.015 mg/kg, 0.450 mg/kg, 0.090 mg/kg, 0.180 mg/kg, 0.300 mg/kg, 0.450 mg/kg) were included in the dose escalation phase of schedule A, which was expanded to include 2 cohorts at 0.045 mg/kg and 0.090 mg/kg Q3W. A fractionated schedule was also evaluated but was not pursued due to comparative safety and antileukemia findings with schedule A.

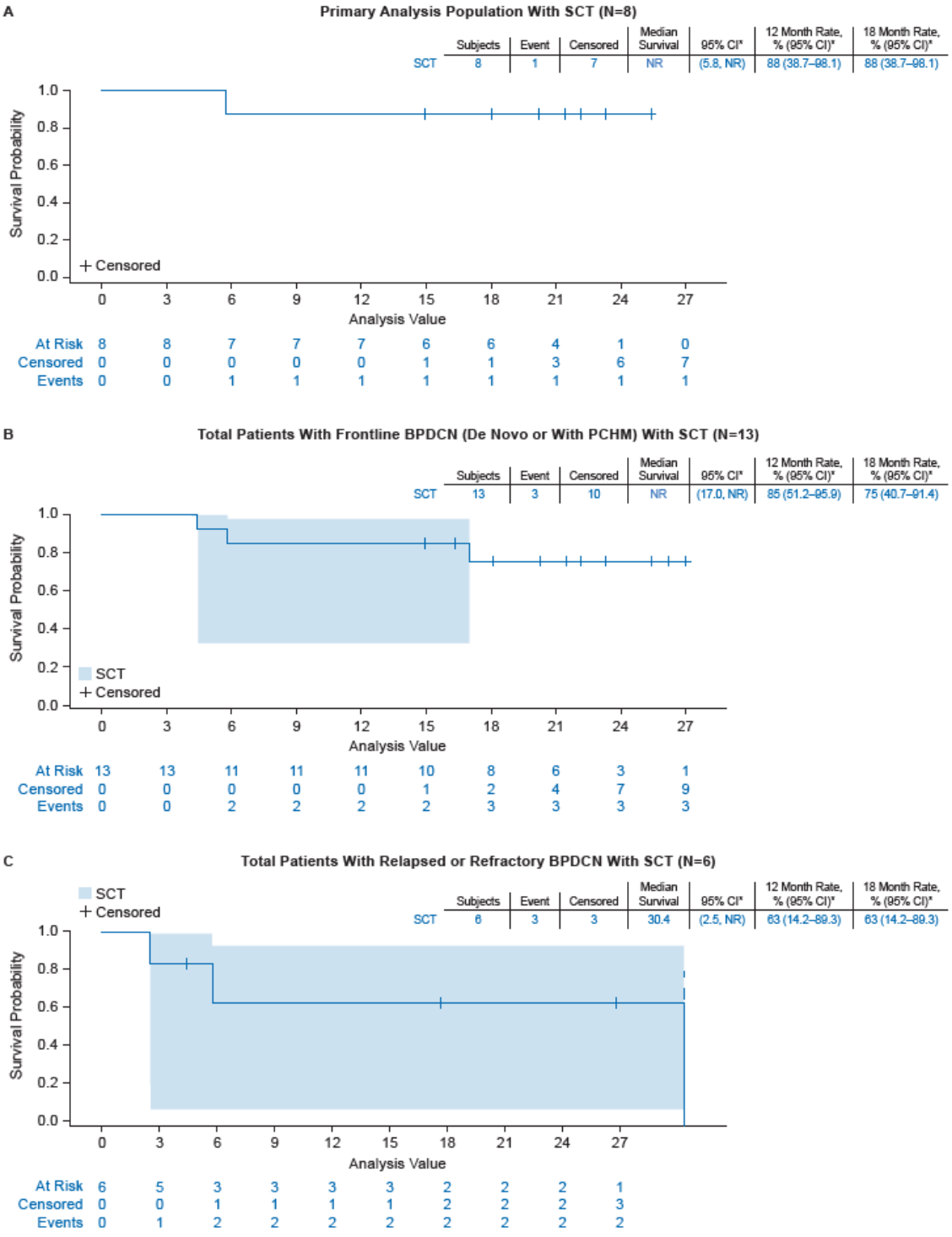
Across the 68 patients included in both dose escalation and expansion phases of schedule A, three dose-limiting toxicities were observed at doses 0.180, 0.300, and 0.450 mg/kg each, although no dose-limiting toxicity-based maximum tolerated dose was reached. Reversible VOD disease occurred in 2 participants at 0.180 mg/kg and 0.450 mg/kg, and prolonged neutropenia occurred in 1 participant at 0.300 mg/kg. The 0.090 mg/kg did not show antileukemia advantage compared with 0.045 mg/kg which led to 0.045 mg/kg Q3W being chosen as a recommended phase 2 dose. At the recommended phase 2 dose (n=29), the most common grade ≥3 treatment-related AEs were febrile neutropenia (10%), infusion related reactions, and anemia at 7% each. The overall response rate was 21% and the composite complete response rate was 17%.

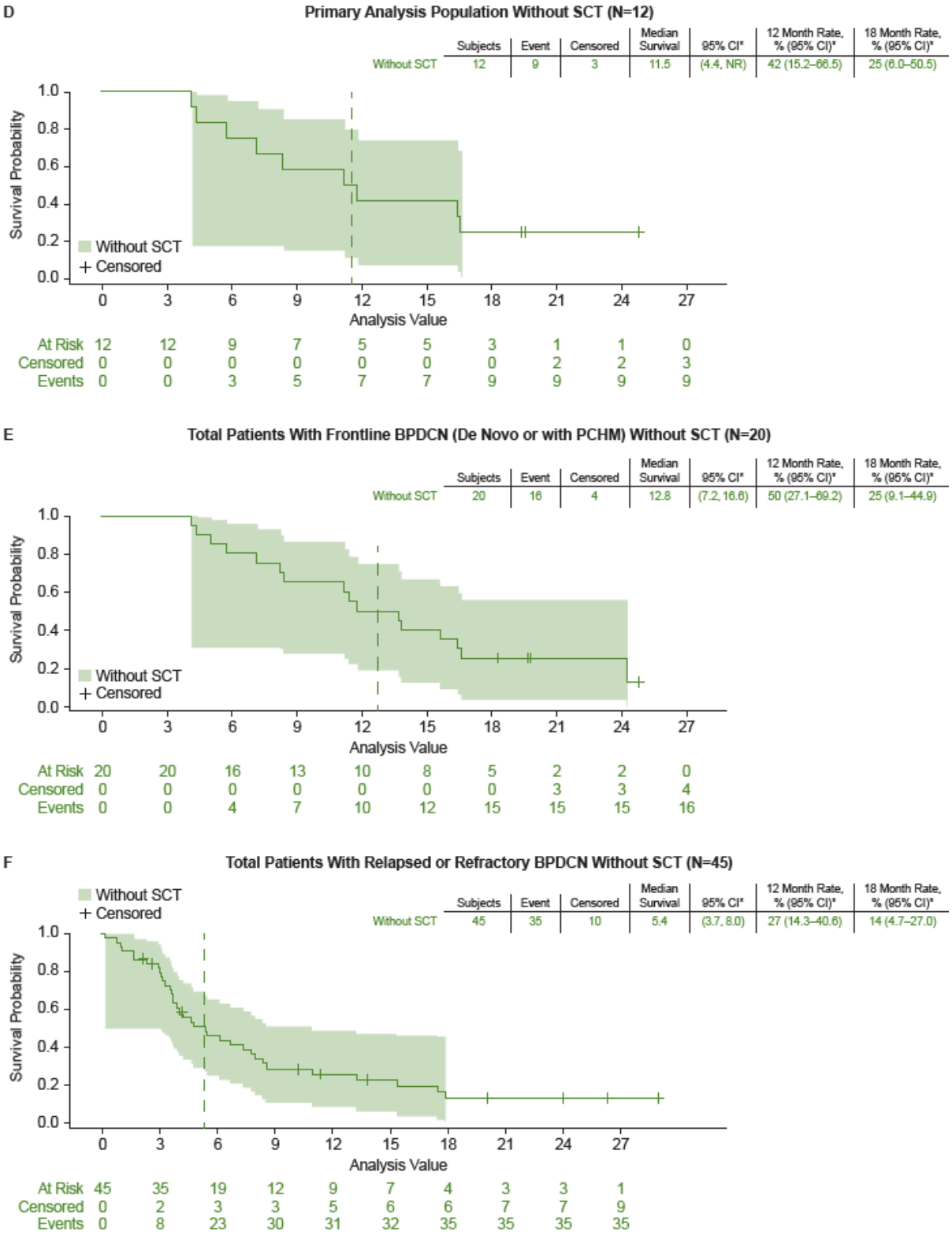
FIG S1. Individual treatment response for additional post hoc analysis of efficacy components in the primary analysis population (A), overall frontline group (B), and relapsed or refractory group (C).



Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; CR, complete response; CRc, clinical complete response; CRh, clinical response with partial hematologic recovery; CRi, clinical response with incomplete recovery; PCHM, prior or concomitant hematologic malignancy; PR, partial response.

FIG S2. Kaplan–Meier estimate in months for additional post hoc, exploratory analysis of overall survival in patients who received stem cell transplant for all patients in the primary analysis population (A), overall frontline group (B), and relapsed or refractory group (C) or among those who did not receive stem cell transplant for all patients in the primary (D), overall frontline (E) and relapsed or refractory (F) groups



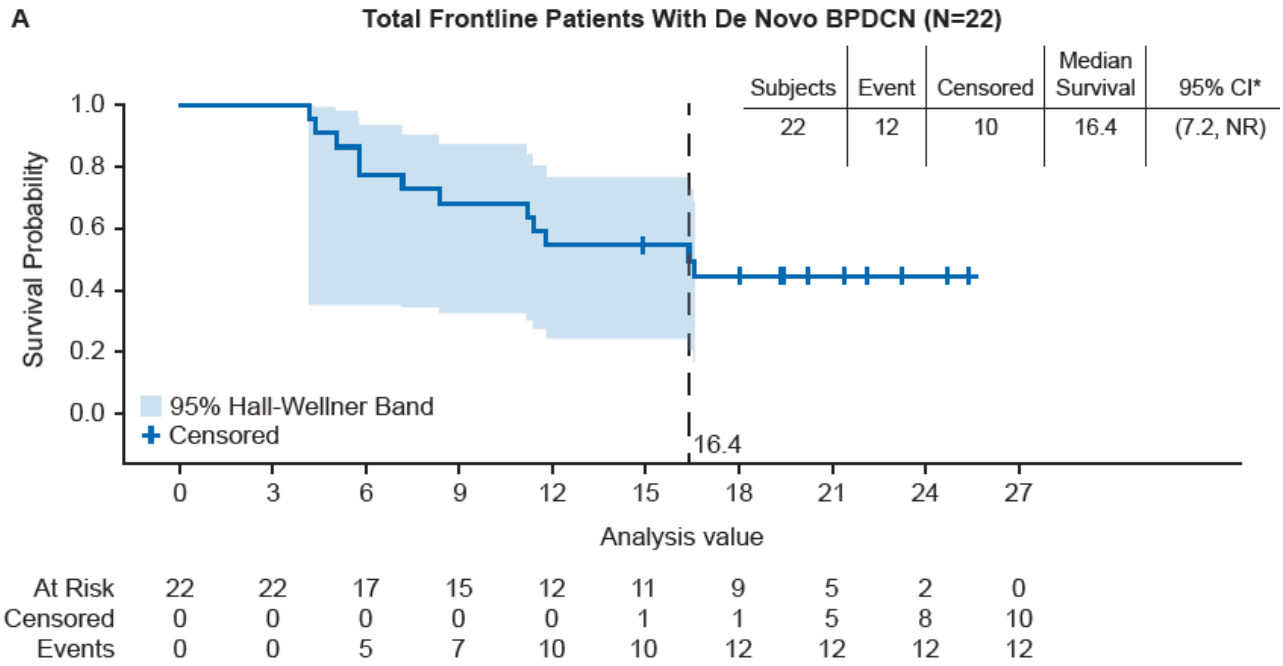


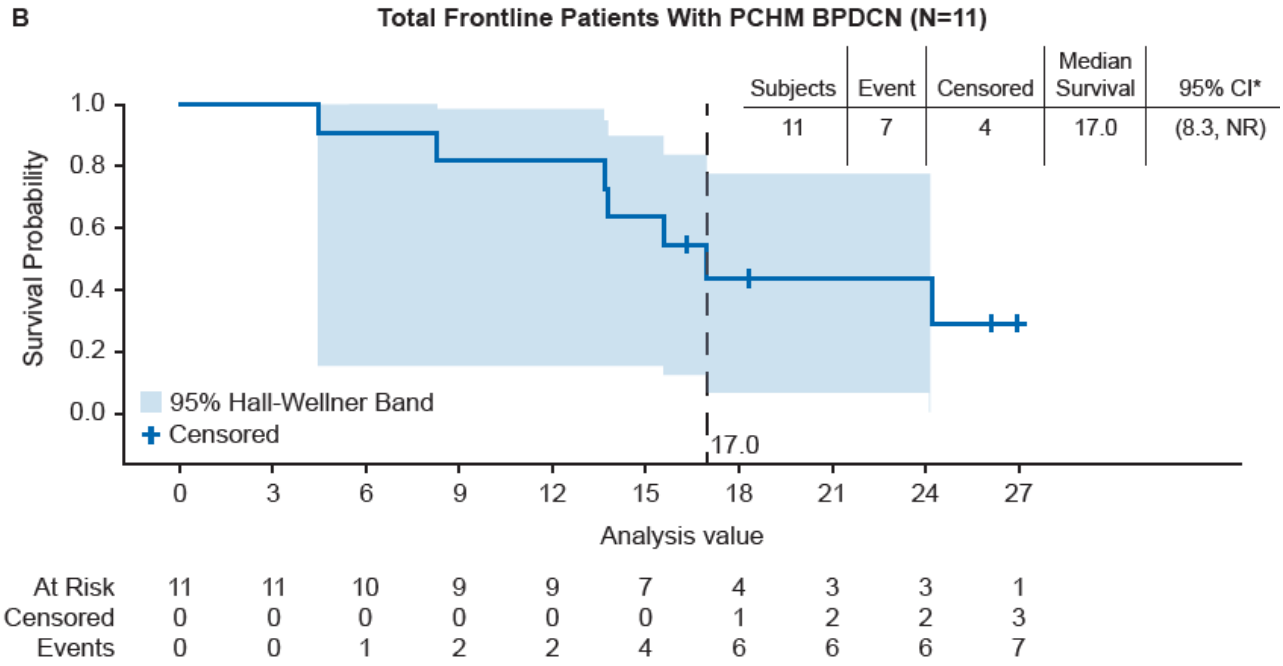
*The 2-sided CIs do not have multiplicity adjustment and should not be used for hypothesis testing.

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; CI, confidence interval; NR, not reached; PCHM,

prior or concomitant hematologic malignancy; SCT, stem-cell transplant.

FIG S3. Kaplan–Meier estimate for additional post hoc analysis of overall survival by presence of prior or concomitant hematologic malignancy





*The 2-sided CIs do not have multiplicity adjustment and should not be used for hypothesis testing.

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; CI, confidence interval; PCHM, prior or concomitant hematologic malignancy.

Table S5. Prespecified Subgroup Analysis of the Primary Endpoint, Composite Complete Response, and Secondary Endpoints in Patients With Relapsed or Refractory BPDCN With Prior Tagraxofusp Exposure and Exploratory Post Hoc Analysis by SCT Status

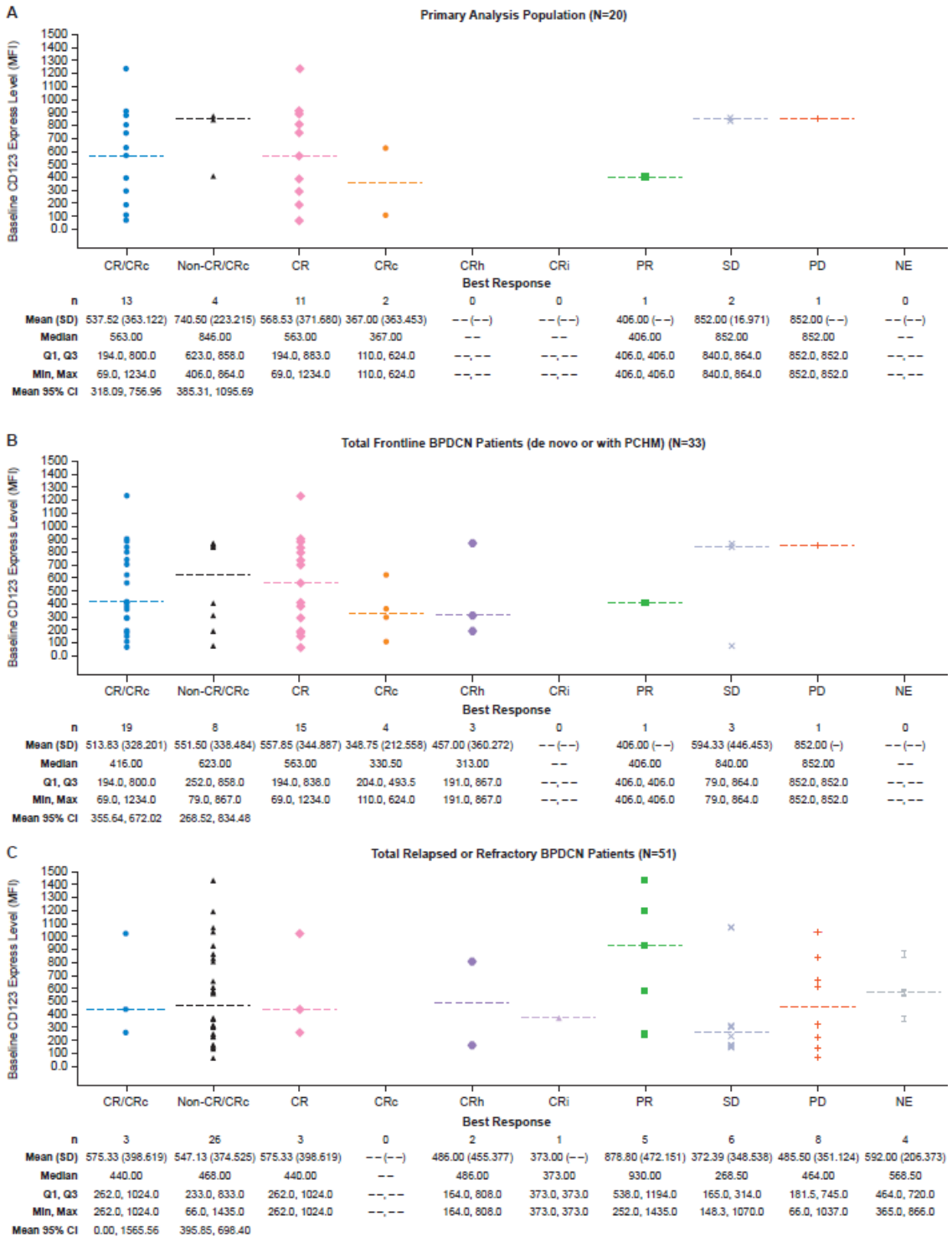
Endpoint	With Prior Tagraxofusp Exposure[a] (n=29)	Without Prior Tagraxofusp Exposure (n=22)	With Prior SCT (n=16)	Without Prior SCT (n=35)
Best overall response rate				
CCR (CR + CRc), n (%; 95% CI[b])	4 (14; 4–32)	3 (14; 3–35)	3 (19; 4–46)	4 (11; 3–27)
ORR (CR + CRc + CRh + CRi + PR), n (%; 95% CI[b])	10 (35; 18–54)	8 (36; 17–59)	8 (50; 25–75)	10 (29, 15–46)
Duration of response, months				
CCR (CR + CRc), median (95% CI[b])	9.2 (4.1 not reached)	3.1 (2.4-not reached)	9.2 (4.1–not reached)	Not reached (2.4–not reached)
ORR (CR + CRc + CRh + CRi + PR), median (95% CI[b])	4.1 (0.8–not reached)	6.9 (2.4–not reached)	6.9 (0.8–not reached)	2.7 (0.9–not reached)
Overall survival				
Months, median (95% CI[b])	7.4 (4.2– 13.2)	3.9 (3.1– 8.0)	10.9 (4.2– not reached)	4.8 (3.3– 8.0)
Rate at 12 months, % (95% CI[b])	35 (17.8–53.5)	24 (8.8–43.5)	43 (17.1–66.5)	25 (11.9–40.6)
Rate at 18 months, % (95% CI[b])	16 (3.6–36.9)	19 (6.0–38.2)	32 (9.2–58.2)	13 (4.0–28.5)

[a]The median time (interquartile range) from prior tagraxofusp exposure to the first dose of pivekimab sunirine was 3.1 (1.2–8.5) months.

[b]The 2-sided CIs do not have multiplicity adjustment and should not be used for hypothesis testing.

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; CCR, composite complete response; CI, confidence interval; CR, complete remission; CRc, clinical complete remission; CRh, complete remission with partial hematologic recovery; CRi, complete remission with incomplete recovery; ORR, overall response rate; PR, partial response; SCT, stem-cell transplant.

FIG S4. Exploratory analysis of CD123+ expression by response for the primary analysis population (A), overall frontline group (B), and relapsed or refractory group (C)



A) Primary analysis population: In 3 of the 20 patients, no CD123 data were available from central testing lab due no distinct pDC population

B) Frontline patients with BPDCN: In 4 of the 33 patients, no CD123 data were available from central testing lab due no distinct pDC population. In 1 of the 33 patients, no CD123 data were available from central testing lab due to missing CD303 biomarker data

C) Relapsed or refractory patients: In 4 of the 51 patients, no CD123 data were available from central testing lab due no distinct pDC population. In 15 of the 51 patients, no CD123 data were available from central testing lab due to missing CD303 biomarker data. In 3 of the 51 patients, samples were not tested at central lab.

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; CI, confidence interval; CR, complete response; CRc, clinical complete response; CRh, clinical response with partial hematologic recovery; CRi, clinical response with incomplete recovery; MFI, median fluorescence intensity; NE, not evaluable; PCHM, prior or concomitant hematologic malignancy; PD, progressive disease; pDC, plasmacytoid dendritic cells; PR, partial response; Q, quartile; SD, stable disease.

Table S6. Prespecified Subgroup Analysis for the Primary Endpoint, Composite Complete Response Rate, and Additional Post Hoc Analysis of the Secondary Endpoint of Overall Response Rate

	Frontline De Novo BPDCN[a]		**Frontline (De Novo and PCHM) BPDCN**		**Relapsed or Refractory BPDCN**	
	CCR (CR + CRc), n/N (%; 95% CI[b])	**ORR (CR + CRc + CRh + CRi + PR) n/N (%, 95% CI[b])**	**CCR (CR + CRc), n/N (%; 95% CI[b])**	**ORR (CR + CRc + CRh + CRi + PR), n/N (%, 95% CI[b])**	**CCR (CR + CRc), n/N (%; 95% CI[b])**	**ORR (CR + CRc + CRh + CRi + PR) n/N (%, 95% CI[b])**
All patients	15/20 (75; 51–91)	16/20 (80; 56–94)	23/33 (70; 51–84)	28/33 (85; 68–95)	7/51 (14; 6–26)	18/51 (35; 22–50)
Subgroups						
Age, years						
18 to <65	2/3 (67; 9–99)	2/3 (67; 9–99)	2/3 (67; 9–99)	2/3 (67; 9–99)	3/21 (14; 3–36)	9/21 (43; 22–66)
65 to <75	7/10 (70; 35–93)	8/10 (80; 44–98)	12/17 (71; 44–90)	15/17 (88; 64–99)	3/16 (19; 4–46)	7/16 (44; 20–70)
≥65	13/17 (77; 50–93)	14/17 (82; 57–96)	21/30 (70; 51–85)	26/30 (87; 69–96)	4/30 (13; 4–31)	9/30 (30; 15–49)
≥75	6/7 (86; 42–100)	6/7 (86; 42–100)	9/13 (69; 39–91)	11/13 (85; 55–98)	1/14 (7; 0–34)	2/14 (14; 2–43)
Race						
White	12/15 (80; 52–96)	13/15 (87; 60–98)	19/27 (70; 50–86)	24/27 (89; 71–98)	5/42 (12; 4–26)	16/42 (38; 24–54)
Black or African American	1/1 (100; NE)	1/1 (100; NE)	1/1 (100; NE)	1/1 (100; NE)	0/2 (0; 0–84)	0/2 (0; 0–84)
Not reported	2/4 (50; 7–93)	2/4 (50; 7–93)	3/5 (60; 15–95)	3/5 (60; 15–95)	2/6 (33; 4–78)	2/6 (33; 4–78)
Asian	NE	NE	NE	NE	0/1 (0; NE)	0/1 (0; NE)
Native American or Alaskan Native	NR	NR	NR	NR	NR	NR
Native Hawaiian/other Pacific Islander	NR	NR	NR	NR	NR	NR
Other	NR	NR	NR	NR	NR	NR

Ethnicity						
Hispanic or Latino	3/3 (100; 29–100)	3/3 (100; 29–100)	3/4 (75; 19–99)	3/4 (75; 19–99)	2/8 (25; 3–65)	6/8 (75; 35–97)
Not Hispanic or Latino	12/17 (71; 44–90)	13/17 (77; 50–93)	19/28 (68; 48–84)	24/28 (86; 67–96)	4/38 (11; 3–25)	10/38 (26; 13–43)
Unknown	NE	NE	1/1 (100; NE)	1/1 (100; NE)	1/5 (20; 1–72)	2/5 (40; 5–85)
Baseline renal function[c]						
Normal	6/8 (75; 35–97)	6/8 (75; 35–97)	10/13 (77; 46–95)	11/13 (85; 55–98)	5/26 (19; 7–39)	15/26 (58; 37–77)
Mild impairment	9/12 (75; 43–95)	10/12 (83; 52–98)	11/18 (61; 36–83)	15/18 (83; 59–96)	2/20 (10; 1–32)	3/20 (15; 3–38)
Moderate impairment	NE	NE	2/2 (100; 16–100)	2/2 (100; 16–100)	0/5 (0; 0–52)	0/5 (0; 0–52)
Severe impairment	NR	NR	NR	NR	NR	NR
Baseline hepatic function[d]						
Normal	11/16 (69; 41–89)	12/16 (75; 48–93)	18/27 (67; 46–84)	22/27 (82; 62–94)	6/43 (14; 5–28)	13/43 (30; 17–46)
Mild impairment	3/3 (100; 29–100)	3/3 (100; 29–100)	4/4 (100; 40–100)	4/4 (100; 40–100)	1/6 (17; 0–64)	5/6 (83; 36–100)
Moderate impairment	1/1 (100; NE)	1/1 (100; NE)	1/2 (50; 1–99)	2/2 (100; 16–100)	0/2 (0; 0–84)	0/2 (0; 0–84)
Severe impairment	NR	NR	NR	NR	NR	NR
Post-treatment HSCT status						
With HSCT	8/8 (100; 63–100)	8/8 (100; 63–100)	12/13 (92; 64–100)	12/13 (92; 64–100)	2/6 (33; 4–78)	6/6 (100; 54–100)
Without HSCT	7/12 (58; 28–85)	8/12 (67; 35–90)	11/20 (55; 32–77)	16/20 (80; 56–94)	5/45 (11; 4–24)	12/45 (27; 15–42)

[a]Primary analysis population.

[b]95% CI were calculated using the Clopper–Pearson method. The 2-sided CIs do not have multiplicity adjustment and should not be used for hypothesis testing.

[c]Baseline renal function: (normal: creatinine clearance ≥90 mL/min; mild impairment: 60 to <90 mL/min; moderate impairment: 30 to <60 mL/min; severe impairment: <30 mL/min).

[d]Baseline hepatic function: (normal: bilirubin ≤ ULN and aspartate transferase ≤ ULN; mild impairment: bilirubin ≤ ULN and aspartate transferase >ULN or ULN < bilirubin ≤1.5-fold ULN; moderate impairment: 1.5-fold ULN < bilirubin ≤3-fold ULN; severe impairment: bilirubin >3-fold ULN).

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; CCR, composite complete response; CI, confidence interval; CR, complete remission; CRc, clinical complete remission; CRh, complete remission with partial progressive disease; CRi, complete remission with incomplete recovery; HSCT, hematopoietic stem-cell transplant; NE, not estimated; NR, not reported; ORR, overall response rate; PCHM, prior or concomitant hematologic malignancy; PR, partial response; ULN, upper limit of normal.

Table S7. Adverse Events[a] Leading to Dose Delay, Reductions, or Discontinuation in Any BPDCN Group

Adverse Event, Number of Events (%)	Frontline De Novo BPDCN (n=20)	All Frontline BPDCN (n=33)	Relapsed or Refractory BPDCN (n=51)	Total (N=84)
Any events leading to dose delay	7 (35)	14 (42)	7 (14)	21 (25)
Peripheral edema	1 (5)	3 (9)	1 (2)	4 (5)
Blood bilirubin increase	1 (5)	1 (3)	0	1 (1)
COVID-19	1 (5)	1 (3)	0	1 (1)
Cardiac failure	0	1 (3)	0	1 (1)
Catheter site hemorrhage	0	1 (3)	0	1 (1)
Coagulopathy	0	0	1 (2)	1 (1)
Cough	1 (5)	1 (3)	0	1 (1)
Dehydration	0	1 (3)	0	1 (1)
Dizziness	1 (5)	1 (3)	0	1 (1)
Dyspnea	1 (5)	1 (3)	0	1 (1)
Erysipelas	0	1 (3)	0	1 (1)
Fall	0	1 (3)	0	1 (1)
Fatigue	1 (5)	1 (3)	0	1 (1)
Gamma-glutamyl transferase increase	1 (5)	1 (3)	0	1 (1)
Gastric hemorrhage	0	0	1 (2)	1 (1)
Gastrointestinal hemorrhage	0	0	1 (2)	1 (1)
Generalized edema	0	1 (3)	0	1 (1)
Hypokalemia	0	1 (3)	0	1 (1)
Impaired healing	0	1 (3)	0	1 (1)
Large intestine perforation	0	0	1 (2)	1 (1)
Mobility decreased	1 (5)	1 (3)	0	1 (1)
Muscular weakness	1 (5)	1 (3)	0	1 (1)
Neutrophil count decrease	0	0	1 (2)	1 (1)
Pancytopenia	0	0	1 (2)	1 (1)
Pneumocystis jirovecii pneumonia	1 (5)	1 (3)	0	1 (1)
Pneumonia	1 (5)	1 (3)	1 (2)	2 (2)
Pneumonitis	1 (5)	1 (3)	1 (2)	2 (2)
Pulmonary embolism	0	1 (3)	0	1 (1)

Pyrexia	0	1 (3)	1 (2)	2 (2)
Upper respiratory tract infection	0	1 (3)	0	1 (1)
Any events leading to dose reduction	2 (10)	3 (9)	1 (2)	4 (5)
Peripheral edema	1 (5)	2 (6)	0	2 (2)
Generalized edema	1 (5)	1 (3)	0	1 (1)
Alanine aminotransferase increase	0	0	1 (2)	1 (1)
Any events leading to dose discontinuation	3 (15)	6 (18)	5 (10)	11 (13)
Pneumonitis	2 (10)	2 (6)	0	2 (2)
Veno-occlusive disease	0	2 (6)	0	2 (2)
Alanine aminotransferase increase	1 (5)	1 (3)	0	1 (1)
Aspartate aminotransferase increase	1 (5)	1 (3)	0	1 (1)
Blood lactic acid level increase	0	0	1 (2)	1 (1)
Clostridium difficile infection	0	0	1 (2)	1 (1)
Dysarthria	0	0	1 (2)	1 (1)
Facial nerve disorder	0	0	1 (2)	1 (1)
Failure to thrive	0	1 (3)	0	1 (1)
Graft versus host disease	0	0	1 (2)	1 (1)
IIIrd nerve disorder	0	0	1 (2)	1 (1)
Left ventricular failure	0	0	1 (2)	1 (1)
Peripheral edema	0	1 (3)	0	1 (1)

[a]Events include preferred terms defined with the use of the *Medical Dictionary of Regulatory Activities*, version 27.1. Adverse event severity is assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03b.

One person could experience more than one event leading to dose delay, reduction, or discontinuation.

Abbreviation: BPDCN, blastic plasmacytoid dendritic cell neoplasm.

Table S8. Adverse Events by Grade ≥3 Severity[a] Occurring in ≥10% Patients in Any BPDCN Group

Grade ≥3 Adverse Event, n (%)	Frontline De Novo Patients With BPDCN (n=20)	Frontline (De Novo and PCHM) Patients With BPDCN (n=33)	Patients with Relapsed or Refractory BPDCN (n=51)	All Patients With BPDCN (N=84)
Any grade ≥3 adverse event	16 (80)	28 (85)	38 (75)	66 (79)
Peripheral edema	2 (10)	8 (24)	2 (4)	10 (12)
Decreased platelet count	1 (5)	5 (15)	3 (6)	8 (10)
Hypophosphatemia	3 (15)	4 (12)	0	4 (5)
Pneumonitis	2 (10)	2 (6)	0	2 (2)
Generalized edema	2 (10)	3 (9)	0	3 (4)
Neutropenia	0	5 (15)	8 (16)	13 (16)
Pneumonia[b]	2 (10)	2 (6)	4 (8)	6 (7)
Leukopenia / white blood cell count decreased	0	4 (12)	8 (16)	12 (14)
Lymphocyte count decreased	2 (10)	3 (9)	2 (4)	5 (6)
Headache	2 (10)	2 (6)	1 (2)	3 (4)
Hypoxia	2 (10)	2 (6)	0	2 (2)
Thrombocytopenia	0	3 (9)	9 (18)	12 (14)
COVID-19	2 (10)	2 (6)	1 (2)	3 (4)
Hypertension	2 (10)	2 (6)	1 (2)	3 (4)
Hypotension	2 (10)	2 (6)	0	2 (2)

[a]Events include preferred terms defined with the use of the *Medical Dictionary of Regulatory Activities*, version 27.1. Adverse event severity is assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03b.

[b]Study conducted during COVID-19 pandemic.

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; PCHM, prior or concomitant hematologic malignancy.

Table S9. Overview of Veno-occlusive Disease (Sinusoidal Obstruction Syndrome) in Patients With On-treatment Events (A) and Post Treatment Stem-Cell Transplant Events (B)

A.

Case	BPDCN Group	Severity	Outcome	Median Time to Event Onset[b]	Median Time to Event Resolution[c]
1	Frontline (de novo)	Grade 3	Study drug discontinuation; recovered/resolved with sequalae[a]	92 days	15 days
2	Frontline (PCHM)	Grade 2	Study drug discontinuation; recovered/resolved	170 days	27 days

B.

Case[d]	BPDCN Group	Severity	Outcome (Additional Factors)	Days From Last Treatment Dose to SCT (cycles received)	Days From SCT Start Date to Post-SCT VOD
1	Frontline	Unknown	Fatal (busulfan-based conditioning; other conditioning)	45 days (3 cycles)	25 days
2	Relapsed/ refractory	Grade 4	Unknown (melphalan-based conditioning)	20 days (3 cycles)	7 days
3	Relapsed/ refractory	Grade 5	Fatal (busulfan-based conditioning)	63 days (5 cycles)	11 days
4	Relapsed/ refractory	Unknown	Continuing at time of analysis (other conditioning)	44 days (3 cycles)	9 days
5	Relapsed/ refractory	Grade 4	Recovered/resolved (other conditioning)	57 days (4 cycles)	22 days

[a]Sequalae not specified.

[b]Time to onset is calculated as date of first event onset – date of first dose of study drug for patients with at least one event.

[c]Time to resolution calculated as event end date − event onset date +1 if the event resolved and a complete end date was recorded.

[d]Includes cases of veno-occlusive disease occurring after post-treatment stem-cell transplant in the Adverse Event Form and veno-occlusive disease or sinusoidal obstruction syndrome diagnosed within the first 60 days after most recent stem-cell transplant collected in the post stem-cell transplant report.

Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; PCHM, prior or concomitant hematologic malignancy; SCT, stem-cell transplant; VOD, veno-occlusive disease.

Table S10. Pre-specified Subgroup Analysis of Adverse Events in Patients With Relapsed or Refractory BPDCN by Prior Tagraxofusp Exposure

Adverse Event,[a] n (%)	Relapsed or Refractory BPDCN (n=51)	Relapsed or Refractory BPDCN	
		With Prior Tagraxofusp Exposure[b] (n=29)	Without Prior Tagraxofusp Exposure (n=22)
Any adverse event	50 (98)	28 (97)	22 (100)
Drug-related adverse event[c]	32 (63)	19 (66)	13 (59)
Any Grade ≥3 adverse event[d]	38 (75)	19 (66)	19 (86)
Drug-related adverse event[c]	16 (31)	12 (41)	4 (18)
Any serious adverse event	20 (39)	13 (45)	7 (32)
Any adverse event leading to:			
Dose delay	7 (14)	4 (14)	3 (14)
Dose reduction	1 (2)	0	1 (5)
Drug discontinuation	5 (10)	2 (7)	3 (14)
Death	1 (2)	0	1 (5)

[a]Events include preferred terms defined with the use of the *Medical Dictionary of Regulatory Activities*, version 27.1.

[b]The median (interquartile range) time from prior tagraxofusp exposure to the first dose of pivekimab sunirine was 3.1 (1.2–8.5) months.

[c]Adverse events that are definitely, probably, or possibly related to the study drug are considered as related to the study drug. Adverse events with missing or unknown relationship to the study drug are considered as related to the study drug. Adverse events with the closest relatedness to the study drug are used for summaries.

[d]Adverse event severity is assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.

Abbreviation: BPDCN, blastic plasmacytoid dendritic cell neoplasm.

Table S11. Summary of Safety Results From Phase 1 Dose Escalation/Expansion Study (Schedule A Escalation and Cohorts 2 and 5 in Expansion)[a,8]

Safety	**Relapsed or refractory AML (N=68), n (%)**
TEAEs	
All Grades	67 (99)
Grade ≥3	59 (87)
Grade ≥3 TEAEs in ≥10% of patients	
Febrile neutropenia	24 (35)
Pneumonia	19 (28)
Anemia	9 (13)
Sepsis	8 (12)
Thrombocytopenia	8 (12)
Dose reduction due to TEAE	0
Treatment discontinuation due to TEAEs	8 (12)
Treatment discontinuation due to TRAEs	4 (6)
DLTs	3
Veno-occlusive liver disease (0.18 mg/kg)	1
Veno-occlusive disease (0.45 mg/kg)	1
Neutropenia (0.3 mg/kg)	1
Grade 3 infusion-related reaction	1
Treatment-related death	1 (1)
Unknown cause (0.300 mg/kg)	1 (1)
Death within 30 days of the last pivekimab sunirine dose	12 (18)
Disease progression	7

Respiratory failure	1
Lung infection	1
Hemoptysis	1
Depressed level of consciousness	1
Unknown	1

[a]On schedule A, pivekimab sunirine was administered intravenously once every 3 weeks, on day 1 of a 3-week cycle, starting at 0.015 mg/kg of bodyweight with five escalations up to 0.45 mg/kg on a modified Fibonacci schema. On the basis of the safety, antileukemia activity, pharmacokinetics, and pharmacodynamics data during the dose-escalation phase, two doses on schedule A were chosen for the dose-expansion phase: 0.045 mg/kg (cohort 2) and 0.090 mg/kg (cohort 5) to further optimize the selection of the recommended phase 2 dose.

Abbreviations: AML, acute myeloid leukemia; DLTs, dose-limiting toxicities; TEAE, treatment-emergent adverse event; TREA, treatment-related adverse event.

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