



## Letter to the Editor

### A therapeutic dilemma between the two “R”s: additional rituximab or radiotherapy for limited, non-bulky diffuse large B-cell lymphoma

**TO THE EDITOR:** Limited disease, defined as Ann Arbor stage I and non-bulky stage II, accounts for approximately 25% of diffuse large B-cell lymphomas (DLBCLs). Since the Southwest Oncology Group (SWOG) study 8736 demonstrated that 3 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) followed by involved-field radiotherapy (IFRT) was superior to 8 cycles of CHOP [1], a short course of chemotherapy followed by IFRT has been the main treatment for limited, non-bulky DLBCL. This treatment strategy has not changed even after the efficacy of rituximab-CHOP (R-CHOP) was proved in the Groupe d'Etude des Lymphomes de l'Adulte (GELA) study of advanced-stage DLBCL [2]. Hence, the current National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (Version 1. 2011) recommend 2 treatment options for stage I/II, non-bulky DLBCL: 3 cycles of R-CHOP with subsequent IFRT and 6 cycles of R-CHOP with or without IFRT. However, the role of radiotherapy for controlling localized DLBCL has been debatable because radiotherapy-associated toxicity may deteriorate the quality of life as well as survival outcome, and in many patients, the disease may relapse outside the radiation field [1, 3]. There is also the risk of secondary malignancies caused by exposure to the radiation field [1, 3]. This controversial use of radiotherapy for consolidation has been augmented by the result of a GELA trial (LNH 93-4) that compared 4 cycles of CHOP with or without IFRT for patients older than 60 years with

limited DLBCL and showed similar outcomes [3].

The need for radiotherapy has been challenged since R-CHOP was used as standard treatment for patients with DLBCL. No study has compared the effect of a short course of R-CHOP plus radiotherapy with extended cycles of R-CHOP alone for limited DLBCL; hence, physicians can choose to perform IFRT or 3 additional cycles of R-CHOP at their discretion. Because the selection of a treatment modality for consolidation after 3 cycles of R-CHOP is debatable, 3 additional cycles of R-CHOP or IFRT are suggested as a therapeutic option in the NCCN guidelines.

In the previous issue, Hong et al. reported the results of comparing 3-4 cycles of R-CHOP plus IFRT with 6-8 cycles of R-CHOP alone in limited, non-bulky DLBCL [4]. The 2 groups that were compared showed similar 3-year overall survival (OS). Their OS was comparable to that observed in a previous study (SWOG 0014) that tested the utility of adding 4 doses of rituximab to 3 cycles of CHOP with subsequent IFRT [5]. However, the study by Hong et al. involved a retrospective analysis with a small number of patients. Their results do not provide information helpful in selecting a treatment strategy. Furthermore, extended cycles of R-CHOP might increase the risk of febrile neutropenia, as evidenced by 1 treatment-related mortality that occurred in the group that underwent 6-8 cycles of R-CHOP [4]. Therefore, the selection of additional R-CHOP or IFRT as a consolidation for limited, non-bulky DLBCL will remain a therapeutic dilemma until a prospective study involving a large study population is conducted.

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