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# Economic evaluation of first-line treatment strategies for locally advanced or metastatic urothelial carcinoma: toward optimizing value-based care

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## CONCLUSIONS

- Healthcare costs in France associated with treating locally advanced or metastatic urothelial carcinoma (la/mUC) continue to be significant
- The estimated total cost of care per patient treated with induction chemotherapy with or without avelumab (AVE)- or best supportive care (BSC)-based maintenance therapy (chemo ± maintenance) was €76,257 over 3 years, 54% lower than with enfortumab vedotin in combination with pembrolizumab (EV+P) (€165,094)
- Adjusting for clinical outcomes, the costs per month in progression-free survival (PFS) and overall survival (OS) were lower with chemo ± maintenance (€4,494 and €3,535, respectively) than with EV+P (€8,870 and €6,527, respectively)
- The incremental cost per additional survivor after 3 years for EV+P vs chemo ± maintenance was estimated at €543,604 over 3 years (€181,201 annually)
- Within a fixed budget, chemo ± maintenance would enable treatment of more patients and result in more patients alive after 3 years than EV+P
- This study underscores the economic impact of therapy for la/mUC, supporting sustainable, value-oriented cancer care that considers costs in shared treatment decision-making

## PLAIN LANGUAGE SUMMARY

- In this study researchers estimated the costs of care over 3 years for two different treatments for patients with advanced urothelial cancer in France
  - The treatments looked at in this study were chemotherapy with or without maintenance therapy (chemo ± maintenance) and enfortumab vedotin plus pembrolizumab
  - The costs of care looked at in this study included buying the drugs, giving the drugs to patients, managing side effects, monitoring the disease, and other drugs received after disease progression
- Total costs per patient were 54% lower with chemo ± maintenance than with enfortumab vedotin plus pembrolizumab
  - This reduced cost was mainly due to lower cost of buying the drugs
- The cost per month of survival was 46% lower with chemo ± maintenance than with enfortumab vedotin plus pembrolizumab
- The cost of keeping one additional patient alive after 3 years as a result of enfortumab vedotin plus pembrolizumab treatment instead of chemo ± maintenance was over €180,000 per year
- Within a fixed budget to treat patients with this disease, the healthcare system could treat more patients, and more patients would remain alive after 3 years if it used chemo ± maintenance rather than enfortumab vedotin plus pembrolizumab
- These findings highlight the need to balance health benefits with economic sustainability when selecting treatments for patients with advanced urothelial cancer

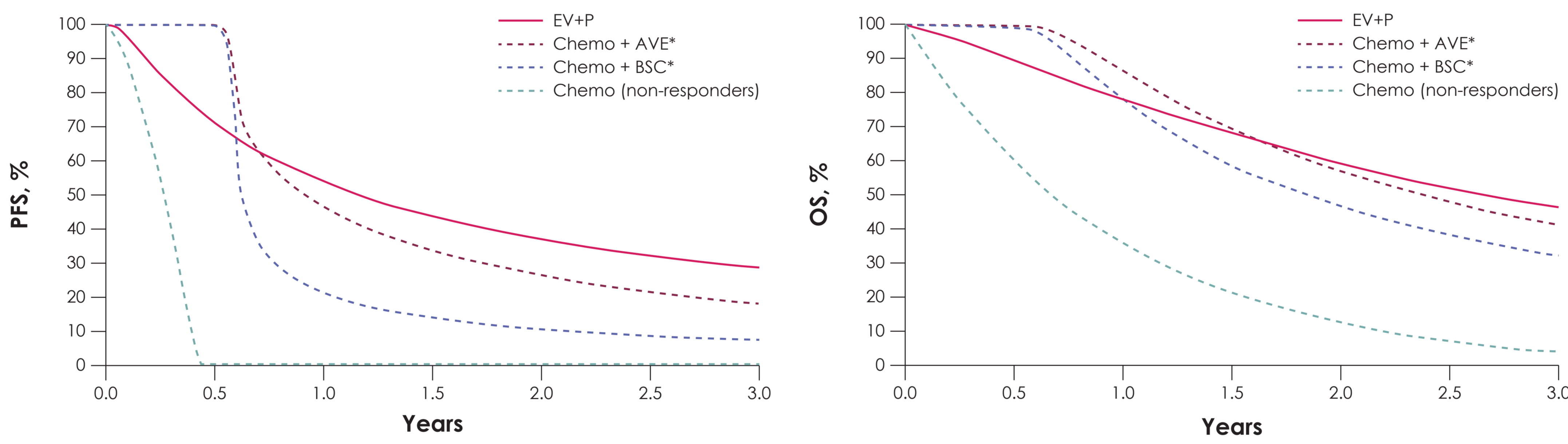
## BACKGROUND

- Bladder cancer is the fifth most common cancer in France,<sup>1</sup> with 8,319–9,481 new cases of, and 5,239 deaths from la/mUC annually between 2017 and 2020.<sup>1</sup> Five-year survival rates for muscle-invasive tumors are 55% in men and 49% in women;<sup>2</sup> this drops to just 5% in the metastatic setting<sup>3</sup>
- la/mUC presents a significant treatment and economic challenge, especially given its poor long-term prognosis<sup>4,5</sup>
- Recent regulatory approvals in France have expanded first-line (1L) treatment options for platinum-eligible patients with la/mUC. In July 2024, the European Medicines Agency's Committee for Medicinal Products for Human Use issued a positive opinion for EV+P,<sup>6</sup> which was followed by European Commission approval in August 2024<sup>7</sup>

## METHODS

- A health economic model compared costs and clinical outcomes between 2 1L treatment strategies over a 3-year period: chemo ± maintenance and EV+P
- Mean treatment duration, PFS, and OS were estimated using restricted mean survival over a 3-year period (ie, area under the curve up to 3 years), derived from parametric survival analyses
- For chemo ± maintenance, the model included patients with chemo-controlled disease who received AVE (chemo + AVE), those with chemo-controlled disease who did not receive AVE (chemo + BSC), and those with uncontrolled disease
  - In JAVELIN Bladder 100, the mean time from induction chemotherapy to randomization was 5.2 months in the AVE arm and 5.3 months in the BSC arm. Accordingly, the model assumed that patients who received chemo + AVE or chemo + BSC were progression free and alive for 5.2 and 5.3 months, respectively. Subsequently, PFS and OS reflected JAVELIN Bladder 100.<sup>10</sup> For patients with uncontrolled disease, PFS and OS were simulated based on the control arm of KEYNOTE-361<sup>13</sup> (Figure 1)
  - To estimate results for this strategy, the model averaged the costs and outcomes for each of these groups, weighted by the proportion of patients in each group
  - Market research data was validated with 3 local medical oncologists and urologists to assign assumptions about the proportions of patients in each segment of the patient journey. This resulted in assuming that 72% of patients receiving induction chemotherapy do not have disease progression and are eligible for maintenance treatment. Among those, 81% receive AVE maintenance. Therefore, among all 1L patients, 58% receive chemo + AVE, 14% receive chemo + BSC, and 28% receive chemo and their disease does not respond

Figure 1. PFS and OS for each treatment



PFS and OS curves for chemo ± maintenance, from 1L, are derived by taking the weighted average of the chemo + AVE, chemo + BSC, and chemo (non-responders) curves. AVE, avelumab; BSC, best supportive care; chemo, chemotherapy; EV, enfortumab vedotin; OS, overall survival; P, pembrolizumab; PFS, progression-free survival. \*Analysis includes patients who were progression-free following chemotherapy; patients who had progression or died prior to initiation of avelumab or BSC were not included.

Table 1. Key model inputs

	Chemo ± maintenance			EV+P
	Chemo + AVE	Chemo + BSC	Chemo (non-responder)	
<b>Efficacy, months<sup>a</sup></b>				
Restricted mean duration of treatment	Chemo: 3.4 <sup>b</sup> AVE: 11.5 <sup>10</sup>	Chemo: 3.4 <sup>b</sup>	3.2 <sup>c</sup>	EV: 9.9 <sup>12</sup> P: 10.7 <sup>10,12</sup>
Restricted mean PFS <sup>a</sup>	16.8 <sup>10</sup>	11.5 <sup>10</sup>	3.2 <sup>12</sup>	18.2 <sup>14</sup>
Restricted mean OS <sup>a</sup>	26.1 <sup>10</sup>	23.4 <sup>10</sup>	11.3 <sup>13</sup>	25.3 <sup>14</sup>
<b>Distribution of chemotherapies (induction therapy), %<sup>a</sup></b>				
Carboplatin	61.5			
Cisplatin	27.9			
Gemcitabine	100			
<b>Rate of subsequent therapy (among patients whose disease progressed during 3 years), %</b>	88.5	91.6	65.0	83.7
<b>Distribution of subsequent treatments, % (median duration of treatment, months)<sup>b</sup></b>				
EV	68.0 (5.00)	50.0 (5.00)	30.0 (5.00)	5.0 (5.00)
P	2.5 (4.49)	75.0 (5.71)	100 (4.57)	2.5 (4.49)
Carboplatin	5.0 (3.68)	12.5 (3.82)	0 (3.06)	55.0 (3.68)
Cisplatin	0 (3.68)	2.5 (3.82)	0 (3.06)	20.0 (3.68)
Gemcitabine	5.0 (3.68)	15.0 (3.82)	0 (3.06)	75.0 (3.68)
Docetaxel	5.0 (3.68)	0 (3.82)	0 (3.06)	0 (3.68)
Paclitaxel	10.0 (3.68)	5.0 (3.82)	5.0 (3.06)	5.0 (3.68)
Erdafitinib	7.0 (4.80)	5.0 (4.80)	5.0 (4.80)	7.0 (4.80)
<b>Cost per month, 2024 €</b>				
<b>Drug and administration cost, €</b>	Induction: 2,090 Maintenance: 6,840 <sup>a</sup>	Induction: 2,090 Maintenance: 0	2,090	EV: 7,694 <sup>d</sup> P: 7,817 <sup>a</sup>
<b>Disease management costs (per month unless noted), €<sup>a</sup></b>				
Disease management: pre-progression/on-treatment	Induction: 65 Maintenance: 65	Induction: 65 Maintenance: 57	65	65
Disease management: pre-progression/off-treatment	57			
One-time cost of progression	631			
Disease management: post-progression/on subsequent active treatment	84			
Disease management: post-progression/off-treatment	86			
<b>Monthly cost of subsequent treatments, €</b>	2,998	7,193	5,131	677
<b>AE management cost<sup>e</sup> (one-off), €</b>	Induction: 1,235 Maintenance: 281	Induction: 1,235 Maintenance: 169	1,147	532

1L, first line; AE, adverse event; AVE, avelumab; BSC, best supportive care; chemo, chemotherapy; EV, enfortumab vedotin; IQOL, key opinion leader; OS, overall survival; P, pembrolizumab; PFS, progression-free survival. <sup>a</sup>Estimated using restricted mean survival over a 3-year period, derived from parametric survival analyses. <sup>b</sup>Induction phase duration assumed as 13 weeks based on JAVELIN Bladder 100 trial. <sup>c</sup>Assumed to match PFS (treated to progression). <sup>d</sup>Maximum treatment duration of 24 months for P was taken into account in this estimate. <sup>e</sup>From the initiation of chemo. <sup>f</sup>Distribution was based on average clinic input; durations were from trials.<sup>10,11</sup> For chemo (non-responder), duration of P and chemo was assumed to be 20% shorter than those for chemo + BSC, based on clinic input. <sup>a</sup>AVE cost based on a 200-mg vial price of €665.02.<sup>10</sup> EV cost based on a 200-mg vial price of €641.97.<sup>12</sup> P cost is based on a 100-mg vial price of €2,482.05.<sup>11</sup> <sup>b</sup>Calculated from monthly frequency, percentages of patients using each resource provided by clinicians, and unit costs. <sup>c</sup>Included grade ≥3 AEs that occurred in ≥2% in any of the treatment options. <sup>d</sup>Calculated based on frequency of AEs from trial data<sup>10,11</sup> and unit cost sourced from published literature and databases.

- AVE maintenance therapy after chemotherapy remains a recommended option, supported by real-world French data from the AVENANCE study<sup>8</sup>
- In 2021, the French National Authority for Health (HAS) approved AVE for la/mUC without disease progression on or after 1L platinum-based induction chemotherapy<sup>9</sup> (based on the JAVELIN Bladder 100 trial<sup>10</sup>). In 2025, it approved EV+P for treatment-naïve la/mUC<sup>11</sup> (based on the EV-302 trial<sup>12</sup>)
- Given the differing costs of these novel therapies, this study sought to estimate the economic value of these treatments in the 1L settings

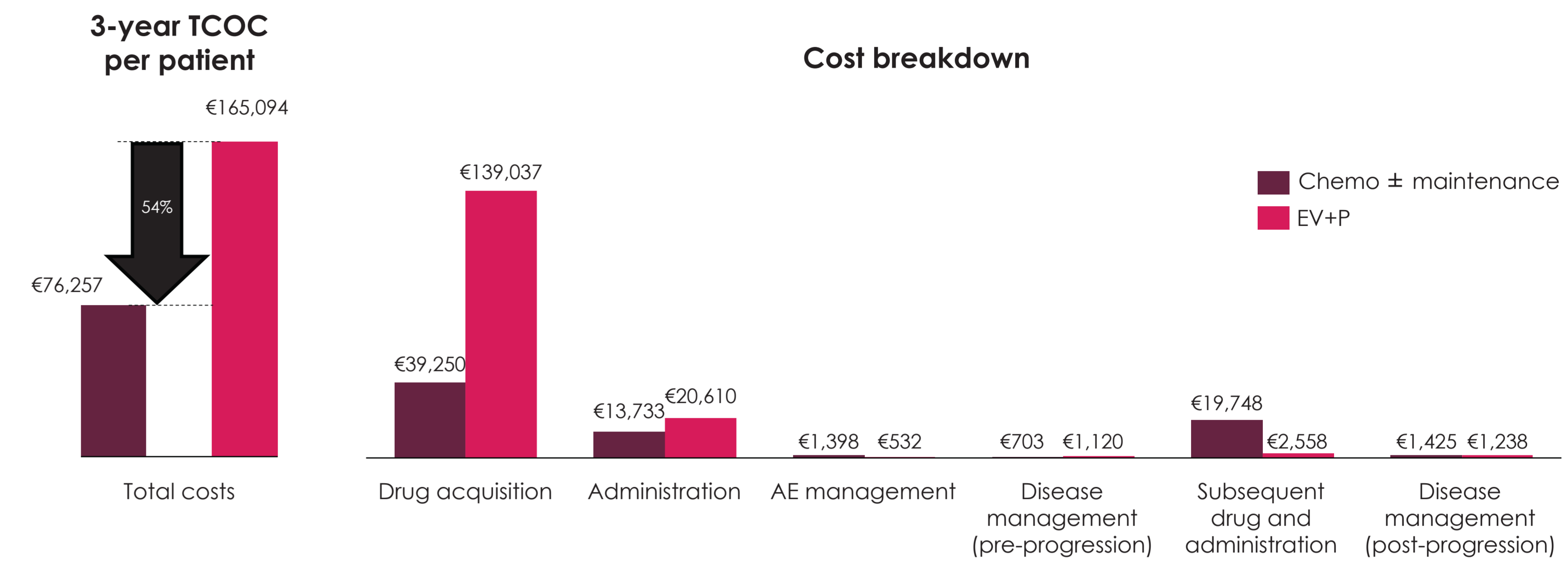
- The latest available costs (2024 EUR)—including drug acquisition and administration, disease management (not including hospitalization cost), adverse event (AE) management, and subsequent therapy (second line or later) costs—were calculated based on treatment duration, PFS, OS, and AE incidence from key clinical trials (JAVELIN Bladder 100, EV-302, and KEYNOTE-361<sup>10,12,14</sup>)
- Treatment dosing schedules were obtained from French product prescribing information, and costs came from public French databases and published literature;<sup>15-17</sup> it was assumed that BSC incurred no drug costs
- Subsequent treatment distribution included pembrolizumab, EV, erdafitinib, and standard chemotherapy care, based on clinical trials and expert opinion
- Main inputs are presented in Table 1
- The model outcomes comprise:
  - 3-year total cost of care per patient
  - Cost per month in PFS and OS: total costs incurred during PFS and OS were divided by the 3-year restricted mean PFS and mean OS, respectively
  - Incremental cost per additional survivor after 3 years: the difference in total per-patient cost between strategies was divided by the 3-year absolute reduction in the risk of death
  - Treatable patients and potential survivors within a fixed budget: the number of treatable patients was the total budget over 3 years divided by the per-patient cost for each strategy; the potential survivors after 3 years was the number of treatable patients multiplied by the 3-year OS rate for that strategy

## RESULTS

### Base case results

- As shown in Figure 2, the estimated total cost of care per patient over 3 years was 54% lower with chemo ± maintenance than with EV+P, with a cost of €76,257 compared with €165,094, respectively. This was driven by drug costs for EV+P, despite chemo ± maintenance incurring higher AE management and subsequent therapy costs
- Monthly costs of PFS and OS with chemo ± maintenance are 49% and 46% lower than those of EV+P, respectively (Table 2)

Figure 2. Base case results



AE, adverse event; AVE, avelumab; chemo, chemotherapy; EV, enfortumab vedotin; P, pembrolizumab; TCOC, total cost of care.

Table 2. Cost per month in PFS and OS

	Total per-patient cost during PFS, €	Total per-patient cost during OS, €	Mean PFS, months	Mean OS, months	Cost per month in PFS, €	Cost per month in OS, €
Chemo ± maintenance	55,084	76,257	12.3	21.6	4,494	3,535
EV+P	161,298	165,094	18.2	25.3	8,870	6,527
Difference (chemo ± maintenance vs EV+P), %					-49.33	-45.83

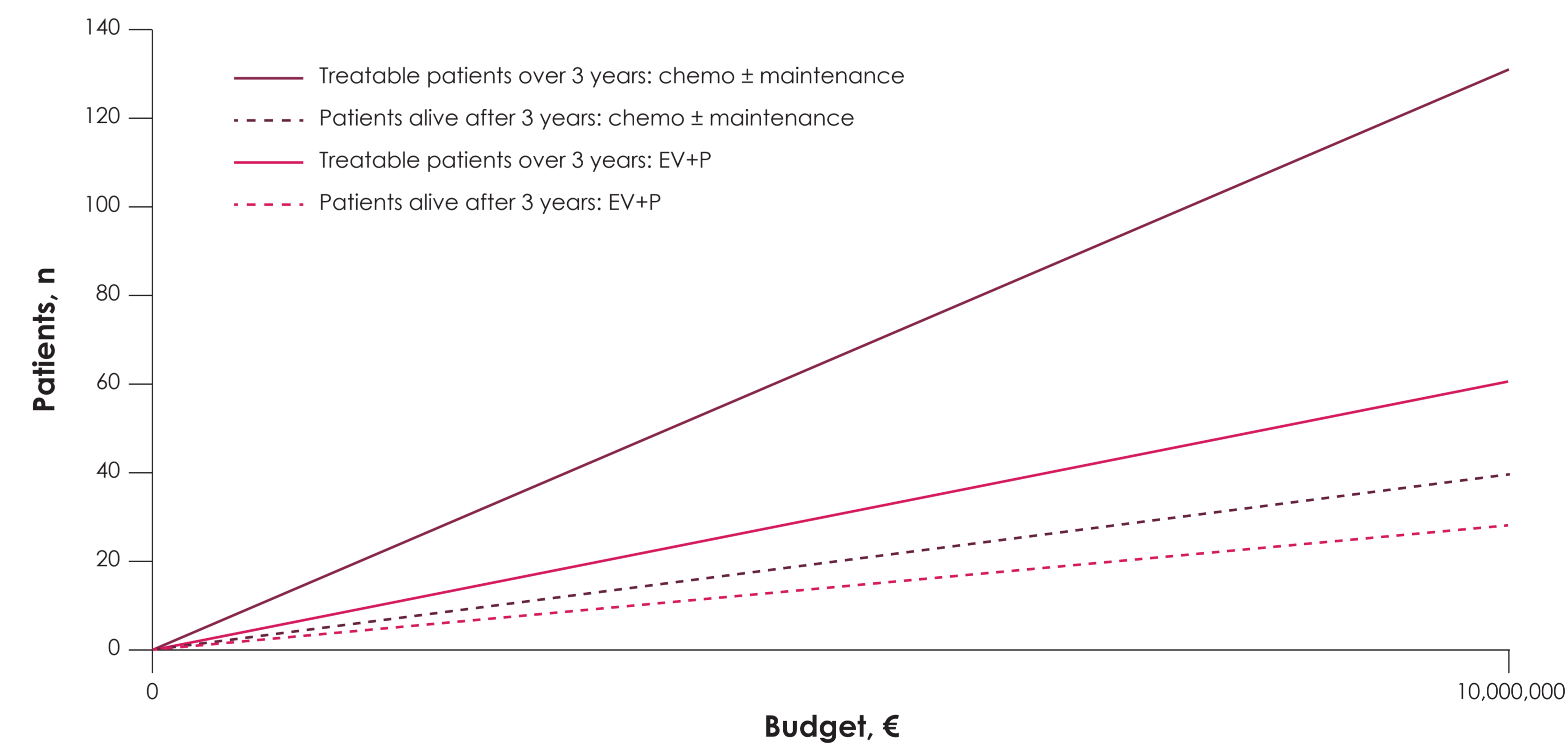
Chemo, chemotherapy; EV, enfortumab vedotin; OS, overall survival; P, pembrolizumab; PFS, progression-free survival.

Table 3. Cost per additional survivor

	3-year TCOC, €	OS rate at 3 years, %	Incremental 3-year TCOC, €	Absolute risk reduction, %	Cost of keeping 1 additional patient alive after 3 years, €
Chemo ± maintenance	76,257	30.2	—	—	—
EV+P	165,094	46.5	88,838	16.3	543,604 (181,201 annually)

Chemo, chemotherapy; EV, enfortumab vedotin; OS, overall survival; P, pembrolizumab; TCOC, total cost of care.

Figure 3. Treatable patients and potential survivors within fixed a budget



AVE, avelumab; BSC, best supportive care; chemo, chemotherapy; EV, enfortumab vedotin; P, pembrolizumab.

## LIMITATIONS

- Clinical inputs, such as treatment duration, PFS, OS, and AE profiles, were based on clinical trials and assumed to be representative of real-world practice in France
- Costs and outcomes are disconnected, as clinical inputs were derived from published trials and data, while other inputs, such as disease management, were based on published literature and input from local clinicians
- To minimize uncertainty about long-term outcomes and costs, the model used a 3-year time horizon; therefore, the clinical and economic effects beyond 3 years are not captured in the model
- AEs associated with subsequent treatments were not considered in the model
- Efficacy of subsequent treatments was assumed to be captured in the OS obtained from the clinical trials. Given the evolving treatment landscape for la/mUC, subsequent treatments used in the clinical trials may not represent those currently used

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