



Book Reviews

Resistance to ibritumomab in lymphoma, M. Hosono, J.F. Chatal, editors (Springer International Publishing, Switzerland) 2018. 158 pages. Price: Not mentioned.

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Non-Hodgkin's lymphoma (NHL) is a clinically and molecularly heterogeneous group of malignant lymphoproliferative diseases. Diffuse large B cell NHL (DLBCL) is the most common subtype followed by indolent or low-grade lymphomas [follicular lymphoma (FL), being the most common subtype among indolent-type lymphoma]. Addition of anti-CD20 therapy (immunotherapy, rituximab) to cyclophosphamide, doxorubicin, vincristine and prednisone results in cure in over half of the patients and is currently the standard of care. For asymptomatic, low-tumour burden FL, a 'wait-and-watch' policy is generally followed. Early-stage FL is treated with local radiation. For symptomatic FL the first-line treatment is chemo-immunotherapy followed by two-year maintenance therapy with anti-CD20 monoclonal antibodies. The CD20 antigen is a transmembrane protein that acts as a calcium channel and plays a key role in cell cycle progression and differentiation of B cells. CD20 antigen is present in approximately 9 per cent of peripheral blood mononuclear fraction and >90 per cent of B cells from blood and lymphoid organs. Lymphoma cells from >90 per cent of patients with B cell NHL express this antigen. Therefore, CD20 is an attractive target molecule in the treatment of B cell NHL.

A number of radionuclides are being used in medicine either for diagnosis or therapy. Monoclonal antibodies are considered efficient carriers for radionuclides to be delivered to the target (also called radio-immunotherapy, RIT). Radiolabelled compounds (therapeutic radiopharmaceuticals) once administered reach to the target molecule present on the surface of

tumour cells and directly interact with these cells. The ^{90}Y -labelled ibritumomab tiuxetan is one such therapeutic radiopharmaceutical that conjugates an anti-CD20 monoclonal antibody with the beta-emitting radionuclide ^{90}Y using the chelating agent tiuxetan; ^{90}Y is a pure beta emitter with a half-life of 64 h (2.7 days) that decays to ^{90}Zr . It has an effective path length of 5.3 mm, meaning that 90 per cent of its energy is absorbed within a sphere with 5.3 mm radius.

Ibritumomab tiuxetan, the ^{90}Y immunotherapy (^{90}Y -IT), was approved for the treatment of relapsed indolent or low-grade FLs or transformed B cell NHL and for patients with rituximab-refractory follicular NHL. This therapy should be considered for patients with indolent lymphoma in the first relapse, who have tumour long-axis diameter ≤ 2.5 cm and $\text{SUV}_{\text{max}} \leq 6.5$. ^{90}Y -IT improves the response rate and outcomes of relapsed/refractory DLBCL patients and in mantle cell lymphoma (MCL) where it has been used to treat minimal residual disease (as consolidation) after first-line chemotherapy. In addition to RIT, recently, there has been development of new classes of highly effective immunotherapeutic approaches including chimeric antigen receptor T cell therapy that are designed to bypass cancer immune evasion.

This book is arranged in 10 chapters: the first chapter gives a comprehensive overview of the clinical use, efficacy, toxicity and safety profile of ibritumomab. ^{90}Y -IT uses an antibody to mediate complement-mediated cytotoxicity, along with the delivery of high-energy, short path length (5 mm) beta irradiation from ^{90}Y to both CD20-lymphoma cells and neighbouring tumour cells that are inaccessible to the antibody or have insufficient antigen expression as a result of a cross-fire effect, with little effect on other solid organs. The expected short-term toxicity associated with ^{90}Y -IT is mainly reversible myelosuppression followed by the

potential development of myelodysplastic syndrome and secondary leukaemia in long term. The second chapter deals with the biology and pathology of B cell lymphomas. The heterogeneity of B cell NHL is nicely captured through WHO classification and the cellular origin of B of mature B cell neoplasms. Better understanding of the microenvironmental interactions in B cell lymphomas has led to the identification of targets and development of newer targeted therapies. The third chapter deals with the issue of resistance to ^{90}Y ibritumomab tiuxetan therapy. It has been suggested that bulky disease, downregulation of CD20 or activation of NF- κB or a combination of these factors is the potential cause of resistance to ^{90}Y -IT.

The next three chapters deal with the characteristics of ibritumomab, radiation dosimetry and response evaluation. ^{18}F -fluorodeoxyglucose positron emission tomography (^{18}F -FDG PET)/computed tomography scan is currently the standard investigation for the evaluation of response for lymphoma. Negative PET finding at three months after ^{90}Y -IT is highly predictive of complete response. However, metabolic response to ^{90}Y -IT could be gradual with continued declines of FDG uptake occurring between 7 and 9 months after therapy; therefore, PET-positive result after three months does not warrant immediate additional therapy.

The subsequent chapter deals with the preparation and schedule of ^{90}Y -IT administration, resistance and heterogeneity of intratumoral antibody distribution and data on radiation dosimetry for patients receiving ibritumomab therapy. The authors described combining radionuclide therapy and other immune-based therapies to overcome resistance in cancer. In the concluding chapter the authors describe prospects for enhancing the efficacy of RIT which has been little utilized because of a variety of medical, financial and logistic obstacles. Newer technologies employing multistep 'pre-targeting' methods, particularly those utilizing bi-specific antibodies, have greatly enhanced the therapeutic efficacy of RIT and diminished its toxicities.

This multi-authored book serves as a reference book on the use of RIT in the treatment of B cell indolent-type lymphoma with good summary of data, potential mechanisms of resistance and possible options for minimizing resistance and improving results. A few details are missing, especially data on

DLBCL, MCL, high-dose chemotherapy and stem cell transplant would have been of interest.

Overall, the book will be a useful companion for oncologists, lymphoma pathologists, nuclear medicine specialists, researchers and physicians involved in the management of lymphomas with radionuclide therapy. This would be a good reference book in the medical libraries.

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