MaHTAS
Malaysian Health Technology Assessment Section

SELECTIVE INTERNAL RADIATION THERAPY USING YTTRIUM-90 RADIOEMBOLIZATION FOR HEPATOCELLULAR CARCINOMA

Executive Summary

[Adapted from the report by DR. NOOR AISHAH YUSSOF]

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2017

Introduction

Hepatocellular carcinoma (HCC) is a primary malignant tumour of the liver that accounts for an important health problem worldwide. It is the sixth most common cancer worldwide with an incidence of 626,000 new patients a year, and the third most common cause of cancer related death. Several risk factors have been identified as being associated with HCC such as hepatitis B and chronic hepatitis C infections, alcohol use, smoking, and aflatoxin. An increase of these risk factors might play an important role in escalating the number of cases of HCC.

Secondary metastatic liver are more common than primary tumour. The most common sites of primary tumour are breast, lung, and colorectal cancer with the majority of secondary liver cancers are metastases from colorectal cancer.

For those with early stage HCC, transplantation or radiofrequency ablation (RFA) offer the best prospect of a cure. Overall survival is reported as 61% at five years after transplantation and 64% at four years after resection. However, early recognition remains an obstacle and lack of it results in poor outcomes for HCC. It is most frequently diagnosed at an intermediate or advanced stage when ablative therapies, curative surgeries or liver transplantation are no longer feasible with only 15–25% suitable for resection. It is also relatively resistant to systemic chemotherapy because expression of drug resistance proteins and mutations in the cancer cell. In addition, liver dysfunction, which presents in the majority of patients with HCC, tends to limit the amount and type of chemotherapy that can be given.

In view of that, currently several locoregional catherer-based therapies options are available such as transarterial chemoembolism (TACE), drug eluting bead chemoembolism and yttrium-90 radioembolization for treatment of choice for unresectable HCC. It is claim to be very effective in reducing the tumour burden, providing palliation of symptoms, and increased survival. It is used for patients with larger, infiltrating, or multifocal disease where resection or ablation is not feasible.

This technology review was conducted following a request by a Medical Officer from Nuclear Medicine Department, Hospital Sultanah Aminah Johor Bahru to review the available evidence on the effectiveness, safety and cost-effectiveness of selective internal radiation therapy (SIRT) using yttrium-90 radioembolisation for the treatment of HCC.

Objective/Aim

The objective of this technology review was to assess the effectiveness, safety and cost-effectiveness of SIRT using yttrium-90 microspheres for the treatment of HCC.

Results and Conclusions

Seventeen articles related to SIRT using Y-90 Microspheres for HCC were included in this report in term of safety and effectiveness: one systematic review, five randomised controlled trials, four non-randomised controlled trials, six cross sectional studies and one case control study. However, there was no retrievable evidence on cost-effectiveness of this technology.

Primary HCC

- There was limited fair level of retrievable evidence to demonstrate that ytrrium-90 radioembolization increased clinical response rates (partial response and stable disease) and successfully downstaging tumour for resection or

transplant in patients with unresectable primary HCC.
- Better prognosis (overall survival) was demonstrated in patients presented with early staging of HCC without portal vein thrombosis.

Liver Metastasis

a) Metastatic Colorectal Cancer (mCRC)

- There was limited fair level of retrievable evidence to suggest that the use of yttrium-90 radioembolization in combination with systemic chemotherapy as first line with floxuridine (FUDR) and 5-fluorouracil with leucovorin (5-FU/LV) in patients with unresectable mCRC of the liver showed improvement in clinical response rates (complete response, partial response and stable disease), longer median time to liver progression and overall survival.
- There was limited fair level of retrievable evidence on the use of yttrium-90 radioembolization in combination with systemic chemotherapy as second line (failed 5-FU) and third line (failed oxaliplatin and irinotecan).
- Salvage treatment for chemotherapy refractory disease also demonstrated improvement in clinical response rates (complete response, partial response and stable disease), median time to tumour and liver progression and overall median survival in patients who had failed a median of three lines of chemotherapy (range 2–5).

b) Metastatic Neuroendocrine Tumour

- There was limited low level of retrievable evidence to suggest the use of yttrium-90 radioembolization improved clinical response rates (partial response and stable disease) and overall survival.

Safety

There was sufficient fair level of retrievable to suggest that yttrium-90 radioembolization is a safe and well-tolerated procedure. However, generally radioembolization with Y-90 was associated with common symptoms which included nausea, vomiting, fatigue, and mild abdominal pain. Radioembolization specific complications include gastrointestinal ulceration cholecystitis, radiation induced liver disease and hepatotoxicity. The majority of laboratory toxicities were low-grade and included derangements of alkaline phosphatase, grade 3/4 bilirubin toxicity and transaminases. However, there was one death related to radiation hepatitis.

Both glass and resin types of microsphere had received approval from U. S. Food and Drug Administration (FDA) for treatment of unresectable primary HCC and liver mCRC concurrent with fluorodeoxyuridine (FUDR) respectively.

Cost/Cost-Effectiveness

There was no retrievable evidence on the cost-effectiveness of the ytrrium-90 radioembolization in the treatment of unresectable primary or secondary HCC. In MOH hospitals, the estimated cost for SIRT is RM34,000 while the approximate cost in private hospitals is RM70,000 to RM90,000.

Methods

Electronic databases searched through the Ovid interface using MEDLINE (R) In-Process and Other Non-Indexed Citations and Ovid MEDLINE (R) 1946 to present, EBM Reviews- Cochrane Central Registered of Controlled Trials February 2016, EBM Reviews- Database of Abstracts of Review of Effects – 1st Quarter 2016, EBM Reviews- Cochrane Database of Systematic Reviews - 2005 to Feb 2016, EBM Reviews- Health Technology Assessment – 1st Quarter 2016, EBM Reviews-NHS Economic Evaluation Database – 1st Quarter 2016. Searches were also run in PubMed. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 25th February 2016