Budget impact analysis of pembrolizumab plus enfortumab vedotin as first-line treatment of cisplatin-ineligible locally advanced or metastatic urothelial carcinoma in the United States

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Background

- Bladder cancer is the sixth most common cancer and the tenth leading cause of cancer death in the United States (US), with over 80,000 new cases and 17,000 deaths in 2022.[1] More than 90% of bladder cancers are urothelial carcinoma[2]
- Patients diagnosed with regional or metastatic bladder cancer have poor prognosis. The 5-year relative survival is 39% for regional stage and only 8% for metastatic stage[1]
- Pembrolizumab is a programmed death receptor-1 (PD-1)-blocking antibody. In the US, pembrolizumab is indicated for the treatment of patients with locally advanced or metastatic urothelial cancer (la/mUC) who are not eligible for any platinum-containing chemotherapy or who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy[3]
- Enfortumab vedotin (EV) is a Nectin-4–directed antibody and microtubule inhibitor conjugate. EV is indicated for the treatment of adult patients with la/mUC who have previously received a PD-1 or PD-L1 inhibitor and platinum-containing chemotherapy or who are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy[4]
- On April 3, 2023, the Food and Drug Administration granted accelerated approval for pembrolizumab in combination with enfortumab vedotin-ejfvto (Pem+EV) for the treatment of adult patients with la/mUC who are not eligible for cisplatin-containing chemotherapy. Encouraging efficacy was shown in KN-869/EV-103, a Phase I/II open label, randomized, multi-cohort global study for the treatment of urothelial cancer (NCT03288545)[5,6]

Objective

- To estimate the budget impact of including Pem+EV to a US health plan formulary as 1L treatment of adult patients with la/mUC who are not eligible for cisplatin-containing chemotherapy

Methods

- A cohort-based budget impact analysis was performed over 3-year time horizon from an overall US payer perspective (including a mix of commercial and Medicare plans)
- The budget impact was estimated by calculating the cost difference between two scenarios:
  - Reference scenario: Pem+EV is not available for the treatment of la/mUC
  - New drug scenario: Pem+EV is available for the treatment of la/mUC
- A hypothetical health plan of 1 million members was assumed. The size of the eligible population was calculated based on epidemiological inputs and RWE data (**Figure 1**)
- Comparators were selected based on NCCN guideline: gemcitabine plus carboplatin with/without avelumab maintenance (GC w/wo avelumab), pembrolizumab, atezolizumab, gemcitabine, gemcitabine plus paclitaxel. Specifically, proportion of receiving avelumab maintenance after GC was assumed to be 30%[7,8]
- Subsequent treatments in second and further lines (2L+) included pembrolizumab, EV, GC, erdafitinib, avelumab, nivolumab and atezolizumab based on NCCN guideline
- Market shares were estimated from market research and claims data for comparators in 1L and 2L+. For Pem+EV, it was assumed a constant 25% for over 3 years, and after progression, patients would receive GC given they already failed anti-PD-1 therapy and EV in combination in 1L (**Table 1**)
- Costs included drug acquisition, administration, monitoring, grade 3-5 adverse event (AE) management, and subsequent treatments. All costs are in 2022 US dollars
- Treatment duration for Pem+EV was derived from KN-869/EV-103, and the published literature for comparators and subsequent treatments
- One-way sensitivity analyses (varying the parameters by +/-20%) and scenario analyses (varying key model assumptions) were conducted to assess model uncertainty

Results

- For a hypothetical 1,000,000-member health plan, there are 17 patients estimated to eligible for Pem+EV as a 1L treatment, annually over a three-year time horizon
- The total costs for a patient over the treatment course were $488,666 for Pem+EV, followed by $286,284 for pembrolizumab, and $283,172 for atezolizumab (**Table 2**). The subsequent treatment cost for Pem+EV was significantly lower than comparators, reflecting a delayed progression with Pem+EV and a higher usage of chemotherapies in subsequent lines
- The inclusion of Pem+EV resulted in an annual budget increase of $364,817, $799,598, and $920,093 in year 1-3, and $694,836 on average (**Table 3**)
- On a per-member per-month (PMPM) basis, the budget impact was $0.0304, $0.0664, and $0.0761 in year 1-3, and $0.0577 on average (**Table 3**)
- The model results remained robust in sensitivity analyses, and most sensitive to time horizon, market share of Pem+EV, EV's relative dose intensity (RDI, defined as actual dose per unit of time/ intended dose intensity), and subsequent treatment costs (**Figure 2**)
- A scenario of Medicare perspective, by assuming 20% coinsurance rate, was tested and found to decrease the budget impact (**Figure 2**)

Conclusions

- Pem+EV can be an affordable and valuable treatment option for la/mUC patients in the 1L setting.
- The introduction of Pem+EV for 1L cis-IE la/mUC patients in a US healthcare plan of 1 million members is projected to lead to a modest budget impact (average 0.06 PMPM)

Adoption of Pem+EV for 1L treatment of advanced bladder cancer will have a modest budget impact on US health plans.

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References

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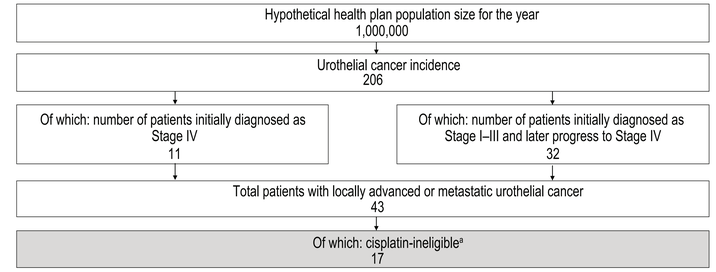
Figure 1. Patient flow and the population size in the indication of interest



[a]Pem+EV eligible la/mUC population

Table 1. Market shares of 1L treatments

Treatments	Reference scenario (years 1–3)	New drug scenario (years 1–3)
Pem+EV	0.0%	25.0%
GC w/wo avelumab	24.8%	20.0%
Pembrolizumab	27.8%	11.0%
Atezolizumab	4.7%	2.0%
Gemcitabine	2.2%	2.0%
Gemcitabine plus paclitaxel	0.4%	0.0%
Untreated	40.1%	40.0%
Total	**100.0%**	**100.0%**

Table 2. Cost per treated patient per treatment course

Treatments	1L drug acquisition, administration	Subsequent drug acquisition, administration	Monitoring	AE management	Total costs
Pem+EV	$474,384	$1,111	$1,907	$11,264	$488,666
Pembrolizumab	$103,916	$179,352	$1,331	$1,685	$286,284
Atezolizumab	$100,632	$179,337	$1,844	$1,358	$283,172
GC w/wo avelumab	$42,244	$181,594	$1,591	$16,265	$241,695
Gemcitabine	$1,454	$126,217	$455	$936	$129,062
Gemcitabine plus paclitaxel	$2,793	$126,626	$927	$11,179	$141,526

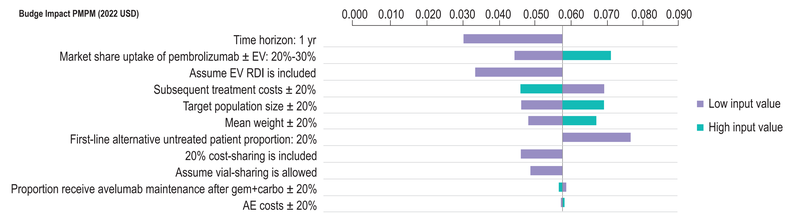
Note: the administration of IV drugs in 1L and subsequent lines (2L+) were accounted for in the costs.

Table 3. Budget impact of adding Pem+EV in 1L la/mUC

Period year	Reference scenario	New drug scenario	Budget impact, total	Budget impact, PMPM
Year 1	$1,880,711	$2,245,527	$364,817	$0.0304
Year 2	$2,578,281	$3,377,879	$799,598	$0.0664
Year 3	$2,696,573	$3,616,667	$920,093	$0.0761
3-year total	$7,155,565	$9,240,073	$2,084,508	N/A
3-year average	$2,385,188	$3,080,024	$694,836	$0.0577

N/A, not applicable.

Figure 2. Budget impact PMPM from one-way sensitivity analyses and scenario analyses



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