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Outcomes with first-line platinum-based chemotherapy and avelumab first-line maintenance in locally advanced or metastatic urothelial carcinoma by *NECTIN4* and *ERBB2* amplification status: exploratory analyses from JAVELIN Bladder 100

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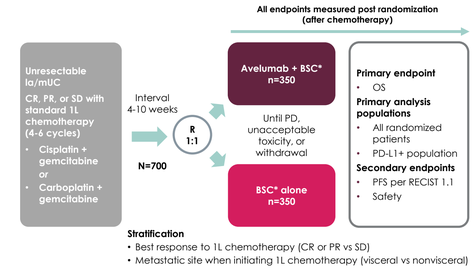
BACKGROUND

- Nectin-4 and HER2 (encoded by *ERBB2*) are relevant therapeutic targets and potential biomarkers for the treatment of muscle-invasive bladder cancer (MIBC) and la/mUC[2-6]
  - Nectin-4 is the molecular target of enfortumab vedotin, an antibody-drug conjugate (ADC) that is approved in MIBC (EU: cisplatin ineligible only) and la/mUC in combination with pembrolizumab, as monotherapy for patients with prior PBC and PD-(L)1 inhibitor treatment (US and Europe), and as monotherapy for cisplatin-ineligible patients with any prior treatment (US)[7,8]
  - HER2 is the molecular target of disitamab vedotin, an ADC in clinical development for the treatment of HER2-expressing la/mUC[9] (approved in China as 1L treatment in combination with toripalimab),[10] and trastuzumab deruxtecan, an ADC that is approved as a later-line treatment for patients with HER2-positive (immunohistochemistry 3+) solid tumors[11,12]
- *NECTIN4* amplification is a frequent genomic event in metastatic UC and is associated with increased nectin-4 membrane expression[13]; *ERBB2* amplification is observed in ≈12% of advanced UCs and is associated with increased HER2 membrane expression[14]
- Previous studies have demonstrated that *NECTIN4* amplification is associated with improved response to enfortumab vedotin-containing treatment[13,15,16]; similarly, improved response to trastuzumab deruxtecan has been observed in gastrointestinal tumors with *ERBB2* amplification[17,18]
  - However, the association between *NECTIN4* and *ERBB2* amplification and treatment outcomes with PBC and PD-(L)1 inhibitors is unclear
- In the JAVELIN Bladder 100 trial, avelumab + BSC significantly prolonged OS and PFS vs BSC alone in patients with la/mUC that had not progressed with 1L PBC[1,19]
  - After ≥2 years of follow-up, median OS was 23.8 vs 15.0 months (hazard ratio [HR], 0.76 [95% CI, 0.63-0.91]; p=0.0036), and median PFS was 5.5 vs 2.1 months, respectively (HR, 0.54 [95% CI, 0.46-0.64]; p<0.0001)[1]
- Here, we report post hoc exploratory biomarker analyses in the JAVELIN Bladder 100 trial population evaluating response to 1L PBC and survival outcomes with avelumab 1L maintenance treatment in subgroups defined by tumor *NECTIN4* and *ERBB2* amplification status

METHODS

- JAVELIN Bladder 100 (NCT02603432) was an international, randomized, phase 3 trial that enrolled patients with unresectable la/mUC who were progression free after 4-6 cycles of 1L PBC (**Figure 1**)
  - Patients were randomized 1:1 to receive avelumab + BSC or BSC alone until cancer progression, unacceptable toxicity, or patient withdrawal
  - The primary endpoint was OS, measured from randomization after chemotherapy
- For the current analysis, tumor samples obtained prior to 1L PBC were processed for copy number variation (CNV) using Genedata Profiler to assess *NECTIN4* and *ERBB2* amplification status
  - A cutoff value of 7 gene copies was used to define a gene as amplified
  - *NECTIN4* and *ERBB2* amplification were assessed as dichotomous variables for subgroups defined by response to 1L PBC and for survival analyses
  - Outcomes were assessed descriptively, without formal comparisons or adjustment for multiplicity; p-values are nominal, unadjusted for multiplicity, and provided for descriptive purposes only

Figure 1. JAVELIN Bladder 100 study design[19]



1L, first line; **BSC**, best supportive care; **CR**, complete response; **la/mUC**, locally advanced or metastatic urothelial carcinoma; **OS**, overall survival; **PD**, progressive disease; **PFS**, progression-free survival; **PR**, partial response; **R**, randomization; **SD**, stable disease.
*BSC (eg, antibiotics, nutritional support, hydration, and pain management) was administered per local practice based on patient needs and clinical judgment; other antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable.

RESULTS

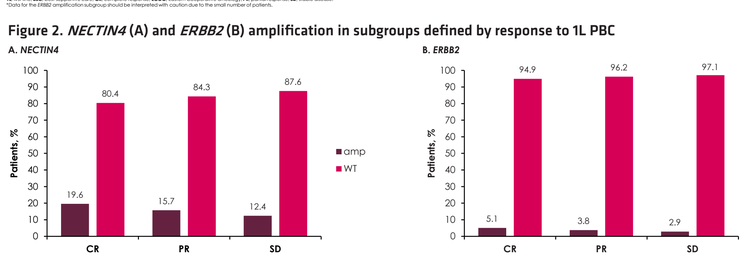
- Overall, 614 patients had tumor samples available for CNV assessment (avelumab + BSC arm, n=316; BSC alone arm, n=298)
  - In the overall population, 97 patients (15.8%) had *NECTIN4* amplification and 24 (3.9%) had *ERBB2* amplification
  - *NECTIN4* and *ERBB2* amplification was observed in 42 (13.3%) and 7 (2.2%), respectively, in the avelumab + BSC arm, and 55 (18.5%) and 17 (5.7%), respectively, in the BSC alone arm
- Patient characteristics in the avelumab + BSC and BSC alone arms in subgroups defined by *NECTIN4* and *ERBB2* amplification status are shown in **Table 1**
  - A higher proportion of patients with *NECTIN4* and *ERBB2* amplification had PD-L1–positive tumors compared with patients with wild type
- In patients who had CR (n=158), PR (n=286), or SD (n=170) to 1L PBC, *NECTIN4* amplification was observed in 31 (19.6%), 45 (15.7%), and 21 (12.4%), respectively, and *ERBB2* amplification was observed in 8 (5.1%), 11 (3.8%), and 5 (2.9%), respectively
- Differences in *NECTIN4* and *ERBB2* amplification in subgroups defined by response to 1L PBC are shown in **Figure 2**

Table 1. Patient characteristics at baseline

	Avelumab + BSC		BSC alone		Avelumab + BSC		BSC alone	
	NECTIN4 amplified (n=42)	*NECTIN4* wild type (n=274)	*NECTIN4* amplified (n=55)	*NECTIN4* wild type (n=243)	*ERBB2* amplified* (n=7)	*ERBB2* wild type (n=309)	*ERBB2* amplified* (n=17)	*ERBB2* wild type (n=281)
Age, median (range), years	69.5 (49-84)	69 (37-90)	71 (46-83)	69 (32-89)	72 (54-81)	69 (37-90)	76 (39-82)	69 (32-89)
Sex, n (%)								
Female	11 (26.2)	63 (23.0)	7 (12.7)	57 (23.5)	0 (0)	74 (23.9)	5 (29.4)	59 (21.0)
Male	31 (73.8)	211 (77.0)	48 (87.3)	186 (76.5)	7 (100)	235 (76.1)	12 (70.6)	222 (79.0)
Pooled geographic region, n (%)								
Asia	9 (21.4)	57 (20.8)	9 (16.4)	50 (20.6)	0 (0)	66 (21.4)	3 (17.6)	56 (19.9)
Australasia	7 (16.7)	26 (9.5)	7 (12.7)	29 (11.9)	1 (14.3)	32 (10.4)	6 (35.3)	30 (10.7)
Europe	22 (52.4)	169 (61.7)	34 (61.8)	142 (58.4)	4 (57.1)	187 (60.5)	8 (47.1)	168 (59.8)
North America	1 (2.4)	11 (4.0)	5 (9.1)	13 (5.3)	1 (14.3)	11 (3.6)	0 (0)	18 (6.4)
Rest of the world	3 (7.1)	11 (4.0)	0 (0)	9 (3.7)	1 (14.3)	13 (4.2)	0 (0)	9 (3.2)
ECOG performance status, n (%)								
0	20 (47.6)	170 (62.0)	33 (60.0)	142 (58.4)	3 (42.9)	187 (60.5)	9 (52.9)	166 (59.1)
≥1	22 (52.4)	104 (38.0)	22 (40.0)	101 (41.6)	4 (57.1)	122 (39.5)	8 (47.1)	115 (40.9)
PD-L1 status, n (%)								
Positive	29 (69.0)	149 (54.4)	37 (67.3)	122 (50.2)	5 (71.4)	173 (56.0)	11 (64.7)	148 (52.7)
Negative	13 (31.0)	115 (42.0)	17 (30.9)	101 (41.6)	2 (28.6)	126 (40.8)	5 (29.4)	113 (40.2)
Unknown	0 (0)	10 (3.6)	1 (1.8)	20 (8.2)	0 (0)	10 (3.2)	1 (5.9)	20 (7.1)
Site of primary tumor, n (%)								
Upper tract	8 (19.0)	80 (29.2)	11 (20.0)	53 (21.8)	2 (28.6)	86 (27.8)	2 (11.8)	62 (22.1)
Lower tract	34 (81.0)	194 (70.8)	44 (80.0)	190 (78.2)	5 (71.4)	223 (72.2)	15 (88.2)	219 (77.9)
Metastatic site at start of 1L chemotherapy, n (%)								
Visceral	19 (45.2)	155 (56.6)	31 (56.4)	128 (52.7)	3 (42.9)	171 (55.3)	6 (35.3)	153 (54.4)
Nonvisceral	23 (54.8)	119 (43.4)	24 (43.6)	115 (47.3)	4 (57.1)	138 (44.7)	11 (64.7)	128 (45.6)
Best response to 1L chemotherapy, n (%)								
CR or PR	35 (83.3)	195 (71.2)	41 (74.5)	173 (71.2)	7 (100)	223 (72.2)	12 (70.6)	202 (71.9)
SD	7 (16.7)	79 (28.8)	14 (25.5)	70 (28.8)	0 (0)	86 (27.8)	5 (29.4)	79 (28.1)

1L, first line; **BSC**, best supportive care; **CR**, complete response; **ECOG**, Eastern Cooperative Oncology; **PR**, partial response; **SD**, stable disease.
*Data for the *ERBB2* amplification subgroup should be interpreted with caution due to the small number of patients.

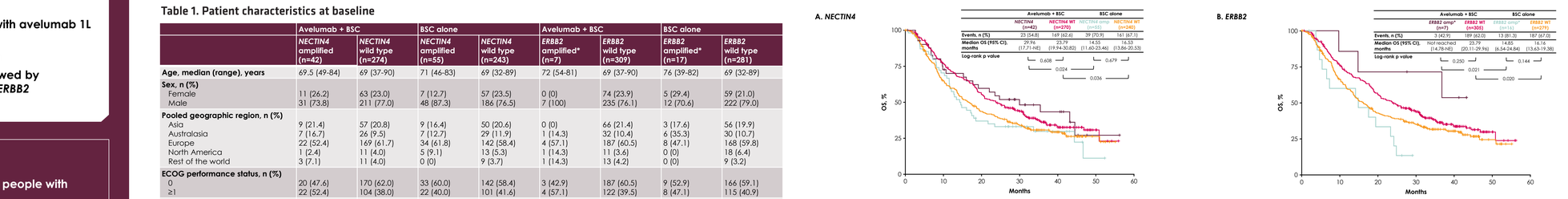
Figure 2. *NECTIN4* (A) and *ERBB2* (B) amplification in subgroups defined by response to 1L PBC



1L, first line; **amp**, amplification; **CR**, complete response; **PBC**, platinum-based chemotherapy; **PR**, partial response; **SD**, stable disease; **WT**, wild type.

- Median OS and PFS in subgroups defined by *NECTIN4* and *ERBB2* amplification status were longer with avelumab + BSC vs BSC alone (**Figures 3** and **4**)
  - In patients with *NECTIN4* amplification, median OS was 29.96 (95% CI, 17.71-not estimable [NE]) vs 14.55 (95% CI, 11.60-23.46) months and median PFS was 5.09 (95% CI, 3.12-13.01) vs 3.50 (95% CI, 1.91-3.75) months, respectively
  - In patients with *NECTIN4* wild type, median OS was 23.79 (95% CI, 19.94-30.82) vs 16.53 (95% CI, 13.86-20.53) months and median PFS was 5.59 (95% CI, 4.30-7.49) vs 2.07 (95% CI, 1.91-3.52) months, respectively
  - In patients with *ERBB2* amplification, median OS was not reached (95% CI, 14.78-NE) vs 14.85 (95% CI, 6.54-24.84) months and median PFS was not reached (95% CI, 5.52-NE) vs 2.25 (95% CI, 1.87-6.01) months, respectively; however, due to the small number of patients with *ERBB2* amplification, these results should be interpreted with caution
  - In patients with *ERBB2* wild type, median OS was 23.79 (95% CI, 20.11-29.96) vs 16.16 (95% CI, 13.63-19.38) months and median PFS was 5.45 (95% CI, 4.21-7.33) vs 2.30 (95% CI, 1.94-3.65) months, respectively

Figure 3. OS in subgroups defined by *NECTIN4* (A) and *ERBB2* (B) amplification status



For exploratory survival analyses, only patients who received treatment were included; 7/614 patients with a CNV assessment did not receive any treatment because of withdrawal of consent or the development of health issues.
Amp, amplification; **BSC**, best supportive care; **CNV**, copy number variation; **NE**, not estimable; **OS**, overall survival; **WT**, wild type.
*Data for the *ERBB2* amplification subgroup should be interpreted with caution due to the small number of patients.

Figure 4. PFS in subgroups defined by *NECTIN4* (A) and *ERBB2* (B) amplification status

For exploratory survival analyses, only patients who received treatment were included; 7/614 patients with a CNV assessment did not receive any treatment because of withdrawal of consent or the development of health issues.
Amp, amplification; **BSC**, best supportive care; **CNV**, copy number variation; **NE**, not estimable; **PFS**, progression-free survival; **WT**, wild type.
*Data for the *ERBB2* amplification subgroup should be interpreted with caution due to the small number of patients.

CONCLUSIONS

- **We report exploratory biomarker analyses of patients with locally advanced or metastatic urothelial carcinoma (la/mUC) in the JAVELIN Bladder 100 phase 3 trial population to evaluate response to first-line (1L) platinum-based chemotherapy (PBC) and survival outcomes with avelumab 1L maintenance treatment in subgroups defined by *NECTIN4* and *ERBB2* amplification status in tumor samples obtained prior to 1L PBC**
- **A similar proportion of patients with *NECTIN4* or *ERBB2* amplification had complete response (CR), partial response (PR), or stable disease (SD) to 1L PBC**
- **Median overall survival (OS) and progression-free survival (PFS) in patients with *NECTIN4* or *ERBB2* amplification and wild type tended to be longer with avelumab + best supportive care (BSC) vs BSC alone, consistent with the overall population[1]**
  - **However, patients with *NECTIN4* amplification tended to have longer OS with avelumab 1L maintenance than patients with wild type**
  - **Median PFS was similar in patients with and without *NECTIN4* amplification**
- **Overall, exploratory analyses from JAVELIN Bladder 100 suggest 1L PBC followed by avelumab 1L maintenance is a treatment option regardless of *NECTIN4* and *ERBB2* amplification status in tumors; results are hypothesis-generating only**

PLAIN LANGUAGE SUMMARY

- **In the JAVELIN Bladder 100 study, avelumab maintenance treatment helped people with advanced urothelial cancer live longer**
  - **Maintenance treatment means treating people whose cancer disappeared, shrank, or stopped growing with chemotherapy**
- **Nectin-4 and HER2 (made from the *ERBB2* gene) are proteins that are present in most urothelial cancers**
  - **Both proteins are targets for drugs used to treat urothelial cancer**
- **This new analysis from the JAVELIN Bladder 100 study looked at results with prior chemotherapy or avelumab maintenance treatment in people whose tumors had extra copies of the *NECTIN4* or *ERBB2* genes**
- **A similar number of people whose tumors had extra copies of the *NECTIN4* or *ERBB2* gene had cancer that disappeared, shrank, or stopped growing with prior chemotherapy**
- **Researchers found that, on average, people treated with avelumab maintenance whose tumors had extra copies of the *NECTIN4* gene lived for ≈30 months, while the average survival time for those with extra copies of the *ERBB2* gene could not yet be estimated due to the small number of people included**
- **These results suggest that chemotherapy followed by avelumab maintenance is a treatment option for people with advanced urothelial cancer whose tumors have extra copies of the *NECTIN4* and *ERBB2* genes**

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REFERENCES 1. Powles T, et al. J Clin Oncol. 2023;41(19):3486-92. 2. Meric-Bernstam F, et al. J Clin Oncol. 2024;42(1):47-58. 3. Sanguedolce F, et al. Int J Mol Sci. 2023;24(4):3720. 4. Stemschus M, et al. J Clin Oncol. 2026;44(7 Suppl):Abstract 801. 5. Klümper N, et al. Clin Cancer Res. 2023;29(8):1496-505. 6. Heath EI, et al. Nat Rev Urol. 2021;18(2):93-103. 7. Padcev (enfortumab vedotin). Prescribing information. Astellas Pharma US, Inc.; 2026. 8. Padcev (enfortumab vedotin). Summary of product characteristics. Astellas Pharma Europe B.V.; 2026. 9. Sheng X, et al. J Clin Oncol. 2023;42(12):1391-402. 10. Junshi Biosciences. News release. Accessed August 27, 2026. https://www.junshipharma.com/en/junshi-biosciences-announces-the-acceptance-of-the-snda-for-toripalimab-as-the-1st-line-treatment-of-her2-expressing-urothelial-carcinoma/. 11. Enhertu (fam-trastuzumab deruxtecan-nxki). Prescribing information. Daiichi Sankyo, Inc.; 2026. 12. Enhertu (trastuzumab deruxtecan). Summary of product characteristics. Daiichi Sankyo Europe GmbH; 2026. 13. Klümper N, et al. J Clin Oncol. 2024;42:2446-55. 14. Koshkin VS, et al. JCO Precis Oncol. 2025;9:e2400879. 15. Klümper N, et al. Ann Oncol. 2025;36:Abstract 309P. 16. Klümper N, et al. Ann Oncol. 2025;36:Abstract 308P. 17. Siena S, et al. Nat Commun. 2024;15:10213. 18. Shitara K, et al. Nat Med. 2024;30(7):1933-42. 19. Powles T, et al. N Engl J Med. 2020;383(13):1218-30.

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