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Cost-effectiveness of afatinib, gefitinib, erlotinib and pemetrexed-based chemotherapy as first-line treatments for advanced non-small cell lung cancer in China

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ABSTRACT

Purpose: Tyrosine kinase inhibitors (TKI) of the epidermal growth factor receptor (EGFR) are becoming the standard treatments for Chinese patients with advanced non-small cell lung cancer (NSCLC) harboring an EGFR mutation. However, the economic impact is unclear yet in China.

Materials and methods: A decision-analytic model was developed to simulate 1-month patient transitions in a 10-year time horizon from Chinese heath care system perspective. The health and economic outcomes of four first-line strategies (pemetrexed plus cisplatin [PC], gefitinib, erlotinib, and afatinib) among NSCLC patients harboring EGFR mutations were estimated and assessed via indirect comparisons. Costs in the Chinese setting were estimated by using local hospital data and literatures. A 5% annual discount rate was applied to both costs and outcomes. The primary outcome was the incremental cost-effectiveness ratio (ICER). Sensitivity analyses were performed.

Results: Afatinib achieved additional 0.382, 0.216 and 0.174 quality-adjusted life-years (QALYs) with marginal $7930, $3680 and $2818 costs in comparison with PC, gefitinib and erlotinib, which resulted in the ICERs of $20,758, $17,693 and $16,197 per QALY gained, respectively. The hazard ratios (HR) of overall survival (OS) of afatinib against gefitinib, erlotinib and PC strategy had substantial influential parameters.

Conclusions: First-line afatinib is cost-effective compared with gefitinib, erlotinib and PC treatment for Chinese patients with EGFR mutation-positive NSCLC.

1. Introduction

Lung cancer is the most incident malignant cancer and is the leading cause of cancer-related death in males and in particular, females in developed countries [1]. Based on the Chinese Cancer Registry Annual Report, lung cancer also showed the highest incidence (48.32 per 100,000) and mortality (39.27 per 100,000) in China in 2011 [2]. Non-small cell lung cancer (NSCLC) represents approximately 85% of all lung cancers, and approximately 46% of NSCLCs are locally advanced or metastatic at the time of diagnosis [3,4]. Four to six cycles of first-line, platinum-based, doublet chemotherapy have been recommended for patients with advanced NSCLC [3]. However, the efficacy of traditional chemotherapy reaches a plateau with a nearly 1-year median overall survival (OS) [5–7]. Thus, novel treatments for advanced NSCLC are necessary to improve the poor clinical outcomes of patients.

Tyrosine kinase inhibitors (TKI) of the epidermal growth factor receptor (EGFR) is a standard treatment for patients with advanced non-small cell lung cancer (NSCLC) harboring an EGFR mutation [8]. The most common mutations in EGFR include exon 19 deletion mutations and L858R (exon 21) substitution mutations [9]. The first-generation reversible EGFR tyrosine kinase oral inhibitors gefitinib and erlotinib specifically target the EGFR receptor and have efficacy in patients with EGFR mutations, while the resistance to these agents can occur most

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commonly through the acquisition of a secondary mutation such as T790M, which is found on exon 20 [10,11]. Afatinib is a second-generation anilinoquinazoline that irreversibly binds to an intracellular tyrosine kinase domain, subsequently inhibiting members of the ErbB receptor family [12]. Afatinib's irreversible binding properties may also be an advantage in inhibiting mutant cell lines, including EGFR L858R/T790M mutations, which are often resistant to gefitinib and erlotinib [13]. Currently, afatinib has been approved as a first-line treatment for patients with advanced non-small cell lung cancer with EGFR mutations [14].

For decision makers, the selection between TKIs or chemotherapy ultimately depends on their comparative costs and effectiveness. The primary objective of this study is to compare the cost-effectiveness of afatinib with traditional chemotherapy and other EGFR-TKIs (gefitinib and erlotinib) for the first-line treatment of advanced NSCLC from the perspective of Chinese health care system.

2. Materials and methods

2.1. Analytical overview and model structure

A mathematical model was constructed to project the ten-year clinical and economic outcomes of first-line treatments for patients with newly diagnosed advanced NSCLC. The following four potential competing strategies were evaluated: four-cycle chemotherapy based on pemetrexed plus cisplatin (PC), gefitinib, erlotinib and afatinib (Fig. 1A). After the disease progressed, salvage chemotherapy or supportive care was administered. Health and economic outcomes were measured with a Markov model (Fig. 1B) including three exclusive health states: progression-free survival (PFS), progressed survival (PS) and death. The Markov cycle length was one month, and the initial health state for all patients was assumed to be PFS. The risk of disease progression or death was determined based on the published literatures. Given the good tolerability of the four alternatives [15–18], the impact of tolerability was not considered in simplifying the model.

Life year (LY), quality-adjusted life-years (QALYs) and cost were measured. Cost and QALYs were discounted at an annual rate of 5%, in line with Chinese guidelines for pharmacoeconomic evaluations [19]. Incremental cost-effectiveness ratios (ICERs), presented as cost per additional QALY gained, were estimated for judging cost-effectiveness. Three times of the per capita gross domestic product (GDP) of China in 2016 (US $ 23,815/QALY) was used as the cost-effectiveness threshold according to the Chinese guidelines for pharmacoeconomic evaluations [19].

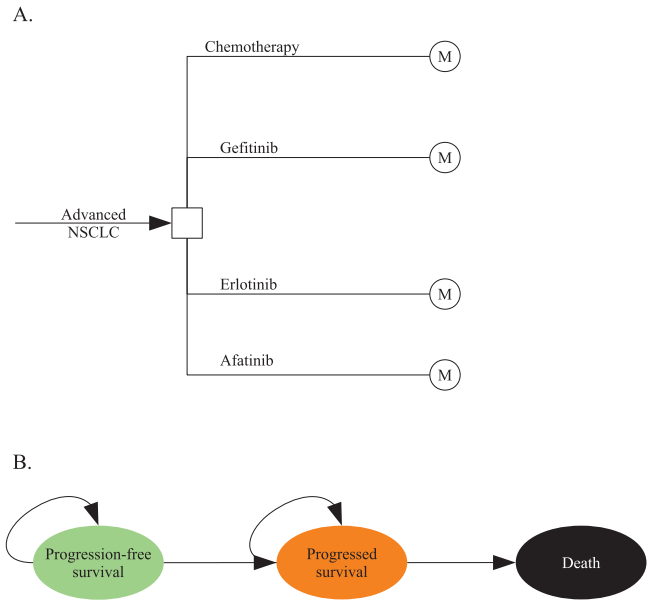

Fig. 1. The framework of the decision tree (A) and the Markov state transition model (B).

2.2. Clinical data

Indirect comparisons of the four strategies were conducted using the survival rate for afatinib from the LUX-Lung 3, 6 and 7 trials. In LUX-Lung 6 trial [20,21], afatinib was compared with PC chemotherapy, which found afatinib gained a 4.2 and 13 months improvement in PFS and OS compared with PC strategy, respectively. In comparison with gefitinib, afatinib significantly improved PFS in newly diagnosed patients with advanced NSCLC and harboring EGFR mutation (median PFS time: 11.0 vs 10.9 months, HR = 0.73; 95% CI: 0.57–0.95) [18].

Weibull survival models were fitted to the Kaplan-Meier curves of survival data for the PC and afatinib strategy according to data from the LUX-Lung 3 trials, which showed the best goodness of fit to the Kaplan–Meier survival data according to the adjusted R^2. The estimated Weibull scale (λ) and shape (γ) parameters are shown in Table 1. The survival probability at time t was calculated using the following formula: $S(t) = P(T \geq t) = \exp(-\lambda t^{\gamma})$. The transition probability from PFS to PS at a given cycle t was calculated by using the following formula: $P(t)_{pfs \rightarrow ps} = 1 - \exp[\lambda(t-1)^{\gamma} - \lambda t^{\gamma}]$, where λ and γ are the Weibull parameters of PFS. The Weibull survival curves of the three alternative strategies were derived using the adjusted Weibull scale ($\lambda_{alternative\ strategy} = \lambda_{control\ strategy} \times HR_{network\ meta\text{-}analysis}$) and shape ($\gamma_{alternative\ strategy} = \gamma_{control\ strategy}$) parameters, as previously described in published studies [22,23]. However, given the absence of head-to-head clinical trial data, the HRs of PFS and OS for the gefitinib and erlotinib strategies relative to the afatinib strategy considered in the economic model were generated using network meta-analysis based on fixed-effects model because of the low heterogeneity ($I^2 < 25\%$). This network meta-analysis was performed with a graph-theoretical methodology implemented in the R package netmeta [24,25]. The HRs of PFS from each clinical trial were derived from the previously published 11 studies, including the LUX-Lung 3, 6 and 7, First-SIGNAL, OPTIMAL, EURTAC, ENSURE, WJTOG, IPASS, NEJ002 and WJTOG3405 trials [26]. The details of the network meta-analysis could be found in the appendix file 1. All NMA-based hazard ratios included in the cost-effectiveness model were presented in Table 1. After the disease progressed, patients entered the PS health states. The entire PS duration was estimated according to the basis of the difference between the OS and PFS derived from the parametric survival models. The transition probability from PS to death at a given cycle t was calculated using the following formula: $P(t)_{ps \rightarrow death} = [S(t)_{os} - S(t)_{pfs}]/S(t)_{pfs}$.

2.3. Cost and utility data

The analysis was conducted from the Chinese Health care system perspective. The direct medical costs were considered in the model only, including the cost of detection of EGFR mutations, first and second-line chemotherapy (including prescription, preparation, and administration), concomitant medication during therapy, managing treatment-related sever adverse events (SAEs, grade ≥3), routine follow-up, and laboratory tests (Table 2). The costs are shown as US dollars ($). All the costs were adjusted to 2017 prices with the local Consumer Price Index and were shown as US dollars (1 US dollar = CNY ¥ 6.8).

Gefitinib at a dose of 250 mg per day, erlotinib at a dose of 150 mg per day, or afatinib at a dose of 40 mg per day was assumed to be administered to patients positive for an EGFR mutation until disease progression. Chemotherapy (pemetrexed, 500 mg/m^2 of body surface area (BSA), plus cisplatin, 75 mg/m^2) was administered every 21 days for six cycles. It was assumed that a typical patient had a body surface area (BSA) of 1.72 m^2 (a weight of 65 kg and a height of 1.64 m) to calculate the dosage of agents. Because generic pemetrexed was widely

Table 1
Key clinical inputs.

Parameters	Values	Ranges	Source
Weibull parameters of PFS for PC	$\lambda = 0.0599$; $\gamma = 1.247$	Fixed	[20]
Weibull parameters of PFS for Afatinib	$\lambda = 0.062$; $\gamma = 1.2128$	Fixed	[20]
Weibull parameters of OS for PC	$\lambda = 0.0033$; $\gamma = 1.6009$	Fixed	[21]
Weibull parameters of OS for Afatinib	$\lambda = 0.0037$; $\gamma = 1.5034$	Fixed	[21]
HR of afatinib versus erlotinib for PFS	0.660	0.44–0.96	Network meta-analysis
HR of afatinib versus erlotinib for OS	0.930	0.64–1.3	Network meta-analysis
HR of afatinib versus gefitinib for PFS	0.700	0.55–0.88	Network meta-analysis
HR of afatinib versus gefitinib for OS	0.860	0.58–1.21	Network meta-analysis

Abbreviation: PFS = Progression free survival; PC = Cisplatin; OS = Overall survival; HR = Hazard ratio.

Table 2
Key cost and utility inputs.

Parameters	Values	Ranges	Source
Cost data (US $)			
Gefitinib per day	29	Fixed	Local charge
Erlotinib per day	35	Fixed	Local charge
Afatinib per day	48	Fixed	Local charge
Pemetrexed per 500mg	1970	441–1970	Local charge
Cisplatin per 100mg	21	16–16	Local charge
Salvage therapy after disease progression	293	220–366	[28]
Outpatient visit and intervention per cycle	2180	1635–2725	Estimated
Supportive care per cycle	274	220–366	Estimated
Diarrhea per event	293	220–366	Estimated
Rash/Acne per event	3719	2790–4649	Estimated
Anemia per event	6434	2435–10438	Estimated
Neutropenia per event	466	0–1384	Estimated
Febrile Neutropenia per event	953	715–1191	Estimated
Utility of health states per event			
PFS	0.784	0.766–0.802	[29]
PS	0.58	0.5–0.66	[29]
Disutility of toxicities			
Diarrhea	−0.047	−0.016 to −0.077	[27]
Rash/Acne	−0.032	−0.01 to −0.055	[27]
Anemia	−0.073	−0.037 to −0.11	[27]
Neutropenia	−0.090	−0.059 to −0.12	[27]
Febrile Neutropenia	−0.090	−0.058 to −0.122	[27]

Abbreviation: PFS = Progression free survival; PS = Progressed survival.

used in Chinese clinical practice, the cost of generic pemetrexed was used as the lower boundary in the one-way sensitivity analysis. After the disease progression, salvage therapy and supportive care were prescribed; in this model, the published median second-line PFS durations was used to estimate the portion of the PD period undergoing active salvage therapies, and the rest of the time in the PD phase would undergo BSC, which was estimated by subtracting the time of active salvage therapy from the total PD time.

The utility values used in the model were derived from the LUX-Lung trials in the base case analysis. Utility values from literatures were also tested within the model. The reported disutility caused by SAEs was also considered [27]. The incidence and duration of SAE during first-line treatment could be found in appendix file 2. The health resource consumption and disutilities associated with adverse events were shown in Table 2.

2.4. Sensitivity analyses

Sensitivity analyses included univariate and probabilistic sensitivity analyses. One-way sensitivity analysis was conducted to test the variance of underlying parameter values and assumptions within the models. The parameters and values used in the one-way sensitivity analysis were showed in Tables 1 and 2, which were derived from literatures and collected data.

Probabilistic sensitivity analysis (PSA) was conducted with a Monte Carlo simulation. For the Monte Carlo simulation, probability distributions related to natural history parameters, relative risks and odds ratios, costs, and utilities were incorporated into the analysis. The analysis adopted standard methods for defining uncertainty around parameters. Estimates of incremental costs and QALYs were obtained by re-running of the model employing values from the related probability distributions. Based on the recommendation of ISPOR-SMDM Modeling Good Research Practices Task Force in conducting PSA [30], a beta distribution was assigned to transition probability, proportion and utility parameters, normal distribution to HR parameters, and a gamma distribution to costs. In this study, 1000 replications were conducted; that was, a set of 1000 outcome estimates were obtained. Cost-effectiveness acceptability curves (CEAC) that presented the probability that each treatment was optimal given different values of willingness-to-pay for an additional QALY were derived.

3. Results

3.1. Base-case analysis

From the perspective of health system, afatinib gained additional 0.382, 0.216 and 0.174 QALYs in comparison with PC, gefitinib and erlotinib strategies with incremental cost of $7,930, $3680 and $2818, respectively, which led to the incremental cost of $20,758, $17,693 and $16,197 per QALY gained, respectively (Table 3). The results showed that given Chinese cost-effectiveness threshold of $23,815/QALY,

Table 3
Cost-effectiveness of afatinib, erlotinib, and cisplatin-pemetrexed as first-line treatment of advanced EGFR mutation-positive NSCLC.

Strategies	QALY	LY	Cost(US $)	Incremental QALY[a]	Incremental LY[a]	Incremental cost(US $)[a]	ICER[a] (US $/QALY)
Pemetrexed/Cisplatin	1.415	2.457	35,700	0.382	0.388	7930	20,758 (cost-effective)
Gefitinib	1.589	2.621	39,949	0.208	0.224	3680	17,693 (cost-effective)
Erlotinib	1.623	2.726	40,811	0.174	0.119	2818	16,197 (cost-effective)
Afatinib	1.797	2.845	43,629	NA	NA	NA	NA

Abbreviation: EGFR = Growth factor receptor; NSCLC = Non-small cell lung cancer; QALY = Quality adjusted life year; LY = Life year; ICER = Incremental cost-effectiveness ratio.

[a] Afatinib comparing other strategies. NA: not applicable.

Table 4
Results of one-way sensitivity analysis.

Parameters	Lower limit of parameters		Upper limit of parameters	
	Values of parameters	ICERs (US $/QALY)	Values of parameters	ICERs (US $/QALY)
Afatinib vs Erlotinib				
HR for OS	0.640	25,509	1.300	36,224
Cost of outpatient visit and intervention per cycle	$67	13,694	$2341	78,154
Cost of best supportive care per cycle	$194	18,992	$2395	−28,831
HR for PFS	0.440	9885	0.960	52,343
Afatinib vs Gefitinib				
HR for OS	0.580	26,272	1.210	46,672
Cost of outpatient visit and intervention per cycle	$67	15,341	$2341	58,346
Cost of best supportive care per cycle	$194	11,600	$2395	23,717
HR for PFS	0.550	15,341	0.880	58,346
Afatinib vs PC				
Cost of outpatient visit and intervention per cycle	$67	18,500	$2341	59,456
HR for OS	0.577	23,192	1.056	11,510
HR for PFS	0.361	12,701	0.675	31,210
Chemotherapy cycles	3	43,330	6	20,758
Cost of best supportive care per cycle	$194	21,340	$2395	5373

Abbreviation: ICER = Incremental cost-effectiveness ratio; QALY = quality adjusted life year; HR = Hazard ratio; OS = Overall survival; PFS = Progression free survival; PC = Cisplatin.

afatinib was a cost-effective treatment strategy comparing with traditional chemotherapy, and a dominant alternative against gefitinib and erlotinib.

3.2. Sensitivity analyses

One-way sensitivity analyses showed the HR of OS, the cost of outpatient visit and intervention per cycle, the HR of PFS and the cost of best supportive care per cycle were the most influential parameters. These parameters might yield substantial changes in the ICER by adjusting their values (Table 4). The impact of adverse events had a paucity of impact on the model outcomes.

The cost-effectiveness acceptability curve (Fig. 2) showed that afatinib was the optimal treatment in approximately 90% of the iterations at Chinese willingness-to-pay threshold, compared with other three competing alternatives.

4. Discussion

There was great interest in the oncologist and patients after the report of a clinical benefit from targeted therapies. However, with the widespread use of the EGFR-TKIs, the subsequent dramatic increase of health care costs was concerned by clinicians and administrators. Economic evaluation of the EGFR-TKIs in this clinical setting is

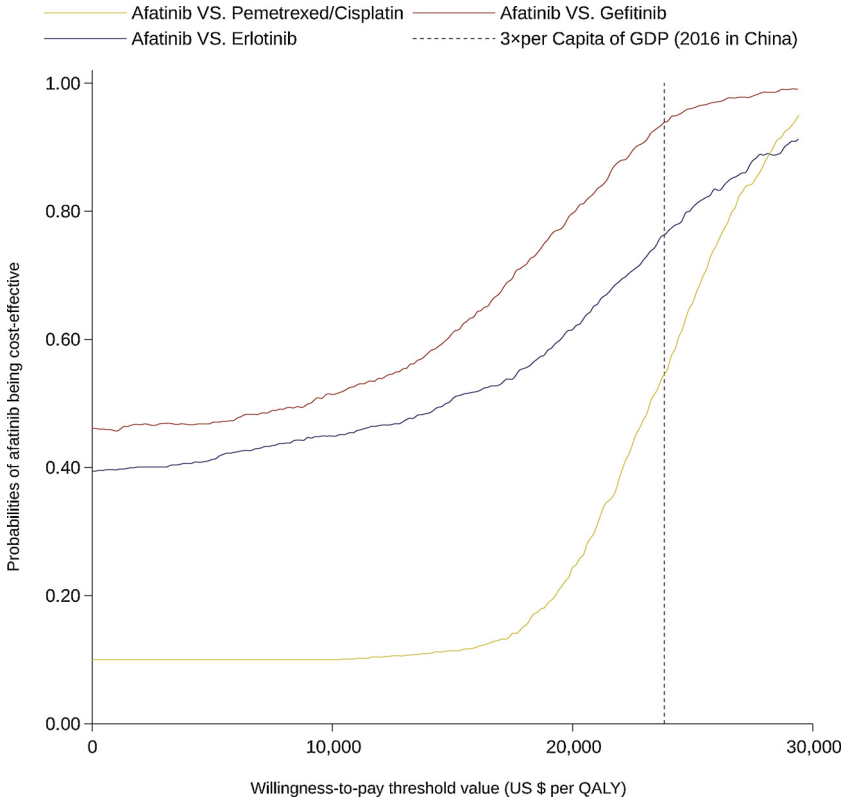

Fig. 2. Cost-effectiveness acceptability curves of afatinib versus other three strategies.

becoming urgent need. The main findings suggested that the afatinib strategy is a cost-effective option in comparison with the PC chemotherapy due to the favorable ICER, and a dominant strategy in comparison with gefitinib and erlotinib strategies due to additional health benefits with lower costs. The probabilistic sensitivity analysis (PSA) also found the highest probabilities of cost-effectiveness of afatinib compared with gefitinib, erlotinib and PC strategy at a threshold of $23,815. Our findings are helpful for determining the preferred 1st-line initial treatments that should be adopted for NSCLC cases.

One recently published French study found that the ICER of afatinib over gefitinib for first-line treatment was €45,211/QALY (0.170 QALY gained for an incremental cost of €7697) [31]. Afatinib also had 100% probability to be cost-effective at a willingness-to-pay threshold of €70,000/QALY. Their conclusion was inherent with our finding that afatinib was a cost-effective option. However, we found that afatinib might be a dominant strategy due to the lower cost and higher health outcomes. The potential reason might be the afatinib's donation program for Chinese patients, which could notably decrease the economic burden of afatinib treatment. Another economic evaluation determined the cost-effectiveness of erlotinib or afatinib, or chemotherapy cisplatin-pemetrexed for first-line treatment of advanced EGFR mutation-positive in the United States reported by Ting et al. [32], which found erlotinib had an incremental $6722 costs with incremental 0.11 QALY that resulted in the incremental cost-effectiveness ratio of $61,809/QALY compared with afatinib. Thus, they showed that erlotinib was the optimal treatment at a willingness-to-pay threshold of $100,000/QALY in the United States, which was opposite with ours. The inconsistency of the study findings might result from the different source of clinical data inputs. In the present analysis, an indirect comparison by employing network meta-analysis was performed by pooling published literatures, which showed the more favorable adjusted HRs of PFS and OS in afatinib arm than erlotinib arm. Ting and colleagues' study directly used the clinical data from LUX-Lung 3 and EURTAC without adjusting HRs of PFS and OS in different trials, which might lead to the more favorable outcomes in erlotinib than afatinib in their study.

The potential ability of afatinib, the first second-generation EGFR-TKI for advanced NSCLC, to improve survival was a major determinant of clinical and economic outcomes. One-way sensitivity analysis showed that the HR of PFS and OS of afatinib against gefitinib, erlotinib and PC strategy was the considerably influential parameter with respect to the robustness of the model. As Table 4 shows, when the HRs of PFS and OS of afatinib against gefitinib, erlotinib and PC strategy were increased or decreased using the upper or lower boundaries, the ICERs increased or decreased dramatically. The one-way sensitivity analysis found that adverse events had a paucity of impact on the model outcomes. One recent real-world observational study found healthcare costs during afatinib and erlotinib appeared to be similar and were largely attributed to hospitalization and anti-cancer therapy [33].

This study has several limitations. First, due to no clinical data evaluating these four first-line alternatives in one trial, a network meta-analysis was performed in this study for an indirect comparison, where the patient characteristics were assumed to be similar although the moderate heterogeneity was detected. Second, a Weibull survival model was used to simulate the lifetime outcomes. This approach was another limitation of this study, although the results of the sensitivity analysis suggested that the model outcome was not sensitive to the variables related to HR of PFS. Third, some key clinical inputs, such as the survival data for the gefitinib and erlotinib strategies, were extracted from distinct RCTs with different study designs conducted on the different population. To minimize potential bias and uncertainty in outcomes, the impact was tested by sensitivity analyses. Fourth, the analysis did not fully examine other potentially competing alternatives for advanced NSCLC, such as bevacizumab, because these agents were not licensed as first-line treatments in China at the time when this study was conducted [34]. Finally, the utility data was not Chinese-specific, which might lead to bias in the model outcomes. However, the sensitivity analyses showed only minor impacts of utility.

In summary, from the perspective of Chinese health care system, afatinib therapy for newly diagnosed advanced NSCLC harboring EGFR mutations is a cost-effective alternative to traditional chemotherapy and first generation EGFR-TKIs.

Conflict of interest statement

Yun-Bo Chu, Yi-Yang Zhao, Yan-Jun Zhang and David Kuo are employees of Boehringer Ingelheim (China). Betty Su and Bin Wu received funding from Boehringer Ingelheim (China). Other authors declared no conflicts of interests. The authors alone are responsible for the content and writing of the article.

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Contributors

MY and BW was involved in the design of the study. YBC, YYZ, YJZ, DK and BS collected the data. BW performed the health economic evaluation and wrote the first draft of the manuscript, which was critically revised by MY, YBC, YYZ, YJZ, DK and BS.

Disclaimer

The views expressed are those of the authors. The funding agencies had no role in the study design, data collection and analysis, decision to publish, or manuscript preparation.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

No additional data are available.

Ethics approval

This economic analysis was based on a literature review and modeling techniques; this study did not require approval from an Institutional Research Ethics Board.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.lungcan.2018.11.029.

References

[1] L.A. Torre, F. Bray, R.L. Siegel, J. Ferlay, J. Lortet-Tieulent, A. Jemal, Global cancer statistics, 2012, CA Cancer J. Clin. 65 (2015) 87–108.
[2] W. Chen, R. Zheng, P.D. Baade, S. Zhang, H. Zeng, F. Bray, A. Jemal, X.Q. Yu, J. He, Cancer statistics in China, 2015, CA Cancer J. Clin. 66 (2016) 115–132.
[3] E. Felip, R.A. Stahel, N. Pavlidis, ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of non-small-cell lung cancer (NSCLC), Ann. Oncol. 16 (Suppl. 1) (2005) i28–i29.
[4] W.J. William, H.Y. Lin, J.J. Lee, S.M. Lippman, J.A. Roth, E.S. Kim, Revisiting stage IIIB and IV non-small cell lung cancer: analysis of the surveillance, epidemiology, and end results data, Chest 136 (2009) 701–709.
[5] The guideline for diagnosis and treatment of Chinese patients with sensitizing EGFR mutation or ALK fusion gene-positive non-small cell lung cancer (2015 Version),

Zhonghua Zhong Liu Za Zhi 37 (2015) 796–799.
[6] D.S. Ettinger, D.E. Wood, W. Akerley, L.A. Bazhenova, H. Borghaei, D.R. Camidge, R.T. Cheney, L.R. Chirieac, T.A. D'Amico, T.L. Demmy, T.J. Dilling, R. Govindan, F.J. Grannis, L. Horn, T.M. Jahan, R. Komaki, M.G. Kris, L.M. Krug, R.P. Lackner, M. Lanuti, R. Lilenbaum, J. Lin, B.J. Loo, R. Martins, G.A. Otterson, J.D. Patel, K.M. Pisters, K. Reckamp, G.J. Riely, E. Rohren, S. Schild, T.A. Shapiro, S.J. Swanson, K. Tauer, S.C. Yang, K. Gregory, M. Hughes, Non-small cell lung cancer, version 1.2015, J. Compr. Canc. Netw. 12 (2014) 1738–1761.
[7] Y. Shi, Y. Sun, C. Ding, Z. Wang, C. Wang, Z. Wang, C. Bai, C. Bai, J. Feng, X. Liu, F. Li, Y. Yang, Y. Shu, M. Wu, J. He, Y. Zhang, S. Zhang, G. Chen, H. Luo, R. Luo, C. Zhou, Y. Zhou, Q. Pang, H. Zhao, Q. Zhao, A. Gu, Y. Ling, C. Huang, B. Han, S. Jiao, H. Jiao, China experts consensus on icotinib for non-small cell lung cancer treatment (2015 version), Ann. Transl. Med. 3 (2015) 260.
[8] X. Zhi, Y. Shi, J. Yu, Standards for the diagnosis and treatment of primary lung cancer (2015 version) in China, Zhonghua Zhong Liu Za Zhi 37 (2015) 67–78.
[9] S.V. Sharma, D.W. Bell, J. Settleman, D.A. Haber, Epidermal growth factor receptor mutations in lung cancer, Nat. Rev. Cancer 7 (2007) 169–181.
[10] G. Gao, S. Ren, A. Li, J. Xu, Q. Xu, C. Su, J. Guo, Q. Deng, C. Zhou, Epidermal growth factor receptor-tyrosine kinase inhibitor therapy is effective as first-line treatment of advanced non-small-cell lung cancer with mutated EGFR: a meta-analysis from six phase III randomized controlled trials, Int. J. Cancer 131 (2012) E822–E829.
[11] J. Ansari, R.E. Shackelford, H. El-Osta, Epigenetics in non-small cell lung cancer: from basics to therapeutics, Transl. Lung Cancer Res. 5 (2016) 155–171.
[12] P. Giordano, A. Manzo, A. Montanino, R. Costanzo, C. Sandomenico, M.C. Piccirillo, G. Daniele, N. Normanno, G. Carillio, G. Rocco, R. Bianco, F. Perrone, A. Morabito, Afatinib: an overview of its clinical development in non-small-cell lung cancer and other tumors, Crit. Rev. Oncol. Hematol. 97 (2016) 143–151.
[13] E.L. Kwak, R. Sordella, D.W. Bell, N. Godin-Heymann, R.A. Okimoto, B.W. Brannigan, P.L. Harris, D.R. Driscoll, P. Fidias, T.J. Lynch, S.K. Rabindran, J.P. McGinnis, A. Wissner, S.V. Sharma, K.J. Isselbacher, J. Settleman, D.A. Haber, Irreversible inhibitors of the EGF receptor may circumvent acquired resistance to gefitinib, Proc. Natl. Acad. Sci. U. S. A. 102 (2005) 7665–7670.
[14] M. Reck, K.F. Rabe, Precision diagnosis and treatment for advanced non-small-Cell lung Cancer, N. Engl. J. Med. 377 (2017) 849–861.
[15] Y.K. Shi, L. Wang, B.H. Han, W. Li, P. Yu, Y.P. Liu, C.M. Ding, X. Song, Z.Y. Ma, X.L. Ren, J.F. Feng, H.L. Zhang, G.Y. Chen, X.H. Han, N. Wu, C. Yao, et al., First-line icotinib versus cisplatine/pemetrexed plus pemetrexed maintenance in advanced NSCLC patients with EGFR mutation, J. Thorac. Oncol. 102 (2015) S205–S206.
[16] L. Paz-Ares, F. de Marinis, M. Dediu, M. Thomas, J.L. Pujol, P. Bidoli, O. Molinier, T.P. Sahoo, E. Laack, M. Reck, J. Corral, S. Melemed, W. John, N. Chouaki, A.H. Zimmermann, C. Visseren-Grul, C. Gridelli, Maintenance therapy with pemetrexed plus best supportive care versus placebo plus best supportive care after induction therapy with pemetrexed plus cisplatin for advanced non-squamous non-small-cell lung cancer (PARAMOUNT): a double-blind, phase 3, randomised controlled trial, Lancet Oncol. 13 (2012) 247–255.
[17] T. Mitsudomi, S. Morita, Y. Yatabe, S. Negoro, I. Okamoto, J. Tsurutani, T. Seto, M. Satouchi, H. Tada, T. Hirashima, K. Asami, N. Katakami, M. Takada, H. Yoshioka, K. Shibata, S. Kudoh, E. Shimizu, H. Saito, S. Toyooka, K. Nakagawa, M. Fukuoka, Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial, Lancet Oncol. 11 (2010) 121–128.
[18] K. Park, E.H. Tan, K. O'Byrne, L. Zhang, M. Boyer, T. Mok, V. Hirsh, J.C. Yang, K.H. Lee, S. Lu, Y. Shi, S.W. Kim, J. Laskin, D.W. Kim, C.D. Arvis, K. Kolbeck, S.A. Laurie, C.M. Tsai, M. Shahidi, M. Kim, D. Massey, V. Zazulina, L. Paz-Ares, Afatinib versus gefitinib as first-line treatment of patients with EGFR mutation-positive non-small-cell lung cancer (LUX-Lung 7): a phase 2B, open-label, randomised controlled trial, Lancet Oncol. 17 (2016) 577–589.
[19] Task group of the chinese guidelines for pharmacoeconomic evaluations: China guidelines for pharmacoeconomic evaluations, China J. Pharm. Econ. 6 (2011) 7–48.
[20] L.V. Sequist, J.C. Yang, N. Yamamoto, K. O'Byrne, V. Hirsh, T. Mok, S.L. Geater, S. Orlov, C.M. Tsai, M. Boyer, W.C. Su, J. Bennouna, T. Kato, V. Gorbunova, K.H. Lee, R. Shah, D. Massey, V. Zazulina, M. Shahidi, M. Schuler, Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations, J. Clin. Oncol. 31 (2013) 3327–3334.
[21] J.C. Yang, Y.L. Wu, M. Schuler, M. Sebastian, S. Popat, N. Yamamoto, C. Zhou, C.P. Hu, K. O'Byrne, J. Feng, S. Lu, Y. Huang, S.L. Geater, K.Y. Lee, C.M. Tsai, V. Gorbunova, V. Hirsh, J. Bennouna, S. Orlov, T. Mok, M. Boyer, W.C. Su, K.H. Lee, T. Kato, D. Massey, M. Shahidi, V. Zazulina, L.V. Sequist, Afatinib versus cisplatin-based chemotherapy for EGFR mutation-positive lung adenocarcinoma (LUX-Lung 3 and LUX-Lung 6): analysis of overall survival data from two randomised, phase 3 trials, Lancet Oncol. 16 (2015) 141–151.
[22] B. Wu, T. Li, J. Cai, Y. Xu, G. Zhao, Cost-effectiveness analysis of adjuvant chemotherapies in patients presenting with gastric cancer after D2 gastrectomy, BMC Cancer 14 (2014) 984.
[23] M. Hoyle, C. Green, J. Thompson-Coon, Z. Liu, K. Welch, T. Moxham, K. Stein, Cost-effectiveness of temsirolimus for first line treatment of advanced renal cell carcinoma, Value Health 13 (2010) 61–68.
[24] B.S. Woods, N. Hawkins, D.A. Scott, Network meta-analysis on the log-hazard scale, combining count and hazard ratio statistics accounting for multi-arm trials: a tutorial, BMC Med. Res. Methodol. 10 (2010) 54.
[25] J.P. Higgins, D. Jackson, J.K. Barrett, G. Lu, A.E. Ades, I.R. White, Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies, Res. Synth. Methods 3 (2012) 98–110.
[26] Y. Zhang, J. Sheng, Y. Yang, W. Fang, S. Kang, Y. He, S. Hong, J. Zhan, Y. Zhao, C. Xue, Y. Ma, T. Zhou, S. Ma, F. Gao, T. Qin, Z. Hu, Y. Tian, X. Hou, Y. Huang, N. Zhou, H. Zhao, L. Zhang, Optimized selection of three major EGFR-TKIs in advanced EGFR-positive non-small cell lung cancer: a network meta-analysis, Oncotarget 7 (2016) 20093–20108.
[27] B. Nafees, M. Stafford, S. Gavriel, S. Bhalla, J. Watkins, Health state utilities for non small cell lung cancer, Health Qual. Life Outcomes 6 (2008) 84.
[28] G. Lewis, M. Peake, R. Aultman, M. Gyldmark, L. Morlotti, J. Creeden, M. de la Orden, Cost-effectiveness of erlotinib versus docetaxel for second-line treatment of advanced non-small-cell lung cancer in the United Kingdom, J. Int. Med. Res. 38 (2010) 9–21.
[29] C. Chouaid, H. Le Caer, C. Locher, C. Dujon, P. Thomas, J.B. Auliac, I. Monnet, A. Vergnenegre, Cost effectivenes of erlotinib versus chemotherapy for first-line treatment of non small cell lung cancer (NSCLC) in fit elderly patients participating in a prospective phase 2 study (GFPC 0504), BMC Cancer 12 (2012) 301.
[30] A.H. Briggs, M.C. Weinstein, E.A.L. Fenwick, J. Karnon, M.J. Sculpher, A.D. Paltiel, M.G.R.P. ISPOR-SMDM, Model parameter estimation and uncertainty analysis: a report of the ISPOR-SMDM modeling good research practices task force working Group-6, Med. Decis. Mak. 32 (2012) 722–732.
[31] C. Chouaid, L. Luciani, K. LeLay, P. Do, J. Bennouna, M. Perol, D. Moro-Sibilot, A. Vergnenegre, G. de Pouvourville, Cost-effectiveness analysis of afatinib versus gefitinib for first-line treatment of advanced EGFR-Mutated advanced non-small cell lung cancers, J. Thorac. Oncol. 12 (2017) 1496–1502.
[32] J. Ting, H.P. Tien, P. Xiang, A. Sugay, M. Abdel-Sattar, L. Wilson, Cost-effectiveness and value of information of erlotinib, afatinib, and cisplatin-pemetrexed for first-line treatment of advanced EGFR mutation-positive non-small-cell lung cancer in the United States, Value Health 18 (2015) 774–782.
[33] K.E. Skinner, A.W. Fernandes, M.S. Walker, M. Pavilack, A. VanderWalde, Healthcare costs in patients with advanced non-small cell lung cancer and disease progression during targeted therapy: a real-world observational study, J. Med. Econ. 21 (2018) 192–200.
[34] M. Takeda, I. Okamoto, T. Yamanaka, K. Nakagawa, Y. Nakanishi, Impact of treatment with bevacizumab beyond disease progression: a randomized phase II study of docetaxel with or without bevacizumab after platinum-based chemotherapy plus bevacizumab in patients with advanced nonsquamous non-small cell lung cancer (WJOG 5910L), BMC Cancer 12 (2012) 327.