# Phase 2 Trial of Ozuriftamab Vedotin (Oz-V), a Conditionally Binding CAB-ROR2-ADC, in Patients with Heavily Pretreated Squamous Cell Carcinoma of the Head and Neck



**Douglas Adkins* MD,[1] Winston Wong MD,[2] Jacob Thomas MD,[3] Jamal Misleh MD,[4] Jochen Lorch MD,[5] Jaspreet Grewal MD,[6] Kathleen C. Kerrigan DO,[7] Jeffery Russell MD,[8] Jeremy Cetnar MD,[9] Kyechin Chen PharmD,[10] Judith Llorin-Sangalang, MD,[10] Kartik Aysola MD,[10] Alan Ho MD,[2]**

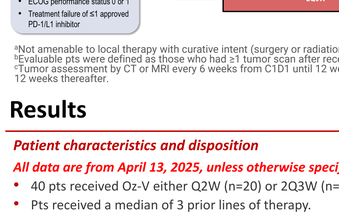
[1]Washington University School of Medicine Robert Ebert and Greg Stubblefield Head and Neck Tumor Center Alvin J. Siteman Cancer Center, and Barnes Jewish Hospital, St. Louis, MO, USA; [2]Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [3]USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [4]Christiana Hospital, Newark, DE, USA; [5]Northwestern University, Chicago, IL, USA; [6]Norton Cancer Institute, Louisville, KY, USA; [7]Huntsman Cancer Institute, Salt Lake City, UT, USA; [8]Tennessee Oncology, Nashville, TN, USA; [9]Oregon Health & Science University, Portland, OR, USA; [10]BioAtla, Inc., San Diego, CA, USA.

## 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 Oropharyngeal Squamous Cell Carcinoma (OPSCC) 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]
- Marked unmet need exists in 2L+ SCCHN for HPV-associated 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.**

### Figure 1. HPV infection drives ROR2 overexpression.[8]

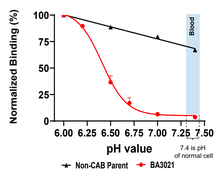



- HPV associated expression of E6 and/or E7 oncoproteins drives progression by upregulating ROR2 expression.[4, 5]
- ROR2 acts as a non-canonical receptor for Wnt family of ligands involved in cell migration in normal tissue formation, which:[4]
  - Can influence cell proliferation and survival by regulating downstream signaling pathways, such as the PI3K/Akt pathway.
  - Can promote or inhibit metastasis potentially 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. [6,7]

**Ozuriftamab vedotin, Oz-V, is an ADC targeting ROR2 that delivers auristatin to malignant cells causing 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. 2).
- 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 2. Oz-V pH binding inflection point designed for TME selectivity.




## Methods

### Figure 3. Multicenter, open-label, 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 April 13, 2025, unless otherwise specified.***

- 40 pts received Oz-V either Q2W (n=20) or 2Q3W (n=20) for a median of 85 days.
- Pts received a median of 3 prior lines of therapy.
- All pts had experienced prior failure of anti–PD-1 therapy and 85% of pts experienced prior failure of platinum therapy **(Table 1)**.
- 22 pts had p16 + OPSCC, constituting the focus of this analysis

## Results (continued)

**Table 1. Patient demographics and clinical characteristics.**

| Ozuriftamab vedotin 1.8 mg/kg | OPSCC P16+[a] | | Full Analysis |
|---|---|---|---|
| | 2Q3W (n=10) | Q2W (n=12) | 2Q3W and Q2W (N=40) |
| **Age, mean (SD), y** | 65 (5) | 62 (7) | 65 (8) |
| **Sex, n (%)** | | | |
| Male | 10 (100) | 11 (92) | 36 (90) |
| Female | 0 | 1 (8) | 4 (10) |
| **ECOG performance, n (%)** | | | |
| 0 | 5 (50) | 8 (67) | 15 (38) |
| 1 | 5 (50) | 4 (33) | 25 (63) |
| **Number of prior lines of therapy, median** | 3 | 3 | 3 |
| **Prior anti–PD-1 exposure, n (%)** | 10 (100) | 12 (100) | 40 (100) |
| **Prior platinum-based chemotherapy exposure, n (%)** | 10 (100) | 10 (83) | 34 (85) |
| **Prior taxane exposure, n(%)** | 7 (70) | 7 (58) | 26 (65) |

[a]HPV status was determined using p16 immunohistochemistry.

***Safety (as of April 13, 2025) – Full data set (N=40)***

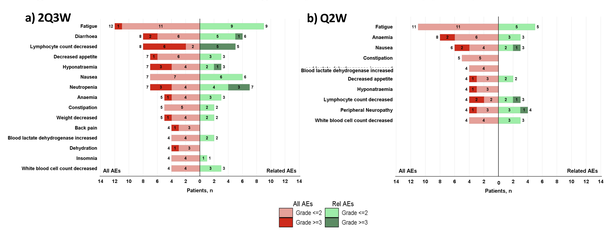
- Most AEs were low grade; fatigue (57%) and anemia (32%) were most frequent. **(Table 2; Figure 4)**
- 9 pts (22%) had grade 3 TRAEs (nausea, diarrhea, decreased lymphocyte count, and decreased neutrophil count, peripheral neuropathy, elevated liver enzymes, and hyperglycemia)
- 3 pts (7%) had grade 4 TRAEs (sepsis, respiratory failure, and hyponatremia).
- No related SAEs were observed with the Q2W regimen.

**Table 2. Summary of AEs – Full data set (N=40)**

| Number of patients with any AE, n (%) | 2Q3W (n=20) | Q2W (n=20) | Total (N=40) |
|---|---|---|---|
| **AE** | 20 (100) | 19 (95) | 39 (97) |
| Related | 19 (95) | 14 (70) | 33 (82) |
| **≥Grade 3 AE[a]** | | | |
| Related grade 3 | 7 (35) | 2 (10) | 9 (22) |
| Related grade 4 | 2 (10) | 1 (5) | 3 (7) |
| **Serious AE** | 11 (55) | 8 (40) | 19 (47) |
| Related | 3 (15) | 0 | 3 (7) |
| **AE leading to treatment discontinuation** | 3 (15) | 2 (10) | 5 (12) |
| Related | 1 (5) | 1 (5) | 2 (5) |
| **AE leading to death** | 2 (10) | 1 (5) | 3 (7) |
| Related | 0 | 0 | 0 |

[a]No grade 5 related AEs observed.

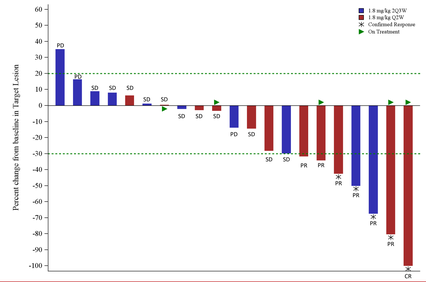
### Figure 4. Most frequent AEs of any grade (>15% of patients) (N=40).




***Efficacy (as of May 14, 2025) – Q2W and 2Q3W HPV+ Oropharyngeal Squamous Cell Carcinoma***

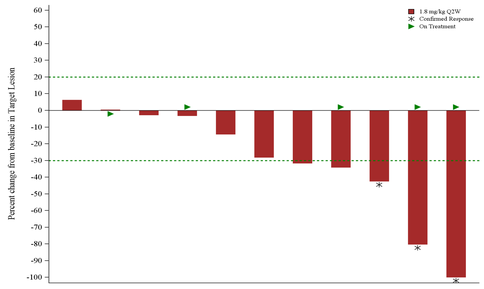
**Disease control rate: 86% (18/21)**

### Figure 5. Oz-V in HPV+ OPSCC continues to demonstrate clinical responses in a heavily pretreated population.




**1.8 mg/kg Q2W selected: Promising anti-tumor activity & better tolerated**

### Figure 6. Q2W Oz-V in HPV+ OPSCC (n=11 evaluable).



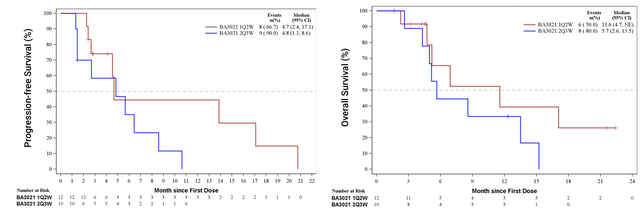

**100% DCR in patients with heavily pre-treated HPV+ OPSCC receiving Q2W**

**Table 3. Best overall response among evaluable HPV+ OPSCC patients treated with Q2W dosing compared to standard of care (SOC).**

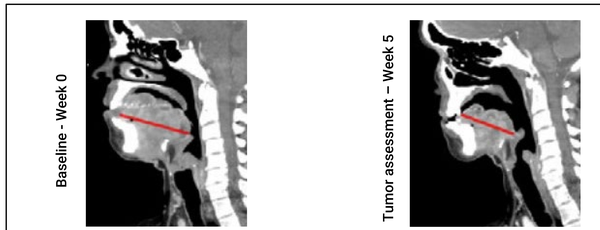
| Treatment** | Median prior lines of therapy | ORR (%) | OS (months) |
|---|---|---|---|
| **Oz-V monotherapy (1.8 mg/kg Q2W)** | **3** | **45%** | **11.6** |
| SOC (methotrexate, docetaxel, or cetuximab)[9] | 2 | 3.4% | 4.4 |

**The comparisons above are not based on data resulting from a head-to-head trial and are not direct comparisons. Different protocol designs, trial designs, patient selection and populations, number of patients, trial endpoints, trial objectives and other parameters that are not the same between the relevant trials may lead to bias in the results causing comparisons from different trials to be unreliable.

### Figure 7. PFS and OS for HPV+ OPSCC pts treated with Oz-V by regimen received




### Figure 8. Confirmed partial response (42% tumor reduction) from Oz-V at 1.8 mg/kg Q2W in HPV+ OPSCC.




51-year-old female with stage IV SCCHN post-radiotherapy. Previous treatments included pembrolizumab, platinum, and arenavirus-based experimental therapy.

## Conclusions

- **Oz-V, a conditionally binding ADC targeting ROR2, achieved promising antitumor activity among heavily pretreated patients with SCCHN.**
- **Oz-V delivered at 1.8 mg/kg Q2W achieved 100% disease control among pts with HPV+ OPSCC and was particularly well-tolerated.**
- **Oz-V has the potential to address the marked unmet need among the recurrent/metastatic HPV+ OPSCC population.**
- **These encouraging findings provide compelling rationale to investigate Oz-V in additional high unmet need HPV-associated cancers.**

## 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.

## 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.** Change, et al. *mAbs*. 2025;17:1, 2490078. doi: 10.1080/19420862.2025.2490078 **6.** Lu, et al. *Oncotarget*. 2015 Jun 15;6(17):15678-15689. doi: 10.18632/oncotarget.3987., **7.** Huang, et al. *Cancer Biol Ther*. 2015 Jul;16(7):1023-1032. doi: 10.1080/15384047.2015.1046789. **8.** Lu, et al. *Cancers*. 2024;16(3474). doi: 10.3390/cancers16093474., **9.** Ferris, et al. *N Engl J Med*. 2016;375:1856-67. doi: 10.1056/NEJMoa1602252.

## 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.**

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**Correspondence: Kartik Aysola, MD** MedicalAffairs@bioatla.com



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