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Response to Comment on: “First-line tagraxofusp leads to durable responses and prolonged survival in adults with blastic plasmacytoid dendritic cell neoplasm regardless of fitness level”

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Contributions

NP and AAL contributed to manuscript writing, editing, and content review, and approved the final draft of the manuscript.

We thank Drs. Kusumoto and Tachibana for their thoughtful comment on our analysis of the pivotal tagraxofusp (TAG) study in blastic plasmacytoid dendritic cell neoplasm (BPDCN) that used the hematopoietic cell transplantation (HCT)–specific comorbidity index to assess TAG outcomes across baseline patient fitness levels.^{1,2} Our post hoc analysis was designed to characterize how baseline fitness relates to TAG efficacy and safety and was not designed or powered to characterize central nervous system (CNS) staging, prophylaxis, or relapse. In the pivotal trial, no cases of overt CNS relapse were observed, but patients with known CNS disease were excluded from enrolling, and routine lumbar punctures (LP) to assess for occult CNS disease were not performed.^{3,4}

We agree with most of the authors' points. First, the distinction between systemic and CNS disease control is well established, and a systemic complete response, including with TAG, should not be assumed to indicate CNS clearance. Second, baseline CNS assessment and a defined CNS management plan are critical components of initial BPDCN management. Third, we agree that prospective CNS assessments in clinical trials, rather than retrospective or nonuniform testing, are the appropriate route for defining incidence, risk stratification, and optimal management of CNS disease in BPDCN and should be a standard component of future BPDCN trial designs. Similarly, the authors' recommendation that patients with cerebrospinal fluid (CSF)–positive disease receive therapeutic rather than prophylactic intrathecal (IT) dosing is consistent with existing BPDCN practice guidance.⁵⁻⁸

Real-world data help illustrate how CNS disease in BPDCN is identified and managed, including the feasibility of combining TAG with CNS-directed therapy, in routine practice, particularly given that TAG is not known to cross the blood-brain barrier. Results from a retrospective review of 26 treatment-naïve patients with BPDCN treated with TAG in the European Named Patient Program showed that 3 (21%) of 14 patients who had baseline CNS status assessed had documented CNS involvement.⁹ Two of these 3 patients received IT chemotherapy before and after TAG initiation and achieved a complete response in marrow with successful bridge to HCT; the third patient, who did not receive IT chemotherapy, achieved a partial response with TAG alone. Separately, 8 patients without documented baseline CNS involvement received IT chemotherapy, predominantly as prophylaxis, with high response rates among evaluable patients. The partial determination of baseline CNS status in this cohort (14 of 26 patients) itself illustrates the nonuniform, incomplete real-world testing that the authors caution against, underscoring the need for standardized, protocol-mandated CNS assessment to ensure appropriate CNS-directed treatment or prophylaxis in future studies.

Importantly, the authors' call for future TAG trials to prospectively incorporate CNS assessment is underway. A phase 2 trial of TAG combined with azacitidine and venetoclax in patients with treatment-naïve and relapsed/refractory BPDCN mandated screening LP for enrollment, and patients with asymptomatic CNS involvement were not

excluded but were enrolled and received IT chemotherapy as part of study treatment.¹⁰ Of 27 enrolled patients, 6 (22%) had asymptomatic CNS disease identified at study entry. Notably, this study does not establish intrinsic CNS activity of TAG or evaluate the optimal CNS treatment strategy. Rather, this trial design directly demonstrates the feasibility of the prospective, protocol-mandated CNS staging and management approach the authors recommend and offers a prototype for incorporating CNS assessment into future TAG-based combination studies. The rationale for this approach is supported by a single-institution analysis of 103 patients with BPDCN, in which CSF involvement during their disease course was identified in 22%, despite LP having been performed in fewer than one-third of patients (n=29).¹¹

We agree that CNS outcomes should be analyzed from treatment initiation rather than restricted to patients bridging to HCT, to avoid undercounting pretransplant events. Because prospective, comparative CNS data from BPDCN trials remain limited, future studies should systematically address this gap. As these data accumulate, we anticipate that evidence-based CNS management strategies for patients receiving first-line TAG, alone or in combination, will become better defined. We appreciate the authors' comment for highlighting this evidence gap and reinforcing the need for CNS-focused reporting standards in future BPDCN trials and registries.

References

1. Kusumoto S, Tachibana T. Central nervous system management remains an evidence gap in first-line tagraxofusp therapy for blastic plasmacytoid dendritic cell neoplasm. Comment on: "First-line tagraxofusp leads to durable responses and prolonged survival in adults with blastic plasmacytoid dendritic cell neoplasm regardless of fitness level". Haematologica. xxx
2. Pemmaraju N, Herling M, Sweet KL, et al. First-line tagraxofusp leads to durable responses and prolonged survival in adults with blastic plasmacytoid dendritic cell neoplasm regardless of fitness level. Haematologica. 2026;111(7):2508-2513.
3. Pemmaraju N, Lane AA, Sweet KL, et al. Tagraxofusp in blastic plasmacytoid dendritic-cell neoplasm. N Engl J Med. 2019;380(17):1628-1637.
4. Pemmaraju N, Sweet KL, Stein AS, et al. Long-term benefits of tagraxofusp for patients with blastic plasmacytoid dendritic cell neoplasm. J Clin Oncol. 2022;40(26):3032-3036.
5. Kharfan-Dabaja MA, Lane AA, Pemmaraju N. How I treat blastic plasmacytoid dendritic cell neoplasm. Blood. 2025;145(6):567-576.
6. Martín-Martín L, Almeida J, Pomares H, et al. Blastic plasmacytoid dendritic cell neoplasm frequently shows occult central nervous system involvement at diagnosis and benefits from intrathecal therapy. Oncotarget. 2016;7(9):10174-10181.
7. Shimony S, Luskin MR, Gangat N, LeBoeuf NR, Feraco AM, Lane AA. Blastic plasmacytoid dendritic cell neoplasm (BPDCN): 2025 update on diagnosis, pathophysiology, risk assessment, and management. Am J Hematol. 2025;100(8):1408-1422.
8. Pemmaraju N, Kantarjian H, Sweet K, et al. North American Blastic Plasmacytoid Dendritic Cell Neoplasm Consortium: position on standards of care and areas of need. Blood. 2023;141(6):567-578.
9. Herling M, Angelucci E, Benoit TM, et al. Durable outcomes with manageable safety leading to prolonged survival with tagraxofusp for treatment-naïve patients with blastic plasmacytoid dendritic cell neoplasm: real world results from a European Named Patient Program. Ann Hematol. 2025;104(8):4121-4131.
10. Pemmaraju N, Wilson NR, Khoury JD, et al. Central nervous system involvement in blastic plasmacytoid dendritic cell neoplasm. Blood. 2021;138(15):1373-1377.

11. Lane AA, Luskin MR, Keating JH, et al. Tagraxofusp, azacitidine, and venetoclax in blastic plasmacytoid dendritic cell neoplasm. *Blood*. 2026 Jul 7;blood.2026033906. doi:10.1182/blood.2026033906. [Epub ahead of print]