

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

Health Technology Appraisal

Issued: October 2014

• بيانات المستحضر محل الدراسة:

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

• الهدف:

تقييم الفعالية لقاء التكلفة لمستحضر Lipiodol Ultra Fluid في علاج مرضي سرطان الكبد. وذلك لضمان أفضل النتائج العلاجية بالنسبة للمريض وبأقل تكلفة ممكنة من خلال الإلتزام بالخطوط العلاجية الاستراتيجية العالمية وفي ضوء الممارسة الإكلينيكية المحلية.

• توصية لجنة اقتصاديات الدواء:

بناء على الطلب المحول من إدارة الدعم ونواقص الادوية إلى وحدة اقتصاديات الدواء لعمل دراسة اقتصادية لدراسة وبحث دعم الدولة للمستحضر ليتم توفيره لجميع المرضى. فقد تم التصديق على المنهج المتبع في الدراسة الاقتصادية التي قامت بإجرائها وحدة اقتصاديات الدواء بعد الاطلاع عليها وتقييمها من خبراء ومتخصصين في مجال علاج امراض الكبد والأشعة التداخلية. حيث تم تحديد Drug Eluting Beads كأفضل comparator، وذلك في ضوء الممارسة الإكلينيكية المحلية وبما يتماشى مع القواعد الاستراتيجية العالمية في علاج المرض.

وتبين من نتائج الدراسة ان السعر المقدم من الشركة لمستحضر lipiodol هو الأقل تكلفة لمتابعة وعلاج المريض عن Drug Eluting Beads. كما توصي اللجنة بالتنسيق بين أعضاء اللجنة القومية لمكافحة الفيروسات الكبدية ولجنة التسعير بالإدارة المركزية للشئون الصيدلية، وذلك لمناقشة الدراسة الاقتصادية التي قامت باعدادها وحدة اقتصاديات الدواء للوصول الي أفضل اتفاق حول السعر وبما يضمن توافره للمريض المصري.

- علما ان الدراسة التي قامت باجرائها وحدة اقتصاديات الدواء شملت بيانات التكلفة الخاصة بالمستحضرات والتي تم تجميعها من تسعيرة مستشفيات وزارة الصحة والسكان، بالإضافة إلى باقي التكلفة المرتبطة بالإقامة بالمستشفى والأدوية والفحوصات الدورية وباقي التبعات الناتجة عن استخدام كل بروتوكول على حدة. كما تم تجميع البيانات الخاصة بالقيمة العلاجية ونسبة الحالات المستجيبة للعلاج من الدراسات المنشورة عالمياً .

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]**

Key Features:	
year of the document	October 2014
Affiliation of authors	Pharmacoeconomic Unit, Central Administration For Pharmaceutical Affairs
Purpose of the document	Evaluate the Cost-Effectiveness Of Using cTACE Versus DEB TACE For The Treatment Of Hepatocellular Carcinoma In Egyptian Patients
Standard reporting format included	Yes
Disclosure	Yes
Target audience of funding/ author's interests	Public And Private Payers, Healthcare Industries And Clinicians
Perspective	Ministry of Health perspective
Indication	Treatment Of Hepatocellular Carcinoma
Target population	Both those who are insured and uninsured by the Egyptian health care system.
Subgroup analysis	No Subgroup analysis
Choice of comparator	DEB TACE
Time horizon	over a one-year period
Assumptions required	yes
Analytical technique	Cost-effectiveness analysis
Costs to be included	Direct medical costs include costs of treatment and managing strategies according to the Egyptian current practice.
Source of costs	Official sources of unit cost data for products (e.g. The Ministry of Health Hospitals)
Modeling	Decision tree
Systematic review of evidences	yes
Preference for effectiveness over efficacy	yes
Outcome measure	The outcomes of the two treatments were measured in terms of total survival days

Method to derive utility	No utility was measured
Equity issues stated	All lives and life years are valued equally, regardless of age, gender, or socioeconomic status of individuals in the population
Discounting costs	No discounting was conducted.
Discounting outcomes	No discounting was conducted.
Sensitivity analysis-parameters and range	Critical component(s) in the calculation is varied through a relevant range or from worst case to best case.
Sensitivity analysis-methods	One-way sensitivity analysis is performed.
Presenting results	cTACE strategy is cost-effective intervention compared to DEB TACE in patients with hepatocellular carcinoma.
Incremental analysis	yes
Total costs vs. effectiveness (cost/effectiveness ratio)	yes
Portability of results (Generalizability)	The generalizability and extent to which the clinical efficacy data and the economic data are representative is identified and discussed.

- 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.

Page 5 of 7

- **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:

Prof. Magdy Bassiouni, Professor of Radiology, Faculty of Medicine, Cairo University.

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

Prof. Randa El-Dessoki, Scientific director of global initiatives of the Organization of the economics of medicine management and research outputs.

Dr. Mahmoud El-Mahdawy, General Director of Hospital pharmacy administration, Central Administration for Pharmaceutical Affairs, Ministry of Health.

Dr. Gihan Hamdy, Head of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.

Dr. Samah Ragab, Head of the technical office, Central Administration for Pharmaceutical Affairs, Ministry of Health.

Prof. Heba Nassar, Professor at the Faculty of Economics and Political Science, Cairo University.

- **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:**

- 1-The National Cancer Registry Program of Egypt (NCRPE). Reports and Statistics: Aswan, Damietta & El-Minia. Available at: <<http://www.cancerregistry.gov.eg/reports.aspx>> (accessed on 05.09.12) [online].
- 2-Miller FD, Abu-Raddad LJ. Evidence of intense ongoing endemic transmission of hepatitis C virus in Egypt. Proc Natl Acad Sci USA. 2010;107:14757–14762J.

3-Marelli, R. Stigliano, C. Triantos, M. Senzolo, E. Cholongitas, N. Davies, et al. Transarterial therapy for hepatocellular carcinoma: which technique is more effective? A systematic review of cohort and randomised studies Cardiovascular and Interventional Radiology, 30 (2007), pp. 6–25

4-J.Lammer, K. Malagari, T. Vogl, F. Pilleul, A. Denys, A. Watkinson, et al. Prospective randomized study of doxorubicin-eluting bead embolization in the treatment of hepatocellular carcinoma: results of the PRECISION

- V study Cardiovasc Intervent Radiol, 33 (2010), pp. 41–52 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].
- 5-C.Malbranche, M. Boulin, B. Guiu, C. Pernot, J.P. Cercueil, L.S. Aho, et al. Impact économique de la chimioembolisation avec billes chargées dans le traitement du carcinoma hépatocellulaire Bull Cancer, 98 (2011), pp. 671–678.
- 6-Philipp Wiggermann, Dominik Sieron, Christiane Brosche, etal. Transarterial Chemoembolization of Child-A hepatocellular carcinoma: Drug-eluting bead TACE (DEB TACE) vs. TACE with Cisplatin/Lipiodol (cTACE). Med Sci Monit, 2011; 17(4): CR189-195.
- 7-Elsisi GH, Kaló Z, Eldessouki R, etal. Recommendations for reporting pharmacoeconomic evaluations in Egypt. Value Health Regional 2013;2:319–27.