Cost-effectiveness analysis of avelumab plus best supportive care (BSC) as first-line maintenance treatment in locally advanced or metastatic urothelial carcinoma (la/mUC) in France

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SCOPE

- **To evaluate the cost-effectiveness of avelumab + BSC vs BSC alone for first-line (1L) maintenance treatment of adult patients with la/mUC who are progression-free following platinum-based chemotherapy in France**

CONCLUSION

- **This cost-effectiveness analysis provided insight into the incremental benefits and associated costs of maintenance therapy with avelumab + BSC in patients with la/mUC who are progression-free following platinum-based chemotherapy**
- **The Haute Autorité de Santé (HAS; French National Authority for Health) found the evaluation to be acceptable and robust, with limited uncertainty. Multiple scenario analyses were conducted, and the HAS deemed the incremental cost effectiveness ratio (ICER) reliable**
- **The analysis demonstrated that avelumab + BSC is likely to be cost effective vs BSC alone in patients eligible for 1L maintenance treatment for la/mUC in France**

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BACKGROUND

- Urothelial carcinoma is the most common type of bladder cancer and accounts for approximately 90% of all bladder cancer cases.[1,2] Treatment for locally advanced or metastatic bladder cancer aims to improve patients' overall survival (OS) and quality of life. Before the introduction of avelumab, the watch-and-wait approach was recommended after chemotherapy in patients with stable disease or objective response[3]
- The phase 3, randomized, open-label, multicenter JAVELIN Bladder 100 trial demonstrated that avelumab + BSC significantly prolonged OS vs BSC alone in patients with la/mUC receiving 1L maintenance treatment
- Avelumab has been assessed by the Commission d'Évaluation Économique et de Santé Publique from the HAS and has been reimbursed in this indication in France since September 2022

METHODS

- This analysis is based on a direct comparison of avelumab + BSC vs BSC alone. A partitioned survival model was developed, including progression-free, postprogression, and death as health states, based on extrapolated outcomes from the phase 3 trial[4] and considering a 10-year time horizon and weekly cycle length
- Utilities by health state were based on EQ-5D-5L values from the trial using the French value set[5]
- Treatment discontinuations, grade 1/2 adverse events (AEs) with the greatest impact on quality of life, and all grade 3/4 AEs were accounted for. AE-associated disutilities were sourced from the literature
- Costs were estimated from a collective perspective and included treatment acquisition, administration, follow-up, AE-related hospitalization, transport, postprogression, and end-of-life costs. The acquisition price of avelumab considered in the model corresponds to the post-negotiation list price. Costs and clinical outcomes were discounted at 2.5% per annum
- Deterministic probabilistic sensitivity and scenario analyses were conducted to assess the level of uncertainty
- Scientific committees consisting of 3 external clinical experts and an economist were organized to assess the model structure, inputs, and model validity and discuss results

RESULTS

- This analysis used clinical data derived from the JAVELIN Bladder 100 trial, which included a high number of French patients (n=82). JAVELIN Bladder 100 patient characteristics were representative of the French population in terms of age, sex distribution, metastatic site, and response to 1L chemotherapy

DETERMINISTIC RESULTS

- Health-related results are presented in **Table 1**. Patients in the avelumab + BSC arm lived on average 0.77 years longer than patients in the BSC alone arm (+36.2%), which translated into 0.67 additional quality-adjusted life years (QALYs). This gain was driven by 0.48 and 0.29 additional years in the progression-free and postprogression health states, respectively
- The difference in cost between the 2 strategies was mainly due to the acquisition and administration costs of avelumab, which represented 72% and 13% of overall costs for the avelumab + BSC strategy, respectively
- Subsequent treatment costs and end-of-life costs represented 76% and 16% of overall costs for the BSC alone strategy, respectively. An incremental cost of -€20,424 for subsequent treatment and -€351 for end-of-life costs was estimated in favor of avelumab + BSC vs BSC alone
- Avelumab + BSC was associated with €97,166 in additional costs compared with BSC alone, which resulted in an ICER of €145,626 per QALY gained (**Table 2**)

SENSITIVITY ANALYSES RESULTS

- The results from the sensitivity analyses were consistent with the base case, and showed that efficacy parameters (OS, time to death), postprogression time on immunotherapy, and postprogression costs had the biggest impact on the ICER (**Figure 1**)
- The results from the probabilistic sensitivity analysis were consistent with the base case, with a variation of -0.4% vs the deterministic analysis results
- All simulations showed avelumab + BSC to be more effective and more expensive than BSC alone
- The probability of avelumab + BSC being cost-effective was 81% for a willingness-to-pay threshold of €300,000/QALY

Table 1. Effectiveness outcomes

	Avelumab + BSC	BSC alone
Total life years	**2.9126**	**2.1379**
Progression-free	1.0161	0.5327
Postprogression	1.8965	1.6052
Time on treatment	1.4085	0.6158
Total quality-adjusted life years	**2.4918**	**1.8246**
Progression-free	0.9084	0.4762
Postprogression	1.5931	1.3484

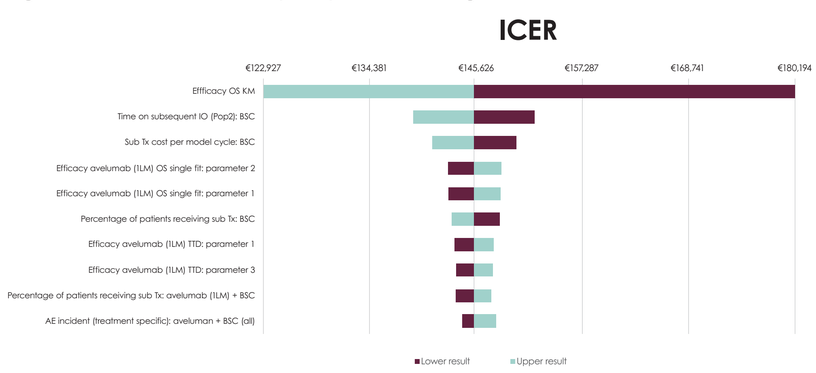
BSC, best supportive care.

Table 2. Incremental outcomes and ICER

	Total Cost, €	QALY	LYG	Incremental			ICER	
				Cost, €	QALY	LYG	€/QALY	€/LYG
Avelumab + BSC	136,917	2.4918	2.9126	97,166	0.6672	0.7747	145,626	125,429
BSC alone	39,751	1.8246	2.1379					

BSC, best supportive care; **ICER,** incremental cost-effectiveness ratio; **LYG,** life year gained; **QALY,** quality-adjusted life year.
The acquisition price of avelumab considered in the model corresponds to the post-negotiation list price.

Figure 1. Deterministic sensitivity analysis: tornado diagram



1LM, first-line maintenance; **AE,** adverse event; **BSC,** best supportive care; **ICER,** incremental cost-effectiveness ratio; **IO,** immunotherapy; **KM,** Kaplan-Meier; **OS,** overall survival; **Pop2,** population2; **sub,** subsequent; **TTD,** time to death; **Tx,** treatment.

DISCUSSION

- This analysis showed limited uncertainty in endpoints and outcomes (within ±5%)
- Utility data from the EQ-5D-5L questionnaire used in the JAVELIN Bladder 100 study were weighted according to French preferences, as recommended by the HAS[6]
- Disutilities related to AEs were not specific to UC. A scenario analysis not considering disutilities showed no major impact on ICERs (-1.4%)
- As requested by the HAS, Kaplan-Meier curves for the entire duration of the trial follow-up were included, although this was not the most conservative choice. Scenario analyses considering parametric choices were conducted
- Distributions that were not the best statistical fit were chosen to avoid clinically implausible extrapolations (curves crossing). Thus, a shorter time horizon (10 years) was considered to limit the uncertainty associated with extrapolations

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