Subgroup analysis by fitness criteria of patients (pts) with blastic plasmacytoid dendritic cell neoplasm (BPDCN) treated with first-line (1L) tagraxofusp (TAG)

Poster # AML-1310

Naveen Pemmaraju,[1] Marco Herling,[2] Kendra L. Sweet,[3] Anthony S. Stein,[4] Sumithira Vasu,[5] Todd L. Rosenblat,[6] David A. Rizzieri,[7] Cristina Papayannidis,[8] Eunice S. Wang,[9] Marina Konopleva,[10] Michael Zuurman,[11] Alessandra Tosolini,[12] Muzaffar Qazilbash,[1] Andrew A. Lane[13]

[1]MD Anderson Cancer Center, Houston, TX, USA; [2]University Hospital Leipzig and Cancer Center Central Germany (CCCG) Leipzig-Jena, Germany; [3]Moffitt Cancer Center, Tampa, FL, USA; [4]City of Hope, Duarte, CA, USA; [5]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [6]Columbia University Herbert Irving Comprehensive Cancer Center, New York, NY, USA; [7]Novant Health Cancer Institute, Charlotte, NC, USA; [8]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna, Italy; [9]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [10]Albert Einstein College of Medicine/Montefiore Cancer Center, Bronx, NY, USA; [11]Menarini Group, Machelen, Belgium, [12]Menarini Group, New York, NY, USA; [13]Dana-Farber Cancer Institute, Boston, MA, USA

BACKGROUND

- Blastic plasmacytoid dendritic cell neoplasm (BPDCN), an aggressive, rare hematologic neoplasm, expresses CD123 and other markers and presents in skin, bone marrow, blood, and viscera.[1-3]
- For patients eligible to undergo hematopoietic cell transplantation (HCT), the first-line treatment goal is to rapidly induce a complete response (CR), and without prolonged myelosuppression, before HCT.
- Tagraxofusp (TAG) is a first-in-class CD123-targeted therapy with a well-characterized and manageable safety profile, importantly without cumulative myelosuppression, and the only drug approved to treat BPDCN.[4,5]
- In a phase 1/2 prospective trial with prespecified and multisystem response criteria, TAG demonstrated a 75% overall response rate (ORR) and a 24.9-month median duration of CR/clinical CR (CRc; CR with residual skin abnormalities not indicative of active BPDCN) in treatment-naïve (1L) patients who had a median age of 68 years.[6] In addition, 51% of patients with CR/CRc were able to bridge to HCT.
- Multi-agent intensive chemotherapy is still used prior to HCT, particularly in young, fit patients, despite short- and long-term toxicity and myelosuppression and despite short durations of response (DOR). Moreover, these modalities have neither been approved nor have they shown clinical benefit in a prospective trial with prespecified success parameters. In addition, many patients with BPDCN are ineligible for intensive chemotherapy before HCT.

OBJECTIVE

- To determine the safety and efficacy of 1L TAG treatment based on pretreatment comorbidity burden and fitness group in patients who received 1L TAG for BPDCN in the pivotal trial (NCT02113982).

METHODS

- Patients who prospectively received 1L TAG 12 µg/kg IV on days 1-5 of a 21-day cycle were assigned, post hoc, to categories by their hematopoietic cell transplantation-specific comorbidity index (HCT-CI) score. HCT-CI is a risk-stratification model based on combined comorbidity scores.[7]
- Points used to calculate HCT-CI scores were determined using baseline medical history, concomitant medications, and labs. HCT-CI categories were then assigned based on the sum of points as follows: 0 (low risk), 1-2 (intermediate risk), and 3+ (high risk).
- Outcomes assessed in this analysis included best response, time to response (TTR), duration of response (DOR), overall survival (OS), HCT rate, treatment-related adverse events (TRAEs), and capillary leak syndrome (CLS).

RESULTS

Patient demographics and baseline characteristics

- Sixty-five treatment-naïve patients were included in this analysis, with HCT-CI scores of 0 (low risk) in 15 (23%), 1-2 (intermediate risk) in 22 (34%), and 3+ (high risk) in 28 (43%) (**Table 1**).
- All patients in the low and intermediate groups had ECOG PS of 0-1; two patients in the high-risk group had ECOG PS 2.
- The most common disease sites in all three groups were skin, bone marrow, and lymph node, with more extensive BPDCN involvement in the high-risk group.
- Median follow-up time was 27.7 mo (range, 2.6-51.7) in low risk; 36.6 mo (0.2-58.1) in intermediate risk, and 36.3 mo (3.9-54) in high-risk groups.

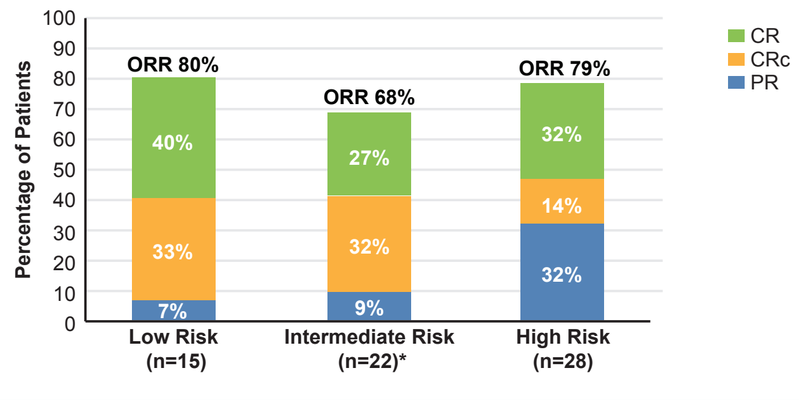
Table 1. Patient characteristics

Characteristic	Low Risk (n=15)	Intermediate Risk (n=22)	High Risk (n=28)
Median age, years (range)	61 (22-79)	67.5 (22-84)	70 (23-84)
Gender, no. (%)			
Male	14 (93)	14 (64)	24 (86)
Race, no. (%)			
White	11 (73)	19 (86)	27 (96)
Ethnicity, no. (%)			
Not Hispanic or Latino	13 (87)	20 (91)	26 (93)
ECOG PS score, no. (%)			
0	10 (67)	11 (50)	10 (36)
1	4 (27)	11 (50)	16 (57)
2	0	0	2 (7)
Median BMI, kg/m² (range)	28 (23-35)	29 (22-48)	31 (21-40)
Disease involvement at baseline, no. (%)			
Skin	13 (87)	22 (100)	25 (89)
Bone marrow	5 (33)	6 (27)	21 (75)
Lymph node	7 (47)	8 (36)	18 (64)
Peripheral blood	2 (13)	3 (14)	12 (43)
Visceral	3 (20)	0	6 (21)
≥2 disease sites	9 (60)	11 (50)	25 (89)
Time since diagnosis (months), median (range)	1.4 (0-2.9)	1.1 (0-4.8)	0.9 (0-3.2)

High overall response rates were achieved regardless of fitness group

- ORRs were high regardless of fitness group; ORRs in low-, intermediate-, and high-risk groups were 80%, 68%, and 79%, respectively (**Figure 1**).
- Median time to response was similar in the three groups:
  - Low risk: 23.5 days (range, 20-49)
  - Intermediate risk: 22 days (range, 14-53)
  - High risk: 25 days (range, 14-97)
- Median DORs were longer in the low- and intermediate-risk groups:
  - Low risk: 24.9 months (range, 1.0-51.1)
  - Intermediate risk: not reached (range, 0.9-57.4)
  - High risk: 3.9 months (range, 0.7-52.3)

Figure 1. Overall response rate in overall population

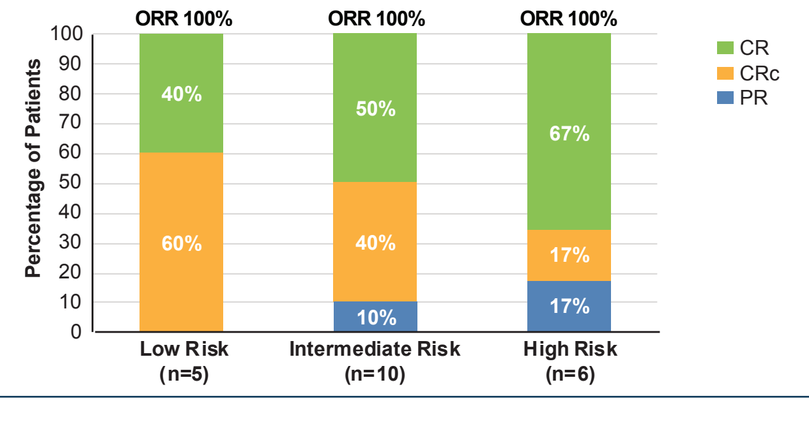


*4 patients not evaluable

In patients who bridged to transplant, high and durable responses to treatment were seen in all patients regardless of fitness level

- Twenty-one patients were bridged to HCT: 5 (33%) in low-, 10 (46%) in intermediate-, and 6 (21%) in high-risk patients.
- In patients bridged to HCT, the median age (range) was 40 (22-69), 58 (22-75), and 68.5 (57-78) years, respectively, and the median BMI (range) was 28 (24-35), 30 (22-48), and 32 (26-38) kg/m², in low-, intermediate-, and high-risk patients, respectively.
- High response rates, including complete responses, were observed in all patients bridged to HCT, regardless of fitness group (**Figure 2**). Pre-transplant CR/CRc rates were 100%, 90%, and 83%, respectively.
- Median time to overall response was shortest in low- and intermediate-risk groups for patients who bridged to HCT:
  - Low risk: 21 days (range, 20-49)
  - Intermediate risk: 22.5 days (range, 14-53)
  - High risk: 41 days (range, 23-57)
- Median DOR was not reached in any of the fitness groups for patients who bridged to HCT.
- Median time from diagnosis to HCT was similar in all fitness groups for patients who bridged to HCT:
  - Low risk: 5.4 mo (range, 4.2-7.7)
  - Intermediate risk: 5.8 mo (range, 2.8-8.4)
  - High risk: 5.4 mo (range, 3.6-8.0)
- Median time from first TAG dose to HCT was also similar across fitness groups for patients who bridged to HCT:
  - Low risk: 3.9 mo (range, 3.0-5.5)
  - Intermediate risk: 3.4 mo (range, 2.4-6.5)
  - High risk: 4.1 mo (range, 2.5-6.7)

Figure 2. Overall response rate in patients who bridged to transplant



Overall survival was prolonged in the overall population and not reached in intermediate- and high-risk patients who bridged to transplant

- Median OS in the overall population (**Figure 3A**) was as follows:
  - Low risk: 38.4 months (range, 2.6-51.7)
  - Intermediate risk: 15.8 months (range, 0.2-58.1)
  - High risk: 11.8 months (range, 3.9-54.0)
- Median OS for patients who bridged to HCT (**Figure 3B**) was as follows:
  - Low risk: 38.4 months (range, 17.8-51.7)
  - Intermediate risk: not reached (range, 3.5-58.1)
  - High risk: not reached (range, 4.1-38.7)

Figure 3A. Overall survival in overall population

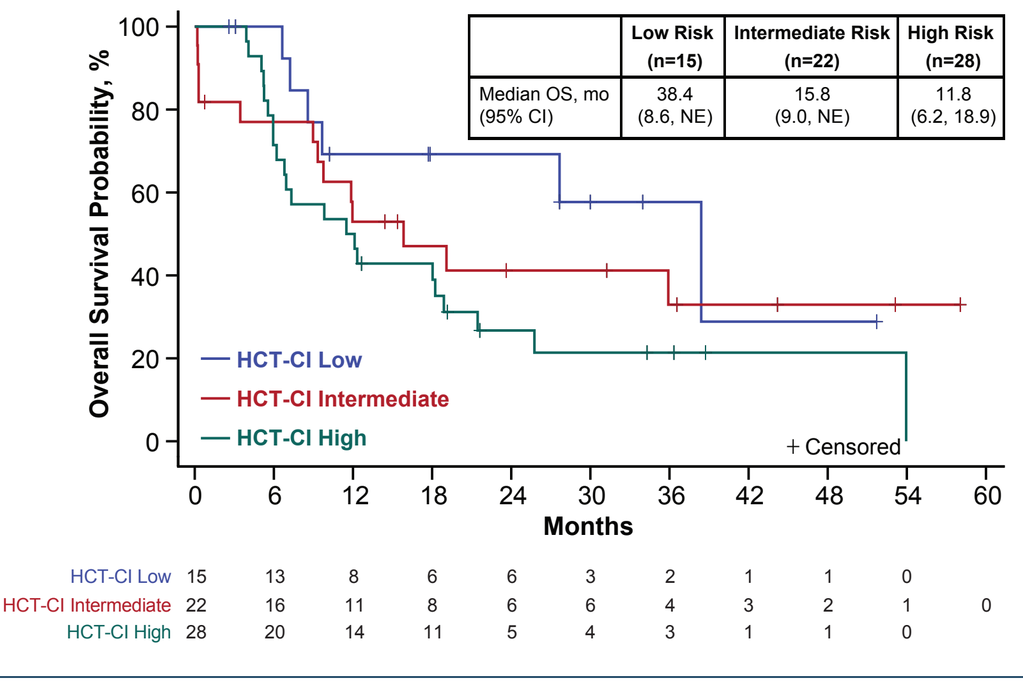
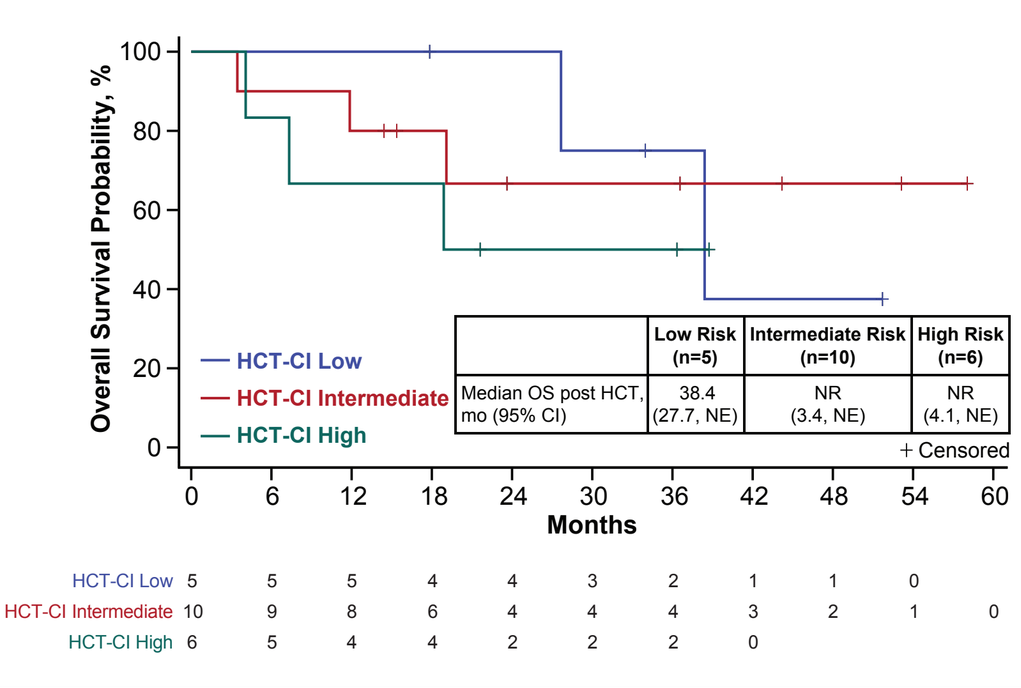


Figure 3B. Overall survival in patients who bridged to HCT



All CLS events occurred in cycle 1 and all grade 1-4 CLS events resolved

- Treatment-related CLS was reported in patients in low-, intermediate-, and high-risk groups as follows:
  - Grade 1-2: 7%, 5%, and 18%, respectively
  - Grade 3-4: 0%, 9%, and 4%, respectively
  - Two patients in the intermediate-risk group died from CLS.

Most TRAEs occurred in cycle 1 and were transient

- The most frequent any-grade TRAEs in ≥ 40% of patients in any subgroup were thrombocytopenia, increased ALT, increased AST, chills, pyrexia, and hypoalbuminemia.
- In each group, the most common grade 3-4 TRAEs were thrombocytopenia and increased ALT and AST; most were in cycle 1 and were transient.
  - Low risk: thrombocytopenia 33%, ALT increased 40%, AST increased 40%
  - Intermediate risk: thrombocytopenia 14%, ALT increased 14%, AST increased 14%
  - High risk: thrombocytopenia 14%, ALT increased 29%, AST increased 29%

CONCLUSIONS

- First-line treatment with TAG for BPDCN yielded high response rates regardless of HCT-CI fitness level.
  - ORR in low-, intermediate-, and high-risk groups was 80%, 68%, and 79%, respectively.
- The safety profile of tagraxofusp was similar across HCT-CI groups.
- TAG, which was not associated with prolonged myelosuppression seen with intensive chemotherapy, enabled bridge to HCT across all fitness groups, including high-risk patients who would have possibly been ineligible for intensive chemotherapy.
- These results affirm TAG as the standard of care for first-line treatment of patients with BPDCN.

REFERENCES:

1. Economides MP, et al. *Ther Adv Hematol*. 2019;10:1-9. 2. Chaperot L, et al. *Blood*. 2001;97:3210-3217. 3. Petrella T, et al. *Am J Surg Pathol*. 2002;26:852-862. 4. ELZONRIS® (tagraxofusp-erzs) injection [prescribing information]. New York, NY: Stemline Therapeutics; 2023. 5. ELZONRIS [summary of product characteristics]. Amsterdam, Netherlands: Stemline Therapeutics B.V.; 2023. 6. Pemmaraju N, et al. *J Clin Oncol*. 2022;40:3032-3036. 7. Sorror ML, et al. *J Clin Oncol*. 2007;25:4246-4254.

ABBREVIATIONS:

1L, first-line; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BPDCN, blastic plasmacytoid dendritic cell neoplasm; CI, confidence interval; CLS, capillary leak syndrome; CR, complete response; CRc, clinical complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HCT, hematopoietic stem cell transplantation; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; kg, kilogram; µg, microgram; mo, months; NE, not estimable; no., number; ORR, overall response rate; OS, overall survival; pts, patients; PR, partial response; TAG, tagraxofusp; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; TTR, time to response.

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:

NP: Institutional research grant from NIH/NCI, US Dept of Defense; Consultant/scientific advisor board/speaking for AbbVie, Aplastic Anemia and 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, Paradox, 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. **MH:** Research funding from BeiGene, JanPix; Consulting or advisory role for BeiGene, Janssen, Stemline Menarini, Takeda; Honoraria from BeiGene, Janssen, Stemline Menarini, Takeda, Roche; Expert testimony for Stemline Menarini; Travel accommodations/expenses from BeiGene, Janssen. **KLS:** Institutional research funding from Incyte, Jazz; Advisory/ consultant role for Jazzfin, Ikarta, 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, Syndax Bio, Debio Pharma; Consultant for Debio Pharma, Syndax Bio. **SV:** Institutional research funding from Sanofi; Participation on a DSMB or advisory board for Alexion. **TLR:** Nothing to disclose. **DAR:** Data safety monitoring board or advisory board for Cellectis. **CP:** Consulting/advisory role and participation on a data safety monitoring board or advisory board for AbbVie, Astellas, Blueprint, Delbert Laboratories, GSK, ImCheck, Istituto Gentili, Janssen, Jazz Pharmaceuticals, Pfizer; Honoraria from AbbVie, Amgen, Astellas, Bristol Myers Squibb, Incyte, Janssen, Menarini/Stemline, Novartis, Pfizer, Servier. **ESW:** Advisory/consulting for AbbVie, Blueprint, Daiichi-Sankyo, ImmunoGen, Kite, Kura, Novartis, Qiagen, Rigel, Ryvu, Schrödinger, Servier, Stemline, Syndax, Takeda; Speaking for Pfizer, Astellas, Daiva; DSMC for Gilead, AbbVie; Other: section editor for UpToDate. **MK:** Institutional research funding from AbbVie, Janssen, Klondike Biopharma; Consulting/advisory role for AbbVie, Adaptive, AnnMax, Curis, Janssen, Kyowa Kirin, Menarini/Stemline Therapeutics, Novartis, Sanofi Aventis, Servier, Vincerx; Participation on a DSMB or advisory board for AbbVie, Auservion GmbH, Dark Blue Therapeutics, Legend, MEI Pharma, Menarini/Stemline Therapeutics, Novartis, Syndax. **MZ & AT:** Employment with Menarini Group. **MQ:** Research funding from Janssen, Sanofi, Angiocrine; Consulting/advisory role for Sanofi; Participation on a DSMB or advisory board for Autolus. **AAL:** Institutional research funding from AbbVie, Stemline Therapeutics; Consulting or advisory role for Cimeio Therapeutics, IDRx, Jnana Therapeutics, ProtenQure, Qiagen, Stelexis BioSciences; Steering Committee for Stemline Therapeutics; Stock or stock options with Medzown, Stelexis BioSciences.

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