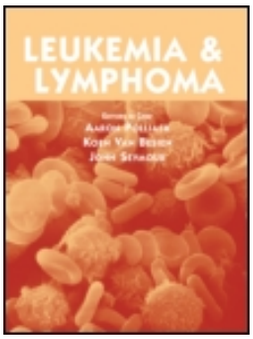

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COMMENTARY

Peripheral T-cell lymphomas: in "real life" experience are we really improving?

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Peripheral T-cell lymphomas (PTCLs) represent the "bad cousins" of the non-Hodgkin lymphoma (NHL) family. PTCLs are a heterogeneous group of malignancies derived from post-thymic T cells, representing approximately 11% of all cases of NHL included in the International Lymphoma Study Group [1]. The most commonly encountered subtypes are the so-called nodal PTCLs: PTCL not otherwise specified (PTCL-NOS), systemic anaplastic large cell lymphoma (ALCL) and angioimmunoblastic T cell lymphoma (AITL). With the exception of ALCL (particularly the subtype positive for anaplastic lymphoma kinase), they are mostly characterized by a dismal prognosis. Several clinical studies have reported a median survival of less than 2 years for patients with PTCLs and 5-year overall survival (OS) rates of less than 30% [2,3]. In their article published in this issue of ***Leukemia and Lymphoma***, Broussais-Guillaumot *et al.* [4] report the daily experience in the treatment and outcome of patients with PTCL in "reality." Their data are the reflection of the true situation we in fact have and witness in hematologic institutions around the world: 48% of patients achieved a complete response to the CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy induction regimen, with 5-year OS and event-free survival rates of 28% and 18%, respectively, for the entire population.

Unfortunately, CHOP still remains the standard front-line chemotherapy regimen. The evolution of PTCL biology and therapy has lagged behind that of B-cell lymphomas, partly due to the fact that in the lymphoproliferative world, PTCLs have only relatively recently been identified as distinct from their B-cell counterparts [5]. The explanation for the poor treatment outcome in patients with PTCLs in contrast to those with aggressive B-cell lymphomas remains uncertain. However, one possibility is that the rarity of these disorders has made them difficult to study, and the results for patients with PTCLs in studies relating to the therapy of aggressive NHL are "lost," because these cases represent such a small proportion of all those being studied. The one thing that can be said with certainty is: what we currently consider optimal treatment for diffuse large B-cell lymphoma is not equally efficacious for PTCL. Durable remissions are uncommon with CHOP-based chemotherapy, particularly in those patients with high risk disease [6]; however, some patients respond to secondary treatment and are able to proceed to high dose chemotherapy and stem cell transplant [7], which is considered the standard of care in this setting.

Relapsed/refractory PTCL is a rare disease that follows a more aggressive clinical course than other lymphomas and is associated with the poorest prognosis of all histological subtypes of NHL. Patients who do not respond to front-line treatment or who relapse after a response to such treatment are in fact often either ineligible for transplant or relapse after transplant. The availability of agents with the potential to induce a response and prevent the disease from further progression is critical for the treatment and continued survival of these patients. The survival rates in PTCL fall even lower following relapse from second and further lines of treatment, as evidenced by the survival after failure. Recognizing the fact that relapsed/refractory PTCL represents an unmet medical need, in the last several years there have been a number of novel therapies tested specifically in relapsed/refractory PTCLs [8]. Further, data are emerging to suggest that PTCLs may be selectively sensitive to drugs that are not as active in aggressive B-cell lymphomas [8], providing a strong rationale to study these diseases separately.

The history of PTCL is abundant, and significant advances have been made over the past few years. From a therapeutic perspective, the new biopathologic and pharmarmacologic advances have led to a "boost" in the development of novel therapeutic approaches for PTCLs. Among these new agents, most recently, three agents have obtained Food and Drug Administration (FDA) approval for relapsed/refractory patients: pralatrexate, a folate antagonist; romidepsin, a histone deacetylase inhibitor; and brentuximab vedotin (only for patients with ALCL), an anti-CD30 antibody–drug conjugate [9–12]. On the basis of these interesting advances on pretreated patients with PTCL, the next probable step

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will be to add these T-cell specific agents to the conventional front-line CHOP regimen; and there are in fact some phase III trials including CHOP with these three approved agents in the up-front setting.

Finally, as several factors contribute to the prognosis of patients with PTCL (e.g. subtype and demographics), not all therapies achieve the same efficacy for all patients with PTCL, and the majority of patients will ultimately relapse, even following initially effective therapy. Thus, it is critical that the treating physicians keep an armamentarium of available validated therapeutic options to sequentially treat patients and thereby keep PTCL at bay for as long as possible.

Potential conflict of interest: A disclosure form provided by the author is available with the full text of this article at www.informahealthcare.com/lal.

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