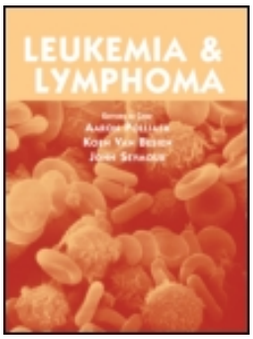

Leukemia & Lymphoma

ISSN: 1042-8194 (Print) 1029-2403 (Online) Journal homepage: informahealthcare.com/journals/ilal20

Intensive chemotherapy without stem cell transplant for indolent lymphomas

Clemens-Martin Wendtner

To cite this article: Clemens-Martin Wendtner (2011) Intensive chemotherapy without stem cell transplant for indolent lymphomas, Leukemia & Lymphoma, 52:11, 2039-2040, DOI: 10.3109/10428194.2011.606385

To link to this article: https://doi.org/10.3109/10428194.2011.606385

Leukemia & Lymphoma, November 2011; 52(11): 2039–2040

ISSN: 1042-8194 print / 1029-2403 online
DOI: 10.3109/10428194.2011.606385

informa
healthcare

COMMENTARY

Intensive chemotherapy without stem cell transplant for indolent lymphomas

Clemens-Martin Wendtner

University of Cologne, Cologne, Germany and Klinikum München-Schwabing, Munich, Germany

Based on the many treatment options for front-line therapy, indolent lymphomas seem to have lost their threat. Generally accepted approaches now include the more or less toxic induction chemotherapeutic regimens such as cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP), bendamustine and others, including use of the anti-CD20 monoclonal antibody rituximab. Nowadays the major threat, however, is that the disease becomes chronic in a negative sense, i.e. that it inevitably relapses after a variable period of time. Douglas Gladstone and his colleagues try to address this problem by a consolidation strategy using a non-transplant approach [1]. Patients with indolent lymphomas were offered treatment with high-dose cyclophosphamide combined with high-dose rituximab without stem-cell support. How do their results impact on current strategies in this setting?

Before putting the data into context, some limitations of the study have to be critically discussed. The trial included subgroups of indolent lymphomas with quite different prognoses, ranging from chronic lymphocytic leukemia (CLL) to transformed lymphomas and mantle cell lymphoma. This is critically important because the overall sample size with 81 patients is limited. Second, patients receiving consolidation treatment after first complete remission were analyzed together with individuals receiving cyclophosphamide and rituximab after a partial response or even after salvage therapy. Third, the outcome figures presented in this study seem to be inferior to data presented for patients receiving aggressive transplant conditioning regimens and stem cell rescue as have been studied by the Nordic Lymphoma Study Group and the M. D. Anderson Cancer Center Group [2,3]. But this comparison might be unfair, given that a less toxic outpatient-based treatment approach was intended by the authors. A more relevant question may be whether this non-transplant approach was truly non-toxic and allowed patients to avoid hospitalization. The authors report that about half of their patients required admission to the hospital, albeit the majority only for a short duration.

Despite all these limitations, this article adds to the currently available strategies for consolidation of indolent lymphomas in order to prevent disease relapse. Do we have nowadays even less toxic options available besides autologous transplant and the doublet cyclophosphamide and rituximab therapy described here? At least for the group of patients with follicular lymphomas, the time for chemotherapy-based consolidation, whether based on stem-cell support or not, seems to be over. Instead of consolidation, maintenance with rituximab over a longer period of time, currently defined as 2 years by data from the PRIMA trial (Primary RItuximab and MAintenance), is the accepted standard [4]. Toxicity is less compared to the cyclophosphamide/rituximab combination. And high efficacy with respect to event-free survival (EFS) and overall survival (OS) seems to be achievable with rituximab alone as maintenance treatment in indolent lymphomas. Longer treatment episodes with rituximab being given 1 day every 2 or 3 months over a total period of up to 4 years or even indefinitely (until disease progression) are currently undergoing evaluation in different trials worldwide. Drugs besides rituximab might also come into play, such as lenalidomide or even some of the new-generation small molecules interfering with the malignant B cell signaling, i.e. the phosphoinositide-3 (PI3) kinase inhibitor CAL-101, Bruton's tyrosine kinase inhibitor PCI-32765 and others [5,6]. They offer hope of a better tolerated treatment that assures prolonged control of indolent lymphomas in all, including the elderly, and that ultimately indolent lymphoma will be rendered into a chronic disease without the need for aggressive interventions.

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.

References

[1] Gladstone DE, Bolaños-Meade J, Huff CA, et al. High-dose cyclophosphamide and rituximab without stem cell transplant: a feasibility study for low grade B-cell, transformed and mantle cell lymphomas. Leuk Lymphoma 2011;52:2076–2081.
[2] Tam CS, Bassett R, Ledesma C, et al. Mature results of the MD Anderson Cancer Center risk-adapted transplantation strategy in mantle cell lymphoma. Blood 2009;113:4144–4152.

Correspondence: Prof. Clemens-Martin Wendtner, University of Cologne, Cologne, Germany and Klinikum München-Schwabing, Munich, Germany. E-mail: clemens.wendtner@uni-koeln.de
This commentary accompanies an article to be published in *Leukemia & Lymphoma*. Please refer to the table of contents of the print issue in which this commentary appears.

[3] Geisler CH, Kolstad A, Laurell A, et al. Long-term progression-free survival of mantle cell lymphoma after intensive front-line immunochemotherapy with in vivo-purged stem cell rescue: a nonrandomized phase 2 multicenter study by the Nordic Lymphoma Group. Blood 2008;112:2687–2693.
[4] Salles G, Seymour JF, Offner F, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomized controlled trial. Lancet 2011;377:42–51.
[5] Herman SEM, Gordon AL, Wagner AJ, et al. The phosphatidylinositol 3-kinase-delta inhibitor CAL-101 demonstrates promising preclinical activity in chronic lymphocytic leukemia by antagonizing intrinsic and extrinsic cellular survival signals. Blood 2010;116:2078–2088.
[6] Burger JA, O'Brien S, Fowler N, et al. The Bruton's tyrosine kinase inhibitor PCI-32675 is well tolerated and demonstrates promising clinical activity in chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL): an update on ongoing phase 1 studies. Blood 2010;116(Suppl. 1): Abstract 57.