Longer survival with tagraxofusp versus venetoclax in patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN): Results of a real-world analysis

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BACKGROUND

- Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an aggressive, orphan hematologic malignancy characterized by CD123 expression and frequent involvement of the skin, bone marrow, blood, lymph nodes, liver, and spleen.
- An objective of first-line (1L) therapy is to induce a rapid and durable complete response without extended myelosuppression, enabling timely transition to hematopoietic stem cell transplantation (HSCT) in eligible patients.
- Tagraxofusp (TAG), a first-in-class CD123-targeted agent, is the first approved treatment for BPDCN in the US and EU, with approval based on a multicenter phase 2 trial (NCT02113982)—the largest prospective study in BPDCN using predefined multisystem response criteria.
- In both clinical and real-world settings, TAG has demonstrated high rates of rapid, durable responses that allow effective bridging to HSCT with associated long-term survival.[1,2]
- Although venetoclax (VEN) is not approved for BPDCN, real-world use has been reported in limited studies.[3,4]

OBJECTIVE

- To evaluate overall survival (OS) in BPDCN patients treated with a TAG- or VEN-based regimen in a US real-world setting.

METHODS

- This retrospective cohort study used US claims data from the Komodo Research Database (January 2016 – December 2023).
- Patients with ≥1 diagnosis of BPDCN and subsequent initiation of a TAG- or VEN-based regimen were included (**Table 1**).
  - The index date was defined as the first administration of a TAG-based regimen or initiation of a VEN-based regimen.
- Patients were additionally required to have continuous enrollment or sufficient claims activity from 3 months prior to the initial BPDCN diagnosis until the index date.
- Two cohorts were identified and matched 1:1 by number of prior lines of therapy (LOTs) (**Table 2**):
  - TAG-based cohort: Patients who initiated a TAG-based regimen in an inpatient setting.
  - VEN-based cohort: Patients who received a VEN-based regimen and no TAG at any time.
- The following subgroups were assessed within each cohort:
  - (1) Patients without post-index HSCT, (2) patients who received a TAG-based or VEN-based regimen in the 1L setting, (3) patients who received TAG or VEN monotherapy (± intrathecal [IT] chemotherapy), (4) patients who received combination therapy (among VEN patients, patients who received VEN + hypomethylating agents [HMAs]), and (5) patients who received IT chemotherapy.

Table 1. Sample selection of BPDCN patients

TAG-based Cohort	n
1. Patients had ≥1 claim with a diagnosis for BPDCN	2962
2. Patients had ≥1 claim with a diagnosis for BPDCN on or after TAG approval date[a]	1836
3. Patients had ≥1 prescription fill for (or administration of) TAG on or after their initial BPDCN diagnosis	165
4. Patients had ≥1 medical and pharmacy claims or continuous enrollment between the initial BPDCN diagnosis to the index date (exclusive)	108
5. Patients had ≥1 medical claim or continuous enrollment during the 3-month period before the initial BPDCN diagnosis	97
6. Patients with eligible TAG LOT and the first TAG dose in an inpatient setting	47

VEN-based Cohort	n
1. Patients had ≥1 claim with a diagnosis for BPDCN	2962
2. Patients had ≥1 prescription fill for (or administration of) VEN on or after the initial BPDCN diagnosis	198
3. Patients had no prescription fill for (or administration of) TAG at any time	157
4. Patients had ≥1 medical and pharmacy claims or continuous enrollment between the initial BPDCN diagnosis and last claim of BPDCN-related treatments	149
5. Patients had ≥1 medical claims or continuous enrollment during the 3-month period before the initial BPDCN diagnosis	139
6. Patients with eligible VEN LOTs	106 (119 VEN LOTs)

[a]TAG approval date: December 21, 2018.

Table 2. LOT matching

Index LOT	TAG-based Cohort N=47	VEN-based Cohort Unmatched N=119	VEN-based Cohort Matched N=47
1L	42	81	42
2L	4	24	4
3L	1	11	1
4L+	0	3	0

Statistical analysis

- OS was defined as time from index date to death from any cause and estimated using Kaplan-Meier analysis.
  - Patients without a death event were censored at the last date of data availability.
  - A sensitivity analysis was conducted, censoring patients at the earlier of last date of data availability or time of first post-index HSCT.
- OS was analyzed by descriptive statistics only.

RESULTS

Patient demographics, patient baseline characteristics, and treatment patterns

- Forty-seven patients treated with TAG-based regimens and 47 patients with VEN-based regimens were included (**Table 3**).
- The mean patient age was 60.9 years for the TAG-based cohort and 67.3 years for the VEN-based cohort.
- Mean Charlson Comorbidity Index (CCI) scores were 0.8 for the TAG-based cohort and 1.1 for the VEN-based cohort.
- Common CCI comorbidities for patients receiving TAG-based regimens and VEN-based regimens, respectively, included diabetes (30% vs 40%), peripheral vascular disease (13% vs 26%), and chronic pulmonary disease (21% vs 15%).
- Monotherapy was used in 85% of patients in the TAG-based cohort and 49% of patients in the VEN-based cohort (**Table 4**).
- In the 24 patients who received a VEN-based combination regimen, 21 received VEN with HMAs.
- IT chemotherapy was administered in 34% of patients in the TAG-based cohort and 19% of patients in the VEN-based cohort.
- Median follow-up was 13.4 months for the TAG-based cohort and 7.4 months for the VEN-based cohort.

Table 3. Patient characteristics (LOT matched cohorts)

Characteristic	TAG-based Cohort (N=47)	VEN-based Cohort (N=47)
Age (years),[a] mean (SD)	60.9 (19.6)	67.3 (18.8)
Sex,[a] n (%)		
Female	13 (28)	8 (17)
Male	34 (72)	39 (83)
Race/ethnicity,[a] n (%)		
White or Caucasian	26 (55)	30 (64)
Black or African American	6 (13)	3 (6)
Asian or Pacific Islander	0 (0)	3 (6)
Hispanic or Latino	7 (15)	3 (6)
Other	2 (4)	3 (6)
Unknown	6 (13)	5 (11)
Year of index date, n (%)		
2017	-	0 (0)
2018	-	9 (19)
2019	5 (11)	7 (15)
2020	13 (28)	13 (28)
2021	7 (15)	6 (13)
2022	11 (23)	1 (2)
2023	11 (23)	10 (21)
BPDCN duration at index (months),[b] mean (SD)	4.2 (8.1)	5.9 (9.0)
Prior or concomitant additional hematologic malignancies,[c] n (%)		
Multiple myeloma	2 (4)	6 (13)
Myelodysplastic syndromes	4 (9)	4 (9)
Acute lymphoblastic leukemia	3 (6)	8 (17)
Chronic myelomonocytic leukemia	2 (4)	1 (2)
Hodgkin lymphoma	0 (0)	1 (2)
CCI comorbidity score (excluding cancer),[d] mean (SD)	0.8 (1.3)	1.1 (1.5)
CCI comorbidities in >5% of patients,[d] n (%)		
Diabetes without chronic complication	10 (21)	14 (30)
Chronic pulmonary disease	10 (21)	7 (15)
Peripheral vascular disease	6 (13)	12 (26)
Mild liver disease	5 (11)	6 (13)
Congestive heart failure	5 (11)	9 (19)
Renal disease	5 (11)	4 (9)
Diabetes with chronic complication	4 (9)	5 (11)
Cerebrovascular disease	3 (6)	7 (15)
Myocardial infarction	2 (4)	3 (6)

[a]Measured at index date; [b]BPDCN at index was defined as time from the initial BPDCN diagnosis to the index date; [c]Measured during the 90-day period prior to the initial BPDCN diagnosis; [d]Measured during the 6-month baseline period prior to the index date.

Table 4. Treatment patterns of matched BPDCN patients treated with TAG or VEN[a]

Characteristic	TAG-based Cohort (N=47)	VEN-based Cohort (N=47)
Index LOT regimen, n (%)		
Monotherapy[b]	40 (85)	23 (49)
Combination therapy	7 (15)	24 (51)
VEN + HMA	-	21 (45)
Received IT chemotherapy during index LOT, n (%)	16 (34)	9 (19)
IT methotrexate	15 (32)	7 (15)
IT cytarabine	8 (17)	8 (17)
Treatment regimens received as index LOT among all TAG patients, n (%)		
TAG monotherapy	28 (60)	-
TAG combination[c]	3 (6)	-
TAG monotherapy + IT chemotherapy[d]	12 (26)	-
TAG combination + IT chemotherapy[e]	4 (9)	-
Treatment regimens received as index LOT among all VEN patients, n (%)		
VEN monotherapy	-	22 (47)
VEN combination[f]	-	16 (34)
VEN monotherapy + IT chemotherapy[g]	-	1 (2)
VEN combination + IT chemotherapy[h]	-	8 (17)
Proceeded to any HSCT, n (%)	12 (26)	13 (28)
Allogeneic only	12 (26)	12 (26)
Autologous only	0 (0)	1 (2)

[a]Treatment patterns and LOTs were identified from the initial BPDCN diagnosis until the later of (a) the end of continuous eligibility or (b) the date of the last claim for BPDCN-related treatment; [b]Monotherapy was defined as treatment with TAG or VEN alone, or in combination with IT chemotherapy; [c]TAG + azacitidine (AZA) (n=1), TAG + VEN (n=1), TAG + cytarabine (n=1); [d]TAG + IT methotrexate (MTX) (n=6), TAG + IT cytarabine + IT MTX (n=5), TAG + IT cytarabine (n=1); [e]TAG + VEN + IT cytarabine + IT MTX (n=2), TAG + daunorubicin + vincristine + IT MTX (n=1), TAG + VEN + IT MTX (n=1); [f]VEN + AZA (n=9), VEN + decitabine (n=5), VEN + decitabine + fludarabine (n=1), VEN + vincristine (n=1); [g]VEN + IT cytarabine + IT MTX (n=1); [h]VEN + AZA + IT cytarabine + IT MTX (n=3), VEN + AZA + IT cytarabine (n=2), VEN + cyclophosphamide + cytarabine + doxorubicin + vincristine + IT cytarabine + IT MTX (n=1), VEN + decitabine + IT cytarabine + IT MTX (n=1), VEN + vincristine + IT MTX (n=1).

More patients were able to receive a subsequent line of therapy after TAG-based regimens

- A subsequent LOT was received in 47% of patients who received a TAG-based regimen and 11% of patients who received a VEN-based regimen.
- Of the 22 patients in the TAG-based cohort who received a subsequent LOT:
  - Five patients received a TAG-based regimen as a subsequent LOT.
  - Eleven patients received a VEN-based regimen as a subsequent LOT.

Median overall survival was longer in patients treated with TAG-based regimens as compared to VEN-based regimens

- Median OS was 35.3 months for the TAG-based cohort and 10.5 months for the VEN-based cohort (**Figure 1**), with 12-month survival rates of 72.1% and 42.8%, respectively.
- Among 1L-treated patients, median OS remained longer for the TAG-based cohort (35.3 months) vs the VEN-based cohort (11.8 months) (**Figure 2**), with 12-month survival rates of 74.9% and 46.7%, respectively.

Figure 1. Overall survival of LOT-matched cohorts

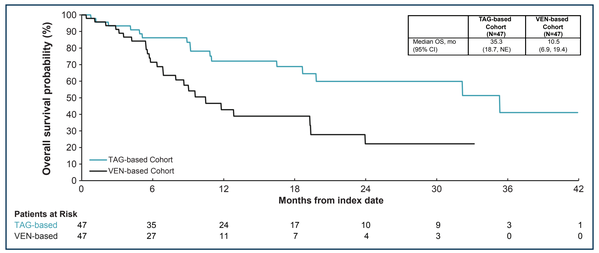
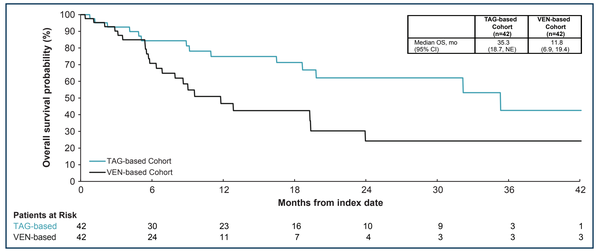


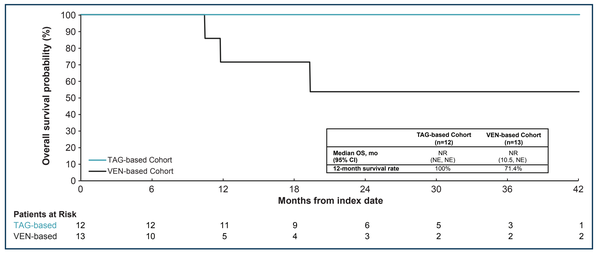
Figure 2. Overall survival of LOT-matched cohorts in 1L-treated patients



Regardless of HSCT, treatment with a TAG-based regimen was associated with a clinically meaningful longer overall survival compared to VEN-based regimens

- OS in patients with HSCT:
  - Median OS was not reached (NR) for the TAG-based cohort and VEN-based cohort (**Figure 3**), with 12-month survival rates of 100% and 71.4%, respectively.
- OS in patients without HSCT:
  - Median OS was 18.7 months (95% CI, 9.2-not estimable [NE]) for the TAG-based cohort and 6.9 months for the VEN-based cohort (95% CI, 5.6-12.9), with 12-month survival rates of 59.6% and 33.1%, respectively.

Figure 3. Overall survival among LOT-matched BPDCN patients with HSCT



Overall survival was longer in the TAG-based cohort for both monotherapy and combination therapy groups

- Median OS in monotherapy recipients was 35.3 months for the TAG-based cohort vs 10.5 months for the VEN-based cohort.
- Median OS in combination therapy recipients was NR for the TAG-based cohort and 9.6 months for the VEN-based cohort.
  - Median OS in 21 patients receiving VEN + HMA was 19.3 months.
- In patients receiving IT chemotherapy (TAG, n=16; VEN, n=9), median OS was NR in either group.
- Among those not receiving IT (TAG-based cohort, n=31; VEN-based cohort, n=38), median OS was 19.8 months for the TAG-based cohort and 9.6 months for the VEN-based cohort.

LIMITATIONS

- These analyses have inherent limitations common in many real-world analyses and apply to both cohorts, including:
  - Residual confounding due to the limited ability to balance baseline characteristics in a small sample size.
  - Potential OS overestimation due to delayed or incomplete death reporting in real-world data; due to incomplete records, the reported real-world OS for some patients may be longer than what they experience.
  - Potential patient misclassifications due to billing inaccuracies, coding errors, and the use of proxy variables to identify clinical characteristics and treatments.
  - Patient activity may be underestimated due to the use of open claims data, which were needed to achieve a suitable sample size.

CONCLUSIONS

- In this cohort study of patients with BPDCN, treatment with TAG-based regimens was associated with a substantially longer median overall survival (35.3 months vs 10.5 months) compared with VEN-based regimens, independent of subsequent receipt of hematopoietic stem cell transplantation.
- The survival advantage with TAG-based therapy was consistent across treatment contexts, including monotherapy, combination regimens, and in patients who underwent hematopoietic stem cell transplantation.
- Notably, a higher proportion of patients treated with TAG-based regimens were able to proceed to subsequent lines of therapy relative to those treated with VEN-based regimens.
- Collectively, these findings reinforce the role of tagraxofusp as the preferred first-line standard of care for patients with BPDCN, irrespective of transplant eligibility.
- Ongoing clinical studies are investigating combinations with a tagraxofusp backbone to further improve outcomes, including with venetoclax plus azacitidine (NCT03113643) and venetoclax plus multiagent chemotherapy (NCT04216524).

REFERENCES:

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ABBREVIATIONS:

1L, first-line; 2L, second-line; 3L, third-line; 4L+, fourth-line and beyond; AZA, azacitidine; BPDCN, blastic plasmacytoid dendritic cell neoplasm; CCI, Charlson comorbidity index; CI, confidence interval; EU, Europe; HMA, hypomethylating agent; HSCT, hemopoietic stem cell transplantation; IT, intrathecal; LOT, line of therapy; mo, month; MTX, methothrexate; n, number; NE, not estimable; NR, not reached; OS, overall survival; SD, standard deviation; TAG, tagraxofusp; US, United States; VEN, venetoclax.

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CONFLICTS OF INTEREST DISCLOSURES:

GSGM: Honoraria from Aptitude Health, Cardinal Health, Curio Science, DAVA Oncology; Advisory board for BeiGene, BMS, Daiichi Sankyo, Gilead/Kite, Pfizer, Syndax; Speakers' Bureau for Amgen, Rigel. **ASS:** Honoraria from Amgen, Debio Pharma, Syndex Bio; Consultant for Debio Pharma, Syndex Bio. **PV:** Consulting/advisory role with Blueprint Medicines, Bristol Myers Squibb, Cogent Biosciences, DISC medicine, Incyte, Sobi, Genentech, Geron, GlaxoSmith Kline, Kartos, Karyopharm, Merck, Novartis, Prelude Therapeutics, Silence Therapeutics, Stemline, Servier, Syndax, Takeda; Leadership role as a Board member for Alabama Cancer Congress; Speakers' Bureau for Incyte. **SI:** Advisory board for Morphosys. **DG and YG:** Employment with Analysis Group Inc; Research funding from Menarini Group. **JK:** Employment with Menarini Group, and previous employment, stock or stock options with AbbVie. **CP:** Employment with Menarini Group. **TK:** Research funding (to institution) from Glycomimetics, Novartis, Syndax; Consulting/advisory role with Amgen, Astellas, Neogenomics, Stemline, Syndax, Takeda; Honoraria from Rigel, Servier; Participation on DSMB or Advisory Board for Amgen, Neogenomics, Stemline, Syndax, Takeda.

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