131-rituximab Radioimmunotherapy for Non Hodgkin's Lymphoma
Executive Summary

[Adapted from the report by BALQIS ABDUL GHANI]

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Introduction

Non-Hodgkin's lymphoma (NHL) is the main type of lymphoma which comprises a heterogonous group of B-cell or T-cell malignancies with a wide range of aggressiveness. Non-Hodgkin's lymphoma may be indolent (slow growing) or aggressive (fast growing). The most common types of NHL in adults are diffuse large B-cell lymphoma (DLBCL), which is usually aggressive, and follicular lymphoma (FL), which is usually indolent. Rituximab, an anti-CD20 monoclonal antibody has favourably improved the outcomes of patients with NHL, particularly those with DLBCL and FL. Radioimmunotherapy (RIT) with Iodine-131-rituximab (I-131-rituximab) has been shown as a more effective treatment compared to treatment with rituximab alone. There are two commercially RIT agents approved by United State Food and Drug Administration (US FDA); ibritumomab tiuxetan (Zevalin®) which delivers yttrium-90 (Y-90) and tositumomab (Bexxar®), which delivers iodine-131 (I-131). Iodine-131-tositumomab has been withdrawn from the market in 2014 due to dramatic decline in its used. Both Y-90 and I-131 are beta emitters, but I-131 is much more accessible and cheaper in Malaysia and has longer life compared to Y-90. Ibritumomab and tositumomab are both murine anti-CD20 monoclonal antibody, but it is not available in Malaysia. Rituximab is more accessible in Malaysia and there are established methods available for self-labelling of I-131-rituximab with lower cost compared to the commercial Zevalin® and Bexxar®.

This technology review was conducted to review the safety and efficacy of I-131-rituximab RIT in patients with NHL.

Objective/Aim

The objective of this systematic review was to assess the safety, effectiveness, cost-effectiveness of I-131-rituximab RIT in patients with NHL.

Results and Conclusions

A total of 323 titles were identified through the Ovid interface and PubMed. There were fourteen articles included in this review; two cohort studies and twelve clinical trials.

Efficacy

There was limited fair level of retrievable evidence to suggest that I-131-rituximab RIT was effective as a first line treatment for NHL. Evidence demonstrated that I-131-rituximab RIT was effective for newly diagnosed, advanced stage, symptomatic follicular NHL. The overall response rate (ORR) at three months was 99% with 88% achieving Deauville category 1 to 3

There was fair level of retrievable evidence that showed I-131-rituximab RIT was effective for treatment of relapsed or refractory NHL. However, the response rate and median survival rate varies greatly. The ORR range from 29% to 97%, complete response (CR) range from 12.5% to 77%, and partial response (PR) range from 17% to 29%. The median overall survivor range from 11.3 months to 87 months while the median progression free survival (PFS) range from 13 months to 71 months. It seems to be more effective for indolent NHL compared to aggressive NHL.

Evidence also suggest that I-131-rituximab RIT was effective when used as repeated treatment for patients with relapsed or refractory NHL including those with aggressive NHL. It was also effective when used as combination treatment for NHL with longer PFS.

However, there was no study retrieved comparing the effectiveness of I-131-rituximab with other established RIT like Y-90-ibritumomab and I-131-tositumomab.

Safety

There was fair level of retrievable evidence to suggest that treatment using I-131-rituximab NHL was safe and tolerable. However, most common toxicity reported was grade III or IV haematological toxicities and hypothyroidism. Combination of I-131-rituximab RIT and high dose chemotherapy increased the toxicity. There was one treatment related mortality (5%) which occurred in patient treated with I-131-rituximab RIT plus high dose chemotherapy. A study reported that radiation exposure to carers and family members of outpatients undergoing I-131-rituximab RIT were compliance with international guidelines.

Cost /cost-effectiveness

There was no retrievable evidence on cost-effectiveness.

Methods

Electronic databases were searched through the Ovid interface: Ovid MEDLINE® In-process and other Non-indexed citations and Ovid MEDLINE® 1946 to present, EMBASE – 1996 to November 2016, EBM Reviews - Cochrane Central Register of Controlled Trials - November 2016, EBM Reviews - Cochrane Database of Systematic Reviews - 2005 to November 2016, EBM Reviews - Health Technology Assessment – 4th Quarter 2016, EBM Reviews – NHS Economic Evaluation Database 1st Quarter 2015. Searches were also run in PubMed. Google was used to search for additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 30th November 2016.