COST UTILITY OF DOCETAXEL COMPARED WITH BEST SUPPORTIVE CARE AND PEMETREXED IN SECOND LINE TREATMENT OF NON-SMALL CELL LUNG CANCER IN POLAND

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Rutkowski J[1], Gwiosda B[1], Lisiecka B[1], Wladysiuk M[1], Lis J[2], Plisko R[1], Rys P[1]
1 – HTA Consulting Poland
2 – Sanofi-Aventis Poland

*A study conducted by **HTA Consulting** **www.hta.pl***

Introduction

Lung cancer remains a devastating disease with few effective treatment options. Recent developments in chemotherapy have brought cautious optimism. Docetaxel, as a single agent, is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of prior platinum-based chemotherapy.

Objectives

To demonstrate, from the perspective of the Polish National Health Fund (NHF), the cost-effectiveness of docetaxel administered in a dose of 75 mg/m2 every 3 weeks as second-line therapy in advanced non-small cell lung cancer versus:

- Best supportive care,
- Pemetrexed 500 mg/m2 every 3 weeks.

Clinical data

Studies included in the analysis were identified by means of a systematic review.

All data concerning the comparison of docetaxel versus BSC were based on the study by Shepherd et al. (2000) [3] and all data concerning the comparison of docetaxel versus pemetrexed were based on the study by Hanna et al. (2004) [1].

Interventions

- Docetaxel administered in a dose of 75 mg per 1 m2 of Body Surface Area (BSA) every 3 weeks for a maximum of 4 cycles.
- Pemetrexed administered in a dose of 500 mg per 1 m2 of Body Surface Area (BSA) every 3 weeks for a maximum of 4 cycles.
- Palliative care (representing BSC in Polish setting).

Summary

Objectives: To evaluate cost-utility of docetaxel (75 mg/m2 every 3 weeks) compared with best supportive care (BSC) or pemetrexed (500 mg/m2 every 3 weeks) as second-line therapy in advanced non-small cell lung cancer in Polish setting.

Methods: A cost-utility approach was adopted, evaluating total direct costs incurred by the Polish National Health Fund (NHF), life years gained (LYG) and quality-adjusted life years (QALY). A micro-simulation Markov model was used to estimate utilities and costs of treatment. The first course of chemotherapy was assumed as the starting time-point of the model. Simulation was terminated at the time of the patient's death or after two years following start of the treatment. It was assumed that patients would undergo 4 cycles of chemotherapy or less if progression occurred during treatment. In case of disease progression, chemotherapy would be terminated and patients would receive palliative care until death. Transition probabilities between health states were calculated based on a systematic review of RCTs. Health state utilities were obtained from published literature. Costs were taken from the NHF catalogue. Probabilistic sensitivity analysis was performed in order to estimate the probability that docetaxel was cost effective in Polish setting, with a threshold of approximately 91,000 polish zloty (PLN).

Results: Incremental costs for docetaxel compared with BSC was PLN 57,501 per LYG and PLN 105,964 per QALY. In a 2-year time horizon docetaxel was PLN 13,582 less costly than pemetrexed (CI95%: 8,224; 17,704). The probability of docetaxel cost-effectiveness over BSC was 99.72% for LYG and 32.95% for QALY. The probability of docetaxel cost-effectiveness over pemetrexed was 99.09% for LYG and 100% for QALY.

Conclusions: Docetaxel seems to be cost effective in comparison with BSC and pemetrexed in Polish setting.

Methodology

Structure of the model

A modified Markov model with memory was used to simulate health status of patients. Model states are presented in Figure 1. The simulation begins at the "Progression-Free" state, in which patients remain until progression or death. In the "Progression" state patients remain until death.

Probabilities were determined by nonlinear estimation of Kaplan Meier curves. Regression was based on the method of least squares. The Weibull distribution function was applied to the estimated curve, because it takes into account change of the risk with time. Example of the estimation is presented on the Figure 2.

Figure 1. Markov Model states

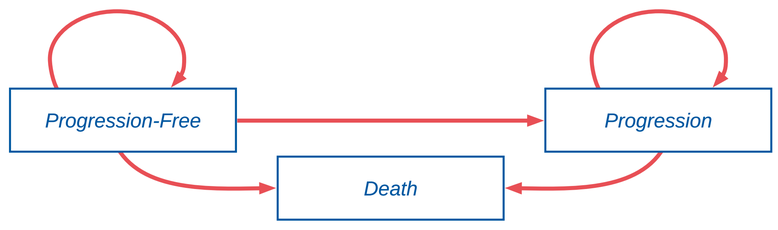
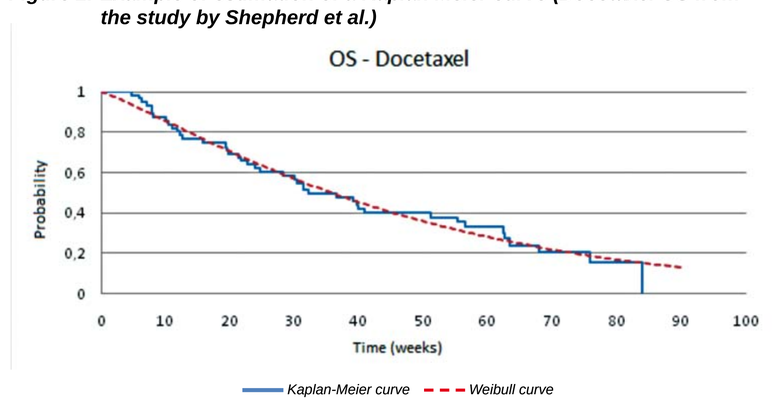


Figure 2. Example of estimation of a Kaplan Meier curve (Docetaxel OS from the study by Shepherd et al.)



Results

Docetaxel vs BSC

The graphs below present the expected costs and QALYs gained for each treatment arm in a 2-year time horizon (Figure 3, Figure 4).

ICER for Docetaxel versus BSC was PLN 57,501 per LYG and PLN 105,964 per QALY.

The probability of docetaxel cost-effectiveness over BSC was 99.72% for LYG (Figure 5, Figure 6) and 32.95% for QALY (it exceeded 80% for a threshold of PLN 120,000 or higher) (Figure 7, Figure 8).

Figure 3. Expected costs for Docetaxel vs BSC

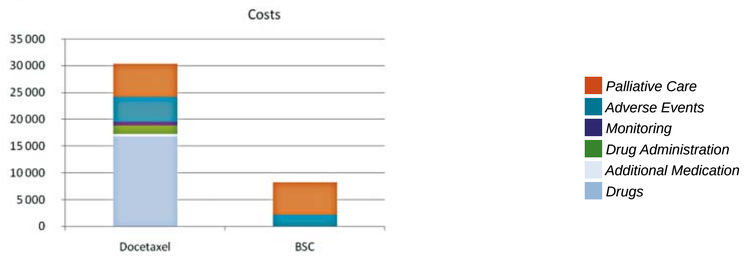
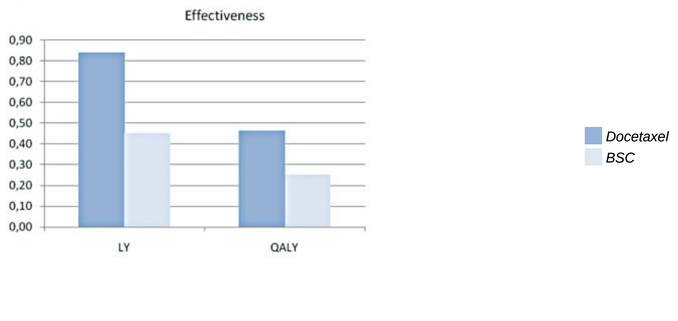


Figure 4. Expected QALY and LY for Docetaxel vs BSC



Graph 5. LYG Scatter Plot – Docetaxel vs BSC

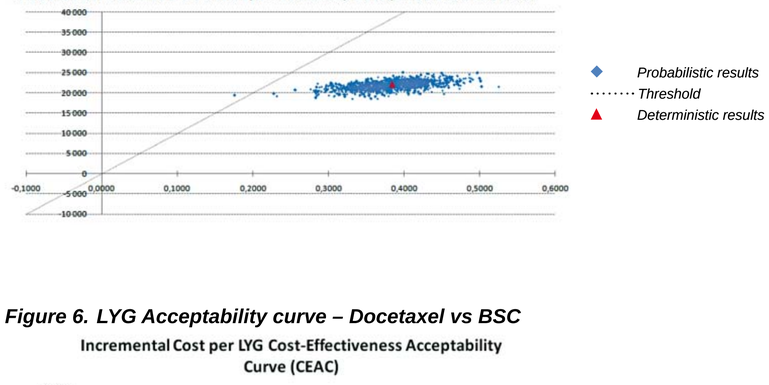


Figure 6. LYG Acceptability curve – Docetaxel vs BSC

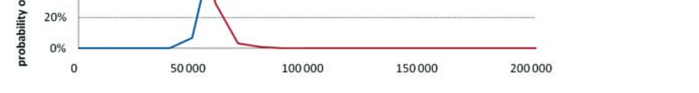


Figure 7. QALY Scatter Plot – Docetaxel vs BSC

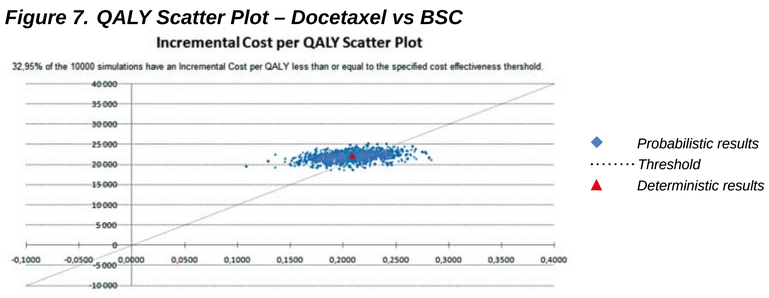
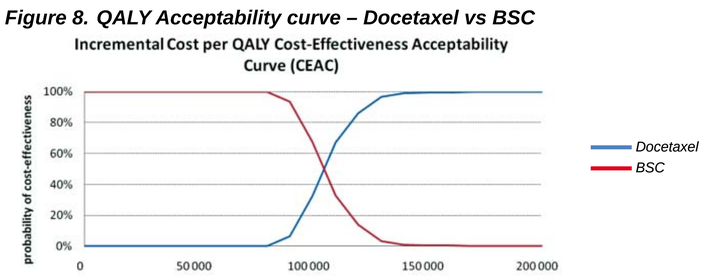


Figure 8. QALY Acceptability curve – Docetaxel vs BSC



Docetaxel vs Pemetrexed

The graphs below present the expected costs and QALYs gained for each treatment arm in a 2-year time horizon (Figure 9, Figure 10).

In a 2-year time horizon, docetaxel was PLN 13,582 less costly than pemetrexed (CI95%: 8,224; 17,704).

The probability of docetaxel cost-effectiveness over pemetrexed was 99.09% for LYG (Figure 11, Figure 12) and 100% for QALY (Figure 13, Figure 14).

Figure 9. Expected costs for Docetaxel vs Pemetrexed

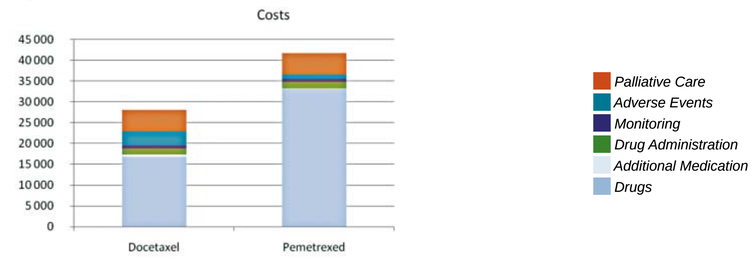


Figure 10. Expected QALY and LY for Docetaxel vs Pemetrexed

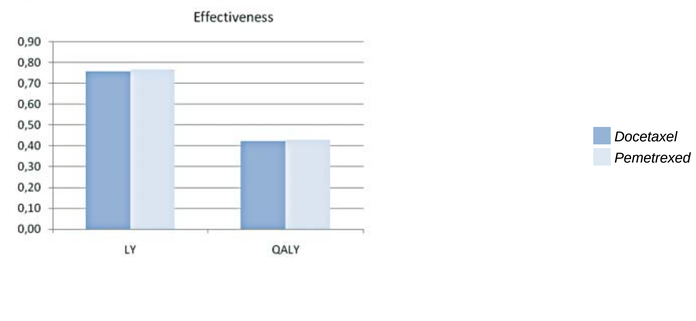


Figure 11 .LYG Scatter Plot – Docetaxel vs Pemetrexed

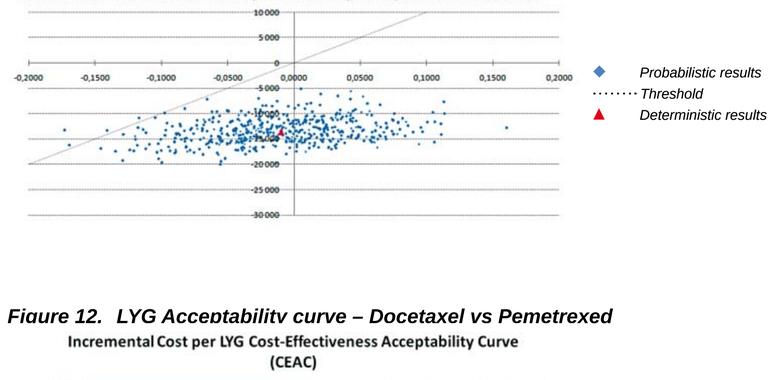


Figure 12. LYG Acceptability curve – Docetaxel vs Pemetrexed

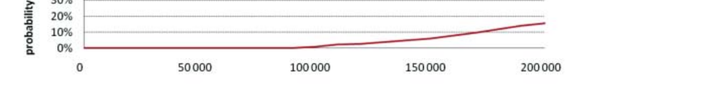


Figure 13. QALY Scatter Plot – Docetaxel vs Pemetrexed

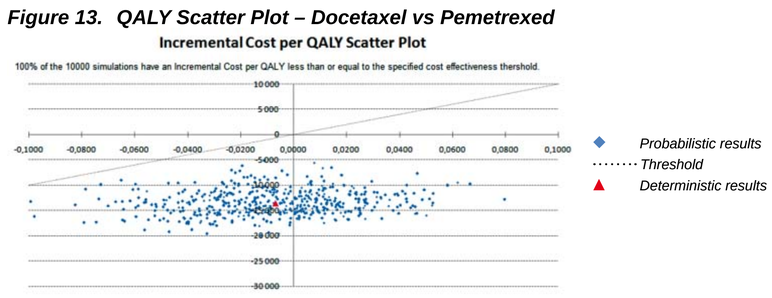


Figure 14. QALY Acceptability curve – Docetaxel vs Pemetrexed

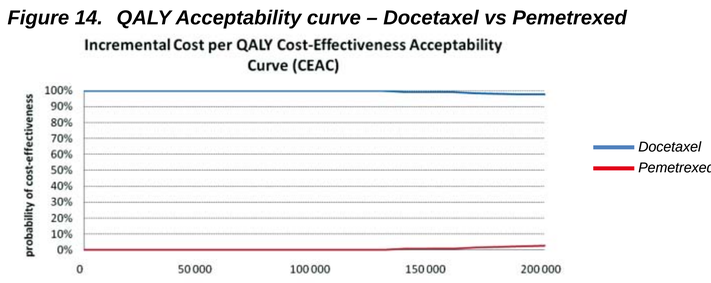


Table 1. Adverse events included in the analysis

AE
Anemia
Diarrhoea
Pulmonary
Thrombocytopenia
Stomatitis
Neuropathy
Rash
Asthenia / Fatigue
Dehydration
Nausea & Vomiting
Neutropenia
Febrile neutropenia
Alopecia

Table 2. Model utilities (based on Nafees 2008 study)

Parameter	Utility value	SE
Stable disease	0,65	0,0222
Progression	-0,18	0,0217
Response	0,02	0,0066
Neutropenia	-0,09	0,0154
Febrile neutropenia	-0,09	0,0163
Fatigue	-0,07	0,0185
Nausea & vomiting	-0,05	0,0162
Diarrhoea	-0,05	0,0155
Hair loss	-0,04	0,0148
Rash	-0,03	0,0117

Partial response to therapy and occurrence of all severe adverse events (grade 3 or 4 and alopecia) reported in the studies were taken into account in the model (Table 1). All these parameters have impact on the utility value.

Utility value

The base utility value, reductions associated with disease progression and adverse events, and increment associated with response were derived from the study by Nafees et al. (2008) [2] (see Table 2).

Costs included in the model

- Chemotherapeutic agents – calculated as the price per 1 unit of a chemotherapeutic multiplied by the dose per 1 m2 and BSA.
- Additional Medication – usage of additional drugs was based on 6 experts' opinion.
- Drug Administration – both docetaxel and pemetrexed are administrated during one-day hospitalization.
- Monitoring – costs associated with each cycle of chemotherapy.
- Adverse Events – costs based on 6 experts' opinion.
- Palliative Care – per each day of progressive disease.

All unit prices were obtained from the 2009 National Health Fund chemotherapy catalogue. Costs were discounted at a 5% annual rate as recommended by the Agency for Health Technology Assessment in Poland (AHTAPol).

Outcome measures of the model

- Progression-Free Life Years
- Progression Life Years
- Total Life Years (LY)
- QALY
- ICER (Cost per LY gained)
- ICER (Cost per QALY gained)
- Cost-Effectiveness acceptability curves
- LY and QALY were discounted at a 3.5% annual rate as recommended by the AOTM.

Conclusions

Based on the obtained results, docetaxel seems to be cost-effective in comparison with BSC and pemetrexed in Polish setting.

References

1. Hanna N, Shepherd FA, Fossella FV, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. J Clin Oncol. 2004 May 1;22(9):1589-97.
2. Nafees B, Stafford M, Gavriel S, Bhalla S, Watkins J. Health state utilities for non small cell lung cancer. October 2008.
3. Shepherd FA. Dancey J. Ramlau R. et al. Prospective randomized trial of docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum- based chemotherapy. Journal of Clinical Oncology. Vol. 18 (10) (pp 2095-2103), 2000.