

Healthcare Costs and Resource Utilisation in 1L Maintenance (1L MT) Treatment (Tx) of Advanced Non-Small Cell Lung Cancer (aNSCLC): A Systematic Literature Review

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Background



- Lung cancer remains the leading cause of cancer deaths worldwide¹
- As of 2020, the age-standardised incidence rate of lung cancer in Europe was 63.5 per 100,000 individuals;² with a 5-year survival rate of 18%³
- Non-small cell lung cancer (NSCLC) is the most common subtype, accounting for 80–85% of cases⁴
- Standard treatment options for stage IIIB-IV NSCLC often include chemotherapy (CT), radiation therapy, immunotherapy and/or surgery^{5,6}
- Treatment recommendations for advanced NSCLC (aNSCLC) without driver mutations and those with high programmed death-ligand 1 (PD-L1) expression (squamous [SQ]/non-(N)SQ) include use of the single-agent PD-L1 inhibitor pembrolizumab (pembro).⁷ Additional treatment options can include CT (e.g., pemetrexed [pmx]) and/or monoclonal antibody targeting vascular endothelial growth factor (bevacizumab [bev])⁷
- In recent years, maintenance (MT) treatment strategies have emerged to sustain response to initial first-line (1L) therapy, typically platinum-based doublets or PD-L1 inhibitors alone (pembro) for patients with high PD-L1^{8–10}



Objectives: To systematically describe the healthcare cost and resource use (HCRU), health-related quality of life (HRQoL), and utilities for 1L MT in patients with stage IIIB-IV aNSCLC and no known targetable driver mutation

Methods

- Searches for peer-reviewed publications were conducted using electronic databases (Table 1). The methodology used was in accordance with the Centre for Reviews and Dissemination guidelines

Table 1. Data sources used to run the searches for eligible articles

	Peer-reviewed search	Grey literature search
Databases	MEDLINE®/MEDLINE® In-process (including e-pubs), Embase® and EconLit	Conference proceedings and Health Technology Assessment websites
Search timeframe	Jan 2015–Feb 2021	2019–2020
Language	English literature only	

Table 2. PICOS framework used to identify eligibility criteria and relevant publications

	Inclusion criteria
	Population: Patients aged ≥18 years receiving 1L MT for stage IIIB (not amenable to definitive chemoradiation)-IV NSCLC (SQ and NSQ histology) - Following a 1L platinum-based chemotherapy regimen - With no known targetable driver mutations
	Study types: Economic models, observational (retrospective/prospective), budget impact analysis, cost-effectiveness (CE)/cost studies, HRQoL and utility studies (prospective interventional [single/multi-arm] and observational [retrospective/prospective])
PICOS, population, Intervention, Comparison, Outcomes and Study	

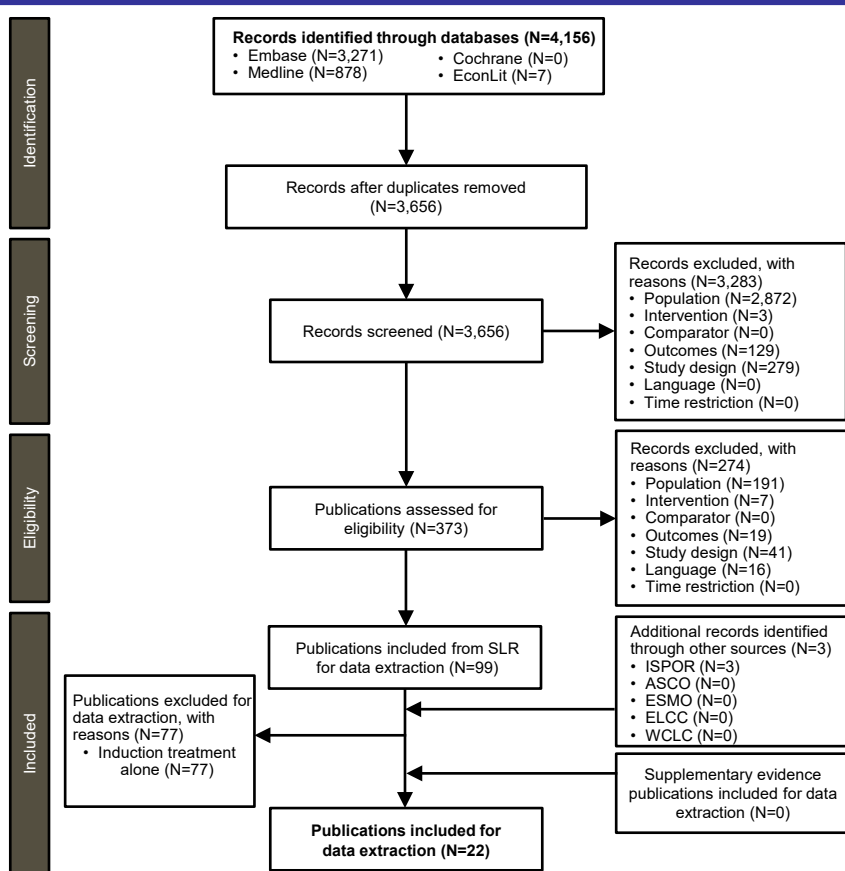
- Data were extracted by one reviewer and independently checked by another

Results

- 22 publications were identified:** 10 were CE analyses (US: 5, China: 3, US & UK: 1, France: 1) of various MT regimens and 12 HRQoL studies

- No HCRU/utility data were found outside CE studies

Figure 1. PRISMA flow chart



ASCO, American Society of Clinical Oncology; ELCC, European Lung Cancer Congress; ESMO, European Society for Medical Oncology; ISPOR, International Society for Pharmacoeconomics and Outcomes Research; PRISMA, preferred reporting items for systematic reviews and meta-analyses; SLR, systematic literature review; WCLC, World Conference on Lung Cancer

Overview of CE studies

- The 10 CE studies were heterogenous in terms of model design, use of treatments and comparators, and time horizon^{11–20}
 - Six studies used Markov model and four used partitioned survival model
 - Time horizon ranged from 3 years to a lifetime across studies
 - >50% were US-based studies
 - 50% of studies included a general NSCLC population; remaining studies targeted histological subtypes
 - 1L MT consisted of: necitumumab (nec), pembro, pmx, bev, gemcitabine (gem) and docetaxel (dxi)

HCRU outcomes from the CE studies

- Table 3 illustrates the major cost inputs

Table 3. Cost inputs from the CE studies*

Author year (country)	Intervention	Cost type	Cost definition	Cost (\$)	Cost year
Georgieva 2018 ¹¹ (UK, USA)	Pembro	DC	Pembro (1 infusion) 200 mg	7,558 (UK) 8,760 (US)	2018
Goldstein 2015 ¹² (USA)	Gem+Cis	AC	Gem-Cis per 3-week cycle	408.96	2014
		DC	Drug: Gem-Cis per 3-week cycle	188.13	
	Gem+Cis+ Nec (+Nec MT)	AC	Gem-Cis-Nec per 3-week cycle	439.58	
			CT administration IV, 1 st hour	143.24	
		DC	Gem 1250 mg/m ² (day 1/day 8) Pal 0.25 mg IV (day 1) Fos 150 mg IV (day 1)	159.60 200.05 259.05	
Huang 2017 ¹³ (USA)	Pembro	AC	Nec MT per 3-week cycle	143.24	2016
		DAC	Drug admin cost	3,854	
	Pembro/SoC	AC	Drug acquisition cost	120,478	
Insinga 2018 ¹⁴ (USA)	Pembro	AC	AC for 1 st hr CTX infusion	224	2017
		DAC	Pembro 200 mg	9,162	
	Pembro+CT	DAC	Drug admin cost	2,848	
Kim 2019 ¹⁵ (USA)	Pmx	DC	Drug acquisition cost	174,436	2018
		DC	Pmx 500 mg/m ²	6,399	
	MT	DC	Osi 80 mg/day, monthly cost Ale 600 mg (BID), monthly cost Cer 3-week cycle, monthly cost Pembro 3-week cycle, monthly cost Bev/Pembro/Gem/Dxl, monthly cost	12,162 12,524 14,868 9,797 7,500	
Lester-Coll 2016 ¹⁶ (USA)	Pac, Car	DC	Pac + Car, monthly cost	10,814	2015
		DC	Bev MT, monthly cost	8,433	
Lu 2018 ¹⁷ (China)	Pmx	DC	2x500 mg Pmx/cycle, unit cost	3,623.14	2016
Shi 2017 ¹⁸ (China)	Pmx MT	DC	Pmx 500 mg, vial cost Pmx 100 mg, vial cost	1,820 364	NR
Taipale 2017 ¹⁹ (France)	Bev	AC	Bev 400 mg	€354.27	2015
		DC	Bev 400 mg, unit cost	€932.94	
	Car	AC	Car 600 mg	€394.27	
			Dxl 160 mg	€394.27	
			Gem 1000 mg	€788.54	
			Pac 300 mg	€394.27	
	Pmx	DC	Pmx 500 mg per 21-day cycle	€354.27	
	Pmx	DC	Pmx 500 mg, unit cost	€1,047.55	
	Vino	AC	Vino 50 mg	€788.54	

*Costs below \$100 are not presented in this table as we assume that they are not major cost drivers
AC, administration cost; Ale, alecinib; BID, twice a day; Car, carboplatin; Cer, ceritinib; Cis, cisplatin; CTX, concurrent cetuximab; DAC, drug acquisition cost; DC, drug cost; Dex, dexamethasone; Fos, fosaprepitant; IV, intravenous; NR, not reported; Ond, ondansetron; Osi, osimertinib; Pac, paclitaxel; Pal, palonosetron; SoC, standard of care; Vino, Vinorelbine

Additional costs inputs included:

- Hospitalisation costs, which varied from €2,288/day in France to \$2,500/day in the US and costing up to \$24,164 for hospitalisation due to neutropenia (US)^{14–16}
- In one study, adverse event (AE)-related hospitalisation costs per event were highest for pneumonitis (\$8,767), followed by anaemia (\$7,970) and thrombocytopenia (\$5,309)¹³
- In addition, other AEs, treatment costs, health state costs and costs of procedure were also reported as the common cost inputs in the CE studies^{11–20}

Median hospital stay ranged from 6.5–8 days for 1L MT and 11 days for 1L induction

HRQoL and utilities outcomes from the HRQoL studies

- No maintenance-specific utility values were identified
- European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core30 (EORTC-QLQ-C30; n=5) was the most frequently used tool to collect the HRQoL data, followed by EQ-5D (n=4) and Lung Cancer Symptom Scale (LCSS; n=3)
 - One study reported significantly worse EORTC-QLQ-C30 and EORTC-QLQ-lung cancer 13 QoL subdomain scores and EQ-5D index score after sunitinib MT versus placebo (mean [standard deviation]: 0.7 [0.2] vs 0.8 [0.2]; P=0.0451, respectively)²⁰
 - The mean maximum improvements reported with pemetrexed MT across LCSS items varied from 0.4 to 24.5 mm on the visual analogue scale²¹

Discussion

- The SLR included publications after 2015, as its focus was to report the recent maintenance treatment landscape in aNSCLC
- No studies assessing healthcare costs or utilities in the 1L MT NSCLC setting were identified
- This type of research can improve our understanding of the implications of 1L MT on cost and QoL in patients with aNSCLC, and can support treatment decisions and cost-effectiveness analyses

Conclusions

- Major cost inputs were drug costs ranging from €364/vial to \$14,868/month and administration costs ranging from \$143.24 to \$3,854 and \$143.24 to \$439.58 for a 3-week cycle
- Contemporary HCRU, HRQoL and utility data are limited in the 1L MT aNSCLC setting
- Further research is needed to evaluate HCRU and HRQoL that reflect the rapidly evolving treatment landscape
- These healthcare cost and resource utilisation data are critical for development of robust economic models to inform decisions about cost-effectiveness of treatments used in aNSCLC

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