Ozuriftamab Vedotin (BA3021), a Conditionally Binding ROR2-ADC in Patients with Heavily Pretreated Squamous Cell Carcinoma of the Head and Neck: Antitumor Activity Observed Among Patients with Both HPV-Related and HPV-Negative Cancers

Winston Wong* MD,[1] Douglas Adkins MD,[2] Jamal Misleh MD,[3] Jochen Lorch MD,[4] Jaspreet Grewal MD,[5] Kathleen C. Kerrigan MD,[6] Jeffery Russell MD,[6] Jeremy Cetnar MD,[7] Alan Ho MD,[1] Kyechin Chen PharmD,[8] Judith Llorin-Sangalang, MD,[8] Kartik Aysola MD,[8] Jacob Thomas MD[9]

[1]Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [2]Washington University School of Medicine, St. Louis, MO, USA; [3]Christiana Hospital, Newark, DE, USA; [4]Northwestern University, Chicago, IL, USA; [5]Norton Cancer Institute, Louisville, KY, USA; [6]Huntsman Cancer Institute, Salt Lake City, UT, USA; [7]Oregon Health & Science University, Portland, OR, USA; [8]BioAtla, Inc., San Diego, CA, USA; [9]USC Norris Comprehensive Cancer Center, Los Angeles, CA, US

Background

- Survival for pts with SCCHN after treatment failure with platinum and anti-PD-1 therapy remains poor with mOS after failure of first-line treatment of only 3-6 months.[1]
- HPV-associated SCCHN pts refractory to treatment are minimally responsive to salvage therapy.
  - 0% (0/31 pts) ORR to cetuximab post-platinum therapy.[2]
  - 0% (0/18 pts) ORR to cetuximab post-platinum and anti-PD-(L)1.[3]
- Unmet need exists in 2L+ SCCHN for both HPV positive and negative patients in large part due to the general lack of efficacy observed with the use of EGFR-targeted therapy.

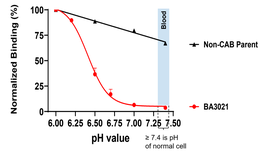
HPV oncoproteins drive increased proliferation and invasiveness through ROR2 overexpression.

- HPV associated expression of E6 and/or E7 oncoproteins drives progression by upregulating ROR2 expression.[4]
- ROR2 acts as a non-canonical receptor for Wnt family of ligands involved in cell migration in normal tissue formation, which:[4]
  - influences cell proliferation and survival by regulating downstream signaling pathways, such as the PI3K/Akt pathway.
  - can promote metastasis by modulating cell migration, invasion, and angiogenesis.
- Increased ROR2 expression has been associated with acquired resistance to chemotherapy, PD-(L)1 inhibitors, molecular targeted therapy, and radiation therapy.[5,6]

Ozuriftamab vedotin, Oz-V, is an ADC targeting ROR2 that delivers auristatin to malignant cells causing tubulin inhibition and immunogenic cell death.

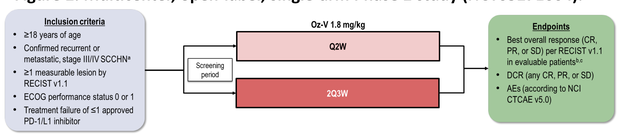
- Ozuriftamab vedotin (Oz-V, BA3021) is a Conditionally Active Biologic or CAB anti-ROR2 antibody–drug conjugate (CAB-ROR2-ADC) employing an MMAE payload (DAR 4) and protease-cleavable linker.
- Oz-V conditionally and reversibly binds to the ROR2 target under the low-pH conditions (pH 5.3 to 6.7) of the tumor microenvironment, thus sparing normal cells **(Fig. 1)**.
- The antibody binding is designed to reduce off-tumor toxicity utilizing a novel mechanism that avoids tissue-mediated drug disposition.
- Oz-V was recently granted FDA Fast Track Designation for treatment of pts with R/M SCCHN who have experienced disease progression following platinum-based chemotherapy and anti-PD-(L)1 antibody therapy.

Figure 1. Oz-V pH binding inflection point designed for TME selectivity.



Methods

Figure 2. Multicenter, open-label, single-arm Phase 2 study (NCT05271604).



[a]Not amenable to local therapy with curative intent (surgery or radiation therapy with or without chemotherapy).
[b]Evaluable pts were defined as those who had ≥1 tumor scan after receiving the study drug.
[c]Tumor assessment by CT or MRI every 6 weeks from C1D1 until 12 weeks, then every 8 weeks up to 1 year, then every 12 weeks thereafter.

Results

Patient characteristics and disposition

All data are from a live database cut from March 24, 2025, unless otherwise specified.

- 40 pts received 1.8 mg/kg Oz-V either Q2W (n=20) or 2Q3W (n=20).
- 60% (26 of 40) pts had tumors associated with HPV infection.
- Pts received a median of 3 prior lines of therapy.
- 95%, 85%, and 65% of pts had experienced prior failure of anti–PD-1 and/or platinum therapy and/or taxane, respectively **(Table 1)**.

Results (continued)

Table 1. Patient demographics and clinical characteristics.

Ozuriftamab vedotin 1.8 mg/kg	Q2W (n=20)	2Q3W (n=20)	Total (N=40)
Age, mean (SD), y	64 (9)	66 (7)	65 (8)
Sex, n (%)			
Male	18 (90)	18 (90)	36 (90)
Female	2 (10)	2 (10)	4 (10)
ECOG performance, n (%)			
0	7 (35)	8 (40)	15 (38)
1	13 (65)	12 (60)	25 (63)
Location of primary disease, n (%)			
Oropharynx	14 (70)	14 (70)	28 (70)
Oral cavity	2 (10)	3 (15)	5 (13)
Larynx	4 (20)	3 (15)	7 (18)
Number of prior lines of therapy, median	3	3	3
Prior anti–PD-1 exposure, n (%)	20 (100)	20 (100)	40 (100)
Prior platinum-based chemotherapy exposure, n (%)	17 (85)	17 (85)	34 (85)
Prior Taxanes	13 (65)	13 (65)	26 (65)
HPV p16 status, n (%)			
Positive	14 (70)	12 (60)	26 (60)
Negative	5 (25)	7 (35)	12 (30)
Missing/not reported	1 (5)	1 (5)	2 (5)

Safety (as of May 31, 2024)

- Most AEs were low-grade **(Table 2)**. Fatigue (59%) and nausea (34%) were the most frequent AEs.
  - Six pts (19%) had grade 3 TRAEs (nausea, diarrhea, decreased lymphocyte count, and decreased neutrophil count, peripheral neuropathy, elevated liver enzymes, and hyperglycemia);
  - 1 pt (3%) experienced TRAE grade 4 hyponatremia in the 2Q3W cohort.
  - No grade 5 related AEs were observed.
- Most frequent grade 3-4 TEAEs were hyponatremia (13%), decreased lymphocyte count (13%), anemia (9%), and hypoxia (9%).
- Two pts discontinued Oz-V due to related AEs (peripheral neuropathy; 1 in Q2W and 1 in 2Q3W).

Table 2. Summary of AEs (as of May 31, 2024).

Number of patients with any AE, n (%)	Q2W (n=12*)	2Q3W (n=20)	Total (N=32)
AE	11 (92)	20 (100)	31 (97)
Related	8 (67)	19 (95)	27 (84)
≥Grade 3 AE[a]			
Related grade 3	1 (8)	5 (25)	6 (19)
Related grade 4	0	1 (3)	1 (3)
Serious AE	8 (67)	9 (45)	17 (53)
Related	1 (8)	3 (15)	4 (13)
AE leading to treatment discontinuation	2 (17)	1 (5)	3 (9)
Related	1 (8)	1 (5)	2 (6)
AE leading to death	0	1 (5)	1 (3)
Related	0	0	0

*8 pts were recently enrolled post-safety data cut.

Efficacy

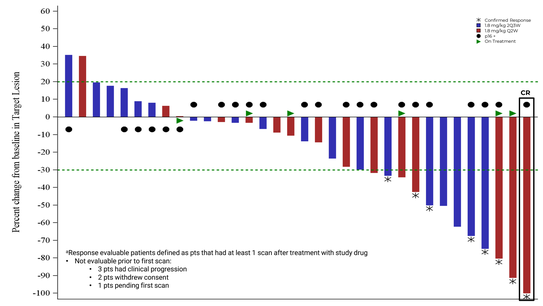
- ORR for total population (HPV positive, negative, and unknown): 38% (13/34); 1 confirmed CR who remains in continued CR for >16 months follow-up **(Figure 5)**, 7 confirmed **(*e.g.*, Figure 6)** and 5 unconfirmed PRs, and 16 SD among 34 evaluable* pts.
- Disease control rate: 85% (29/34).

*Completed at least one post-dose tumor assessment.

Table 2. Best overall response amongst evaluable patients.

Ozuriftamab vedotin 1.8 mg/kg	Q2W (n=15)[a]	Total (n=34)[a]
Responses, % (n)	40 (6)	38 (13)
Confirmed responses	27 (4)	24 (8)
DCR, % (n)	93 (14)	85 (29)

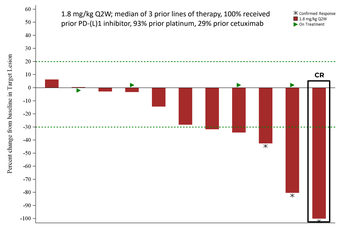
Figure 3. Oz-V in SCCHN continues to demonstrate clinical responses and median overall survival of ~9 months in a heavily pretreated population.



[a]Response evaluable patients defined as pts that had at least 1 scan after treatment with study drug
- Not evaluable prior to first scan:
  - 3 pts had clinical progression
  - 2 pts withdrew consent
  - 1 pts pending first scan

100% disease control among pts with heavily pre-treated HPV⁺ SCCHN.

Figure 4. Oz-V in HPV⁺ R/M SCCHN (n=14[b]).

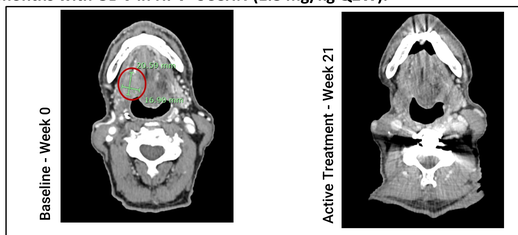


[b]Response evaluable patients defined as pts that had at least 1 scan after treatment with study drug
- Not evaluable prior to first scan:
  - 1 pt had clinical progression
  - 1 pt withdrew consent
  - 1 pts pending first scan

Table 3. Best overall response amongst evaluable HPV⁺ pts at Q2W.

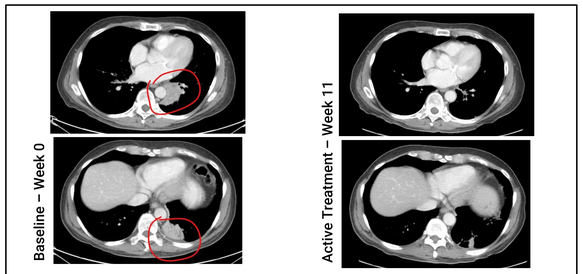
Ozuriftamab vedotin 1.8 mg/kg	Q2W (n=11)[b]
Responses, % (n)	45 (5)
Confirmed responses	27 (3)
DCR, % (n)	100 (11)
DOR	*ongoing*
PFS	*ongoing*
OS	*ongoing*

Figure 5. Confirmed complete response who remains in continued CR for > 16 months with Oz-V in HPV⁺ SCCHN (1.8 mg/kg Q2W).



76-year-old male with stage IV SCCHN post-surgery and radiotherapy. Previous treatments included pembrolizumab; clinical trial bispecific anti-PD1/CD47. Pt experiencing continued CR >16 months and currently off therapy per pt personal preference; active follow-up of disease status continuing.

Figure 6. Confirmed partial response (-80%) ongoing with Oz-V in HPV⁺ oropharyngeal squamous cell carcinoma (1.8 mg/kg Q2W).



63-year-old male with stage IV OPSCC post- surgery and chemo-radiotherapy. Prior treatments included platinum-based chemo-radiotherapy, pembrolizumab and arena-virus based investigational study. At baseline, pt had biopsy proven progression with new mediastinal nodal disease, large left hilar mass, increased hepatic metastases, and small bowel metastasis. Continues on Oz-V treatment with active follow-up of disease status.

Conclusions

- **Oz-V, a conditionally binding ADC targeting ROR2, achieved promising antitumor activity among pts with HPV⁺, as well as HPV⁻ SCCHN.**
- **Oz-V achieved 100% disease control among pts with heavily pretreated HPV⁺ tumors - one of whom remains in continued CR at 16 mo. follow-up.**
- **Oz-V delivered at 1.8 mg/kg Q2W was particularly well-tolerated.**
- **Oz-V has the differentiated potential to address the marked unmet need among the R/M SCCHN population, including HPV⁺ patients.**

References

1. He, et al. *J Cancer Res Clin Oncol*. 2022 May;148(5):1235-1245. doi: 10.3390/cancers14184472., **2.** Kochanny, et al. Cancer 126.10 (2020): 2146-2152. doi. 10.1002/cncr.32762., **3.** Fayette, et al. *Annals of Oncology*. 2023. 34 (suppl_2): S554-S593. 10.1016/S0923-7534(23)01938-5., **4.** Avincsal, et al. *Oncol Rep*. 2021 Jul;46(1):148. doi: 10.3892/or.2021.8099. Epub 2021 Jun 3., **5.** Lu, et al. *Oncotarget*. 2015 Jun 15;6(17):15678-15689. doi: 10.18632/oncotarget.3987., **6.** Huang, et al. *Cancer Biol Ther*. 2015 Jul;16(7):1023-1032. doi: 10.1080/15384047.2015.1046789.

Abbreviations

2Q3W, days 1 and 8 every 3 weeks; AE, adverse event; BOR, best overall response; CAB, conditionally active biologic; CR, complete response; CT, computed tomography; CTCAE, Common Terminology Criteria for Adverse Events; D, day; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; ELISA, enzyme-linked immunosorbent assay; FDA, US Food and Drug Administration; G, grade; HPV, human papillomavirus; mOS, median overall survival; MMAE, monomethyl auristatin E; MRI, magnetic resonance imaging; NCI, National Cancer Institute; NE, not estimable; NR, not reached; OD, optical density; OPSCC, oropharyngeal squamous cell carcinoma; ORR, objective response rate; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PR, partial response; Q2W, days 1 and 15 every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; ROR2, receptor tyrosine kinase orphan receptor 2; RP2D, recommended phase 2 dose; s/p, status post; SCCHN, squamous cell carcinoma of the head and neck; SD, stable disease; TEAE, treatment-emergent adverse event; TME, tumor microenvironment; TRAEs, treatment-related adverse events; v, version.

Clinical Trial Identifier

A Phase 2 Multi-center, Open-label, Single-Arm Study Of BA3021 (ozuriftamab vedotin) in Patients With R/M SCCHN previously treated with anti-PD-1 agents.
Clinical Trial Registry Number: NCT05271604.

Acknowledgements and Funding

This study was funded by BioAtla, Inc.

Correspondence: Kartik Aysola, MD MedicalAffairs@bioatla.com

Presented at Mayo Multidisciplinary Head and Neck Cancer Symposium • Scottsdale, AZ • March 27, 2025 to March 29, 2025