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Response depth rather than treatment intensity may define prognosis in primary plasma cell leukemia. Comment on: "The prognostic factors and immune microenvironment of primary plasma cell leukemia: the KMMWP-2204 study"

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Author contributions

All listed authors have contributed significantly, directly, and intellectually to the work, and have approved it for publication.

Disclosure

The authors declare no conflict of interest.

To the Editor,

We read with great interest the study by Kim et al[1]. describing prognostic factors and immune features in the KMMWP-2204 cohort of primary plasma cell leukemia (pPCL). The authors should be commended for assembling one of the largest contemporary multicenter pPCL cohorts and for addressing several longstanding questions regarding circulating plasma cell burden, autologous stem cell transplantation (ASCT), and early mortality. Their findings further support the clinical applicability of the revised International Myeloma Working Group diagnostic threshold and provide valuable real-world insights into outcomes in this highly aggressive disease.

Among the many observations reported, we believe that the relationship between treatment intensity and response depth deserves particular attention. Although intensive triplet or quadruplet regimens and ASCT were used more frequently in the post-2016 era, overall survival and progression-free survival remained broadly unchanged at the cohort level. In contrast, achievement of complete remission (CR) emerged as the most consistent favorable prognostic factor across both conventional and time-dependent analyses. Patients achieving CR experienced substantially longer survival, and CR remained independently associated with improved overall and progression-free survival after multivariable adjustment[2].

These findings raise an important conceptual question. In pPCL, should treatment success be defined primarily by the therapeutic strategy employed or by the depth of disease eradication achieved? Historically, treatment discussions in pPCL have focused on specific modalities, including proteasome inhibitor–based combinations, anti-CD38 monoclonal antibodies, and ASCT. However, the attenuation of the apparent ASCT benefit in time-dependent models suggests that treatment selection alone may not adequately explain outcome differences. Instead, therapies may derive their prognostic value largely through their ability to induce deep responses[3]. This interpretation is particularly relevant as novel therapeutic approaches continue to emerge. Future studies may benefit from incorporating response depth, and ultimately measurable residual disease (MRD) status, as central efficacy endpoints rather than relying predominantly on treatment category comparisons. Such an approach may better capture biological treatment effectiveness and facilitate comparisons across increasingly heterogeneous therapeutic strategies.

Importantly, this perspective may also help reconcile the apparent discrepancy between the absence of clear survival improvement across treatment eras in the present study and the favorable outcomes reported in other contemporary pPCL series. If response depth rather than treatment intensity is the principal determinant of outcome, variations in baseline risk, cytogenetic composition, and the proportion of patients achieving CR may be more informative than treatment exposure alone. In summary, the study by Kim et al. suggests that achieving deep remission may be more important than the specific therapeutic pathway used to achieve it. Future prospective pPCL studies should consider shifting from a treatment-centered framework toward a response-centered framework, with particular emphasis on CR and MRD-directed endpoints.

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