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Real-World Frontline Use of Enfortumab Vedotin - Pembrolizumab (EV+P) After Adjuvant Nivolumab in Advanced Urothelial Cancer (aUC)

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Introduction

- EV+P received accelerated FDA approval in April 2023 (EV-103) and full approval in December 2023 (EV-302) for the treatment of advanced urothelial cancer (aUC). By April 2024, EV+P had become the most common frontline (1L) regimen in the US, accounting for 50% of treatment starts.[1] EV-302 excluded patients who had received prior immunotherapy in the perioperative setting. Treatment selection in this emerging post-immunotherapy population remains poorly understood. We examined real-world 1L treatment choices among aUC patients with prior exposure to adjuvant nivolumab.

Objective

- To describe adjuvant treatment patterns among 1L treated mUC patients who had prior radical cystectomy and received nivolumab treatment post radical cystectomy, and to describe the sequence of systemic treatments received (i.e., 1L, 2L, etc.) in the metastatic setting.

Methods

Study design: Retrospective cohort.

Data source: Data were obtained from the Flatiron Health EHR-derived database, a geographically diverse United States database comprised of patient-level structured and unstructured data, curated via technology-enabled abstraction. The de-identified data originate from approximately 280 cancer clinics (~800 sites of care), representing more than 2.2 million patients with cancer.

Study identification period: From April 3, 2023, with follow-up through April 30, 2025.

Study population: The study sample included patients that were 18 years or older, diagnosed with de novo or recurrence stage IV urothelial cancer (bladder, renal pelvis, ureter, or urethra) with ≥2 clinical encounters after advanced diagnosis, and patients who initiated 1L therapy who had prior surgery and received adjuvant nivolumab monotherapy within 6 months of curative-intent surgery.

Statistical analysis: Descriptive statistics summarized baseline characteristics and 1L treatment regimens.

Results

Patient characteristics

Among eligible aUC patients initiating 1L treatment (n=1447), 54 had received prior adjuvant nivolumab (mean age = 71 y, 79.6% male, 92.2% White, 19.1% ECOG performance status 2+, 66.7% cisplatin-ineligible, 70.4% bladder as primary site, and 82.4% from community practice) **(Table 1)**.

Table 1. Baseline characteristics among adjuvant nivolumab subgroup who later received 1L therapy, overall and by top regimens

		Overall (N = 54)	1L EV-P (n = 26)	1L EV mono (n = 13)
Sex	Male, n (%)	43 (79.6%)	20 (76.9%)	10 (76.9)
Age	Mean years (SD)	71.46 (7.94)	71.31 (9.16)	70.38 (5.64)
Race	White, n (%)	47 (92.2%)	24 (96.0%)	11 (91.7%)
	Black or African American, n (%)	2 (3.9%)	1 (4.0%)	0 (0.0%)
	Hispanic or Latino, n (%)	1 (2.0%)	0 (0.0%)	1 (8.3%)
	Asian, n (%)	1 (2.0%)	0 (0.0%)	0 (0.0%)
	Missing, n	3	1	1
Smoking	Yes, n (%)	38 (70.3%)	16 (61.5%)	11 (84.6%)
Creatinine clearance	Mean mL/min (SD)	55.5 (24.3)	50.7 (20.3)	64.2 (27.4)
	Missing, n	4	0	1
ECOG performance status	0, n (%)	17 (36.2%)	9 (36.0%)	4 (40.0%)
	1, n (%)	21 (44.7%)	11 (44.0%)	4 (40.0%)
	2+, n (%)	9 (19.1%)	5 (20.0%)	2 (20.0%)
	Missing, n	7	1	3
Cisplatin ineligible*	Yes, n (%)	34 (66.7%)	17 (65.4%)	8 (61.5%)
	Missing, n	3	0	3
Primary site	Bladder, n (%)	38 (70.4%)	22 (84.6%)	10 (76.9%)
	Renal Pelvis, n (%)	5 (9.3%)	0 (0.0%)	2 (15.4%)
	Ureter, n (%)	11 (20.4%)	4 (15.4%)	1 (7.7%)
Insurance type	Commercial, n (%)	46 (85.2%)	25 (96.2%)	11 (84.6%)
	Medicare, n (%)	5 (9.3%)	1 (3.8%)	1 (7.7%)
	Other gov, n (%)	2 (3.7%)	0 (0.0%)	1 (7.7%)
	Other, n (%)	1 (1.9%)	0 (0.0%)	0 (0.0%)
Treatment facility	Community, n (%)	42 (82.4%)	23 (88.5%)	11 (84.6%)
	Academic, n (%)	9 (17.6%)	3 (11.5%)	2 (15.4%)
	Missing, n	3	0	0

***Cisplatin ineligible defined as PS ≥2 and/or creatinine clearance <60**

Treatment patterns and sequencing

Following the accelerated approval of EV-P, EV-P was the most commonly selected regimen, received by 48% (26/54) of patients **(Table 2)**. EV monotherapy was the next most frequently used 1L option (24.1%, 13/54), while a smaller proportion of patients received platinum-based chemotherapy (9.3%, 5/54). Use of later lines of therapy was limited in this subgroup, with relatively few patients progressing to 2L treatment and very few receiving 3L or 4L therapy during observed follow-up.

Table 2. Frequency of treatment selection (top regimens) among patients receiving adjuvant nivolumab (n=54) after accelerated approval of EV-P

Line Name	1L	2L	3L	4L
Enfortumab Vedotin, Pembrolizumab	26	1	0	0
Enfortumab Vedotin	13	5	0	0
Carboplatin, Gemcitabine	3	0	3	0
Pembrolizumab	2	1	0	0
Cisplatin, Gemcitabine	1	0	0	0
Other	9	15	2	4

Adjuvant nivolumab administration

Timing from adjuvant nivolumab exposure to initiation of 1L therapy is summarized in **Tables 3** and **4**. Median follow-up from surgery to last recorded visit was only 474 days **(Table 5)**, indicating limited long-term follow-up for many patients.

Table 3. Time from first adjuvant nivolumab administration date to start of 1L therapy

	Median (months)	IQR
1L EV-P (n = 26)	5.7	(3.6, 8.1)
1L EV mono (n = 13)	7.1	(6.2, 10.4)

Table 4. Time from last adjuvant nivolumab administration date to start of 1L therapy

	Median (months)	IQR
1L EV-P (n = 26)	1.7	(1.0, 6.3)
1L EV mono (n = 13)	3.8	(1.3, 8.3)

Table 5. Follow-up time from surgery date to last visit

Median (IQR), days	474 (336, 64)
[min, max]	[92, 1144]

Limitations

This study has several limitations inherent to retrospective analyses of real-world data including: 1) data lag precluding the ability to examine the impact of newer perioperative strategies (gemcitabine with cisplatin and durvalumab, EV-P, CT DNA-guided adjuvant therapy) on subsequent systemic treatment selection/sequencing; 2) insufficient follow-up to more accurately estimate long-term survival of EV-P users.

Conclusion

Among real-world patients with aUC who previously treated with adjuvant nivolumab, EV+P accounted for nearly half 1L systemic therapies initiated after its FDA approval. EV monotherapy was also common, while platinum-based chemotherapy was used infrequently. Results from this analysis suggest relatively short treatment-free intervals following completion of adjuvant therapy in this subgroup. Further research is needed to better understand 1L treatment decision-making and outcomes in the evolving landscape of perioperative immunotherapy.

References

1. Mamtani R, et al. *Eur Urol.* 2024;86(5):474-476.

Disclosures

MM, RM, and NS are employees of the University of Pennsylvania, Philadelphia, PA, USA. AB, BHM, CR, and HL are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD).

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Presented at International Society for Pharmacoeconomics and Outcomes Research (ISPOR); May 17 - 20, 2026; Philadelphia, PA, USA.