Cost effectiveness of ceritinib in patients previously treated with crizotinib and chemotherapy with anaplastic lymphoma kinase positive (ALK+) non-small cell lung cancer (NSCLC) in the United States

Yichen Zhang
Tulane University
Yixue Shao
Tulane University
Charles Stoecker
Tulane University
Lizheng Shi (lshi1@tulane.edu)
Tulane University

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Abstract

Background

Lung cancer is the leading cause of cancer death in the United States. Among non-small cell lung cancer (NSCLC) patients with anaplastic lymphoma kinase mutation (ALK+) and who were resistant to crizotinib, ceritinib was approved as a following treatment. Ceritinib was found to be cost effective among Canadian patients, but its cost effectiveness among US population remains unknown.

Objective

To evaluate the cost-effectiveness of ceritinib versus chemotherapy among ALK+ NSCLC patients who received treatment of crizotinib and chemotherapy, from the US healthcare perspective.

Methods

A Markov model with three health states (progression-free, progression, and death) and a partitioned survival analysis model (PartSA) were developed, respectively. Survival functions, including progression free survival and overall survival, for ceritinib and chemotherapy were extrapolated from clinical trials ASCEND-2, ASCEND-5, and PROFILE-1007. Costs for the drugs, monitoring, and adverse events, and utilities at each health state were derived from published literature. Costs were inflated to 2018 US dollars. An annual discount rate of 3% was applied to costs and utilities, and a 5-year time horizon was applied to the analysis. Incremental cost per quality-adjusted life year (QALY) gained for ceritinib versus chemotherapy was estimated with $150,000/QALY as the US willingness-to-pay threshold. Sensitivity analyses (i.e., one-way sensitivity analysis and probabilistic sensitivity analysis) were conducted to test the uncertainties of the models.

Results

Both models find ceritinib yields fewer QALYs than chemotherapy. The Markov model indicates modest cost-savings of ceritinib when compared to chemotherapy (-$3,131) and small declines in health (-1.04 QALYs) ($3008.39 per QALY lost). The PartSA model indicates additional costs of ceritinib when compared to chemotherapy ($12,884.95) and similar declines in health (-0.87 QALYs), indicating a dominated strategy. Both models were most sensitive to parameters of medical cost for progression disease and cost of ceritinib.

Conclusions

Ceritinib is not cost effective compared to chemotherapy among patients who were previously treated with crizotinib and chemotherapy, from the US healthcare perspective.

Background

Lung cancer is the leading cause of cancer death in both genders in the United States [1] . The estimated national expenditure on lung cancer care in 2018 was $14.2 billion [2] . The present value of lifetime earnings from lost productivity due to lung cancer diagnosis in 2005 was $36.1 billion [2] . Nearly all patients (85%) with lung cancer were diagnosed with non-small cell lung cancer (NSCLC) [3] . The 5-year overall survival of NSCLC is 23%, though this varies by cancer stage [4] .

Several genetic mutations in NSCLC have been identified recently[5]. The most commonly identified mutations were Kirsten ras (KRAS) gene (24% of all cases), and epidermal growth factor receptor (EGFR) gene (13–22% of all cases)[5]. Anaplastic lymphoma kinase (ALK) mutation occurred in 5–6% of all NSCLC cases[5]. ALK rearranged lung cancer, also called ALK-positive (ALK+), is most often seen in people who have never or rarely smoked[6]. Brain metastatic occurs frequently in patients with ALK + lung cancer[6].

Currently approved treatments for ALK rearrangement include ALK inhibitors crizotinib and ceritinib. Crizotinib was approved by the US Food and Drug Administration (FDA) to treat certain late-stage (locally advanced or metastatic) NSCLC that express the abnormal ALK gene, in 2011[7]. Ceritinib, approved by the US FDA in April 2014, is a next-generation ALK inhibitor and used for ALK + NSCLC patients who have progressed on or are intolerant to crizotinib[8]. Clinical trial data has shown that ceritinib is a more efficacious treatment option compared with chemotherapy (ASCEND-5) in patients previously treated with chemotherapy and crizotinib[9]. A significant improvement in median progressive-free survival was found among the patients with ceritinib comparing with patients with chemotherapy.

Several studies have evaluated the cost-effectiveness of ceritinib. One study has specifically evaluated its cost-effectiveness as a following treatment among patients previously treated with crizotinib in Canadian patients[10]. It suggested that ceritinib is a cost-effective option compared with other alternatives in patients who have progressed or are intolerant to crizotinib in Canada, based on the willingness-to-pay threshold for end-of-life cancer drugs. Only one US study have been conducted about the cost-effectiveness of ceritinib from the third payer perspective, however, ceritinib was considered as a first-line treatment in that study[11]. Ceritinib was cost-effective compared to crizotinib and chemotherapy as the first-line treatment among NSCLC patients with ALK + metastatic. In a recently published study in China, comparing the ceritinib and alectinib with crizotinib, from the Chinese medical system perspective, it found that even ceritinib and alectinib can extend the survival time of patients compared with crizotinib, first-line with crizotinib is the most cost-effective, according to the World Health Organization’s three-times gross domestic product (GDP) recommendation[12].

The cost-effectiveness of ceritinib as a second-line treatment among patients with ALK + mutation who were previously given chemotherapy and crizotinib remains unknown in the US. The aim of this study was to assess the cost-effectiveness of ceritinib among NSCLC patients who were previously treated with chemotherapy and crizotinib, comparing with chemotherapy from the US health payer perspective.

Methods

2.1 Target population

The study population of this analysis was patients with NSCLC with ALK rearrangement who were previously treated with crizotinib and chemotherapy in the United States. The comparators, ceritinib and chemotherapy, were continuing treatment options following the crizotinib and chemotherapy among this population.

2.2 Model structure

In this study we implemented both a Markov model and a Partitioned Survival Analysis (PartSA) model to assess the cost-effectiveness of ceritinib versus chemotherapy as a following treatment after the advent of drug resistance to crizotinib in this population. Following the standard in oncology studies, our models consider three health states: profession-free survival (PFS), progressed disease state (PD), and death (Fig. 1). The PartSA model estimates time spent in PFS and death states through survival curves while the time spent in PD state is calculated using the difference in area between the two curves. Markov models, on the other hand, calculate the three states simultaneously rather than the separate modeling of the two outcomes in PartSA model[13–15].

At the beginning of each model, all patients were assumed to be in the PFS state receiving either ceritinib or chemotherapy. Then after each cycle, patients could either stay in the same state, or enter the PD state or death state, based on the transition probability. Patients in the PD state can only stay in the same health state or move to death state. One key difference in the assumptions in Markov model and PartSA model is that, in PartSA model, one subject can only transit from PFS to PD then to death, in a sequence; while in Markov model, one subject can transit directly from PFS to death.

A 5-year time horizon was implemented in both models, with 30 days in each cycle. An annual discount rate of 3% was applied to cost and utility. The analysis was performed from the US payer perspective. TreeAge 2020 (TreeAge Software, Inc., Williamstown, MA, USA) was used for the construction of Markov model and PartSA model, base case analysis, and sensitivity analysis.

2.3 Model inputs

2.3.1 Clinical data inputs

The comparator of chemotherapy in this study included pemetrexed and docetaxel, which were the same comparators in the ASCEND-5 trial (ClinicalTrials.gov, number NCT01828112)[9]. The probabilities of PFS for ceritinib and chemotherapy were obtained from the ASCEND-5 trial[9]. The ASCEND-5 clinical trial is an open-label phase-3 trial, comparing ceritinib and chemotherapy in patients previously treated with chemotherapy and crizotinib. The probabilities of overall survival (OS) of comparators, however, were from other similar trials because this data was not published for the ASCEND-5 trial. The OS for ceritinib was obtained from the ASCEND-2 trial (ClinicalTrials.gov, number NCT01685060), a single-arm, phase-2 trial of ceritinib in similar NSCLC patients with ALK rearranged (ALK+) previously treated with

chemotherapy and crizotinib[16]. The OS for chemotherapy was obtained from the PROFILE-1007 trial (ClinicalTrials.gov, number NCT00932893), a phase-3 trial of crizotinib versus standard of care in advanced NSCLC patients with ALK + [17]. We assumed that the efficacy data inferred from the other reported study of the ALK + population in PROFILE 1007 was applicable to patients with ALK + NSCLC who have failed treatment with crizotinib. The Graph Digitizer (version 2.26; http://getdata-graph-digitizer.com) was used to extract PFS probabilities and OS probabilities from the progression-free survival (PFS) and OS curves and to construct individual-level data for the Kaplan Meier (KM) curves. SAS was used to fit individual data with parametric survival functions, such as log-logistic, log-normal, exponential, and Weibull. Goodness of fit was examined using Akaike information criterion (AIC) and Bayesian Information Criterion (BIC).

For both ceritinib and chemotherapy, the exponential survival function was selected to predict the OS, and log-logistic survival function was selected to predict the PFS. The reproduced survival curves using the predicted survival functions are shown in **eFigure1**. The proportion of patients in each health state in each cycle was calculated based on the predicted PFS and OS. For example, the probability of staying in PFS state is the proportion of patients who were under the PFS curve, the probability of death is the proportion of patients who were above the OS curve. The probability of PD state is the proportion of patients who were above the PFS curve but below the OS curve. Efficacy inputs are shown in Table 1.

Table 1
Summary of model inputs

Clinical data input					
Interventions	**Details**	n	**Outcomes (months)**	**Parameter functions**	**Reference**
Ceritinib					
PFS	oral ceritinib 750 mg per day fasted (in 21 day treatment cycles)	115 (100%)	Median PFS = 5.4	Log-logistic	ASCEND-5[9]
Death			Median OS = 11.3	Exponential	ASCEND-2[16]
Comparators: chemotherapy (34% pemetrexed & 63% docetaxel)					
PFS	pemetrexed: intravenous 500 mg/m², every 21 days; docetaxel: 75 mg/m², every 21 days	113 (97%)	Median PFS = 1.6	Log-logistic	ASCEND-5[9]
Death			Median OS = 22.8	Exponential	PROFILE-1007[17]
		Input		**Note**	**Reference**
Utility input					
Progression-free state (PFS)					
Ceritinib		0.73		Low: 0.66; High: 0.80	Carlson, J. J. *et al.*, 2017[20]
Chemotherapy		0.69		Low: 0.62; High: 0.76	Blackhall, F. *et al.*, 2014[22], Shaw, A. T. *et al.*, 2017[9]
Progressive Disease (PD)		0.46		Low: 0.28; High: 0.63	Chouaid, C. *et al.*, 2013[23]
Cost input					
Unit cost					
Ceritinib		$ 11,043.83		Adjusted to 2018 USD	Zhou et al, 2018[11]; Truven, 2017[25]
Chemotherapy					

Clinical data input			
Pemetrexed	$ 6,169.94	Adjusted to 2018 USD	Zhou et al, 2018[11]; Huang et al, 2017[18]; Truven, 2017[25]
Docetaxel	$ 1,430.83	Adjusted to 2018 USD	Zhou et al, 2018[11]; Huang et al, 2017[18]; Truven, 2017[25]
Total chemotherapy	$ 3,089.52	Adjusted to 2018 USD	Patient proportion from Shaw, A. T. et al., 2017[8]
Drug delivery cost			
Intravenous (IV) infusion			
Chemo IV push additional drug	$ 59.76	Adjusted to 2018 USD	CMS Physician Fee Schedule (HCPCPS Code: 96411)[19]
Chemo IV infusion 1 hour	$ 144.72	Adjusted to 2018 USD	CMS Physician Fee Schedule (HCPCPS Code: 96413)[19]
Chemo IV infusion additional hour	$ 31.68	Adjusted to 2018 USD	CMS Physician Fee Schedule (HCPCPS Code: 96415)[19]
Intr-muscular injection			
Therapeutic, prophylactic, or diagnostic injection	$ 20.88	Adjusted to 2018 USD	CMS Physician Fee Schedule (HCPCPS Code: 96372)[19]

Clinical data input			
Total administration cost	$ 257.04	Adjusted to 2018 USD	
Monitoring cost (PFS only)	$ 191.15	Adjusted to 2018 USD	Carlson, J. J. *et al.*, 2017[20]
Medical cost of progression disease (monthly)	$ 12,053.68	Adjusted to 2018 USD	Fox *et al.*, 2008[24]; Zhou *et al.*, 2018[11]
Cost associated with terminal care (one-time)	$ 18,232.91	Adjusted to 2018 USD	Chastek *et al.*, 2012[26]; Zhou *et al.*, 2018[11]
Cost associated with AEs (one-time)			
Ceritinib	$ 445.29	Adjusted to 2018 USD	Carlson, J. J. *et al.*, 2017[20]; Arunachalam A *et al.*, 2018[21]
Chemotherapy	$ 99.11	Adjusted to 2018 USD	Carlson, J. J. *et al.*, 2017[20]; Arunachalam A *et al.*, 2018[21]

2.3.2 Utility inputs

The utility of PFS and PD states for ceritinib and chemotherapy were extracted from published literature[11,18–26]. It is assumed that the utility of PD state remains the same, regardless of the treatment arm in both models. The ranges of utility for each state under each arm were extracted for one-way sensitivity analysis. Utility inputs are shown in Table 1.

2.3.3 Cost inputs

In each model, only direct medical costs were included in this study. The costs considered in both models included drug costs, drug delivery costs, adverse events (AEs) management costs, monitoring costs for PD state, and terminal costs at death state. All costs were converted to 2018 USD. Cost inputs are shown in Table 1.

Drug, drug delivery costs. Drug costs of ceritinib, pemetrexed and docetaxel were calculated based on body surface area (BSA) and estimated dosage needed[11,18]. Total cost for chemotherapy was summed

following the usage rates of pemetrexed and docetaxel in the ASCEND-5 trial[9]. Drug delivery costs included intravenous infusion and intra-muscular injection. Unit costs for drug administration were obtained from the 2018 Physician Fee Schedule from the Centers for Medicare & Medicaid Services (CMS)[19]. It was assumed that there were no drug administration costs for oral drugs, thus, no drug administration costs were included for ceritinib treatment arm.

AE management costs. Grade 3 or 4 AEs with greater than 5% incidence rate of ceritinib reported in ASCEND-5 were included in the models[9]. The rate of each AE was based on ASCEND-5 trial[9]. Unit cost of each AE was obtained from public literature[20, 21]. It was assumed that AEs occurred when patients took oral drugs or IV injections in the PFS state in every cycle. Thus, when patients moved into the progressed state, there would be no AE management costs.

Monitoring costs for PD state. When patients were in the PD state, it was assumed that no active treatments were given in this state. Instead, patients in this state would have regular physician visits, and radiologic monitoring.

2.4 Base-case analysis and sensitivity analysis

2.4.1 Base-case analysis

Quality-adjusted life years (QALYs) were used to measure health benefits. The incremental cost-effectiveness ratio (ICER) between ceritinib and chemotherapy was calculated using the differences in costs in 2018 USD divided by the differences in QALYs gained.

2.4.2 Sensitivity analysis

Deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) were conducted to test the impact of uncertainties of model inputs on the models. The DSA, also called one-way sensitivity analysis, was conducted by validating one model input at a time. It can address the methodological uncertainty from model structure, selection of data inputs or model assumptions. Tornado diagram analysis was used to assess the relative weight of each variable on overall uncertainty. The range of each model input used in the DSA was derived from published literature or based on plausible ranges and distributional assumptions followed the recommended guidelines[27]. The parameters tested in DSA included medical cost for PD state, QALY of PFS for each treatment group, disutility of progression in each treatment group, costs of medications, monitoring costs, costs of managing adverse events, costs associated with terminal care at death state, and discount rate.

The PSA was conducted to estimate the probability of ceritinib being cost-effective compared with chemotherapy, using the willingness-to-pay (WTP) threshold of $150,000 USD [28] . A Monte-Carlo simulation with 50,000 iterations was performed, in which model inputs were randomly drawn from the specified distributions at each iteration. In both Markov and PartSA models, PFS and OS functions were assumed to follow a Weibull distribution. Costs were assumed to be Gamma distributed, while utilities for the three health states were assumed to have a Beta distribution.

Results

Base case analysis

The results of the base case analysis from Markov model and PartSA model are presented in Table 2. In the Markov model, at the end of the 5-year time horizon, ceritinib treatment cost $331,297 and yielded 12.93 QALYs, chemotherapy treatment cost $334,428 and yielded13.97 QALYs. A treatment strategy using ceritinib versus chemotherapy saved $3,131 at the cost of 1.04 QALYs. ICER was $3008.39 per QALY lost in the Markov model. Comparing with the willingness-to-pay threshold of $150,000/QALY, ceritinib was not cost-effective versus chemotherapy. When modeled with the PartSA model, ceritinib as a secondline treatment was a dominated treatment (it cost more than chemotherapy and yielded fewer health benefits). The results are shown in Table 2.

Table 2
Base-case results

Markov model					
Strategy	**Cost**	**Incremental Cost**	**QALY**	**Incremental QALY**	**Incr C/E (ICER)**
Chemotherapy	$ 334,428.00		13.97		
Ceritinib	$ 331,297.00	$ (3,131.00)	12.93	-1.04	3008.39
PartSA model					
Strategy	**Cost**	**Incremental Cost**	**QALY**	**Incremental QALY**	**Incr C/E (ICER)**
Chemotherapy	$ 340,702.17		14.13		
Ceritinib	$ 353,587.13	$ 12,884.96	13.26	-0.87	-14859.25

Sensitivity analysis

Deterministic sensitivity analysis (DSA)

The tornado diagrams from two models are shown in Fig. 2a **and** Fig. 2b. Both models were robust from the DSA results. In both models, the calculated incremental cost per QALY gained from ceritinib versus chemotherapy was the most sensitive to medical cost for PD state, cost of ceritinib, and utility of PFS state in ceritinib arm.

Probabilistic sensitivity analysis (PSA)

PSA of the Markov model comparing ceritinib and chemotherapy indicated there is a higher chance that ceritinib was not cost-effective at the WTP threshold of $150,000, as 61.59% of the iterations had ceritinib above the WTP threshold in the incremental cost-effectiveness (ICE) scatter plot (**eFigure2a)**. The cost-

effectiveness acceptability curve (CEAC) is shown in Fig. 3a. The probability that ceritinib was cost-effective increased from 28.2–40.0% as the WTP per QALY increased from $0 to $300,000.

PSA of the PartSA model comparing ceritinib and chemotherapy indicated 60.87% of the iterations indicated that ceritinib was not cost-effective at the WTP threshold of $150,000 (**eFigure2b)**. The cost-effectiveness acceptability curve (CEAC) is shown in Fig. 3b. From the Monte Carlo simulation report, the probability for ceritinib to be cost-effective over chemotherapy in this model increased from 14.7–46.4% as the WTP threshold increased from $0 to $300,000.

Discussion

This study found that ceritinib is not cost-effective as a following treatment among NSCLC patients with ALK + who were previously treated with chemotherapy and crizotinib, from the US health payer perspective. To our best knowledge, this is the first study conducted in the US setting and considering ceritinib as a second-line treatment, instead of a first-line treatment.

This finding was robust to model choice as both Markov and PartSA models, demonstrated that ceritinib was not cost-effective when compared to chemotherapy in the study population. Both models were most sensitive to the same factors in the one-way sensitivity analysis.

The study finding is not consistent with previous studies. The Canadian study found ceritinib to be cost-effective among patients who have progressed or are intolerant to crizotinib, comparing with the willingness-to-pay threshold for end-of-life cancer drugs[10]. This result may not be comparable because of the heterogeneity in study samples, drug costs, parameters, and willingness-to-pay threshold. The Canadian study used a pooled patient population of ASCEND-1 and ASCEND-2 in patients previously treated with crizotinib, while we used ASCEND-5, the most recent appropriate phase 3 clinical trial. Costs for active treatments in the Canadian study also included associated costs of concomitant medications, including dexamethasone, NSAIDs, bisphosphonate, and morphine for chemotherapy, and folic acid associated with pemetrexed, while we did not consider these, because information on specific concomitant medications used in ASCEND-5 trial was unavailable. In both strategies there will be concomitant medication expenditures, so we are unable to anticipate if this will bias our findings in favor of one particular strategy. In addition, which adverse events were included in the Canadian study were not explicitly specified, so we are unable to predict how our selection of adverse events may affect the results. Further, as both arms in our study are from the same clinical trial, we were able to extract adverse events from a single study for both arms. In comparison, the Canadian study pulled data on the two strategies from different clinical trials which may bias that study in favor of one arm over the other if there are differences between the two. The Canadian study compared certinib to pemetrexed monotherapy, whereas we followed the ASCEND-5 trial and compared certinib to a combination of pemetrexed and docetaxel. And lastly, the Canadian study was conducted from the Canadian public healthcare perspective which has lower prices than in the US perspective used here.

Prior work has shown ceritinib was cost-effective as a first-line treatment among NSCLC patients in the US, compared with chemotherapy, using ASCEND-4 clinical trial data[11]. However, when ceritinib is used for a continuing treatment option after crizotinib, it is assumed that the patients have already experienced cancer progression or intolerant on crizotinib. Thus, the progression rate or progression free survival is different among patients using ceritinib as first-line treatment and patients with ceritinib as a following treatment after crizotinib. The comparator platinum doublet (with maintenance) in ASCEND-4 included pemetrexed in combination with cisplatin, or carboplatin followed by pemetrexed maintenance therapy. The chemotherapy combination is different from what we adapted from ASCEND-5 trial in our study as mentioned above. In addition, comparing the predicted PFS and OS curves for ceritinib and chemotherapy from ASCEND-4 trial adapted in the US study (Fig. 2 from Zhou *et al.*, 2018[11]), the proportions of patients remaining alive under ceritinib and platinum doublet treatments at 60 months from ASCEND-4 were higher than the proportion that we predicted from ASCEND-5 trial. This may be able to explain the difference in cost-effectiveness of ceritinib when it is used at different lines.

In addition, the PFS curves and OS curves in eFigure1 supported our findings. Even the PFS from ceritinib is longer than the PFS from chemotherapy (median time of 5.4 months from ceritinib vs. median time of 1.6 months from chemotherapy, the OS from ceritinib is significantly shorter than the OS from chemotherapy (median time of 11.3 months from ceritinib vs. median time of 53.1 months from chemotherapy). Thus, ceritinib may be cost-effective in short term, but it may lead to the opposite direction in long term.

One of our strengths is that two models for the same cost-effectiveness analysis were performed in this study. Ceritinib was not cost-effective in both models. And both models were most sensitive to the same parameters including medical cost for PD state, cost of ceritinib, and utility of PFS state in ceritinib arm in the one-way sensitivity analysis, even the calculated ICERs were different. Another strength is that the survival rates (i.e., progression free survival and overall survival) were extrapolated from clinical trials, instead of using transition probabilities from published literature, using survival rates from real-world clinical trials provided more reliability in our data inputs.

While ceritinib performs more poorly on ultimate survival than chemotherapy, patients on ceritinib spend less time on the progressed disease state, which is an expensive state to maintain. The PartSA model finds increased costs of certinib over chemotherapy (compared to the Markov model) since patients in the PartSA model spend more time in the progression free state, magnifying the additional costs patients accrue at that stage under ceritinib. Since the transition from PFS to death is not allowed in the PartSA model, while it is allowed in Markov model, more subjects transited out from PFS to other states in Markov model in each cycle. Though we note that both models found numerous iterations both above and below cost-effectiveness thresholds, so this difference may not be statistically significant.

There are some limitations in this study. First, we extracted survival rates from graphs published in the ASCEND-5 trial. Ideally our study would be based on individual patient data. This extract process may cause measurement error in the survival rates at different cancer stages. Second, the OS curves of

ceritinib and chemotherapy were extracted from two different clinical trials, ASCEND-2 and PROFILE-1007. These two trials had different study population selection criteria. However, the efficacy observed in ASCEND-5 was consistent with the reported results in ASCEND-2, and ASCEND-2 and PROFILE-1007 have similar patient populations with progressed ALK + NSCLC, except for the previous treatment of crizotinib criteria. Median age in both trials was about 50 years, and gender and race distributions were similar. The PROFILE 1007 trial had similar median overall survival as was reported in the ASCEND-5 trial. The populations in these trials most closely matched our study population. Third, this study only included direct medical cost in the analysis, indirect costs such as cost due to loss of productivity and transportation were not considered. The estimated ICER may change accordingly when considering the indirect costs. Ceritinib is taken orally and may be taken at home without physician supervision and thus is accompanied by minimal travel costs. Chemotherapy is taken intravenously once per cycle (e.g. once per month) and thus requires regular travel costs to locations where the injections can be administered. This difference in where drugs can be administered may cause ceritinib to be more cost-effective, potentially reversing our findings if these travel costs and lost productivity costs are high enough. Fourth, although we used the most appropriated parameters to our study population, all model inputs in this study were not all based specifically on NSCLC patients previously treated with crizotinib and chemotherapy. Other factors, such as previous treatment options or numbers of lines of treatments, that may have impacts on utilities were not controlled for in our analysis.

Conclusion

From the payer perspective in the US, ceritinib is not cost effective as a following treatment option for patients who developed drug resistance after crizotinib and chemotherapy. Our findings provide important insight for decision making among payers and other policy makers about the clinical and economic value of ceritinib relative to the chemotherapy as a treatment option for patients previously treated ALK + NSCLC.

Abbreviations

ALK+
anaplastic lymphoma kinase positive
NSCLC
non-small cell lung cancer
PartSA
partitioned survival analysis model
QALY
quality-adjusted life year
KRAS
Kirsten ras gene
EGFR

epidermal growth factor receptor
FDA
US Food and Drug Administration
GDP
gross domestic product
PFS
profession-free survival
PD
progressed disease
OS
overall survival
PFS
progression-free survival
KM
Kaplan Meier curves
AIC
Akaike Information Criterion
BIC
Bayesian Information Criterion
AE
adverse event
BSA
body surface area
CMS
Centers for Medicare & Medicaid Services
ICER
incremental cost-effectiveness ratio
DSA
deterministic sensitivity analysis
PSA
probabilistic sensitivity analysis
WTP
willingness-to-pay

Declarations

Ethics approval and consent to participate

This study used published data for model input. There was no participant in this study nor direct interaction. No ethical approval or consent to participate was in need for this study.

Consent for publication

This study does not have any individual person's data.

Availability of data and materials

This study used published data for model inputs. All the data were reported in the tables.

Competing interests

The authors declare no conflict of interest.

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Author's contribution

Yichen Zhang substantially contributed to the concept of the work, analyzed and interpreted the data for the work, drafted of the work and revised it critically for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Yixue Shao analyzed the data for the work, revised the manuscript critically for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Charles Stoecker interpreted the data for the work, revised the manuscript critically for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Lizheng Shi, the corresponding author, substantially contributed to the conception or design of the work, revised the manuscript critically for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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