To the editor:

Rhenium-labeled anti-CD20 antibody radioimmunotherapy followed by autologous peripheral blood stem cell transplantation in patients with relapsed or refractory non-Hodgkin lymphoma

We read with interest the article of Gopal et al1 on the use of high-dose radioimmunotherapy in relapsed follicular lymphoma. Here, we report on our experience using a rhenium 186 (186Re)–labeled chimeric anti-CD20 antibody (rituximab). We chose 186Re as treatment isotope because of its favorable physical properties (3.7 d half-life; 1070 keV β-energy; 9.5% 137 keV γ-radiation). The γ-radiation enables intratherapeutic imaging and dosimetry. Furthermore, a stable antibody-labeling technique had been developed for both 186Re and 99 metastable (99m) technetium (99mTc). 2,3 186Re was generated by neutron irradiation of 185Re in the high-flux position of the University of Missouri Research Reactor.

We treated 4 patients with refractory or relapsed diffuse large B-cell lymphoma (DLBCL; n = 2), mantle cell lymphoma (MCL; n = 1), and follicular lymphoma (n = 1) (Table 1). To determine antibody uptake in the tumor and to measure blood kinetics, an imaging study with 1.5 to 2 GBq 99mTc-labeled antibody (10-20 mg) was performed. The blood radioactivity curve was fitted biexponentially. While the initial decrease reflected spleen uptake, the second phase matched early kinetics and distribution if predosing was applied as done for treatment. Dose of radioactivity for treatment in order to obtain a blood dose of 25 Gy (n = 3) and 30 Gy (n = 1), respectively, was calculated from the blood kinetics of the test-application and the physical half-life of 186Re. Total antibody dose was 3 mg/kg. A dose of 1.5 to 2 mg was given unlabeled one hour before the Re-antibody infusion. The patients received a total blood dose of 24 to 26 Gy (n = 3) and 38 Gy (n = 1). When residual bone marrow dose was less than 0.3 Gy, the patients’ stem cells (2.92 × 106 CD34+ cells/kg body weight [range, 1.78-4.42 × 106 CD34+ cells/kg body weight]) were reinfused (d 8-13 after treatment). All patients experienced myeloaebitation. Time to neutrophil counts of at least 0.5 × 109/L was 10 days (range, 9-11 days) after transplantation, and time to platelet counts of at least 25 × 109/L was 12 days (range, 11-14 days) after transplantation. Neutropenia lasted 17 days (range, 11-22 days) and thrombocytopenia 16.5 days (range, 10-24 days). Toxicity was limited, with no grade III or grade IV nonhematologic toxicity according to a modified Bearman scale.4 Grade II infection was seen in 2 patients. We observed no treatment-associated mortality.

Two patients with DLBCL received radioimmunotherapy; a 57-year-old woman (no. 1) with refractory disease who had undergone prior high-dose chemotherapy achieved a complete remission that lasted for 42 months; and a 25-year-old male patient (no. 4) with refractory disease achieved mixed response. Patient no. 2 with MCL showed stable disease (SD) initially after radioimmunotherapy. Thus, he received additional chemotherapy. The patient experienced a protracted remission and finally achieved a complete remission (CR) with a duration of 7 months. Patient no. 3, who had follicular non-Hodgkin lymphoma (NHL), did not show a response.

Thus, high-dose radioimmunotherapy with 186Re followed by autologous peripheral blood stem cell transplantation (PBSCT) seems to be a feasible therapeutic option even in extensively pretreated patients with relapsed non-Hodgkin lymphoma.5 Patients achieving CR had a low tumor burden with a lactate dehydrogenase (LDH) level in the normal range. This finding is in accordance with a larger series reported previously.6

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References


Table 1. Patient characteristics

<table>
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<tr>
<th>Patient no.</th>
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<th>Age, y</th>
<th>Histologic type</th>
<th>Stage</th>
<th>Extranodal involvement</th>
<th>LDH elevation</th>
<th>No. prior chemotherapy regimens</th>
<th>Prior high-dose therapy</th>
<th>Response to last therapy</th>
<th>Bulky disease</th>
<th>Outcome after RIT</th>
<th>Duration of response, mos.</th>
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*SD was documented initially after RIT and CR was achieved after additional chemotherapy.

Bulky disease indicates largest tumor manifestation greater than or equal to 10 cm; RIT, radioimmunotherapy; DLBCL, diffuse large B-cell lymphoma; CR, complete remission; MCL, mantle cell lymphoma; FL, follicular lymphoma; PD, progressive disease; —, not applicable (patient did not experience any remission); and MR, mixed response.
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