Measuring the trend of use of targeted therapy and Economic Evaluation of Gefitinib for Advanced Non-small Cell Lung Cancer (NSCLC) in Singapore

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Introduction

- In Singapore, cancer is the leading cause of death, accounting for 30% of total death in 2011. With the tremendous growth of targeted therapy in global market and its high drug expenditures observed in United States, the trends in utilization of targeted therapy are primary focus for health care providers. 1,2
- Among all the incidence of cancers, lung cancer is one of the top ranked cancer with the highest mortality rate in 2006-2010. Novel targeted therapy – Gefitinib has been shown to improve progression free survival (PFS) and a substantially better adverse-effect profile than conventional chemotherapy in NSCLC. 3,4

Objectives

- To determine the trend of use of targeted therapy in National Cancer Centre Singapore (NCCS) from 2007-2011.
- To evaluate the treatment response of Gefitinib in NSCLC patients.
- To conduct an economic evaluation of Gefitinib for advanced non-small cell lung cancer (NSCLC) patients without prior chemotherapy.

Methods

- Study Design = Retrospective study conducted at outpatient clinic in NCCS.
- Study Cohort = All patients who had received outpatient prescriptions for targeted therapy between 1 Jan 2007 to 31 Dec 2011. For evaluation of Gefitinib in NSCLC, 124 patients who received Gefitinib as 1st line treatment without prior chemotherapy were identified.
- Data sources = Outpatient administrative system, pharmacy database and medical case notes.
- Outcome measurements = Number of patients receiving treatment and annual consumption costs for each targeted therapy. Clinical outcomes for Gefitinib include treatment response and PFS.
- Statistical analysis = Descriptive analysis were used to describe quantitative data. Kaplan Meier was performed to analyze survival-time data. Cox proportional hazards model was used to analyze PFS with its associated covariates.
- Economic evaluation = Model structure = Markov model with five exclusive health states: Progressing at entry, partial response (PR), stable disease (SD), progression disease (PD) and death NSCLC (Dead). (Figure 1). Cycle length and time horizon were 21 days and 5 years respectively.
- Probabilities = Probability of staying in each health state or transition to various health states for Gefitinib were derived from 124 patients in the study cohort. The probabilities for CP were determined by using hazard ratio (HR) from IPASS trial. Assumption made: Survival curves were exponential and the rates were constant over time.
- Resources utilization = Medical resources consumed were collected from Gefitinib study cohort. Whereas, expert opinions and IPASS trial were used for CP.
- Costs = Costs were based on the unit selling price listed in NCCS.
- Utilities = Health states, adverse events and administration mode were associated with utilities. All utilities were obtained from published literatures (Evidence Review group report, 2006 and Nafees). 3
- Discounting = Both costs and utilities were discounted at an annual rate of 3%. 
- Perspective = Analyzed from the perspective of health care purchaser (Ministry of Health), hence only direct medical costs were considered.

Demographics

- Characteristics Gefitinib (N=124)
  - Age = Mean ± SD 67.2 ± 10.4
  - Male 20.2 %
  - Female 79.8 %
  - Median duration of treatment (days) 278 (28-1627)
  - Chinese 92.7 %
  - Malay 4.8 %
  - Indian 1.6 %
  - Never-smoker 85.5 %
  - Smoker 2.4 %
  - Former smoker 12.1 %
  - Non-adenocarcinoma 6.5 %
  - Adenocarcinoma 91.1 %
  - Unknown histology 2.4 %
  - Stage IV at entry 12.1 %
  - EGFR positive 34.7 %
  - Unknown EGFR status 65.3 %

Conclusion

- Trends of use:
  - Total number of patients receiving targeted therapy in NCCS increased significantly from 585 patients in 2007 to 1119 patients in 2011 (Fig 2).
  - Fig 3 depicted the trends of annual consumptions cost for each targeted therapy. The cost increased more than two times from $9.1 million in 2007 to $20.6 million in 2011.
  - Trastuzumab has the highest consumption costs accounted for $30.2 million (40.7%). Followed by Gefitinib $15.5 million (20.9%) and Bevacizumab $7.74 million (10.4%). Increasing trend of use for Imatinib, Sunitinib and Cetuximab were observed and approaching annual costs of Bevacizumab in 2011.
  - Treatment response of Gefitinib:
    - None of the patients has complete response. Majority of patients 64.5% has stable disease, 23.4% presented with partial response and minority of patients 12.1% has disease progression.
    - Unadjusted median PFS: 353 days (95% CI 301-404); Adjusted median PFS: 322 days
  - Cost effectiveness and cost-utilty analysis:
    - Progression free days (PFD) gained = Compared to CP the treatment with Gefitinib has gained 73.23 PFD.
    - Quality adjusted life year (QALY) gained = Improved effectiveness expressed as QALY gained, reported as 2.87 QALY’s gained.
  - Incremental cost-effectiveness ratio (ICER) and Incremental cost-utility ratio (ICUR) = As a result, ICER and ICUR were S$420.86 per PFD gained and S$10,749.86 per QALY gained respectively.
  - Sensitivity analysis = The results of one way sensitivity analysis are shown in Fig 3. ICUR was most sensitive to the cost of Gefitinib. Other important parameters identified include PD to D rate, SD to PD rate and utilities values for all the responses. Varying the PFS HR for CP also affected the ICUR.

References

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