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Cost-effectiveness of adjuvant icotinib versus chemotherapy for patients with stage II–IIIA EGFR-mutated non-small cell lung cancer in China

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ABSTRACT

Objective Icotinib has been approved for adjuvant treatment of stage II–IIIA non-small cell lung cancer (NSCLC) patients with activating epidermal growth factor receptor (EGFR) mutations in China, yet the long-term costs and outcomes of this strategy are unknown. Thus, we examined the cost effectiveness of adjuvant icotinib, compared with adjuvant chemotherapy, for the treatment of resected stage II–IIIA EGFR-mutated NSCLC.

Design We performed a cost-effectiveness analysis from the perspective of the Chinese healthcare system, comparing 2-year adjuvant icotinib with four cycles of adjuvant chemotherapy. Costs and quality-adjusted life years (QALYs) were estimated using a Markov model. Model inputs were obtained from local data and literature. The influence of model parameters and assumptions was explored in sensitivity analyses. All costs are expressed in 2022 US dollars, and costs and QALYs were discounted at a rate of 5% per year. The willingness-to-pay (WTP) threshold was set at three times the per capita gross domestic product.

Setting The Chinese healthcare system perspective.

Participants A hypothetical Chinese cohort of patients with resected stage II–IIIA EGFR-mutated NSCLC.

Interventions Icotinib versus chemotherapy.

Primary outcome measure Costs, QALYs, incremental cost-effectiveness ratio.

Results The incremental cost per QALY gained with the use of 2-year icotinib, from the Chinese healthcare system perspective, was $3440.66 compared with adjuvant chemotherapy. At a WTP threshold of $40 500, adjuvant icotinib was the optimal treatment in over 99% of replications. The interpretation of the results was insensitive to model and input assumptions.

Conclusions Compared with adjuvant chemotherapy, adjuvant icotinib may be a cost-effective treatment for resected stage II–IIIA EGFR-mutated NSCLC as the WTP threshold is set at $40 500 per QALY.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Both standard parametric survival models and Royston-Parmar models were taken into consideration for survival extrapolation.
⇒ Two different modelling methods, TreeAge Pro and R, were used to ensure the transparency and reproducibility of the study.
⇒ Parametric survival extrapolation based on immature overall survival data of EVIDENCE trial may introduce bias and uncertainty to findings.

INTRODUCTION

Non-small cell lung cancer (NSCLC) is of the highest incidence and mortality over the world, as well as in China.[1 2] Approximately 50% of Asian NSCLC patients have epidermal growth factor receptor (EGFR) mutations, of higher proportion than the Caucasians.[3] The main types of EGFR gene mutations are exon 19 deletion and L858R mutation in exon 21, accounting for almost 90%.[4] The fact that the incidence of EGFR mutations occurs similarly in both resectable early-stage lung adenocarcinoma and advanced-stage patients shed light on the application of EGFR tyrosine kinase inhibitors (EGFR-TKIs) which are the standard first-line treatment for NSCLC patients with EGFR sensitive mutations.[5–7] However, platinum-based chemotherapy has always been the standard adjuvant treatment in early-stage NSCLC patients with complete resection of stage II–IIIA NSCLC, followed by limited improvement in disease-free survival (DFS) and overall survival (OS).[8–10]

In recent years, new clinical trials have explored the efficacy and safety of EGFR-TKIs in the adjuvant treatment setting for EGFR-mutated NSCLC patients.[11–14] For instance, the EVIDENCE trial, a phase III, multicentre and randomised controlled trial (RCT) based on the Chinese population, included a total of 322 stage II–IIIA R0 resected NSCLC patients with activating EGFR mutations and compared the efficacy and safety of 2-year adjuvant icotinib (N=161) with adjuvant chemotherapy (N=161). The results showed that the icotinib group had a longer median DFS than the chemotherapy group (47.0 months vs 22.1 months, HR 0.36, 95% CI 0.24 to 0.55; p<0.0001), while the data for

OS at a median follow-up of 24.9 months preliminarily revealed the mortality rates in the icotinib group and chemotherapy group were 9% and 11%, respectively.[15] Supported by the positive results of the EVIDENCE trial, the National Medical Products Administration of China approved icotinib for adjuvant treatment of stage II–IIIA NSCLC patients with activating EGFR mutations in June 2021.[15]

Since the cost-effectiveness of targeted therapy for tumours has always been a concern in resource-limited settings in China and the long-term costs and outcomes of adjuvant icotinib for resected stage II–IIIA EGFR-mutated NSCLC are unknown, we conducted this study to evaluate the cost-effectiveness of 2-year adjuvant icotinib from the Chinese healthcare system perspective.[16–19]

METHODS

Patient population

A cost-effectiveness model was constructed to compare postoperative adjuvant icotinib with postoperative adjuvant chemotherapy with the patients included in the model reflecting the cohorts included in the EVIDENCE trial. All the patients, with stage II–IIIA NSCLC but without previous systemic antitumour therapy, had been confirmed the EGFR 19del or 21L858R activating mutations after R0 resection, the median age of whom was 59 years old.[15]

Model construction

A Markov model, with three mutually exclusive health states, including disease-free (DF), post-progression (PP) and death, was constructed to simulate the natural history of the disease. The resected EGFR-mutated NSCLC patients in the model received adjuvant icotinib or chemotherapy. The former received 2 years of icotinib treatment, while the latter received four cycles of platinum-containing double-drug chemotherapy. Otherwise, we assumed that all patients received osimertinib (third-generation EGFR-TKI) after disease relapse.[20] The Markov model had a cycle of 1 week, and the study time horizon was 20 years. The primary endpoint of this study was the incremental cost-effectiveness ratio (ICER), which represented the cost paid to gain one more quality-adjusted life year (QALY). A discount rate of 5% was used for costs and effects according to the China guidelines for pharmacoeconomic evaluations.[21] From the perspective of the Chinese healthcare system, the willingness-to-pay (WTP) threshold was set at three times the per capita gross domestic product of China, which is about $40 500 in 2022.[22] The Markov model was constructed with TreeAge Pro (TreeAge Software, Williamstown, MA), and other statistical analyses and visualisation were performed via R (V.4.3.1).

Transition probabilities

The parameters for transition probabilities in the base-case analysis are shown in table 1. The transition probabilities were calculated from the EVIDENCE trial and Chinese age-specific mortality rates.[15 23] The individual patient-level data were reconstructed using the method established by Guyot *et al*.[24–26] The proportional hazards (PH) assumption was tested to determine whether the icotinib group and the chemotherapy group followed the PH assumption. If the PH assumption was satisfied, a PH model was used; otherwise, separate survival models were fitted to the data of the two groups. The predicted survival curves were compared with the Kaplan-Meier curves, and suitable parametric survival models were selected based on the Akaike information criterion (AIC), Bayesian information criterion (BIC) and plausibility of the extrapolation.[27]

We reconstructed 20 survival curves based on 5 clinical trials including the EVIDENCE trial. The reconstructed DFS and OS data, and the corresponding results of the parametric survival analysis are deposited online (https://mulifeng.shinyapps.io/reconIPD_EGFRmN-SCLC_adj/). Since the DFS data from the EVIDENCE trial followed the PH assumption (p=0.102), exponential, Weibull, Gompertz and Royston-Parmar (RP) models (having greater flexibility than standard parametric survival models) were considered (see online supplemental figures S1 and S2). In the base-case analysis, the RP model (k=3) was selected to fit the DFS data.[27 28] Similar to the DFS data, the test results showed that the OS data from the EVIDENCE trial also followed the PH assumption (p=0.357) (see online supplemental figures S1 and S3). Thus, the Weibull model was selected to fit the OS data in the base-case analysis, based on the AIC, BIC and plausibility of the extrapolation.[27 28]

As both DFS and OS data were fitted with PH models, the HRs were used to measure the difference in efficacy between the icotinib and the chemotherapy strategy in our model.[27] Based on the transition probabilities of the chemotherapy group and HR, the transition probabilities for the icotinib group were calculated using the following formula: $tp_{ico} = 1 - \left(1 - tp_{chemo}\right)^{HR}$, where the transition probabilities from the DF state to the death state were calculated based on age-specific mortality rates in China published by the WHO.[23]

Costs

The cost parameters included in the model are shown in table 1. The cost of the chemotherapy strategy was based on cost data from inpatient at the Affiliated Hospital of North Sichuan Medical College, including three components: cost of platinum drugs, cost of non-platinum antitumour drugs and other inpatient costs (see online supplemental figure S4). Other inpatient costs included costs of non-antitumour drugs, examination fees, treatment fees, bed fees and so on. All these costs were calculated in 2022 US dollars (Consumer Price Index for Medical Care and a ratio of 1 US dollar=6.35 Chinese yuan were applied).[29] For the icotinib strategy, the cost of icotinib and the management cost of grade ≥3 adverse events were considered. The cost of icotinib

Table 1 Model parameters

Parameters	Point estimation (ranges)	Distribution (parameters)	Data source
Starting age	59.0 (52 to 64)¶	Normal (58.299, 8.942)	15
Duration of treatment for icotinib	22.2 (13.8 to 24.8)¶	Fixed	15
RP DFS model of chemotherapy*	gamma0=−7.144, gamma1=2.516, gamma2=−1.413, gamma3=2.639, gamma4=−1.402	Fixed	15
Weibull OS model of chemotherapy	shape=1.994, scale=0.000117	Fixed	15
HR of icotinib versus chemotherapy for DFS†	0.373 (0.250 to 0.557)**	Log-normal (−0.986, 0.205)	15
HR of icotinib versus chemotherapy for OS†	0.837 (0.399 to 1.756)**	Log-normal (−0.178, 0.378)	15
Probability of grade ≥3 adverse event in icotinib	0.109 (0.098 to 0.120)††	Beta (10.9, 89.1)	15
Probability of grade ≥3 adverse event in chemotherapy	0.612 (0.551 to 0.673)††	Beta (61.2, 38.8)	15
Cost per model cycle‡			
Icotinib	131.66 (118.49 to 144.83)††	Fixed	Local charge
Osimertinib	182.49 (164.28 to 200.79)††	Fixed	Local charge
Platinum drugs per cycle§	122.02 (90.53 to 128.49)¶	Gamma (2.728, 0.025)	Local charge
Non-platinum drugs per cycle§	382.96 (380.67 to 382.96)¶	Gamma (9.789, 0.027)	Local charge
Hospital expenses excluding antitumour drugs per cycle§	409.92 (302.97 to 610.30)¶	Gamma (2.463, 0.005)	Local charge
Management grade ≥3 adverse event per unit	362 (272 to 453)	Gamma (2850, 7.874)	16
Cost of disease recurrence per unit	705 (452.5 to 1022)	Gamma (3407, 0.207)	16
Utilities			
DF state	0.82 (0.78 to 0.86)	Beta (82, 18)	49 51
PP state	0.70 (0.66 to 0.74)	Beta (70, 30)	34 49
Disutility of grade ≥3 adverse event	−0.353 (−0.392 to −0.314)	−Beta (35.3, 64.7)	51

*RP model, k=3.
†Estimated from parametric survival analysis based on reconstructed survival data.
‡One model cycle=1 week.
§One chemotherapy cycle=3 weeks.
¶Median (IQR).
**95% CI.
††Point estimate±10%.
DF, disease-free state; DFS, disease-free survival; OS, overall survival; PP, post-progression state; RP, Royston-Parmar.

came from the reference price of the centralised drug procurement.[30–33]

Utilities

The utility values of health states were derived from published literature (table 1). The utility for DF and PP states are 0.82 and 0.70, respectively. The disutility of grade ≥3 adverse events is −0.353.[34 35] QALYs are calculated by weighting the survival years of patients using the utility values for each health state.

Sensitivity analysis

We conducted one-way sensitivity analyses and probabilistic sensitivity analysis to assess the uncertainty of the model. One-way sensitivity analysis evaluated the impact of individual parameters in the model on the ICER within a specified range. In probabilistic sensitivity analysis, parametric distributions were used to describe the input parameters in the Markov model. Then, 1000 Monte Carlo simulations were performed, with model input parameters resampled from the specified distributions, where cost was described by a gamma distribution, baseline age by a normal distribution, HR by a log-normal distribution and probabilities and utility values by beta distributions.

In addition, several scenario analyses were conducted. First, the change in ICER value was considered when the time horizon was shortened to 10 years. Second, other PH models were considered since the differences between different parametric survival models in the base-case analysis may or may not have statistical significance. Survival

data of chemotherapy from other RCTs were also considered. Third, the impact of 3-year adjuvant treatment with icotinib was considered.[13 15 36] Finally, the pooled HRs from two recently published network meta-analyses were used to observe their impact on the ICER.[37 38]

Model validation

The Markov model was validated according to the International Society for Pharmacoeconomics and Outcomes Research guidelines.[39]

As the OS data from the EVIDENCE trial was immature, our model performance was validated using external data, the ICOMPARE trial.[15 36] This study is a phase II RCT that compares 2-year adjuvant icotinib with 1-year adjuvant icotinib in stage II–IIIA EGFR-mutated NSCLC. It has a longer median follow-up time than the EVIDENCE trial, and thus the OS data from the 2-year adjuvant icotinib group in this study was taken to compared with our model simulation performance.[15 36] Furthermore, the reproducibility of the model results was guaranteed by a Markov model reconstruction based on R scripts, followed by the comparison between the two approaches.[40 41]

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Base-case analysis

The total costs of the icotinib and chemotherapy strategies are $24 554.18 and $20 206.56, respectively. The average QALYs for the icotinib and chemotherapy strategies are 5.48 and 4.22, respectively. Compared with chemotherapy, the ICER for the icotinib strategy is $3440.66 per QALY, equivalent to 8.50% of the WTP threshold.

Sensitivity analysis

One-way sensitivity analysis

The results of the one-way sensitivity analysis are shown in figure 1. Among all the model parameters, the HR for DFS is the most sensitive variable to ICER, followed by the duration of treatment for icotinib, the HR for OS, the cost of icotinib, the hospital expenses excluding antitumour drugs and the utility of DF state. When the HR for DFS ranges from 0.25 to 0.56, the estimated ICER increases from $1746.30 per QALY to $6167.80 per QALY. When the cost of icotinib increases from $118.49 to $144.83, the ICER increases from $2579.41 per QALY to $4301.90 per QALY. When the model parameters vary within their specified ranges, the ICER remains below the WTP threshold of $40 500, indicating the robustness of the base-case analysis results.

Probabilistic sensitivity analysis

The cost-effectiveness acceptability curve is shown in figure 2. When the WTP threshold is $40 500 per QALY, the probability of cost-effective adjuvant icotinib exceeds 99%.

Scenario analysis

The results of the scenario analysis are shown in table 2. In the first scenario analysis, when the time horizon is 10 years, the estimated ICER is $3446.16 per QALY. In the second scenario analysis, when the disease recurrence process was described using exponential, Weibull and Gompertz models, the corresponding ICER were $1807.86, $4067.93 and $4932.48 per QALY, respectively. The chemotherapy group showed similar disease

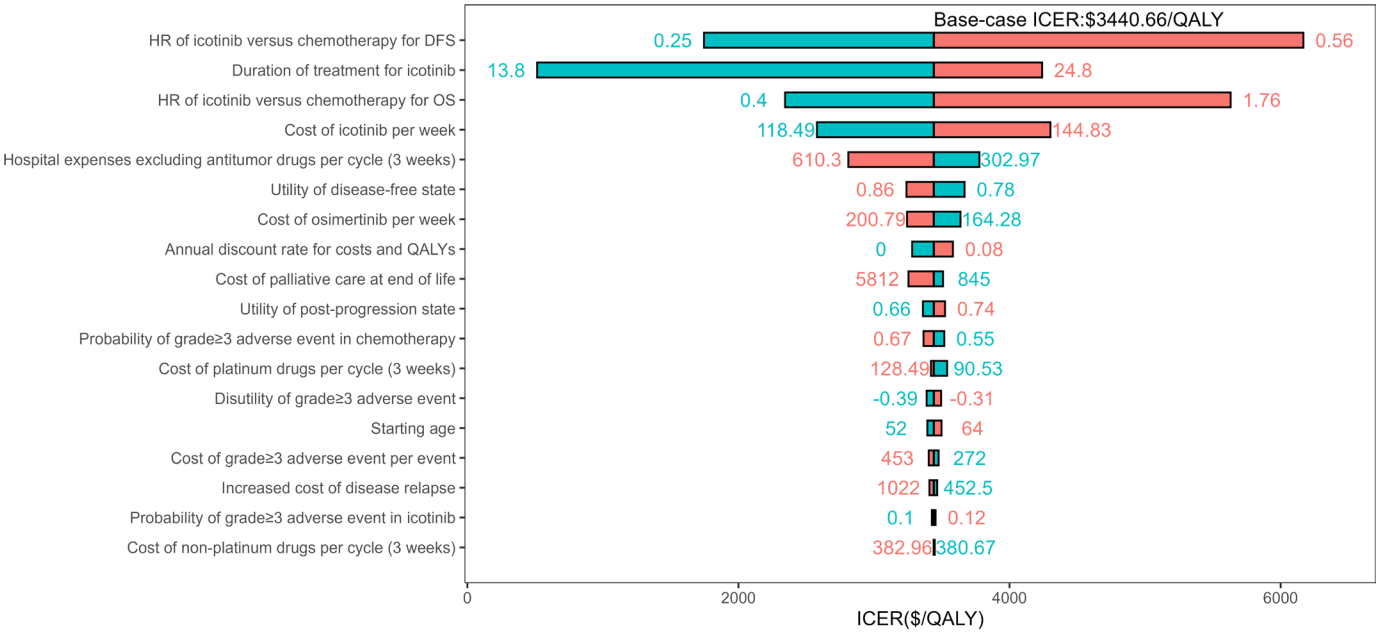

Figure 1 Tornado diagram of the one-way sensitivity analysis of the incremental cost-effectiveness ratio (ICER) of icotinib over chemotherapy. DFS, disease-free survival; OS, overall survival; QALY, quality-adjusted life year.

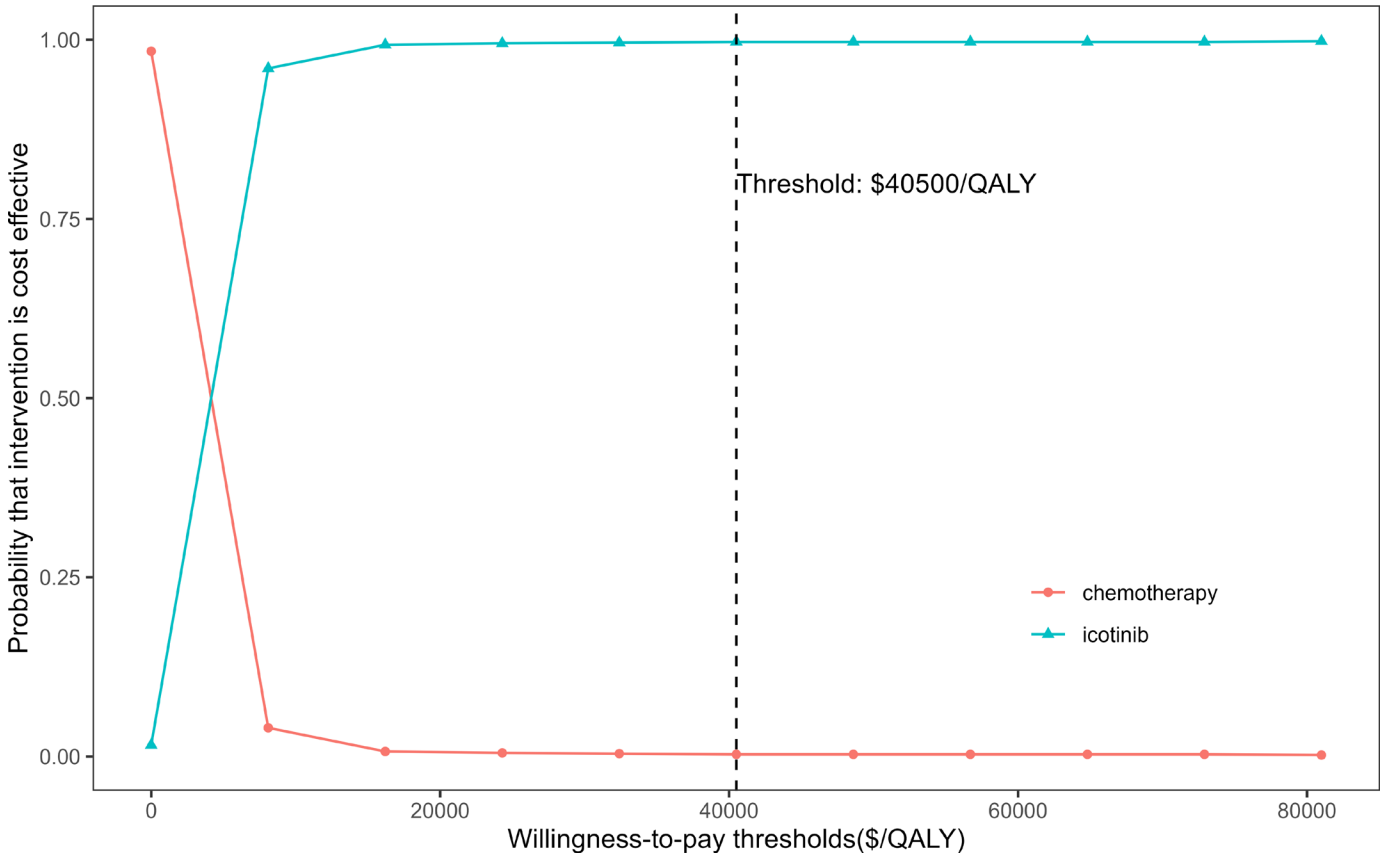

Figure 2 Cost-effectiveness acceptability curve. QALY, quality-adjusted life year.

recurrence patterns while reviewing the RCTs that compared several first-generation EGFR-TKIs with chemotherapy for resected EGFR-mutated NSCLC (see online supplemental figure S5). Therefore, the reconstructed DFS data of the chemotherapy group from the ADJUVANT trial, the IMPACT trial and the EVAN trial were used for the parametric survival analysis, with the ICER values ranging from $346.00 to $6335.53 per QALY under exponential, Weibull, Gompertz and RP (k=3) models.[14 42 43] As to simulating the transition process from PP state to death state, exponential, Gompertz and RP (k=3) models were applied, with the ICERs being $4643.64, $2392.92 and $3344.44 per QALY, respectively. In the third scenario analysis, the icotinib strategy was assumed to require continuous oral administration for 3 years, and no increase in the treatment benefits and costs of treatment-related adverse events. The results showed that, compared with chemotherapy, the incremental QALYs of the 3-year icotinib strategy remained at 1.26 (5.48 vs 4.22), but the incremental cost increased to $9358.30 ($20 206.56 vs $29 564.86), resulting in an ICER of $7406.06 per QALY, which is equivalent to 18.29% of the WTP threshold. In the fourth scenario analysis, the pooled HRs for DFS and OS were adopted from two network meta-analyses, with calculated ICERs being $4872.89 and $5111.90 per QALY, respectively.[37 38]

Model validation

The results of the survival curve extrapolation validation are shown in figure 3. Through visual assessment, the simulated cohort's survival outcomes are close to the OS data of the 2-year icotinib group in the ICOMPARE trial. The simulated survival curve of resected stage II–IIIA EGFR-mutated NSCLC patients is lower than the general population mortality curve (calculated from WHO life table) and falls within the appropriate range. In addition, using the modelling approach based on R scripts, the calculated ICER is $3437.24 per QALY, which is close to the result of the Markov model built by TreeAge Pro (ie, $3440.66 per QALY). The research results can be reproduced, and different parametric survival models can be explored through the online web application (https://mulifeng.shinyapps.io/CEA_icotinib_NSCLC_adj/).

DISCUSSION

As far as we know, this study is the first economic evaluation of icotinib as adjuvant therapy for early-stage NSCLC in China since our thorough literature search showed no published study had evaluated the cost-effectiveness of icotinib for postoperative adjuvant treatment of stage II–IIIA NSCLC. This study compared the cost-effectiveness of icotinib with platinum-based doublet chemotherapy using a Markov model from the Chinese healthcare system perspective. The base-case analysis demonstrated

Table 2 Scenario analyses to assess model robustness

Scenario	ICER, $ per QALY
WTP threshold (3×china GDP per capita)	40 500
Base-case analysis	3440.66
Time horizon 10 years	3446.16
DF→PP curve fit exponential (EVIDENCE)	1807.86
DF→PP curve fit Weibull (EVIDENCE)	4067.93
DF→PP curve fit Gompertz (EVIDENCE)	4932.48
DF→PP curve fit exponential (ADJUVANT)	1779.14
DF→PP curve fit Weibull (ADJUVANT)	1472.87
DF→PP curve fit Gompertz (ADJUVANT)	346.00
DF→PP curve fit RP k=3 (ADJUVANT)	413.41
DF→PP curve fit exponential (IMPACT)	1452.01
DF→PP curve fit Weibull (IMPACT)	1055.87
DF→PP curve fit Gompertz (IMPACT)	660.01
DF→PP curve fit RP k=3 (IMPACT)	633.93
DF→PP curve fit exponential (EVAN)	1832.97
DF→PP curve fit Weibull (EVAN)	5102.65
DF→PP curve fit Gompertz (EVAN)	6335.53
DF→PP curve fit RP k=3 (EVAN)	2964.97
PP→Death curve fit exponential (EVIDENCE)	4643.64
PP→Death curve fit Gompertz (EVIDENCE)	2392.92
PP→Death curve fit RP k=3 (EVIDENCE)	3344.44
3-year adjuvant icotinib	7406.06
HRs from meta-analyses Zhao *et al*[38]	4872.89
HRs from meta-analyses Zhang *et al*[37]	5111.90

DF, disease-free state; ICER, incremental cost-effectiveness ratio; OS, overall survival; PP, post-progression state; WTP, willingness-to-pay.

that the 2-year adjuvant icotinib generated more QALYs but also incurred higher costs, with an ICER of $3440.66 per QALY. The results of one-way sensitivity analyses and scenario analyses showed that the ICERs ranged from $413.41 to $7406.06 per QALY, all of which were below the WTP threshold. These indicate a cost-effectiveness advantage of 2-year adjuvant icotinib compared with chemotherapy.

In the EVIDENCE trial, all patients in the chemotherapy group were treated with vinorelbine plus cisplatin or pemetrexed (adenocarcinoma) plus cisplatin.[15] Nevertheless, in real clinical practice in China, platinum-based doublet chemotherapy regimens including drugs such as pemetrexed or paclitaxel combined with platinum-based drugs (cisplatin, carboplatin, nedaplatin and lobaplatin) are widely used.[44] With the real-world treatment regimens and cost data, the calculated results showed that the cost of 4-cycle adjuvant chemotherapy was equivalent to approximately 28 weeks of icotinib treatment under the current prices, that is, the accumulated cost of 4-cycle chemotherapy was 26.73% of 2-year icotinib adjuvant therapy.

Whether 2 years of treatment should be the endpoint or not remains disputed.[11 45] In our scenario analysis, we assumed 3 years of icotinib adjuvant treatment without considering the increased benefits or increased costs due to more adverse events caused by prolonged treatment. Considering the previous meta-analyses based on RCTs suggesting that the incidence of adverse events in icotinib compared with other EGFR-TKIs is lower, and the high dose intensity in the icotinib group in the EVIDENCE trial (99.8% (IQR 99.2%–100.0%)), we argue that this is a relatively conservative assumption.[15 46 47] Even so, our results showed that 3-year adjuvant icotinib is still cost-effective compared with chemotherapy (ICER was $7406.06 per QALY) under the current prices.

Furthermore, these results were also validated using a modelling method based on R scripts, to guarantee the cost-effectiveness analysis framework of reproducible research results and facilitate the update of new evidence. The base-case analysis results of the two modelling approaches only had slight differences, with ICERs of $3437.24 and 3440.66 per QALY, respectively.

However, there are important limitations in our study. First, immature OS data from the EVIDENCE trial showed an HR of 0.91 (95% CI 0.42 to 1.94, p>0.80), indicating no statistically significant difference.[15] In our study, a PH model was applied to measure the difference in OS between the two treatment strategies, with the HR value for OS was 0.837 (calculated using the Weibull parametric survival model) in base-case analysis, and to explore the impact of HR value fluctuation on ICER within the 95% CI range in one-way sensitivity analysis. The results showed that the calculated ICER was always lower than WTP threshold when HR varied within the range of 0.399–1.756, and the icotinib strategy was still cost-effective compared with the chemotherapy strategy.

Second, since the ICOMPARE trial had a longer median follow-up time than the EVIDENCE study, its OS data was adopted in model validation despite of lack of high maturity.[15 36] Previous studies have shown that parametric survival extrapolation using early survival data might have substantial imprecision compared with updated survival data in economic evaluations.[48] Therefore, assumptions were set to fill the gap, but leave mature OS data from the EVIDENCE trial in the future to calculate the final cost-effectiveness.

Third, post-progression treatment strategies from the EVIDENCE trial are undisclosed.[15] Patients with disease recurrence may have received treatment regimens such as EGFR-TKI, EGFR-TKI combined with chemotherapy, surgery, radiotherapy, surgery plus radiotherapy and so on.[14] To simplify the model, as in published studies, it is assumed that all patients will receive osimertinib (third-generation EGFR-TKI) after disease recurrence.[20]

Finally, we did not include other EGFR-TKIs in our study. Gefitinib and erlotinib are not approved for adjuvant treatment of NSCLC in China, while icotinib is

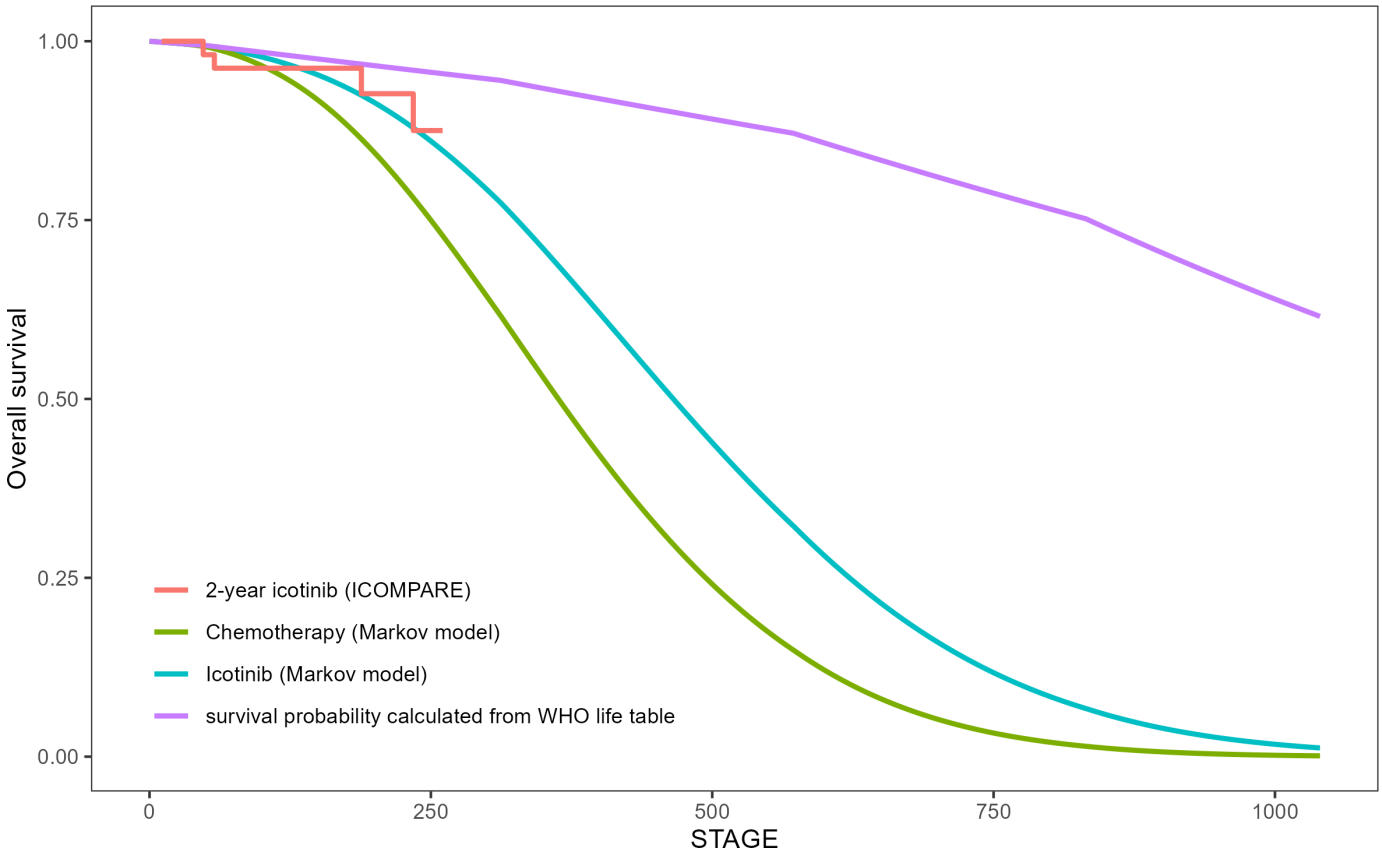

Figure 3 Validation of survival extrapolation. 1 stage is equal to 1 week in Markov model.

currently the only first-generation EGFR-TKI approved for adjuvant treatment of EGFR-mutated NSCLC in China. The ADAURA trial employed a different research design from the EVIDENCE trial, which investigated the use of 3-year adjuvant osimertinib/placebo±adjuvant chemotherapy in patients with resected EGFR-mutated stage IB-IIIA NSCLC.[13 15] Additionally, published studies have evaluated the cost-effectiveness of 3-year adjuvant osimertinib compared with placebo.[20 49 50] For these reasons, our study did not include osimertinib as a comparison strategy. To accurately assess the cost-effectiveness of icotinib versus osimertinib, a properly designed head-to-head clinical trial or disclosure of relevant subgroup data from the ADAURA trial may be necessary.

In conclusion, adjuvant icotinib for stage II–IIIA EGFR-mutated NSCLC is cost-effective with the fact that adjuvant therapy with icotinib leads to increased costs and QALYs, with a calculated ICER of $3440.66 per QALY, which is below the WTP threshold.

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Contributors LM and FL conducted the model, performed the analyses and wrote the manuscript. YF and MH collected the data and interpreted the results. MY contributed to the study concept, reviewed, revised the manuscript, and took responsible for the overall content of the manuscript and serves as the guarantor. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves no sensitive information or ethical issues, so no special ethical review is required.

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Data Supplement for "Cost-effectiveness of adjuvant icotinib versus chemotherapy for patients with stage II-IIIA EGFR-mutated non-small cell lung cancer in China"

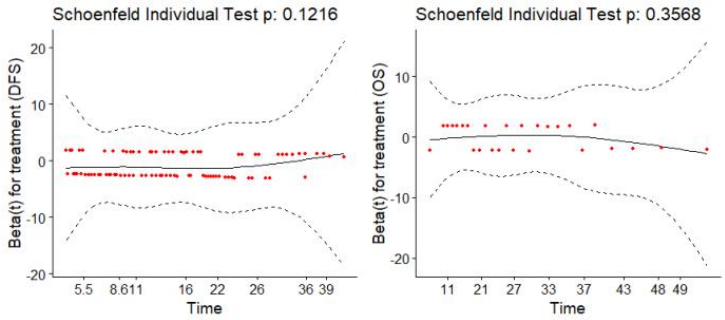

Figure S1 Tests for the proportional hazards assumption

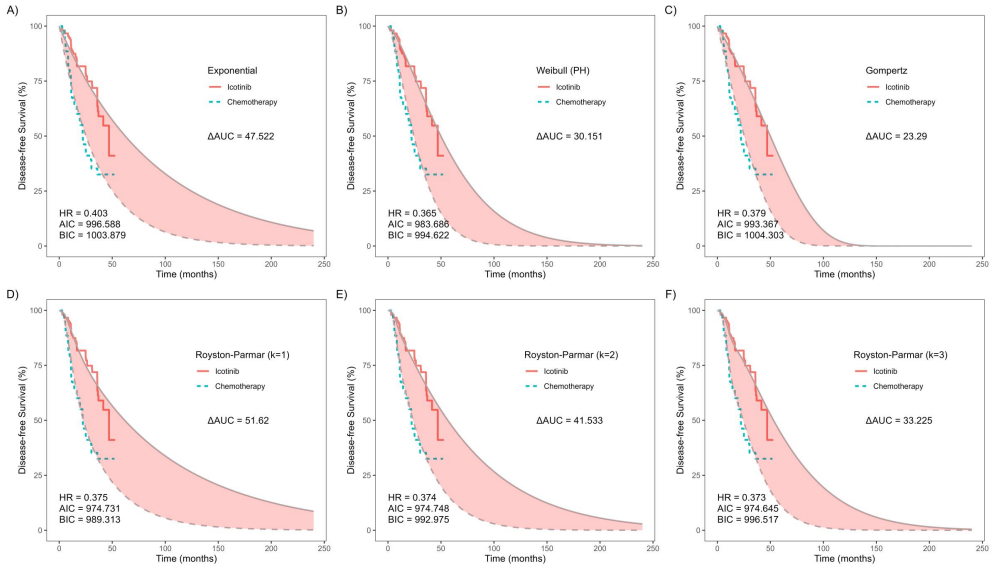

Figure S2 Selection of parametric survival model for DFS
A)Exponential survival model; B) Weibull survival model; C)gompertz survival model; D) Royston-Parmar model k=1; E) Royston-Parmar model k=2; F) Royston-Parmar model k=3.

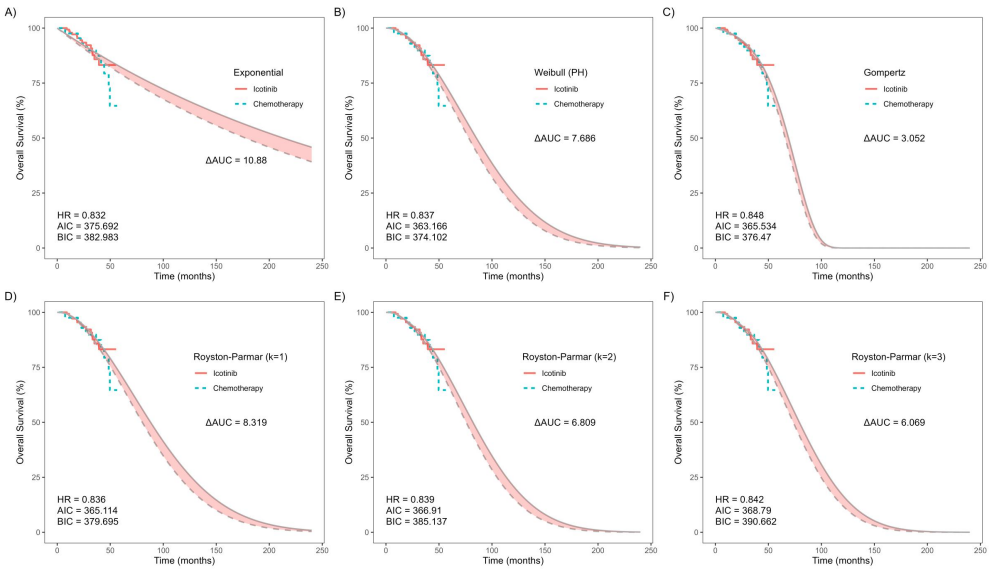

Figure S3 Selection of parametric survival model for OS

A)Exponential survival model; B) Weibull survival model; C)gompertz survival model; D) Royston-Parmar model k=1; E) Royston-Parmar model k=2; F) Royston-Parmar model k=3.

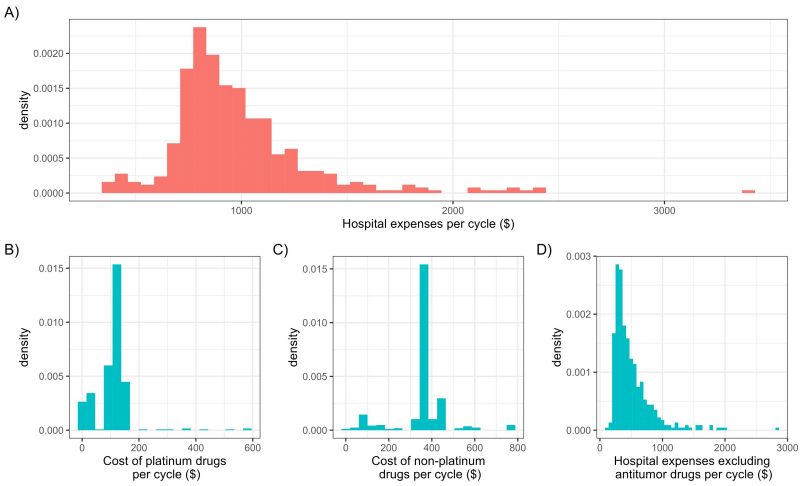

Figure S4 Hospital expenses of adjuvant chemotherapy of II-IIIA NSCLC from Affiliated Hospital of North Sichuan Medical College (including 122 patients, with a total of 409 courses of chemotherapy)

The cost of the chemotherapy group came from stage II-IIIA NSCLC patients who were hospitalized for chemotherapy at the Affiliated Hospital of North Sichuan Medical College from January 2019 to March 2023. Inclusion criteria: 1) diagnosed with stage II-IIIA NSCLC and receive adjuvant chemotherapy after surgery. Exclusion criteria: 1) Patients receiving neoadjuvant therapy; 2) Patients participating in clinical trials; 3) Patients receiving radiotherapy during chemotherapy; 4) Patients receiving triple-drug chemotherapy regimens; 4) Patients receiving adjuvant immunotherapy.

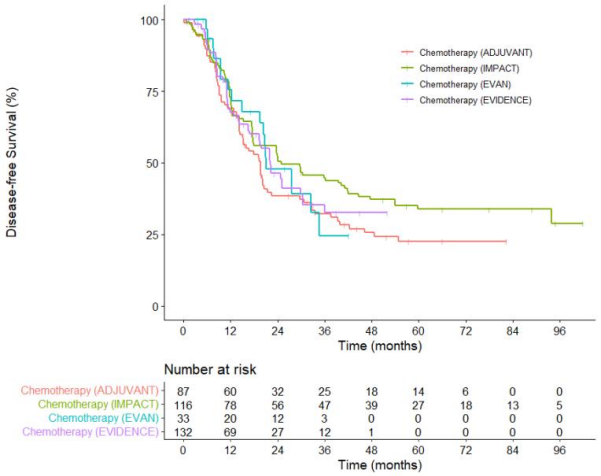

Figure S5 Reconstructed DFS data from the chemotherapy group in 4 randomized controlled trials