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Economic evaluation of PD-1 blockers in Merkel cell carcinoma: A systematic literature review

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INTRODUCTION

- Merkel cell carcinoma (MCC) is a rare, aggressive skin cancer associated with ultraviolet exposure, immunosuppression, and Merkel cell polyomavirus infections primarily reported in the elderly[1]
- The reported prevalence of MCC varies across continents around the globe, with Europe having an incidence rate of 0.13 per 100,000 between 1995–2002, as reported by the Surveillance of Rare Cancers (RARECARE) database.[2] In the US, the most recent data from the Surveillance, Epidemiology, and End Results programme (2011) reported 0.79 cases per 100,000[3]
- Until 2017 there were no approved treatments for MCC. In that year, the US FDA approved avelumab (Bavencio®) for advanced cases. Subsequently, in 2019 pembrolizumab (Keytruda®) was also granted approval to treat this rare and lethal form of skin cancer[4]

OBJECTIVES

- Our objective was to conduct a systematic literature review (SLR) to assess model-based economic evaluations of programmed cell death protein 1 (PD-1) inhibitors used to manage MCC

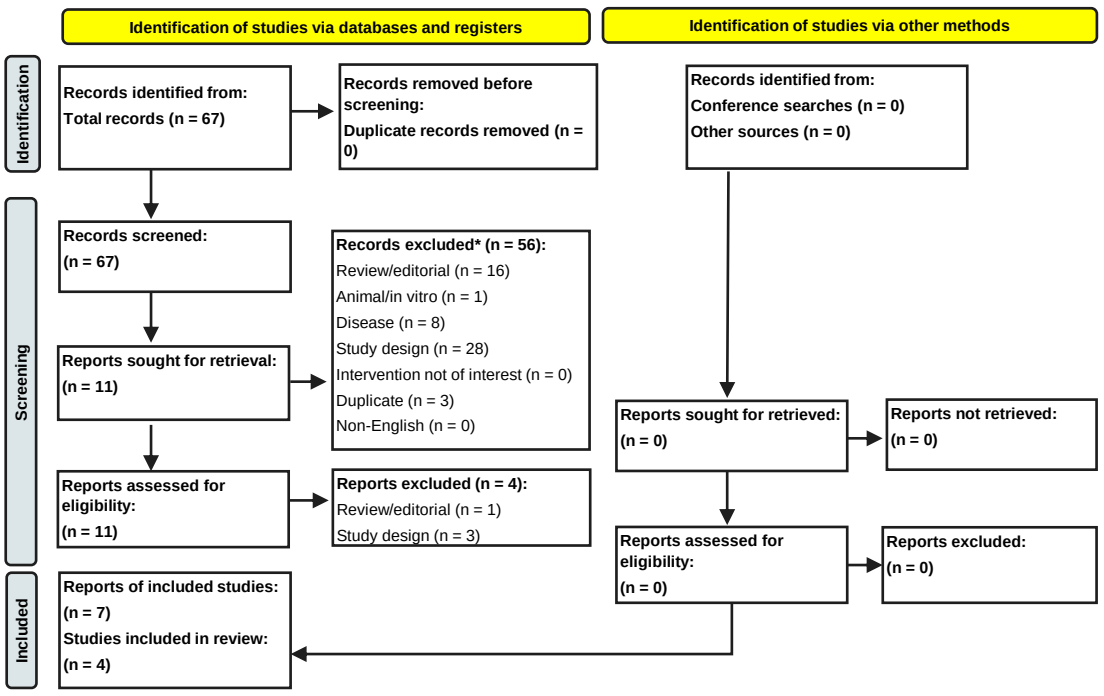
METHODS

- Embase.com (Embase® and MEDLINE®) was systematically searched (from database inception to May 2023) using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, by combining relevant keywords to identify studies that were screened using the Population, Intervention, Comparator, Outcome, Study Design criteria
- The searches were not limited by study country or timeframe. However, searches were restricted to the English language
- Two independent reviewers performed initial screening of the title and abstract for each reference identified by the electronic database search. Any uncertainty regarding the inclusion of a study was reconciled by a third reviewer

RESULTS

- Among the 67 records retrieved from the electronic database search, four original studies from seven records met the inclusion criteria. The details for the flow of studies are presented in Figure 1 using a PRISMA Flow Diagram

Figure 1: PRISMA flow diagram



Key: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
Notes: * All records were manually screened; no automation tools were used. ** Two studies were assessed based on their abstracts only.

SUMMARY OF EVIDENCE

- Among the included studies, one study each was conducted in the UK, Russia, Portugal and Taiwan
- In all four studies, the patient population included patients with metastatic MCC (mMCC) who had previous treatment exposure. However, the UK- and Taiwan-based studies also included treatment-naïve (TN) patients
- The studies performed in the UK, Russia and Taiwan adopted national healthcare perspectives, while the study in Portugal was conducted from a payer perspective
- Partitioned survival models were used in all four studies, with the time horizon spanning from 5 years to a lifetime (assumed to be 40 years)

Table 1: List of included economic evaluation studies

Study name	▪ Intervention ▪ Comparator	Key patient characteristics	Economic analysis	Country
Chang et al. 2021[5]	▪ Avelumab ▪ Chemotherapy regimens[a] and BSC	TN and TE mMCC patients	Cost–utility	Taiwan
Pinheiro et al. 2020[6]	▪ Avelumab ▪ Doxorubicin	TE mMCC patients	Cost–utility	Portugal
Avxentyev et al. 2019[7]	▪ Avelumab ▪ SoC	TE mMCC patients	Cost-effectiveness	Russia
Bullement et al. 2019[8]	▪ Avelumab ▪ SoC[b] and BSC	TN and TE mMCC patients	Cost–utility	UK

Key: BSC, best supportive care; mMCC, metastatic Merkel cell carcinoma; SoC, standard of care; TE, treatment experienced; TN, treatment-naïve.
Note: [a] Chemotherapy regimens included carboplatin etoposide, carboplatin paclitaxel, cisplatin etoposide, cisplatin paclitaxel, cyclophosphamide doxorubicin vincristine, doxorubicin, liposomal doxorubicin, paclitaxel, or topotecan. [b] A combination of palliative chemotherapy, radiotherapy and BSC.

Table 2: Key characteristics of the included studies

Study name (economic analysis type)	Model	Time horizon	Perspective	Price year	Discounting	Model health states
Chang 2021[5] (cost–utility)	Partitioned-survival Microsoft Excel®-based model	Lifetime (40 years)	NHIA	2020	3% for both costs and QALYs	Three key mutually exclusive health states related to survival: ▪ Progression-free disease ▪ Progressed disease ▪ Death
Pinheiro 2020[6] (cost–utility)	Partitioned-survival model	Lifetime	Payer	NR	5% for both costs and outcomes	NR
Avxentyev 2019[7] (cost-effectiveness)	Partitioned survival model	5 year	Healthcare system	NR	NR	NR
Bullement 2019[8] (cost–utility)	Partitioned survival model	Lifetime (40 years)	National Health Service	2015–2016	3.5% per year for both costs and QALYs	Health states based on progression status (categorized by > 100, 30–100, or < 30 days until death): ▪ Pre-progression ▪ Post-progression ▪ Death

Key: NHIA, National Health Insurance Administration; NR, not reported; QALYs, quality-adjusted life years.

KEY FINDINGS

- In Russia, the incremental cost-effectiveness ratio (ICER) for avelumab versus standard of care (SoC) was USD 102,710 per life year gained (LYG) and USD 172,101 per progression-free LYG, suggesting avelumab is a cost-effective second-line treatment option for mMCC compared with SoC
- In the Portuguese setting, avelumab emerged as a cost-effective option when compared with doxorubicin in a previously treated population, presenting with an ICER of EUR 35,057 per quality-adjusted life year and EUR 30,576 per LYG
- In Taiwan, avelumab proved cost-effective for both the TN and treatment-experienced (TE) populations, with ICER of USD 42,993.06 and USD 44,885.06 per quality-adjusted life year gained for TN patients, and USD 26,557.43 and USD 27,243.06 for TE patients, when compared with chemotherapy and best supportive care, respectively
- In the UK, avelumab was found to be cost-effective for both the TN and TE populations, with ICER values ranging from GBP 38,205 to GBP 40,158 for TN patients and GBP 34,113 to GBP 35,335 for TE patients, when compared with chemotherapy, SoC and best supportive care.

Table 3: Results of included studies for TN patients

	Taiwan			UK			
	Avelumab	Chemotherapy	BSC	Avelumab	Chemoth-erapy	SoC[a]	BSC
QALY	3.518	1.322	1.355	3.37	1.34	1.35	1.36
Incremental QALY	-	2.197	2.164	-	2.02	2.02	2.01
LYG	5.426	1.937	1.937	5.50	1.94	1.94	1.94
Incremental LYG	-	3.489	3.489	-	3.56	3.56	3.56
Total cost	USD 100,282	USD 5,845	USD 3,166	GBP 87,899	GBP 10,607	GBP 8,918	GBP 7,229
Incremental cost	-	USD 94,437	USD 97,116	-	GBP 77,292	GBP 78,981	GBP 80,669
ICER	-	USD/QALY 42,993	USD/QALY 44,885	-	GBP/QALY 38,205	GBP/QALY 39,178	GBP/QALY 40,158

Key: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; LYG, life year gained; QALY, quality-adjusted life year; SoC, standard of care; TN, treatment-naïve. **Notes:** [a] Palliative chemotherapy regimens.

Table 4: Results of included studies for TE patients

	Taiwan			Portugal		Russia		UK			
	Avelumab	Chemothe-rapy[a]	BSC	Avel-umab	Doxoru-bicin	Avelu-mab	SoC	Avelu-mab	Chemother-apy[b]	SoC[c]	BSC
QALY	3.107	0.229	0.239	-	-	-	-	2.60	0.30	0.31	0.31
Incremental QALY	-	2.878	2.868	-	2.32	-	-	-	2.30	2.29	2.29
LYG	5.135	0.414	0.414	3.62	-	1.98	0.4	4.15	0.41	0.41	0.41
Incremental LYG	-	4.722	4.722	-	2.66	-	-	-	3.74	3.74	3.74
Total cost	USD 82,025	USD 5,594	USD 3,892	-	-	USD 163,122[d]	USD 1,563[d]	GBP 88,229	GBP 9,834	GBP 7,584	GBP 7,465
Incremental cost	-	USD 76,431	USD 78,133	-	-	-	-	-	GBP 78,395	GBP 80,646	GBP 80,764
ICER	-	USD/QALY 26,557	USD/QALY 27,243	-	EUR/QALY 3,505 EUR/LY 30,576	-	USD/LY 102,710	-	GBP/QALY 34,113	GBP/QALY 35,274	GBP/QALY 35,335

Key: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; LYG, life year gained; QALY, quality-adjusted life year; SoC, standard of care; TE, treatment experienced. **Notes:** [a] Chemotherapy regimens included carboplatin etoposide, carboplatin paclitaxel, cisplatin etoposide, cisplatin paclitaxel, cyclophosphamide doxorubicin vincristine, doxorubicin, liposomal doxorubicin, paclitaxel or topotecan. [b] Palliative chemotherapy regimens. [c] A combination of palliative chemotherapy, radiotherapy and BSC. [d] Total 5-year total medical costs.

CONCLUSIONS

- Our SLR showed that avelumab can be considered a cost-effective option for both TE and TN patients with MCC, as per results from four countries
- The results of the SLR should be interpreted with caution as the populations considered in the current models are heterogeneous in nature due to low disease prevalence and paucity of clinical data
- While the US FDA has granted approval for pembrolizumab to treat patients with MCC, the SLR did not identify any economic evaluations concerning to this indication

REFERENCES

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An electronic version of the poster can be viewed by scanning the QR code.

Poster presented at ISPOR Europe 2023; 12–15 November 2023; Copenhagen, Denmark.