Commentary

Radioimmunotherapy in limited-stage diffuse large B-cell lymphoma

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Patients with limited-stage aggressive B-cell lymphoma without adverse risk factors are generally cured when treated by short-term therapy, with overall survival (OS) at 10 years ranging from 94% to 97% (1,2). However, limited-stage diffuse large B-cell lymphoma (DLBCL) patients with adverse risk factors including stage II disease, age >60 years, elevated serum lactate dehydrogenase (LDH), and poor performance status have a relatively unfavorable outcome, with a 5-year OS of 50% to 77% and a 10-year OS of 0% to 50%, and treatment optimization is needed for this subtype patients (1-4).

Radiolabeled anti-CD20 antibody ibritumomab tiuxetan (Zevalin) has shown promising efficacy in the treatment of patients in the rituximab-naive patients with DLBCL (5). Persky *et al.* investigated that if the addition of Zevalin to cyclophosphamide hydroxydaunomycin oncovin prednisone (CHOP) (3) plus institute for fitness research and training (IFRT) can improve the outcome of patients with limited-stage aggressive B cell lymphoma having at least one high-risk factor in a prospective single-arm phase II study Southwest Oncology Group (SWOG S0313) (6). The outcome of these patients is favorable compared with historical data, with a 5-year propellent feed system (PFS) of 82% and OS of 87%, which was superior to that of patients with limited aggressive non-Hodgkin's lymphoma (NHL). While compared with SWOG S0014 in which four doses of rituximab were combined with CHOP (3) and followed by IFRT, the results of current study appeared to be similar to that of SWOG S0014 (5-year PFS 78%, 5-year OS 83%). However, with longer follow up, the relapse in current study seemed to be fewer than those of prior trials. And treatment side effects was well-managed with no secondary myeloid neoplasms, and only 2 patients truncated due to toxicity, these data support the value of radioimmunotherapy in first-line treatment of limited-stage DLBCL patients with adverse risk factors.

However, several aspects of this study should be addressed. First of all, this was a single-arm, prospective clinical trial, only 46 patients were enrolled into this trial, and the results of this study was compared with historical data. Similar to other SWOG studies (SWOG S0014, SWOG S8736), most patients enrolled in this study were low risk with only one adverse factor who usually have a good prognosis, while stage II patients with bulky disease, which usually have a inferior outcome, are excluded from this study (7,8). Secondly, staging and evaluation using positron emission tomography computer tomography (PET-CT) scan is not required in this study, however, PET-CT scan is very import in the evaluation of the response to chemotherapy, because complete remission evaluated by fluorodeoxyglucose-PET (FDG-PET) scan post induction-chemotherapy always indicate a very favorable outcome in early stage patients treated by CHOP (3) ± R and followed by IFRT (9). Last, the treatment schedule in this study included 40–50 Gy IFRT of radiotherapy, the potential long-term radiation-related side effects should be considered. Although there were no patients who developed treatment-related myeloid neoplasms, data of other solid tumors and long-term side effects were not mentioned.

Introduction of rituximab or Zevalin in treatment protocols has significantly improved the prognosis of limited-stage aggressive B-cell lymphoma with at least one risk factor, compared with treatment of CHOP (3) plus IFRT. The treatment protocols in this study, SWOG S0014 (3 × R – CHOP + IFRT), Ricover-60 and MINT (6 × R – CHOP ± 2R) have significantly improved the outcome of patients with limit-stage DLBCL, and survival of patients in this study seems to be superior to those of others (10-12).

However, it is difficult to draw a final conclusion, because there are no randomized controlled clinical trials to evaluate the efficacy between these different treatment strategies. In conclusion, a randomized controlled clinical trial is needed to determine whether the protocol comprising radioimmunotherapy and CHOP (3) plus IFRT is associated with a better prognosis in patients with limit-stage aggressive B cell lymphoma having at least one risk factor.

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Footnote

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