Nilotinib Versus Imatinib In Chronic Myeloid Leukemia From Health Insurer perspective

Health Technology Appraisal
Issued: February 2016

- **بيانات المستحضر محل الدراسة:**

Intervention	Tasigna (Nilotinib 300 mg, Twice daily)
Company name	Novartis
Comparator	Gleevec (Imatinib 400 mg, Once daily)

- **الهدف:**

تقييم الفعالية لقاء التكلفة لمستحضر Nilotinib مقابل مستحضر Imatinib في علاج مرضي سرطان الدم (Chronic Myeloid Leukemia) وذلك لضمان أفضل النتائج العلاجية بالنسبة للمريض وبأقل تكلفة ممكنة من خلال الإلتزام بالخطوط العلاجية الاسترشادية العالمية وفي ضوء الممارسة الإكلينيكية المحلية.

- **توصية لجنة اقتصاديات الدواء:**

بعد البحث في الأدلة العلمية وبناء علي دراسة الجدوي الإقتصادية التي أجريت من قبل وحدة إقتصاديات الدواء تبين ان مستحضرNilotinib (300mg twice daily) عند سعر ٢٩٠٠ جنيه مصري شهريا هو الأكفأ من حيث الفعالية لقاء التكلفة مقارنة بمستحضر Imatinib (400mg once daily) عند سعر ٢٨٧٥جنيه مصري شهريا في علاج مرض سرطان الدم.

وذلك نظرا إلي التحسن في جودة الحياة المعيشية وقلة احتمالية الاصابة بالاضرار الجانبية المصاحبة لصالح مستحضر الـ Nilotinib مقارنة بمستحضر Imatinib مع وجود فارق بسيط في التكلفه العلاجية بين المستحضرين .

- علما ان الدراسة التي قامت باجرائها وحدة اقتصاديات الدواء شملت بيانات التكلفة الخاصة بالمستحضرات التي تم تجميعها من هيئة التأمين الصحي بالاضافة إلى باقي التكلفة المرتبطة بالإقامة بالمستشفى والأدوية والتبعات المحتملة عن علاج الحالات الغير مستجيبة والحالات الطارئة لاستخدام كل بروتوكول على حدة.

- كما تم تجميع البيانات الخاصة بالقيمة العلاجية الناتجه عن جودة الحياه المعيشية للمريض ونسبة الحالات المستجيبة للعلاج من الدراسات المنشورة عالميًا .

Tel.: +202 – 23684288 +202 – 23648769 +202 -25354100 Ext.: 1902 Fax: +202 – 23684194
Email: peunit@eda.mohp.gov.eg Website: www.eda.mohp.gov.eg

English Summary:

COST EFFECTIVENESS ANALYSIS OF NILOTINIB VERSUS IMATINIB IN CHRONIC MYELOID LEUKEMIA PATIENTS FROM HEALTH INSURER PERSPECTIVE

- **Introduction**

Chronic Myelogenous leukemia (CML) is characterized by the malignant expansion of stem cells in the bone marrow. It is diagnosed using cytogenetic and molecular diagnostic techniques to detect a chromosomal abnormality known as the Philadelphia (Ph) chromosome that is the only known cause of CML. This is a relatively rare disease having an annual incidence of approximately 1 – 2 per 100 000 people [1], and accounts for 15 – 20% of adult leukemias [2 – 4]. The median age at presentation is 50 – 60 years, and 12 – 30% of patients are > 60 years old at diagnosis [5].

The use of BCR-ABL tyrosine kinase inhibitors imatinib improved outcomes for patients with Philadelphia chromosome–positive chronic myeloid leukemia (CML) and established BCR-ABL–targeted therapy as the standard of care for this disease. imatinib was associated with a superior response rate and improved progression-free survival, as compared with the previous standard therapy, interferon alfa plus low-dose cytarabine.[6-8]

Despite the positive effect of imatinib, nearly 20% of patients who take the drug do not have a complete cytogenetic response, and others may have intolerable side effects or drug resistance over time[9], Resistance to imatinib occurs annually in 3% to 4% of patients with CML in chronic phase (CML-CP), and is defined as failure to achieve complete hematologic response (CHR) within 3 months of therapy [10] .Loss of response and transformation to advanced disease occur mainly in the first 3 years of imatinib therapy, and the rate of overall survival is poor in these patients. Thus, improved first-line therapy is needed.

Nilotinib is an orally bioavailable drug with greater potency and selectivity for BCR-ABL than imatinib[11] .Nilotinib was first approved in the United States and elsewhere in 2007 for patients with CML in the chronic or accelerated phase who had resistance to or could not tolerate imatinib[12,13].

Objective

The aim of this study was to evaluate the cost-effectiveness of nilotinib versus imatinib in chronic myeloid leukemia patients from health insurer perspective.

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Economic Evaluation Key Features[14]

Key Features:	
Year of the document	Feb 2016
Affiliation of authors	Pharmacoeconomic Unit, Central Administration For Pharmaceutical Affairs
Purpose of the document	Evaluate the cost-effectiveness of nilotinib versus imatinib in chronic myeloid leukemia patients from health insurer perspective.
Standard reporting format included	Yes
Disclosure	Yes
Target audience of funding/ author's interests	Public Healthcare Industries
Perspective	Health insurer perspective
Indication	Treatment of chronic myeloid leukemia.
Target population	Those who are insured and not insured by the Egyptian health care system.
Subgroup analysis	No subgroup analysis was performed.
Choice of comparator	Imatinib 400 mg
Time horizon	Over 3-year time horizon
Assumptions required	yes
Analytical technique	Cost-effectiveness analysis
Costs to be included	Direct medical costs only included and include the cost of therapy, and the cost of AEs treatment, cost of lab tests done for monitoring.
Source of costs	Health insurance 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 quality-adjusted life-years (QALYs)

Preferred method to derive utility	Time trade off method was used to derive utility in our study.
Equity issues stated	All lives, life years, or QALYs are valued equally, regardless of age, gender, or socioeconomic status of individuals in the population
Discounting costs	Not applied
Discounting outcomes	Not applied
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	Nilotinib is a cost effective intervention in treatment of chronic myeloid leukemia newly diagnosed patients.
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**

Nilotinib has been shown to be a more potent inhibitor of BCR-ABL than imatinib. ENEST trial evaluated the efficacy and safety of nilotinib, as compared with imatinib, in patients with newly diagnosed Philadelphia chromosome–positive chronic myeloid leukemia (CML) in the chronic phase. So the main objective of this study was to evaluate the cost-effectiveness of nilotinib versus imatinib in chronic myeloid leukemia.

The results of the CE study indicated that nilotinib is cost saving versus imatinib in chronic myeloid leukemia at ICER value of -44126 L.E/QALY in ITT scenario and it is also cost effective at ICER value of 76793 L.E/QALY in per-protocol scenario. This result is comparable with that of a systematic review of clinical effectiveness and cost-effectiveness studies in UK which demonstrated that nilotinib was more cost effective as first line therapy than first line imatinib in chronic myeloid leukemia.

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The clinical data of the cost effectiveness study were derived from ENESTnd 3-year follow-up trial which enrolled 846 patients in a phase 3, randomized, open-label, multicenter study, the patients were randomized in a 1:1:1 ratio to receive nilotinib (at a dose of either 300 mg or 400 mg twice daily) or imatinib (at a dose of 400 mg once daily). The primary end point was the rate of major molecular response at 12 months [15].

The current cost effectiveness study measured efficacy in terms of Quality Adjusted Life Years (QALY) which is a final outcome, the time horizon for the cost effectiveness model was 3 years in which cost of managing side effects was calculated.

As in all modeling exercises, several assumptions were made in this study leading to uncertainties in the results. In this analysis for ITT scenario we assumed that patients' withdrawal from core treatment was totally due to treatment failure, so this percent was added to the probability of no MMR response and assigned a utility value of no response state.

To assess the impact of other model structures and assumptions on the cost -effectiveness estimates, one-way sensitivity analysis was performed and revealed that the key driver of the results was the utility value of molecular response state in ITT scenario and the probability of patients still on core treatment of nilotinib was the key driver in per protocol results; these parameters have the major impact on the analysis result.

- **Conclusion**

Compared with our willingness to pay threshold as that stated by WHO (3times GDP/CAPITA) nilotinib is cost effective versus imatinib in chronic myeloid leukemia.

- **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:

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

Tel.: +202 – 23684288 +202 – 23648769 +202 -25354100 Ext.: 1902 Fax: +202 – 23684194
Email: peunit@eda.mohp.gov.eg Website: www.eda.mohp.gov.eg

Prof. Ahmed Hassouna, Biostatistics Consultant.

Dr. Randa El dessouki, Assistant lecturer, Faculty of Medicine , Fayoum university

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

- **Asmaa saad,** Team member of Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs, Ministry of Health.

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