

Radiolabeled Immunotherapy in Non-Hodgkin's Lymphoma: The Perception in Clinical Oncology Needs Further Attention

Andreas Otte*

Division of Biomedical Engineering, Faculty of Electrical Engineering and Information Technology, Offenburg University, Badstr. 24, D-77652 Offenburg, Germany

***Corresponding Author:** Andreas Otte, Division of Biomedical Engineering, Faculty of Electrical Engineering and Information Technology, Offenburg University, Badstr. 24, D-77652 Offenburg, Germany, Email: andreas.otte@hs-offenburg.de

EDITORIAL

Internal radio-immunotherapy (RIT) has achieved fundamental clinical successes in the past. Its commercial availability is, however, poor.¹⁻³ Only few, as e.g. ⁹⁰Y-ibritumomab tiuxetan (Zevalin), have gone to market but still pose a number of challenges since many years, the main one being health economics. In an article published in the *New York Times* of 14 July 2007, entitled 'Market Forces Cited in Lymphoma Drugs' Disuse',⁴ this dilemma of innovation and health politics is presented by three embarrassing case studies of patients having late-stage Non-Hodgkin's lymphoma (NHL): All three recovered after a single dose of Bexxar or Zevalin, and all three were in the prestigious role to receive these treatment options at all, as, at that time, in the United States these options were used little by physicians due to the unacceptable reimbursement situation.⁵

From a cost-effectiveness point of view, this is not understandable, since, already a year before, in 2006, data for Zevalin provided convincing support in favour of its added value in terms of cost per month in remission or cost per disease-free month despite higher initial product acquisition costs⁶.

Even more, in a recent state-of-the-art seminar on NHL, published in one of the premier journals, *The Lancet*,⁷ Shankland and colleagues discussed advances in the understanding of the biology and new, available therapy regimens for this indication. In their comprehensive review they indeed briefly described radiolabeled immunotherapy (RIT) options, such as ⁹⁰Y-ibritumomab tiuxetan for the treatment of follicular lymphoma. However, other indications of this new RIT approach are not mentioned in this article, although there are also

several entities that have been evaluated with convincing results for this new treatment approach, interesting and important enough to mention for patients and treating physicians: e.g., indolent and aggressive NHL⁸, relapsed diffuse large B-cell lymphoma^{e.g., 9}, mantle cell lymphoma^{e.g., 10}, multiple myeloma¹¹, primary central nervous system lymphoma¹², Hodgkin's lymphoma¹³, marginal zone lymphoma¹⁴, or Richter syndrome¹⁵ (for a detailed review, see, e.g.,¹⁶). Zevalin can not only be used as add-on treatment, but can also be considered alone in first-line treatment of follicular NHL.¹⁷

RIT with ⁹⁰Y-ibritumomab tiuxetan offers a lot of advantages to patients if compared to older chemotherapy combinations: The easy clinical setting with only two sessions within a week, no need for preliminary diagnostic imaging to estimate dose prior to treatment, and, last but not least, several quality-of-life advantages (no hair loss, to mention only one).^{18, 19} Today, 2018, the RIT alternative to common chemotherapy regimens in NHL seems still not present in clinical practice.

To conclude, the perception of RIT in NHL, as we think, still needs further attention as it is a valuable aid or even alternative to conventional chemotherapy schemes in NHL. In addition to its efficacy there is also convincing data on cost-effectiveness. Therefore, the perception of RIT in clinical oncology should be updated. This could work if the partners, oncologists, nuclear medicine physicians, and health economists take up the discussion – together, not separately, and as peers.

REFERENCES

- [1] Otte A, Jermann E, Behe M, Goetze M, Bucher HC, Roser HW, Heppeler A, Mueller-Brand J, Maecke HR. DOTATOC - a powerful new tool

- for receptor-mediated radionuclide therapy. *Eur J Nucl Med* 1997; 24:792-795
- [2] Otte A, Mueller-Brand J, Dellas S, Nitzsche EU, Herrmann R, Maecke HR. Yttrium-90-labelled somatostatin-analogue for cancer treatment. *Lancet* 1998; 351:417-418
- [3] Merlo A, Hausmann O, Wasner M, Steiner P, Otte A, Jermann E, Freitag P, Reubi JC, Muller-Brand J, Gratzl O, Macke HR. Locoregional regulatory peptide receptor targeting with the diffusible somatostatin analogue ⁹⁰Y-labeled DOTA⁰-D-Phe¹-Tyr³ octreotide (DOTATOC): a pilot study in human gliomas. *Clin Cancer Res* 1999; 5:1025-1033
- [4] Berenson A. Market forces cited in lymphoma drugs' disuse. *The New York Times* 14 July 2007
- [5] Otte A. Does health economics have an impact on non-Hodgkin's lymphoma patients' options? *Nucl Med Comm* 2008; 29:748-749
- [6] Otte A, Thompson SL. Practical and health economic aspects of radioimmunotherapy for the treatment of patients with non-Hodgkin's lymphoma. *Nucl Med Comm* 2006; 27:753-756
- [7] Shankland KR, Armitage JO, Hancock BW. Non-Hodgkin lymphoma. *Lancet* 2012; 380:848-57
- [8] Emmanouilides C. Radioimmunotherapy for non-hodgkin lymphoma: historical perspective and current status. *J ClinExpHematop* 2007; 47:43-60
- [9] Morschhauser F, Illidge T, Huglo D, Martinelli G, Paganelli G, Zinzani PL, Rule S, Liberati AM, Milpied N, Hess G, Stein H, Kalmus J, Marcus R. Efficacy and safety of yttrium-90 ibritumomab tiuxetan in patients with relapsed or refractory diffuse large B-cell lymphoma not appropriate for autologous stem-cell transplantation. *Blood* 2007;110:54-8
- [10] Bertoni F, Ghilmini M, Cavalli F, Cotter FE, Zucca E. Mantle cell lymphoma: new treatments targeted to the biology. *ClinLymphoma* 2002;3:90-6
- [11] Chatterjee M, Chakraborty T, Tassone P. Multiple myeloma: monoclonal antibodies-based immunotherapeutic strategies and targeted radiotherapy. *Eur J Cancer* 2006; 42:1640-52
- [12] Pitini V, Baldari S, Altavilla G, Arrigo C, Naro C, Perniciaro F. Salvage therapy for primary central nervous system lymphoma with (90)Y-Ibritumomab and Temozolomide. *J Neurooncol* 2007;83:291-293
- [13] Schnell R, Dietlein M, Schomäcker K, Kobe C, Borchmann P, Schicha H, Hallek M, Engert A. Yttrium-90 ibritumomab tiuxetan-induced complete remission in a patient with classical lymphocyte-rich Hodgkin's lymphoma. *Onkologie* 2008; 31:49-51
- [14] Vanazzi A, Ferrucc PF, Grana C, Pruneri G, Crosta C, Pinto A, Chinol M, Paganelli G, Martinelli G. Efficacy of ⁹⁰Y-Ibritumomab Tiuxetan in Marginal-Zone Lymphoma (MZL). *Blood* 2007; 110 (11): abstract 4499
- [15] Tsimberidou AM, Murray JL, O'Brien S, Wierda WG, Keating MJ. Yttrium-90 ibritumomab tiuxetan radioimmunotherapy in Richter syndrome. *Cancer* 2004; 100:2195-200
- [16] Otte A, Van de Wiele C, Dierckx RA. Radiolabelled immunotherapy in non-Hodgkin's lymphoma – the next step. *Nucl Med Commun* 2009; 30:5-15
- [17] Bodet-Milin C, Ferrer L, Pallardy A, Eugène T, Rauscher A, Alain Faivre-Chauvet, Barbet J, Kraeber-Bodéré F. Radioimmunotherapy of B-Cell Non-Hodgkin's Lymphoma. *Front Oncol* 2013; 3:177. doi: 10.3389/fonc.2013.00177. eCollection 2013.
- [18] Otte A. Value of diagnostic imaging prior to ⁹⁰Y-ibritumomab tiuxetan (Zevalin®) treatment in follicular non-Hodgkin's lymphoma (NHL). *Hell J Nucl Med* 2008; 11:12-15.
- [19] Witzig TE, Gordon LI, Cabanillas F, Czuczman MS, Emmanouilides C, Joyce R, Pohlman BL, Bartlett NL, Wiseman GA, Padre N, Grillo-Lopez AJ, Multani P, White CA. Randomized controlled trial of yttrium-90-labeled ibritumomab tiuxetan radioimmunotherapy versus rituximab immunotherapy for patients with relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma. *J ClinOncol* 2002; 20:2453-63

Citation: Andreas Otte. Radiolabeled Immunotherapy in Non-Hodgkin's Lymphoma: The Perception in Clinical Oncology Needs Further Attention. *ARC Journal of Radiology and Medical Imaging* 2018; 3(1): 18-19

Copyright: © 2018 Authors. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.