Transarterial Chemoembolization With Lipiodol For The Treatment Of Hepatocellular Carcinoma In Egyptian Patients

Health Technology Appraisal

Issued: October 2014

**Intervention**

| Lipiodol Ultra Fluid 480mg/l/ml solution for injection (Ethyl ester of iodic oleic acid) |
| Company name |
| Lab. Guerbet, france , imported by Amoun. |
| Comparator |
| Drug Eluting Beads |

**Objective:**

The objective is to evaluate the cost-effectiveness of using Lipiodol Ultra Fluid in the treatment of hepatocellular carcinoma in Egyptian patients, ensuring the best results compared to other treatments, and at the lowest possible cost, while adhering to the guidelines and clinical practice locally and internationally.

**Recommendations:**

- Lipiodol Ultra Fluid is recommended as a treatment for hepatocellular carcinoma.
- Drug Eluting Beads are recommended as a comparator.

**Conclusion:**

The cost-effectiveness study conducted by the Pharmacoeconomic Unit confirms that the price offered by the company for Lipiodol Ultra Fluid is the lowest for continued treatment of the disease.

The recommendations include coordinating with the national committee to combat viral hepatitis and the pricing committee to discuss the economic study conducted by the Pharmacoeconomic Unit to reach the best possible agreement on the price, ensuring its availability for all Egyptian patients.

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**Minister of Health and population**

**Central Administration for Pharmaceutical Affairs**

**Pharmacoconomic Unit**

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**Economic Evaluation Of Transarterial Chemoembolization With Lipiodol Versus Drug Eluting Beads For The Treatment Of Hepatocellular Carcinoma In Egyptian Patients**

- **Introduction**

  Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer. Globally, liver cancer is the 5th and 7th most common cancer in men and women, respectively. In many Egyptian regional registries, liver cancer is the first cancer in men and the second in women [1]. Risk factors for HCC vary among countries, but chronic infections with HBV and HCV are the most important precursors for HCC development on a global scale. In Egypt, HCV is the main risk factor for HCC where 71% of HCC cases are positive for anti-HCV antibodies [2].

  Local ablative procedures, such as percutaneous ethanol injection (PEI), radiofrequency ablation (RFA) or laser-induced thermotherapy (LITT), are potentially curative treatment methods that can be employed with a limited form of the disease; diffusely infiltrating or multifocal tumors, which are often present at the initial diagnosis, are not suitable for these treatment methods. Seventy per cent of patients are diagnosed at an advanced stage and can no longer benefit from curative treatment (surgical resection, liver transplantation, percutaneous ablation) [3].

  Transarterial chemoembolization (TACE) is the treatment recommended in patients with an unresectable, non-metastatic HCC who are in a good general condition with preserved hepatic function (intermediate stage B of the BCLC classification). TACE relies on both local provision of the anticancer agent and on the dual arterial and venous supply to the liver making it possible to temporarily interrupt arterial flow without inducing ischemic necrosis of the organ. Even though TACE has been practiced throughout the world for many years, the technique is still very heterogeneous, and depends on the centers and radiologists in charge of the procedure for the choice of anticancer agents, the doses, the vectors, the embolization agents, the perfusion procedures and the frequency of the courses [4].

  Since 2006, new medical devices, drug-eluting beads (DEB), have been used as the vector for anticancer agents for TACE of HCC. These expensive devices have the twin advantages of reducing the systemic release of the anticancer agent by releasing it in a controlled way on contact with the tumor and of embolizing the vessels supplying the hyper vascularised nodules. These two advantages are still theoretical in as far as the only randomized study published, which compared the efficacy and tolerance of TACE with doxorubicin-eluting beads with conventional TACE using lipiodol as the vector, did not demonstrate any significant difference in terms of efficacy at 6 months between the two techniques [5].
Objective

To evaluate the cost-effectiveness of conventional Transarterial chemoembolization with Lipiodol (cTACE) compared to Drug-Eluting-Bead-Chemoembolization (DEB TACE) in patients with hepatocellular carcinoma (HCC) from the Ministry of health perspective.

- Economic evaluation Key Features:[7]

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<thead>
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<th>Key Features:</th>
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<tr>
<td>year of the document</td>
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<td>Purpose of the document</td>
<td>Evaluate the Cost-Effectiveness Of Using cTACE Versus DEB TACE For The Treatment Of Hepato-cellular Carcinoma In Egyptian Patients</td>
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<td>Disclosure</td>
<td>Yes</td>
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<tr>
<td>Target audience of funding/ author’s interests</td>
<td>Public And Private Payers, Healthcare Industries And Clinicians</td>
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<td>Perspective</td>
<td>Ministry of Health perspective</td>
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<td>Treatment Of Hepatocellular Carcinoma</td>
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<td>Target population</td>
<td>Both those who are insured and uninsured by the Egyptian health care system.</td>
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<td>Subgroup analysis</td>
<td>No Subgroup analysis</td>
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<td>Choice of comparator</td>
<td>DEB TACE</td>
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<td>Time horizon</td>
<td>over a one-year period</td>
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<td>Assumptions required</td>
<td>yes</td>
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<td>Analytical technique</td>
<td>Cost-effectiveness analysis</td>
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<tr>
<td>Costs to be included</td>
<td>Direct medical costs include costs of treatment and managing strategies according to the Egyptian current practice.</td>
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<tr>
<td>Source of costs</td>
<td>Official sources of unit cost data for products (e.g. The Ministry of Health Hospitals)</td>
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<td>Modeling</td>
<td>Decision tree</td>
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<tr>
<td>Systematic review of evidences</td>
<td>yes</td>
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<td>Preference for effectiveness over efficacy</td>
<td>yes</td>
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<tr>
<td>Outcome measure</td>
<td>The outcomes of the two treatments were measured in terms of total survival days</td>
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Committee Discussion

It is important to identify the most cost-effective treatment in patients with hepatocellular carcinoma from a range of alternatives. To support reimbursement decision-making in Egypt, Decision analysis is a quantitative method for synthesizing data from numerous sources for the evaluation of treatment alternatives and was developed to determine the cost-effectiveness of the cTACE strategy, as compared to DEB TACE.

This decision analytical model was constructed to assess the costs and consequences associated with cTACE compared with DEB TACE. The clinical parameters were derived from a retrospective comparison of therapy-associated complications on 44 patients with unresectable HCC and Child-Pugh A Cirrhosis. The evaluation of the therapy in this study was 8.1 months on average (SD±6.6). The results showed that DEB-TACE mean survival was significantly prolonged with 651±76 days vs. 414±43 days for cTACE with Lipiodol [6] (p=0.01) associated with a similar safety profile. The main limitation of the evidence is its retrospective character and the limited number of patients. It is likely that the framework conditions differed so that, for example, technical progress and increasing operator experience led to more frequent achievement of super selective catheter positioning, which might have favorably influenced the results in the DEB-TACE group.
Direct medical costs were obtained from the Ministry of health hospitals in Egypt. Deterministic sensitivity analyses were conducted. No discounting was conducted.

The total survival days of cTACE strategy was estimated to be 414 days whereas that of DEB TACE strategy was estimated to be 651 days. The total costs for cTACE strategy and DEB TACE strategy were EGP 420,529 and EGP 1,351,105 respectively. Thus the incremental cost effectiveness ratio (ICER) for cTACE versus DEB TACE is EGP 3,926 per one day survival gained.

As in all modeling exercises, several assumptions were made in this study leading to uncertainties in the results. In this analysis, we explicitly accounted for these uncertainties by assigning confidence intervals and plausible ranges of the survival days, tumor response, and drug costs based on published sources. To assess the influences of other model structures and assumptions on the cost-effectiveness estimates, one-way sensitivity analyses of various parameters were performed. The Deterministic sensitivity analysis demonstrated that survival associated by DEB TACE strategy and DEB-TACE operation costs have the greatest effect on the results. These various sensitivity analyses did not result in qualitatively different results, and the model proved to be rather robust.

- Conclusion

Results from this study suggest that employing a cTACE strategy is cost-effective intervention compared to DEB TACE in patients with hepatocellular carcinoma based on the willingness to pay threshold stated by world health organization (3xGDP/capita) for low and middle income countries. These findings will help inform health care decisions regarding the allocation of health care system resources to improve the health of the Egyptian population.

- Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

- Appraisal Committee members

Each technology appraisal is appraised by the PE Committee, which is one of CAPA’s standing advisory committees and consist of members who represent different specialties such as statistics, clinical evidence, economics, medicine, clinical pharmacy and pharmacoeconomics. A list of the Committee members who took part in the discussions for this appraisal appears below:
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Prof. Magdy Bassiouni, Professor of Radiology, Faculty of Medicine, Cairo University.

Prof. Emam Waked, Professor of liver diseases, Faculty of Medicine, Cairo University.

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- **PEU project team**
  - Gihan Hamdy El-sisi, Head of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.
  - Shimaa Fouad Ahmed, Team member of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.

- **References:**


Moreover, only one economic study compared the cost of DEB-TACE with conventional TACE, but it only provided information on the costs of the first course [10].

