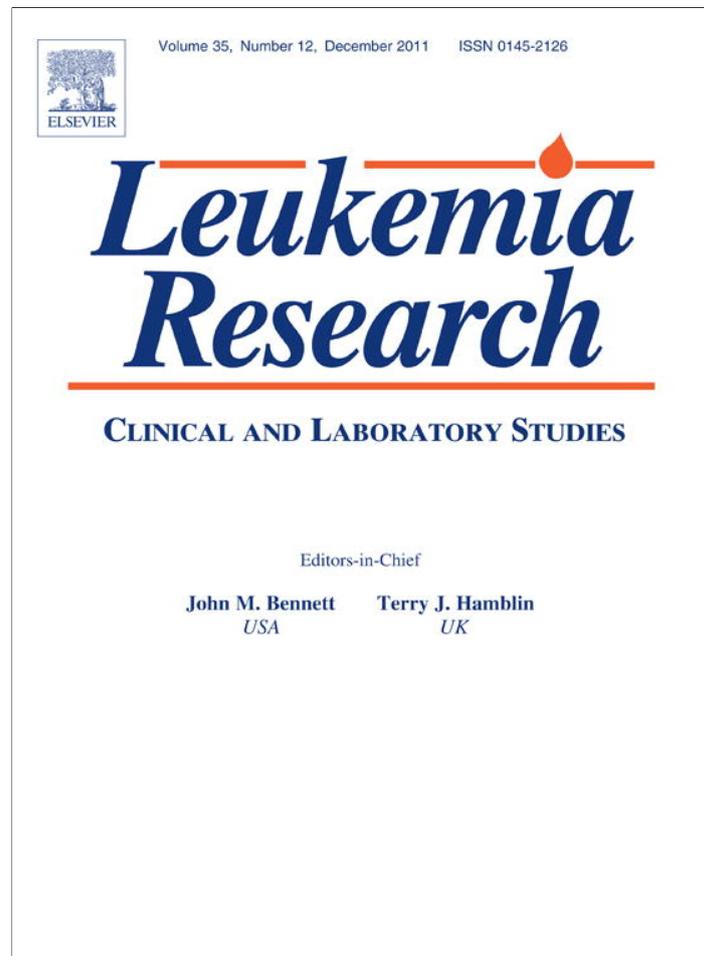


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## Editorial

## Plasmablastic lymphoma: Are more intensive regimens needed?

**Keywords:**

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In this issue of *Leukemia Research*, Liu et al. [1] present one of the largest case series to date on nine patients with a pathological diagnosis of HIV-negative plasmablastic lymphoma (PBL), and suggest that hematopoietic stem cell transplantation (HSCT) in first remission could derive on better outcomes in this rather aggressive B-cell lymphoma. PBL is a rare subtype of diffuse large B-cell lymphoma (DLBCL), which was initially described in patients with HIV infection. However, more recently, several cases of PBL have been identified in patients without HIV infection.

In general, PBL poses a diagnostic challenge given the lack of expression of CD20 by the malignant cells. Nonetheless, based on molecular studies, the B-cell lineage of PBL has been demonstrated. Interestingly, using immuno-histochemical studies, PBL shares several features with plasma cell myeloma, but based on genomic analysis, PBL shows significant overlapping features with DLBCL. Thus, the cell of origin of PBL seems to be an activated post-germinal center B-cell in transformation into a plasma cell. Despite this apparent common ground, several differences have been identified in HIV-positive and HIV-negative patients with PBL [2], which are confirmed in the present study by Liu and colleagues, likely a reflection of the molecular heterogeneity of PBL.

Several studies have emphasized on the poor prognosis that a diagnosis of PBL carries, with median overall survival times ranging between 12 and 15 months, despite the use of intensive chemotherapeutic regimens [3]. Indeed, the clinical course of PBL is characterized by an aggressive course and high rates of relapse. Furthermore, the most common cause of death reported in PBL patients is progression of disease. The clinical aggressiveness of PBL can be explained, in part, by the lack of expression of CD20 and the plasmacytic differentiation seen in PBL cells. In a fairly recent study, CD20-negativity has been associated with inferior survival in patients with DLBCL treated with CHOP or R-CHOP. CD20 negativity was an adverse prognostic factor independent of the International Prognostic Index (IPI). Consistent with these

findings, other aggressive CD20-negative B-cell lymphomas with plasmacytic differentiation such as primary effusion lymphoma or anaplastic lymphoma kinase-positive DLBCL have also been associated with primary chemoresistance, high relapse rates and poor prognosis. Finally, recurrent C-MYC rearrangements have been the most common chromosomal abnormality found in PBL, conferring a poor prognosis.

The treatment of PBL has not been standardized, although it is a common practice to start patients on combination chemotherapy with or without highly active antiretroviral therapy. In the current National Comprehensive Cancer Network guidelines, the recommendation is to treat HIV-positive or HIV-negative PBL with intensive regimens such as CODOX-M/IVAC, EPOCH or hyperC-VAD [4]. Specifically, the guidelines state that standard CHOP is not adequate therapy. It is important to note that no prospective studies have ever been done in patients with PBL; hence, these recommendations are based on consensus derived from case reports and small case series. However, in a recent literature review study that compiled data from 70 HIV-associated PBL patients treated with chemotherapy, there was no statistical difference between 35 patients treated with CHOP or CHOP-like regimens and 16 patients treated with more intensive regimens (18 vs. 16 months, respectively;  $p=0.84$ ) [5].

Nonetheless, the prognosis of PBL patients remains poor and novel approaches are needed. Agents borrowed from the plasma cell myeloma therapy, such as bortezomib, and consolidation with high dose chemotherapy followed by autologous stem cell rescue could prove to be of value in PBL. Although there are just a few cases reporting responses to bortezomib in the relapsed setting, it poses an interesting question since bortezomib in combination with chemotherapy seems to improve response and survival rates in patients with DLBCL of a post-germinal center origin [6]. The data available on HSCT in PBL are rather scant; however, a potential benefit in patients obtaining a first complete remission cannot be discarded. Such approach has shown potential survival benefit in other lymphomas with poor prognosis, such as peripheral T-cell lymphoma. Furthermore, a recent study presented at the most recent American Society of Clinical Oncology Annual Meeting suggests that autologous HSCT is associated with improved survival in patients DLBCL with high-risk IPI scores in first remission [7].

Ideally, therapeutic approaches should be evaluated in prospective settings. However, given the scarcity of PBL cases, this could prove to be a nearly impossible task without multi-institutional and/or international collaboration. In the meantime, recommendations arising from isolated case reports, small case

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series, transplanted data from other more common aggressive B-cell lymphomas and our best clinical judgment will have to do.

#### Conflict of interest

J.J.C. has no conflict of interest to declare.

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*Contribution.* J.J.C. researched and wrote manuscript.

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