

Economic Burden, Utilities, and Cost Effectiveness of
the First-Line Treatment of Extensive-Stage Small Cell
Lung Cancer: A Systematic Literature Review

EE368

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CONCLUSIONS

- The SLRs identified a substantial evidence base of published studies and HTA submissions that presented economic evidence, HCRU and cost data, or HSUV data for patients with 1L ES-SCLC, although limited to US, China, and Japan perspectives
- Based on the findings of this SLR, the following considerations are recommended when developing an economic model for 1L ES-SCLC:
 - Careful consideration of the relevant comparator treatments is required, given the wide range of potential options available
 - Formal indirect treatment comparison methods will be required to compare comparators in the absence of head-to-head trial data
 - Detailed reporting and justification are needed for all structural elements, parameter inputs, and assumptions
 - Use of a three-state partitioned survival analysis or Markov model is likely to be acceptable
 - Evidence from published UK studies on healthcare costs is lacking, therefore it would be sensible to base estimates on precedent from previous NICE submissions (TA638)¹
 - For QALY losses associated with AEs, their duration should be estimated from trial data

INTRODUCTION

- Small cell lung cancer (SCLC) accounts for approximately 15% of all lung cancers, and nearly all cases are attributable to cigarette smoking²⁻⁴
- Extensive-stage SCLC (ES-SCLC) is an incurable, aggressive form of lung cancer with early development of metastases, poor prognosis, and high healthcare resource utilization (HCRU)⁵
- Approximately two-thirds of patients with SCLC have extensive disease at diagnosis, where the cancer is no longer confined to the ipsilateral hemithorax^{6,7}
- Patients with ES-SCLC typically receive chemotherapy plus immunotherapy, followed by maintenance immunotherapy until progression or unacceptable toxicities^{6,8-10}
- In the past decade, programmed death ligand-1 (PD-L1) inhibitors such as atezolizumab and durvalumab have received regulatory approval for use in ES-SCLC, forming the backbone of current immuno-chemotherapy regimens⁷
- While these agents have improved survival outcomes, they are associated with immune-mediated adverse events (AEs) including pneumonitis, colitis, dermatitis, myositis, and hypothyroidism^{15,16}
- Three systematic literature reviews (SLRs) were conducted to assess the economic impact of first-line (1L) treatments for ES-SCLC by identifying studies reporting: 1) economic evaluations; 2) HCRU and cost outcomes; and 3) health state utility values (HSUVs) to inform future health technology assessments (HTAs)

METHODS

- Embase, MEDLINE, Cochrane, and EconLit electronic databases, as well as recent oncology conference proceedings and previous HTA reports, were systematically searched from database inception (economic evaluations and HSUV SLRs) and January 2019 (HCRU and cost SLR) to October 2024 according to best practice guidelines¹¹⁻¹⁶
- Title/abstracts and full-text publications were screened by two independent reviewers according to prespecified inclusion criteria
- To assess the risk of bias of included studies, identified economic evaluations were assessed for quality using the Drummond Checklist¹⁷
- Prespecified eligibility criteria required studies to report on adult patients (aged ≥18 years) with histologically or cytologically confirmed ES-SCLC receiving treatment with immuno-chemotherapy
 - The population for the economic evaluations SLR included 1L patients only; however, the HCRU and costs SLR and HSUV SLR were not restricted by line of therapy to ensure sufficient evidence was identified
 - Full eligibility criteria are presented in **Table 1**
- Across the three SLRs, outcomes of interest were: costs, quality-adjusted life years (QALYs), life years, incremental cost-effectiveness ratios (ICERs), resource use, utilities, and disutilities
- Data from the relevant publications were extracted by one reviewer into standardized, piloted data extraction tables, and all extracted information was quality-checked by a second independent reviewer

Table 1. PICOS Eligibility Criteria

Characteristics	Economic Evaluations		HCRU and Costs		HSUV
Population	Adults (aged ≥18 years) with histologically or cytologically confirmed ES-SCLC, who have received no prior systemic treatment for ES-SCLC		Adults (aged ≥18 years) with histologically or cytologically confirmed ES-SCLC, regardless of the number of lines or nature of prior treatment(s)		Adults (aged ≥18 years) with histologically or cytologically confirmed ES-SCLC, regardless of the number of lines or nature of prior treatment(s)
Interventions	Chemotherapy plus immunotherapies, such as, but not limited to:		No restriction		No restriction
	• Tislelizumab • Nivolumab • Pembrolizumab • Atezolizumab • Durvalumab • Tremelimumab	• Ipilimumab • Serplulimab • Toripalimab • Sintilimab • Benmelstobart			
Comparators	• Platinum-based chemotherapy (cisplatin, carboplatin) • Topoisomerase inhibitor (etoposide, irinotecan, amrubicin) • Taxane (paclitaxel)		No restriction		No restriction
Outcomes	• Costs • Costs per outcome • QALYs	• Life years gained • ICER • Budget impact	• Measures of costs – Direct costs – Indirect costs – Caregiver costs	• Measures of resource use	• Utilities/disutilities/QALYs for health states or adverse events • Mapping algorithms
Study design	• Cost-effectiveness analysis • Cost-utility analysis • Cost-minimization analysis (cost-comparison analysis)	• Cost-consequence analysis • Cost-benefit analysis • Cost-offset analysis • Budget impact analysis	Any studies reporting original cost and/or resource use data		Any studies reporting original HSUV data
Date limits	No restriction		2019-present		No restriction
Countries	No restriction				
Languages	English language publications				

Abbreviations: ES-SCLC, extensive-stage small cell lung cancer; HCRU, healthcare resource utilization; HSUV, health state utility value; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

RESULTS

- Upon completion of full-text review of publications and supplemental handsearching, the three SLRs identified:
 - Thirty-five economic evaluations (29 publications, six HTAs)
 - Fifty-one studies reporting HCRU and costs (43 publications, eight HTAs)
 - Eight studies reporting HSUVs (seven publications, one HTA)

Economic Evaluations

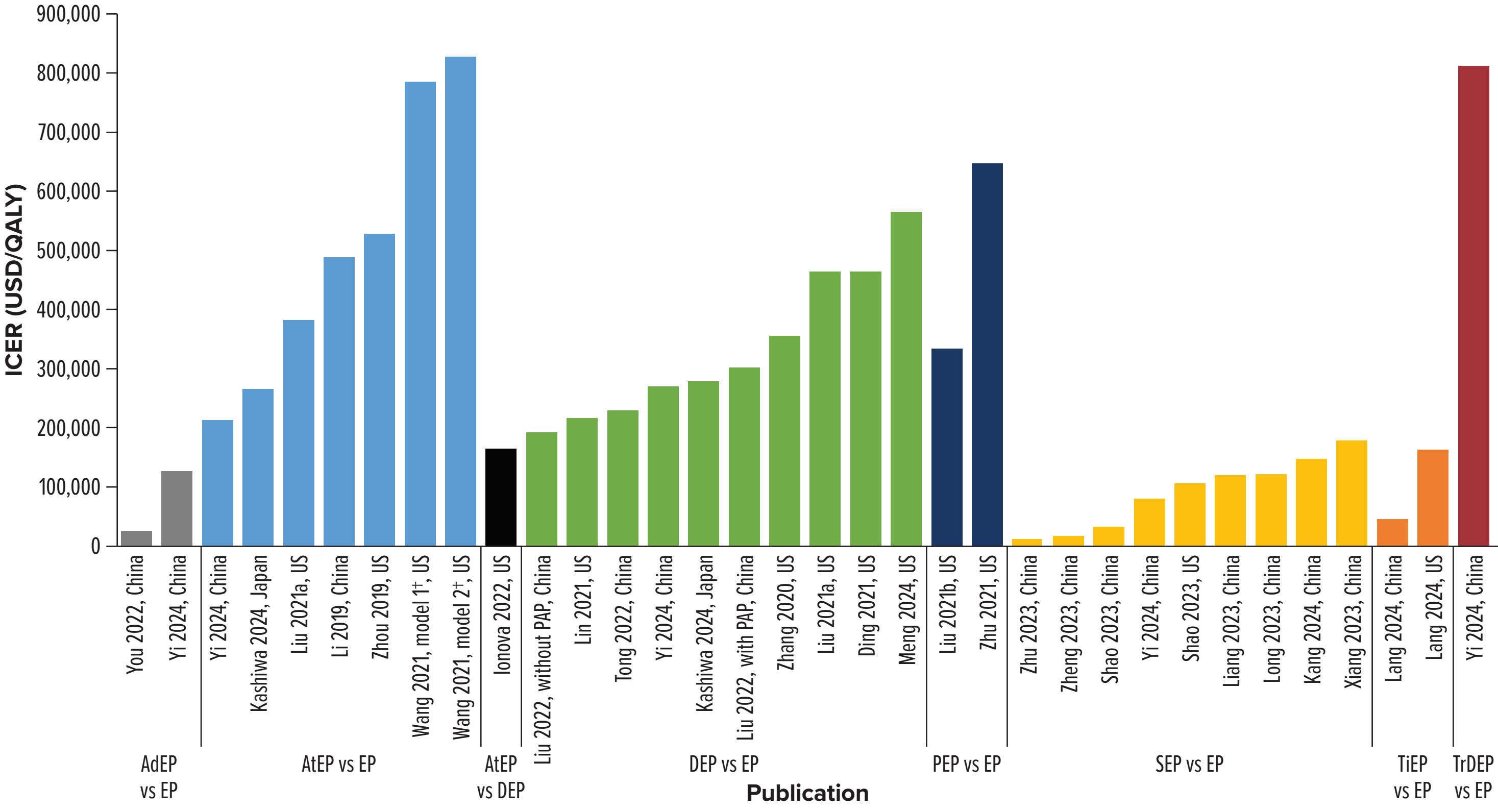
Study Characteristics

- Of the 35 economic evaluations included, most were conducted from a Chinese or United States (US) perspective
- The most commonly assessed treatment combinations were durvalumab + platinum etoposide chemotherapy (n=10), atezolizumab + platinum-etoposide chemotherapy (n=9), and serplulimab + platinum-etoposide chemotherapy (n=9)
 - The most commonly assessed comparator sequence was platinum-etoposide chemotherapy, which was evaluated in 24 studies
- Markov models were utilized in 16 published studies, whereas partitioned survival models were utilized in 10 studies
- Cycle lengths and time horizons ranged from 1 week to 6 weeks, and 12 weeks to lifetime, respectively, with only one study implementing a half-cycle correction
- Utility values derived from non-small cell lung cancer (NSCLC) patients were often used in place of those from SCLC patients, under the assumption that the health states of each disease were similar enough to assume equivalence
 - The most commonly cited sources of utility values were specific to NSCLC and were sourced from Nafees et al 2008¹⁸ and Nafees et al 2017¹⁹

Study Findings

- Total treatment costs ranged from \$6789 for placebo + platinum-etoposide in China to \$418,010 for serplulimab + platinum-etoposide in the US
- Total life-years ranged from 0.57 for placebo + platinum-etoposide in the US to 2.47 for adebreliab + platinum-etoposide in China
- Total QALYs ranged from 0.15 for atezolizumab + platinum-etoposide in the US to 1.51 for serplulimab + platinum-etoposide in China
- ICERs ranged from \$25,914/QALY for adebreliab + platinum-etoposide in China to \$827,610 for atezolizumab + platinum-etoposide in China (**Figure 1**)

Figure 1. ICERs Reported in Published Studies



¹Model 1 was a mixture cure model, and Model 2 was a standard parametric model.
Abbreviations: AdEP, adebreliab + platinum-etoposide; AEP, atezolizumab + platinum-etoposide; DEP, durvalumab + platinum-etoposide; EP, platinum-etoposide; ICER, incremental cost-effectiveness ratio; PAP, patient assistance program; PEP, pembrolizumab + platinum-etoposide; QALY, quality-adjusted life year; SEP, serplulimab + platinum-etoposide; TIEP, tislelizumab + platinum-etoposide; TrDEP, tremelimumab + durvalumab + platinum-etoposide; US, United States; USD, United States dollar.

HCRU and Cost

Study Characteristics

- Of the 43 included HCRU and cost published studies (excluding HTA submissions), 29 studies reported on total costs, 26 on unit costs, and 21 on resource utilization
- Study designs included cost-utility analyses (n=15), cost-effectiveness analyses (n=2), combined cost-effectiveness and cost-utility analyses (n=12), retrospective observational studies (n=12), a budget-impact analysis (n=1), and a survey (n=1)
- Costs and resource use varied widely and were reported across diverse time units, currencies, geographic settings, and outcome types, which limited evidence synthesis

Study Findings

- Reported treatment acquisition costs ranged from \$8429 per 1500 mg dose of durvalumab in the US to \$0.01 per mg of etoposide in China
- The highest reported total treatment cost was \$49,538 for an atezolizumab + etoposide + carboplatin regimen in the US (timeframe not reported)
- In one study, it was reported that the per-cycle drug cost for tislelizumab was \$355.78 in China compared with \$2554.28 in the US
- In one study, it was reported that the monthly cost of treatment with durvalumab + etoposide + platinum (inclusive of drug acquisition and administration) was \$5062.89 for patients in China
- Across all treatments, common AEs that were associated with high treatment and management costs included febrile neutropenia, thrombocytopenia, and decreased platelet count (**Table 2**)
 - In the US, the total cost of managing grade 3-4 AEs with an incidence of ≥3% ranged from \$4743.05 in patients receiving treatment with durvalumab + carboplatin + etoposide, to \$23,323 in patients receiving treatment with durvalumab + tremelimumab + etoposide + platinum chemotherapy
 - In China, the total cost of managing grade 3-4 AEs with an incidence of ≥3% ranged from \$118.35 in patients treated with durvalumab + etoposide + platinum to \$2907.01 for the management of AEs in patients treated with adebreliab + etoposide + carboplatin

Table 2. Summary of Total Adverse Event Cost Data Reported in Published Studies

Publication	Country	Cost Year, Currency	Total Adverse Event Costs
Ionova 2022 ²⁰	US	2020, USD	<i>Monthly cost (low [-25%], high [+25%])</i> Durvalumab: \$66,529.98 (\$48,897.49, \$83,162.48) Atezolizumab: \$51,711.57 (\$38,783.82, \$64,639.45)
Li 2019 ²¹	China	2019, USD	Atezolizumab: \$48 per cycle Placebo: \$47 per cycle
Liu 2021 ²²	US	2020, USD	<i>Grade 3-4 AEs with an incidence of ≥3%, per treatment:</i> 1L atezolizumab + carboplatin + etoposide: \$4959.82 1L durvalumab + carboplatin + etoposide: \$4743.05 1L carboplatin + etoposide: \$6100.94 2L topotecan: \$14,487.33
Liu 2021 ²³	US	2020 (drug cost), USD	1L pembrolizumab + EP: \$8680.05 ^a 1L EP: \$8110.70 ^a Subsequent pembrolizumab + EP: \$5429.48 ^a Subsequent placebo + EP: \$6129.80 ^a
Meng 2024 ²⁴	US	2022, USD	Durvalumab + tremelimumab + etoposide + platinum: \$23,323 ^a Durvalumab + etoposide + platinum: \$23,302 ^a Etoposide + platinum: \$21,728 ^a
Tong 2022 ²⁵	China	NR, USD	<i>Total costs of grade 3-4 AEs, study period:</i> Durvalumab + EP: \$118.35 EP: \$167.77 <i>Total costs of grade 3-4 AEs, per month:</i> Durvalumab + EP: \$4.93 EP: \$6.99
Yi 2024 ²⁶	China	2023, USD	1L chemotherapy: \$215.58 per event 1L atezolizumab + chemotherapy: \$224.20 per event 1L durvalumab + chemotherapy: \$211.27 per event 1L durvalumab + tremelimumab + chemotherapy: \$325.52 per event 1L serplulimab + chemotherapy: \$252.23 per event 1L adebreliab + chemotherapy: \$228.51 per event
Zhou 2019 ²⁷	US	NR, USD	<i>Grade 3+ AEs, per month</i> Carboplatin + etoposide arm: \$621 Atezolizumab + carboplatin + etoposide arm: \$955
Zhou 2023 ²⁸	China	2021, USD	1L adebreliab + etoposide + carboplatin: \$2907.01 per event 1L etoposide + carboplatin: \$2599.55 per event

^aTimeframe not reported.
Abbreviations: 1L, first line; 2L, second line; AE, adverse event; EP, etoposide + platinum; NR, not reported; US, United States, USD, United States dollar.

Health State Utility Values

- Among the five published studies and one National Institute for Health and Care Excellence (NICE) submission that reported utility values, progression-based, time-to-death, and treatment specific utilities were included
- Mean utility scores ranged from 0 for death to 0.85 for patients with a life expectancy of ≥60 days and a treatment response
- Two studies reported progression-based utility values. In both studies, progression-free (PF) utility values (including response and stable disease) were higher than progressive disease (PD) utility values (0.673 [PF] vs 0.473 [PD] and 0.85 [response] vs 0.70 [stable disease] vs 0.55 [PD])
- There was a paucity of data on caregiver costs and HCRU in the PF and PD health states
- Disutility values due to AEs were reported in two studies, with the mean scores ranging from 0.0010 for asthenia to 0.42 for grade 3-4 febrile neutropenia
- The NICE submission presented an economic evaluation conducted from a United Kingdom (UK) perspective, with EQ-5D-5L values mapped to EQ-5D-3L values using the crosswalk algorithm published by van Hout et al 2012²⁹ and UK tariffs

LIMITATIONS

- For economic evaluations, utility values were often derived from patients with NSCLC rather than with SCLC, which assumes equivalent health states
- Data for HCRU were often not reported separately for the different treatment arms within a study, therefore it is difficult to ascertain which treatments, if any, were associated with increased resource use
- The SLR did not identify studies reporting on patients in regions other than North America, Europe, China, or Japan, highlighting a geographical evidence gap

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DISCLOSURES

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