Outcomes in patients (pts) younger than 50 years old (yo) with treatment-naïve blastic plasmacytoid dendritic cell neoplasm (BPDCN) treated with tagraxofusp (TAG): subanalysis of a phase 1/2 trial

Poster # AML-1290

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BACKGROUND

- Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an aggressive, rare hematologic malignancy characterized by cells expressing CD123 and other markers.[1-3]
- In BPDCN patients <50 years old, including the adolescent and young adult population (ie, patients 15-39 years old), data are limited.
- Tagraxofusp (TAG), a first-in-class CD123-targeted therapy, is the only drug approved for adults (US/EU) and pediatric patients aged ≥2 years old (US only) with BPDCN.[4,5]
- Results from the phase 1/2 trial of TAG in BPDCN, prospectively designed with prespecified/multisystem response criteria, demonstrated a high overall response rate (ORR) of 75% and CR/clinical CR (CRc; CR with residual skin abnormalities not indicative of active BPDCN) of 57%, with rapid and durable responses (23 days median time to response and 24.9 months median duration of CR/CRc) in 65 treatment-naïve patients.[6]
- TAG has a well-characterized and manageable safety profile, with transient adverse events (AEs) occurring mostly in cycle 1, no cumulative long-term toxicity, no myelosuppression, and with the majority of patients having restoration of normal hematopoiesis.[7]
- While not approved, multi-agent chemotherapy is used in adolescents and young adults, resulting in short- and long-term toxicity, including prolonged myelosuppression.

OBJECTIVE

- To determine the safety and efficacy of first-line (1L) TAG treatment for BPDCN patients <50 years old from a subgroup analysis of the pivotal TAG monotherapy study (NCT02113982).

METHODS

- We analyzed outcomes in treatment-naïve patients <50 years old who received 1L TAG 12 µg/kg intravenously on days 1-5 of a 21-day cycle.
- Assessed outcomes included best response, time to best response, duration of response (DOR), overall survival (OS), treatment-related adverse events (TRAEs), and capillary leak syndrome (CLS).

RESULTS

Patient demographics and baseline characteristics

- Ten patients (median age of 31.5 years old [range, 22-45]) were included in this analysis, including six young adult patients (**Table 1**).
- All patients had ECOG PS of 0-1.
- 60% of patients had ≥2 sites of disease, most commonly skin (100%) and lymph node (60%).

Table 1. Patient characteristics

Characteristic	Overall Population (N=10)
Median age, years (range)	31.5 (22-45)
Gender	
Male	6 (60)
Race	
White	10 (100)
Ethnicity	
Hispanic or Latino	3 (30)
Not Hispanic or Latino	7 (70)
ECOG PS score	
0	8 (80)
1	2 (20)
Disease involvement at baseline	
Skin	10 (100)
Lymph node	6 (60)
Bone marrow	2 (20)
Peripheral blood	2 (20)
≥2 disease sites	6 (60)
Time since diagnosis (months), median (range)	0.9 (0.0-2.9)

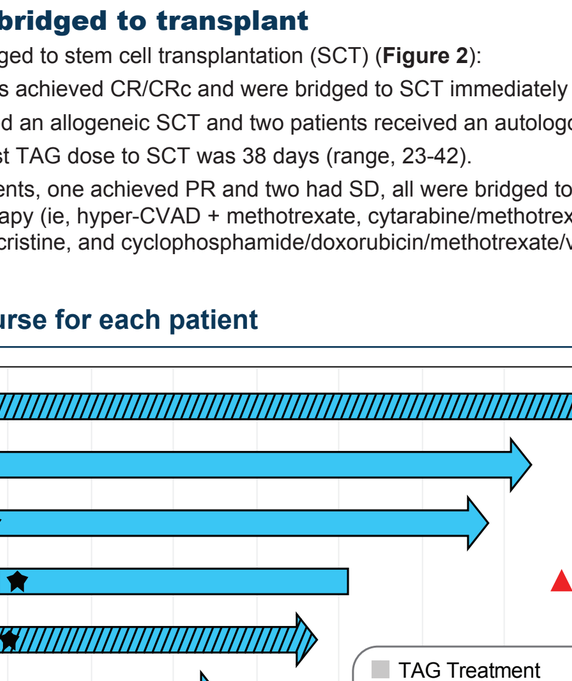
Treatment

- Patients received a median of four (range, 2-7) cycles of TAG.
- Median number of doses in cycle 1 was five (range, 3-5), which is in line with the USPI dosing.

TAG induced high rates of CR/CRc with durable responses

- At a median follow-up of 34 months (range, 10-53), the ORR was 80% (**Figure 1**):
  - Median time to overall response was 21 days (range, 14-44).
  - Median duration of overall response was not reached (range, 0.9-NE).
- 70% of patients had a CR/CRc (**Figure 1**):
  - Median time to CR/CRc was 41 days (range, 14-44).
  - Median duration of CR/CRc response was not reached (range, 8.4-51.8 mo).

Figure 1. Best overall response in all patients



All patients were bridged to transplant

- All ten patients were bridged to stem cell transplantation (SCT) (**Figure 2**):
  - Seven of these patients achieved CR/CRc and were bridged to SCT immediately following TAG treatment:
    - Five patients received an allogeneic SCT and two patients received an autologous SCT.
    - Median time from last TAG dose to SCT was 38 days (range, 23-42).
  - Of the other three patients, one achieved PR and two had SD, all were bridged to SCT following subsequent multi-agent chemotherapy (ie, hyper-CVAD + methotrexate, cytarabine/methotrexate/hydrocortisone [IT] + cyclophosphamide/vincristine, and cyclophosphamide/doxorubicin/methotrexate/vincristine).

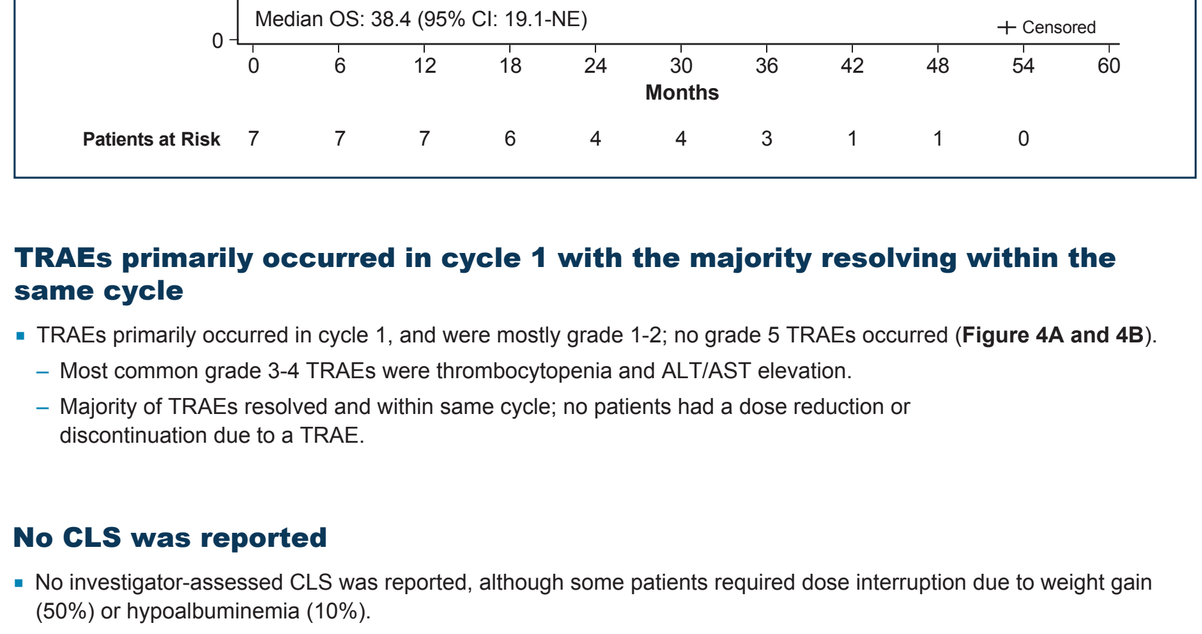
Figure 2. Clinical course for each patient

*Cause of death: study disease, unknown, respiratory failure

TAG led to long-term survival for all patients

- Median OS for all ten patients was 38.4 months (range, 10.2-53.1).
- Median OS for the seven patients bridged to transplant immediately following TAG treatment was 38.4 months (range, 17.8-53.1) (**Figure 3**).

Figure 3. Overall survival for patients bridged to transplant immediately following TAG treatment (n=7)



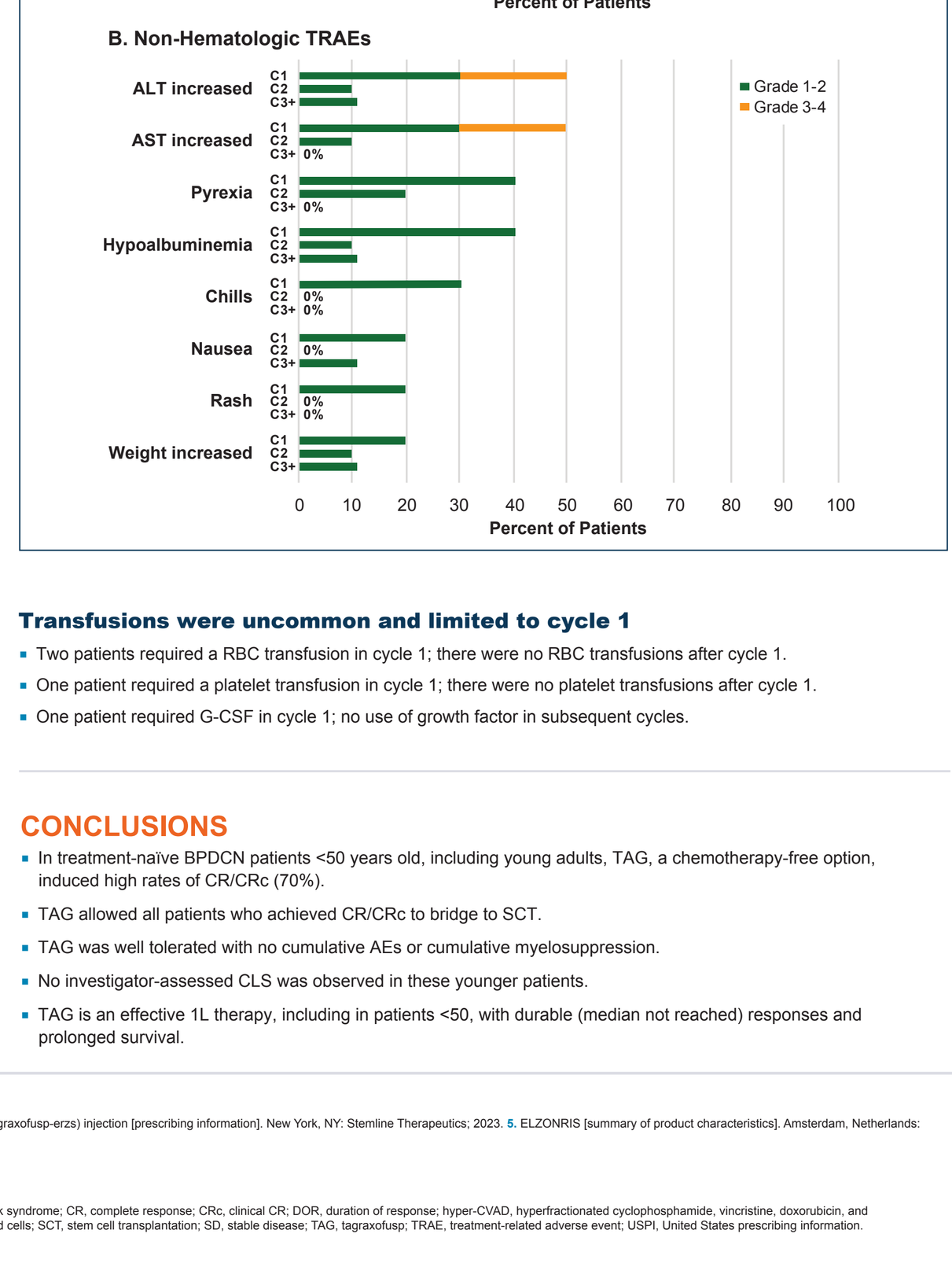
TRAEs primarily occurred in cycle 1 with the majority resolving within the same cycle

- TRAEs primarily occurred in cycle 1, and were mostly grade 1-2; no grade 5 TRAEs occurred (**Figure 4A and 4B**).
  - Most common grade 3-4 TRAEs were thrombocytopenia and ALT/AST elevation.
  - Majority of TRAEs resolved and within same cycle; no patients had a dose reduction or discontinuation due to a TRAE.

No CLS was reported

- No investigator-assessed CLS was reported, although some patients required dose interruption due to weight gain (50%) or hypoalbuminemia (10%).

Figure 4. Treatment-related adverse events in ≥2 patients



Transfusions were uncommon and limited to cycle 1

- Two patients required a RBC transfusion in cycle 1; there were no RBC transfusions after cycle 1.
- One patient required a platelet transfusion in cycle 1; there were no platelet transfusions after cycle 1.
- One patient required G-CSF in cycle 1; no use of growth factor in subsequent cycles.

CONCLUSIONS

- In treatment-naïve BPDCN patients <50 years old, including young adults, TAG, a chemotherapy-free option, induced high rates of CR/CRc (70%).
- TAG allowed all patients who achieved CR/CRc to bridge to SCT.
- TAG was well tolerated with no cumulative AEs or cumulative myelosuppression.
- No investigator-assessed CLS was observed in these younger patients.
- TAG is an effective 1L therapy, including in patients <50, with durable (median not reached) responses and prolonged survival.

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ABBREVIATIONS:

1L, first-line; AE, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BPDCN, blastic plasmacytoid dendritic cell neoplasm; C, cycle; CLS, capillary leak syndrome; CR, complete response; CRc, clinical CR; DOR, duration of response; hyper-CVAD, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone; IT, intrathecally; kg, kilogram; µg, microgram; mo, months; NE, not estimable; ORR, overall response rate; OS, overall survival; PR, partial response; RBC, red blood cells; SCT, stem cell transplantation; SD, stable disease; TAG, tagraxofusp; TRAE, treatment-related adverse event; USPI, United States prescribing information.

ACKNOWLEDGMENTS:

- We thank the patients and their families, and the investigators, co-investigators, and their participating institutions.
- This study was funded by Menarini Group (New York, NY, USA).
- Editorial and medical writing assistance were provided by Kelsi Bates, PharmD, from Phillips Group Oncology Communications, Inc. (Albany, NY, USA), funded by Menarini Group.

DISCLOSURES:

KLS: Institutional research funding from Incyte, Jazz; Advisory/consultant role for JazzBri, Nkarta, Novartis; Honoraria from Bristol Myers Squibb; Expert testimony with Nelson Mullins; Travel accommodations/expenses from Bristol Myers Squibb, Jazz; Participation on a DSMB or advisory board for Karyopharm; Stock or stock options with BeiGene. **ASS:** Honoraria from Amgen, Syndex Bio, Debio Pharma; Consultant for Debio Pharma, Syndex Bio. **AAL:** Institutional research funding from AbbVie, Stemline Therapeutics; Consulting or advisory role for Cimeio Therapeutics, IDRx, Jnana Therapeutics, ProteinQure, Qiagen, Stelexis BioSciences; Steering Committee for Stemline Therapeutics; Stock or stock options with Medzown, Stelexis BioSciences. **SV:** Institutional research funding from Sanofi; Participation on a DSMB or advisory board for Alexion. **AT:** Employment with Menarini Group. **JK:** Employment with Menarini Group and previous employment, stock or stock options with AbbVie. **MK:** Institutional research funding from AbbVie, Janssen, Klondike Biopharma; Consulting/advisory role for AbbVie, Adaptive, AmMax, Curis, Janssen, Kyowa Kirin, Menarini/Stemline Therapeutics, Novartis, Sanofi Aventis, Servier, Vincerx; Participation on a DSMB or advisory board for AbbVie, Auxenion GmbH, Dark Blue Therapeutics, Legend, MEI Pharma, Menarini/Stemline Therapeutics, Novartis, Syndax. **NP:** Institutional research grant from NIH/NCI, US Dept of Defense; Consultant/scientific advisory board/speaking for AbbVie, Aplastic Anemia and MDS International Foundation, Aptitude Health, Astellas Pharma US, Blueprint Medicines, Bristol Myers Squibb, 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, PharmaEssentia, Physician Education Resource (PER); Board of Directors/Management for Dan's House of Hope; Leadership with ASH Committee on Communications, ASCO Cancer.Net Editorial Board; Licenses with Karger Publishers; Editorial board (unpaid) for HemOnc Times/Oncology Times.

Presented at SOHO Annual Meeting 2025, September 3-6, 2025