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RETIFANLIMAB VS AVELUMAB IN PATIENTS WITH METASTATIC MERKEL CELL CARCINOMA: A COST-UTILITY ANALYSIS IN ITALY

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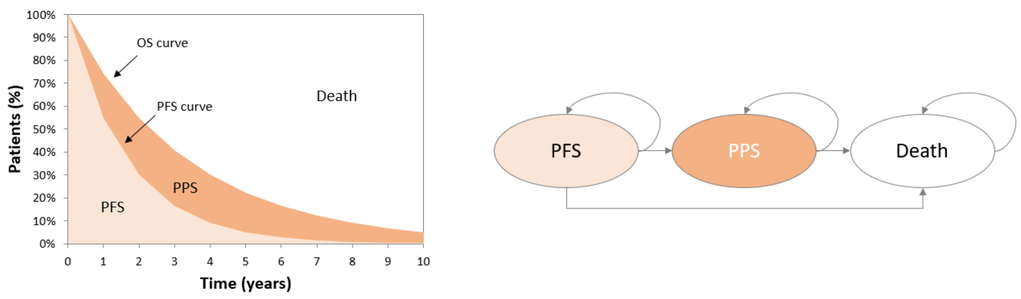
Objective

- Merkel cell carcinoma is an ultra rare but aggressive neuroendocrine skin cancer, with a 5-year survival rate of less ~13 % in patients with distant metastases [1].
- This study aimed to assess the cost-utility of retifanlimab versus avelumab in patients with metastatic Merkel cell carcinoma (mMCC) without prior systemic therapies from the perspective of the Italian National Health Service (SSN).

Methods

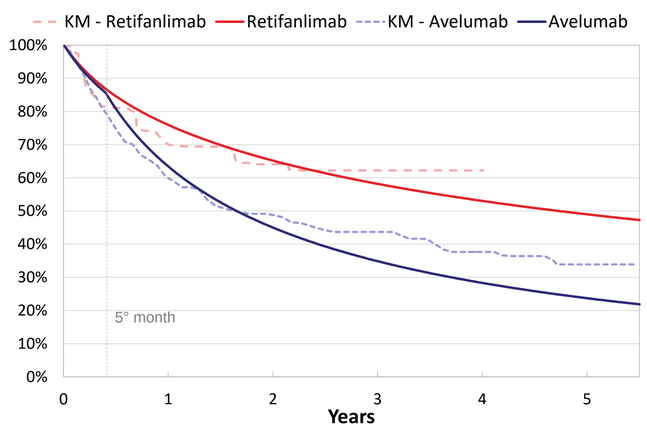
- A 7-day cycles partitioned survival model with three mutually exclusive health states – progression-free, post-progression and death – was adapted to the Italian context to compare lifetime clinical outcomes and costs of patients treated with retifanlimab and avelumab (Figure 1).

Figure 1. Model structure



- Progression-free survival (PFS) and overall (OS) curves were modelled independently and POD1UM-201 anonymized data were used to model the efficacy of retifanlimab (NCT03599713). In the absence of direct head-to-head clinical trial, the efficacy of avelumab was estimated with the hazard ratio (HR) obtained from a matching-adjusted indirect comparisons (MAIC) [2,3] (Figure 2 and 3).
- In line with a previous NICE submission [4], a time-to-death approach was considered for utility values and states were defined as “>266 days to death”, “35-266 days to death”, and “<35 days to death” (Figure 1). The disutility associated with adverse events (AE) was also considered [4].
- Direct healthcare costs, including drug acquisition and administration, disease monitoring, adverse event (AE) management, post-progression therapy, and end of life were collected from Italian sources [5-8] (Table 1).
- Costs and health gains were discounted at an annual 3% rate.
- Deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) evaluated the uncertainties on input parameters.

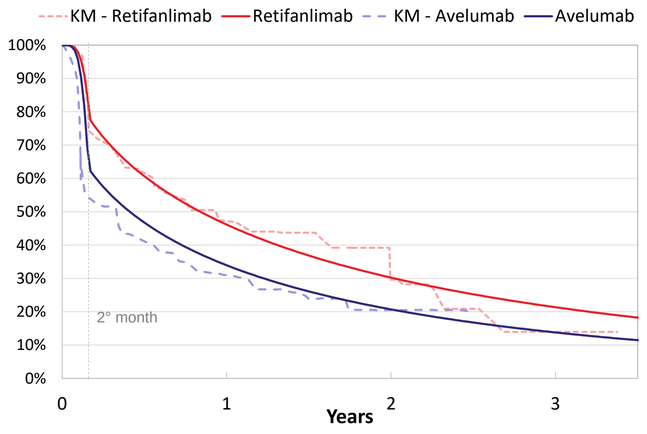
Figure 2 – Long term prediction OS



Retifanlimab	Log-normal distribution
Avelumab	HR 1-5 months: 1.092 (95%CI 0.579; 2.766)
	HR >5 months: 2.243 (95%CI 1.245; 5.545)

Although statistical analyses showed that the proportional hazards assumption was not violated, visual inspection of the Kaplan-Meier plot from the MAIC revealed that the two curves are nearly overlapping in the first period and diverge later on. This is supported by the estimated HRs: the HR in the first period is close to 1, suggesting equivalence between the treatments, while in the second period, the HR significantly favours retifanlimab.

Figure 3 – Long term prediction PFS



Retifanlimab	Piecewise exponential
Avelumab	HR 1-2 months: 2.145 (95%CI 1.503; 4.542)
	HR >2 months: 1.168 (95%CI 0.771; 1.840)

Kaplan-Meier curves showed a high risk of progression/death in the first few months, which decreases over time. To accurately model this, a time-dependent distribution was used for retifanlimab. For avelumab, the PFS curve was estimated by applying a HR of 2.145 for the first 2 months and 1.168 for the following period.

Table 1 – Unit costs

Cost item		Value (€)
Retifanlimab (500 mg)		‡
Avelumab (200 mg)*		985.55
IV administration		37.10
Disease monitoring PFS (weekly)		24.41
Disease monitoring PPS (weekly)		22.99
Post-progression therapy (one-off)		1,484
AE management (one-off)	Retifanlimab	494.45
	Avelumab	176.52
End of life (one-off)		4,023.69

‡ The price of retifanlimab was assumed to be equal to that of the highest-priced PD-1 in Italy, rounded up to the nearest 1,000
* Ex-factory price net of mandatory discounts

Administration costs: The cost of IV administration was estimated based on the corresponding national DRG tariff (DRG 410) reduced by 90% [6].

Disease monitoring: annual frequency of health resources consumption was derived from national guidelines [5] and unit costs were taken from national tariffs [6].

Post-progression therapy: trial data and national tariffs were used to inform the frequency and costs of post-progression therapies [1-2,6].

AE management: frequency of AE was derived from clinical trials and costs per event taken from literature [7] or national DRG tariff [6].

End of life: estimated from literature data [8].

Results

- Retifanlimab demonstrated **greater efficacy** compared to avelumab (6.39 vs 3.42 LYs and 5.11 vs 2.68 QALYs) with an **additional cost** of € 12,228 (Table 2).
- The **ICER** was estimated at **€ 5,037 per QALY** gained (Table 3).

Table 3 – ICERs

	Retifanlimab	Avelumab	Δ	ICER
LYs	6.39	3.42	2.98	4,107 €/LY gained
QALYs	5.11	2.68	2.43	5,037 €/QALY gained
Costs (€)	161,585	149,357	12,228	

Table 2 – Summary results

	Retifanlimab	Avelumab	Δ
Total LYs	**6.39**	**3.42**	**2.98**
PFS	1.92	1.31	0.61
PPS	4.47	2.10	2.37
Total QALYs	**5.11**	**2.68**	**2.43**
>266 days to death	4.78	2.32	2.46
35-266 days to death	0.30	0.33	-0.03
<35 days to death	0.03	0.04	0.00
AE disutility	-0.0011	-0.0004	-0.0006

	Retifanlimab	Avelumab	Δ
Overall costs (€)	**161,585**	**149,357**	**12,228**
Drug	145,809	136,105	9,704
Administration	3,301	4,475	-1,174
AE	494	177	318
Monitoring PFS	2,451	1,673	778
Monitoring PPS	5,360	2,522	2,839
Post-progression therapy	907	790	117
End of life	3,261	3,615	-354

- Sensitivity analyses confirmed the **robustness** of the base case results (Figure 4, Figure 5, and Figure 6).

Figure 4 – DSA: tornado chart

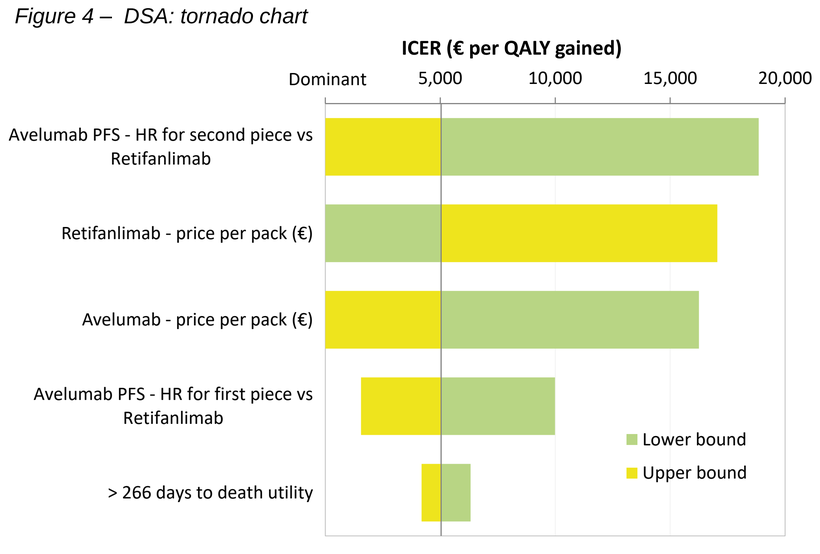


Figure 5 – PSA: scatterplot

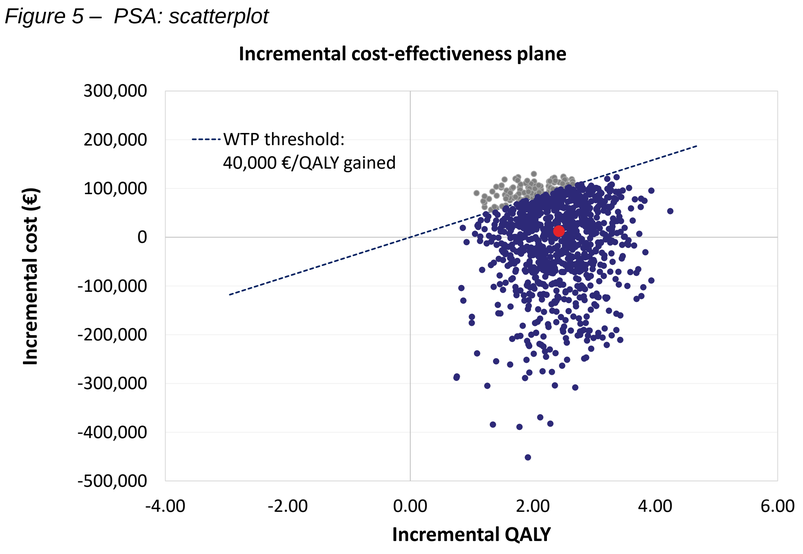
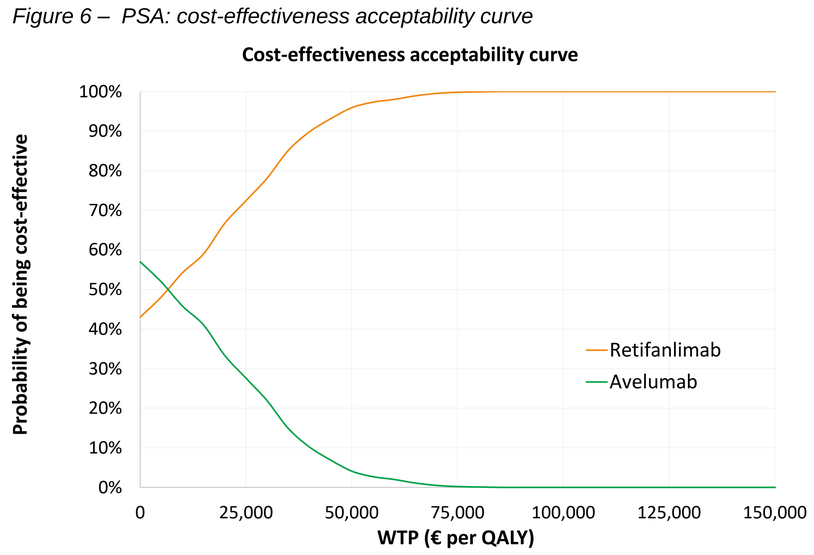


Figure 6 – PSA: cost-effectiveness acceptability curve



Conclusions

Retifanlimab can be considered a **cost-effective option** for Italian patients with mMCC without prior systemic therapies.

Bibliography

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ISPOR Barcelona 2024

Acknowledgements This analysis was funded by Incyte Biosciences Italy Srl