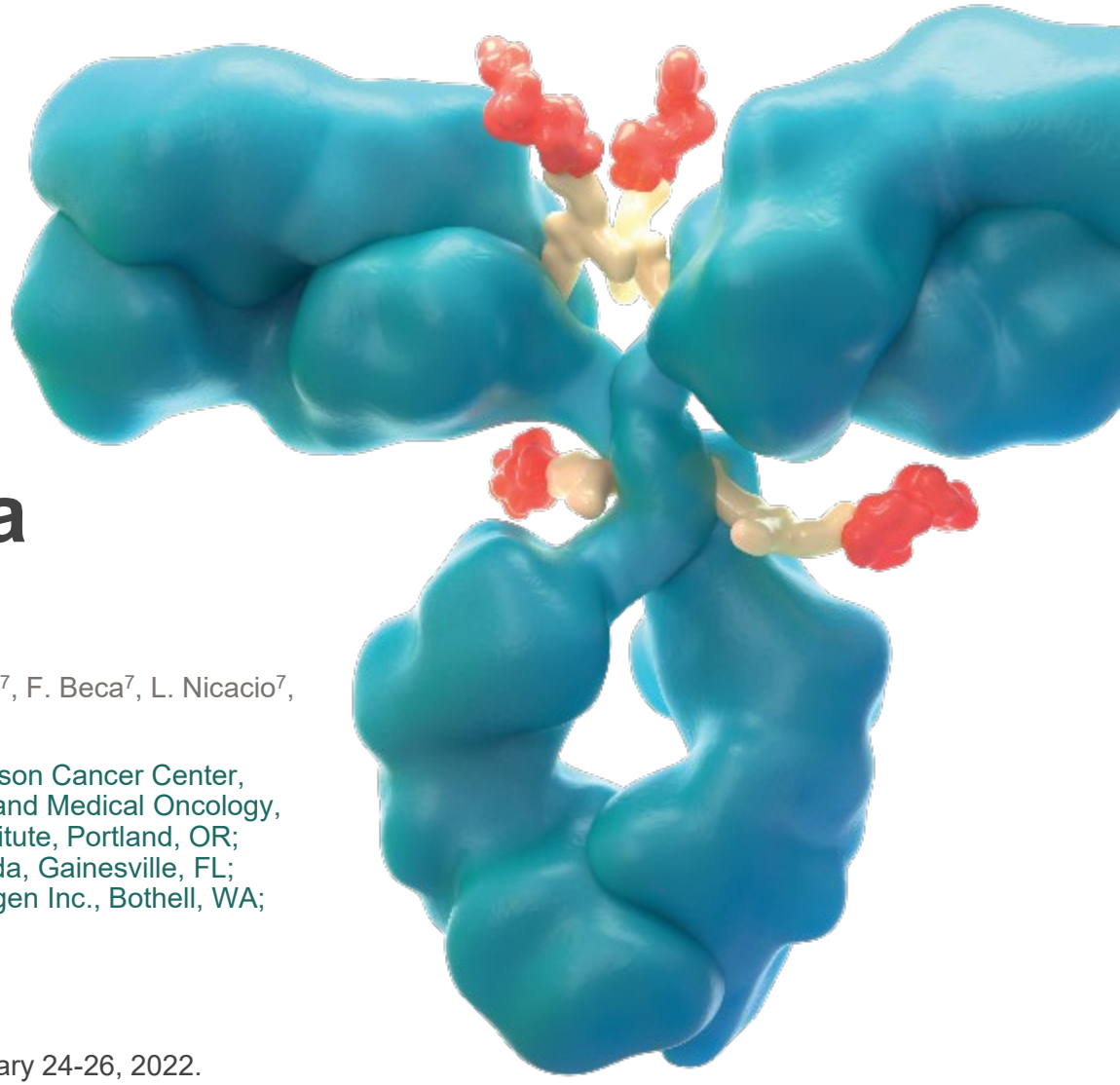
Efficacy and Safety of Tisotumab Vedotin in Patients With Head and Neck Squamous Cell Carcinoma: Results From a Phase II Cohort



D. S. Hong[1], A. Birnbaum[2], C. Steuer[3], M. Taylor[4], T. J. George[5], J. Lacy[6], B. Wang[7], F. Beca[7], L. Nicacio[7], I. Soumaoro[8], and M. Cho[9]

[1]Department of Investigational Cancer Therapeutics, University of Texas MD Anderson Cancer Center, Houston, TX; [2]Rhode Island Hospital, Providence, RI; [3]Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; [4]Providence Cancer Institute, Portland, OR; [5]Division of Hematology and Oncology, Department of Medicine, University of Florida, Gainesville, FL; [6]Department of Medical Oncology, Yale School of Medicine, New Haven, CT; [7]Seagen Inc., Bothell, WA; [8]Genmab US, Princeton, NJ; [9]University of California, Irvine, CA

ASTRO Multidisciplinary Head and Neck Cancers Symposium, Phoenix, AZ; February 24-26, 2022.

Seagen | Genmab

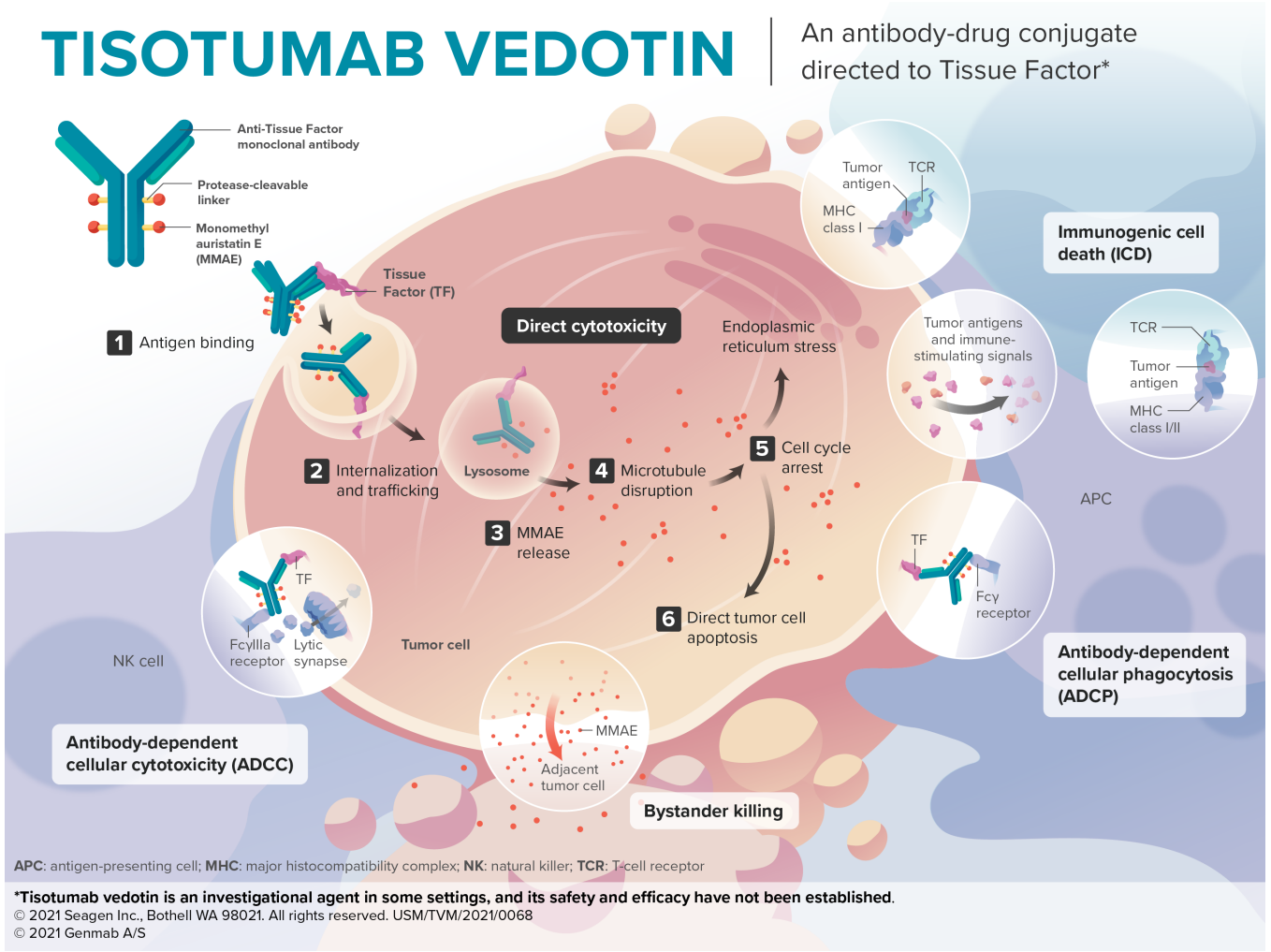
Background

- There is a significant unmet need in previously treated recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) due to limited treatment options and poor outcomes for patients
- For patients with locally advanced or metastatic SCCHN who progress on first-line treatment, the preferred subsequent treatment is a checkpoint inhibitor, if not already used
- Options for patients who progress after platinum-based therapy and checkpoint inhibitors are limited
  - Historically, treatment with cetuximab, taxanes, or methotrexate after platinum-based therapy resulted in objective response rate (ORR) of 6-14% and median overall survival (OS) of 5-7 months[1-3]
- Tisotumab vedotin, an investigational antibody-drug conjugate, was analyzed in a first in human study, studied in additional tumor types known to express tissue factor, and has demonstrated preliminary evidence of activity[4]
- This presentation describes results from a cohort of patients with relapsed, locally advanced, or metastatic SCCHN treated with tisotumab vedotin

1. Vermorken JB, J Clin Oncol. 2007. 2. Machiels J-PH, et al. Lancet Oncol. 2015. 3. Soulières D, et al. Lancet Oncol. 2017. 4. de Bono JS, et al. Lancet Oncol. 2019.

Proposed Mechanism of Action of Tisotumab Vedotin

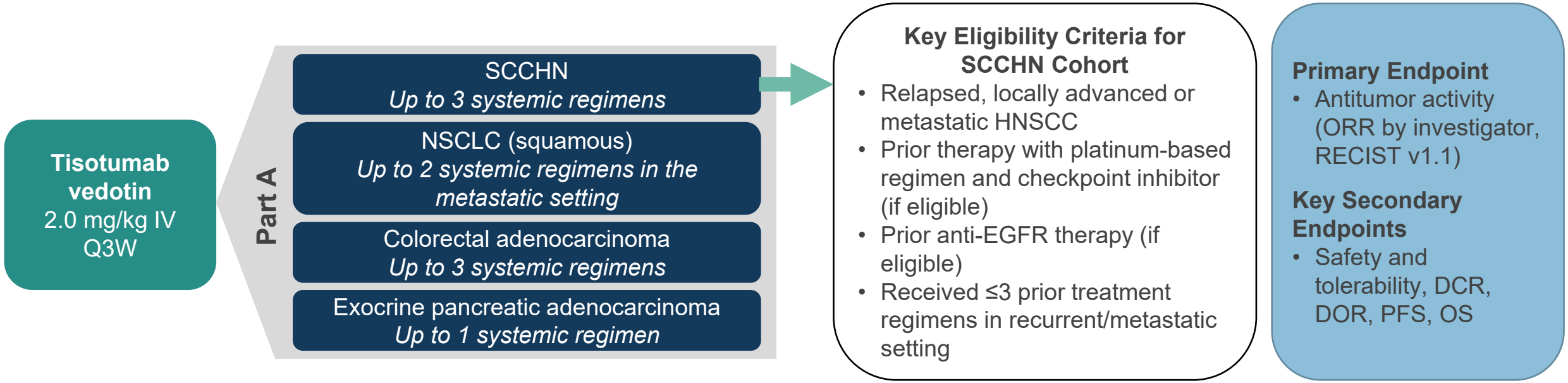
- Tisotumab vedotin is an investigational antibody-drug conjugate directed to tissue factor (TF)
- TF is a transmembrane protein with high differential expression in numerous solid tumors, including SCCHN[1,2]
  - High expression of TF has been associated with promotion of tumor growth, angiogenesis, and metastasis[3,4]
- Tisotumab vedotin received accelerated approval in the US by FDA in September 2021 for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy
- Early data suggests tisotumab vedotin may have activity in other cancers that express TF[5]



1. Forster Y, et al. Clin Chim Acta. 2006. 2. Wojtukiewicz MZ, et al. Thromb Haemost. 1999. 3. van den Berg YW, et al. Blood. 2012. 4. Hisada Y, et al. Semin Thromb Hemost. 2019. 5. de Bono JS, et al. Lancet Oncol. 2019.

innovaTV 207 Study Design

innovaTV 207 (NCT03485209) is an ongoing open-label multicenter (US and Europe) Phase 2 Study evaluating tisotumab vedotin in solid tumors



Note: Study schema for Part A only, currently Parts C and D are ongoing.

DCR, disease control rate; DOR, duration of response; EGFR, epithelial growth factor receptor; SCCHN, squamous cell carcinoma of the head and neck; IV, intravenous; NSCLC, non small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1

Baseline and Prior Treatment Characteristics

	N=31
Age, median (range)	65.0 (47,78)
Race, n (%)	
White	23 (74.2)
Asian	1 (3.2)
Not reportable[a]	7 (22.6)
Geographic region	
North America	21 (67.7)
Europe	10 (32.3)
ECOG performance status	
0	5 (16.1)
1	26 (83.9)
Diagnosis subtype	
Oral cavity	3 (9.7)
Oropharynx	16 (51.6)
Hypopharynx	4 (12.9)
Larynx	6 (19.4)
Sinus	1 (3.2)

	N=31
HPV status[b]	
Positive	10 (32.3)
Negative	5 (16.1)
Unknown	16 (51.6)
P16 status[b]	
Positive	14 (45.2)
Negative	4 (12.9)
Unknown	13 (41.9)
Lines of prior systemic therapies per subject in all settings, median (range)	2.0 (1, 5)
Type of prior therapies	
Systemic therapies	31 (100)
Primary tumor surgery	14 (45.2)
Primary tumor radiation	24 (77.4)
Prior systemic regimens	
Checkpoint inhibitor	27 (87.1)
Cetuximab	18 (58.1)
Platinum-based therapy	31 (100)

[a] Not reportable indicates information was not collected.
[b] As reported per site/investigator.
ECOG, Eastern Cooperative Oncology Group; HPV, human papillomavirus.
Data cutoff Oct 15, 2020. All datapoints displayed as “n (%)” except where otherwise indicated.

Patient Disposition for SCCHN Cohort in Part A

	N=31
Patients with ongoing treatment	1 (3.2)
Patients who discontinued treatment	30 (96.8)
Progressive disease	18 (58.1)
Adverse event	7 (22.6)
Investigator decision	3 (9.7)
Patient decision, non-adverse event	2 (6.5)
Patients who discontinued from the study	23 (74.2)
Death	18 (58.1)
Withdrawal of consent	3 (9.7)
Lost to follow-up	1 (3.2)
Other	1 (3.2)

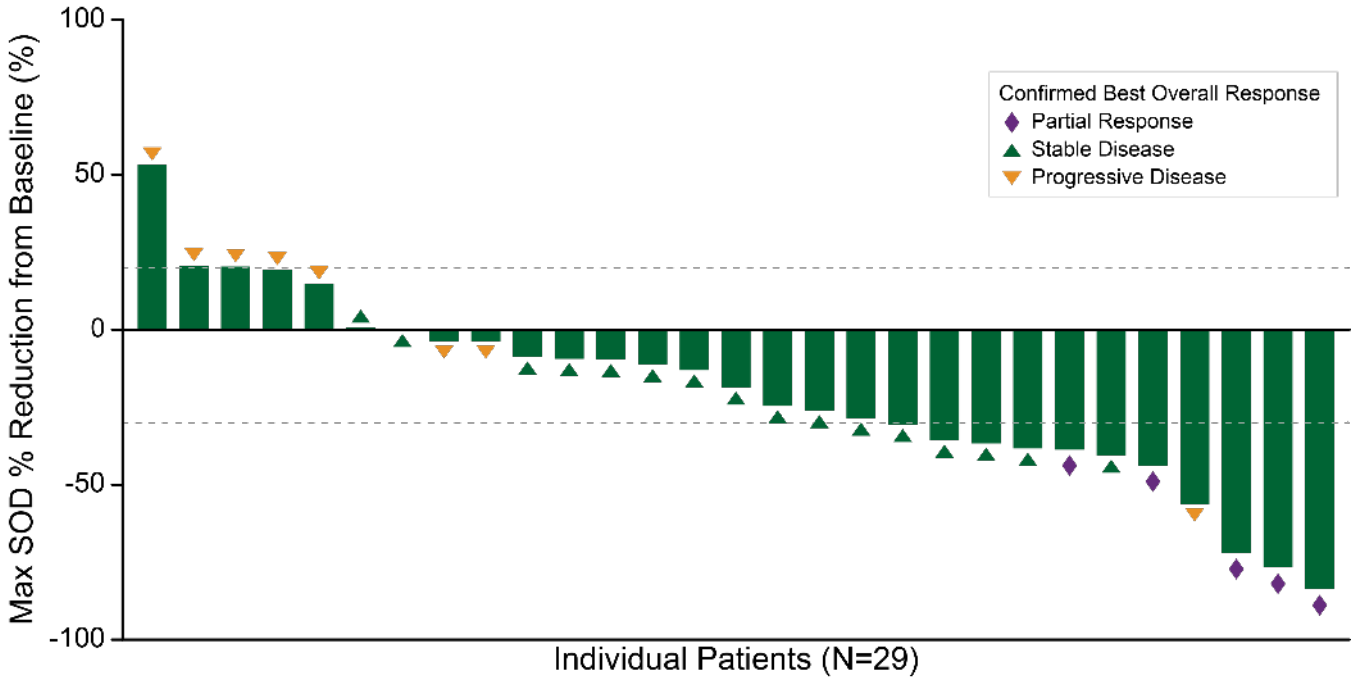
Data cutoff Oct 15, 2020. All datapoints displayed as “n (%)” except where otherwise indicated.

TV Demonstrated Antitumor Activity in SCCHN

Summary of Confirmed Best Overall Response

	N=31
Confirmed best overall response[a], n (%)	
Partial Response	5 (16.1)
Stable Disease	16 (51.6)
Progressive Disease	8 (25.8)
Not evaluable[b]	2 (6.5)
Disease control rate[c], n (%) [95% CI]	18 (58.1) [39.1, 75.5]
Median PFS, in months (95% CI)	4.2 (2.7, 4.8)
Median OS, in months (95% CI)	9.4 (8.1, 11.8)

Maximum Percent Reduction from Baseline

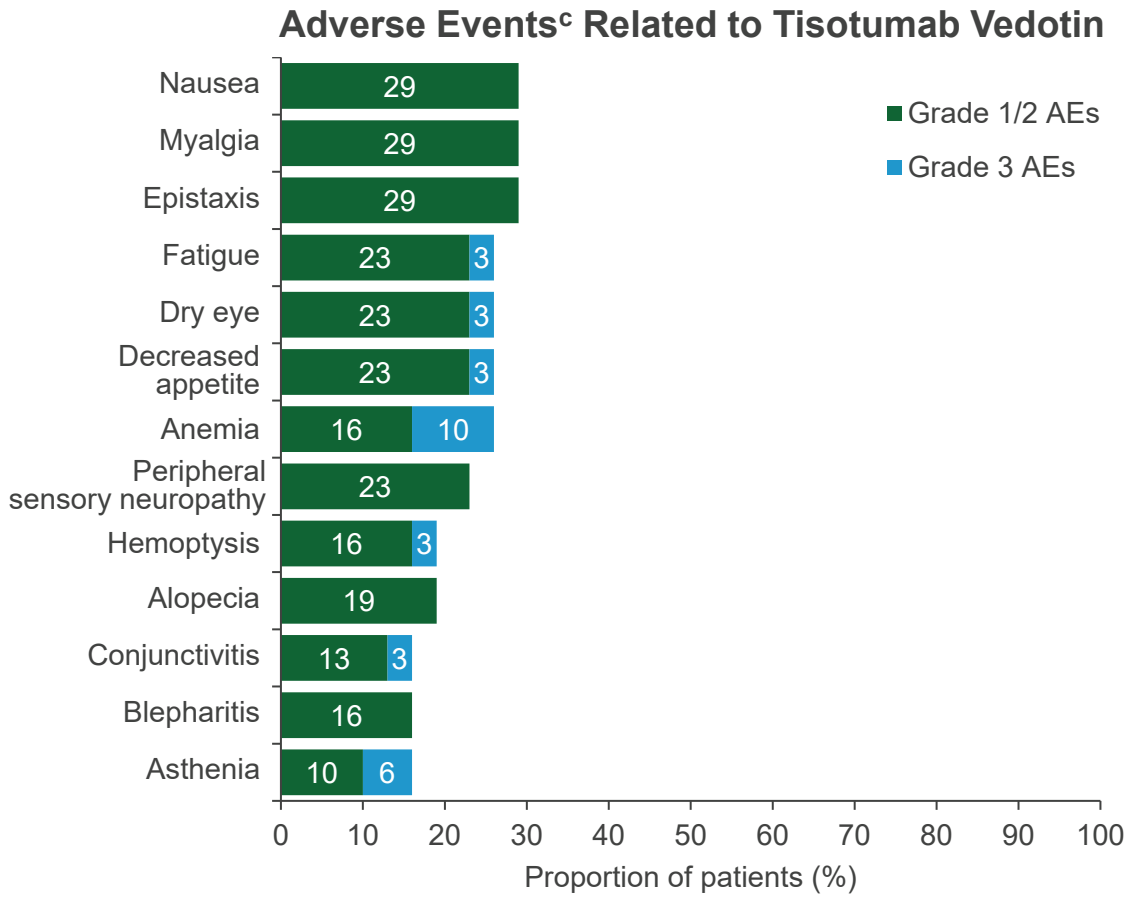


79% (23/29) of evaluable subjects showed a reduction in the size of their target lesions

[a] RECIST v1.1, as assessed by investigator. Confirmed ORR after second confirmatory scan at least 4 weeks since initial response noted.
[b] Not evaluable per RECIST 1.1, may be due to death, discontinuation, or incomplete/not repeated tumor assessment
[c] Disease control rate is defined as the proportion of patients who achieved a confirmed complete response or partial response per RECIST v1.1 as assessed by the investigator, or meet the stable disease criteria at least once after start of study treatment at a minimum interval of 12 weeks.
Data cutoff Oct 15, 2020. All datapoints displayed as "n (%)" except where otherwise indicated.

Adverse Events Observed with Tisotumab Vedotin

	N=31
Patients with ≥1 TEAE, n (%)	31 (100)
TEAE related to TV, n (%)	28 (90.3)
Grade ≥3 TEAE, n (%)	22 (71.0)
Grade ≥3 TEAE related to TV, n (%)	12 (38.7)
SAE, n (%)	16 (51.6)
SAE related to TV[a], n (%)	2 (6.5)
Fatal TEAE[b], n (%)	1 (3.2)
Fatal TEAE related to TV, n (%)	0



[a] 1 each of hemoptysis and post-procedural hemorrhage.
[b] Fatal TEAEs defined as any death occurring within 30 days of last dose of study treatment.
[c] Graph only includes AEs with an incidence of ≥15%.
SAE, serious adverse event; TEAE, treatment-emergent adverse event (defined as newly occurring or worsening AE after the first dose and with AE start date on or before 30 days after the last dose of the study drug).
Data cutoff Oct 15, 2020. All datapoints displayed as "n (%)" except where otherwise indicated.

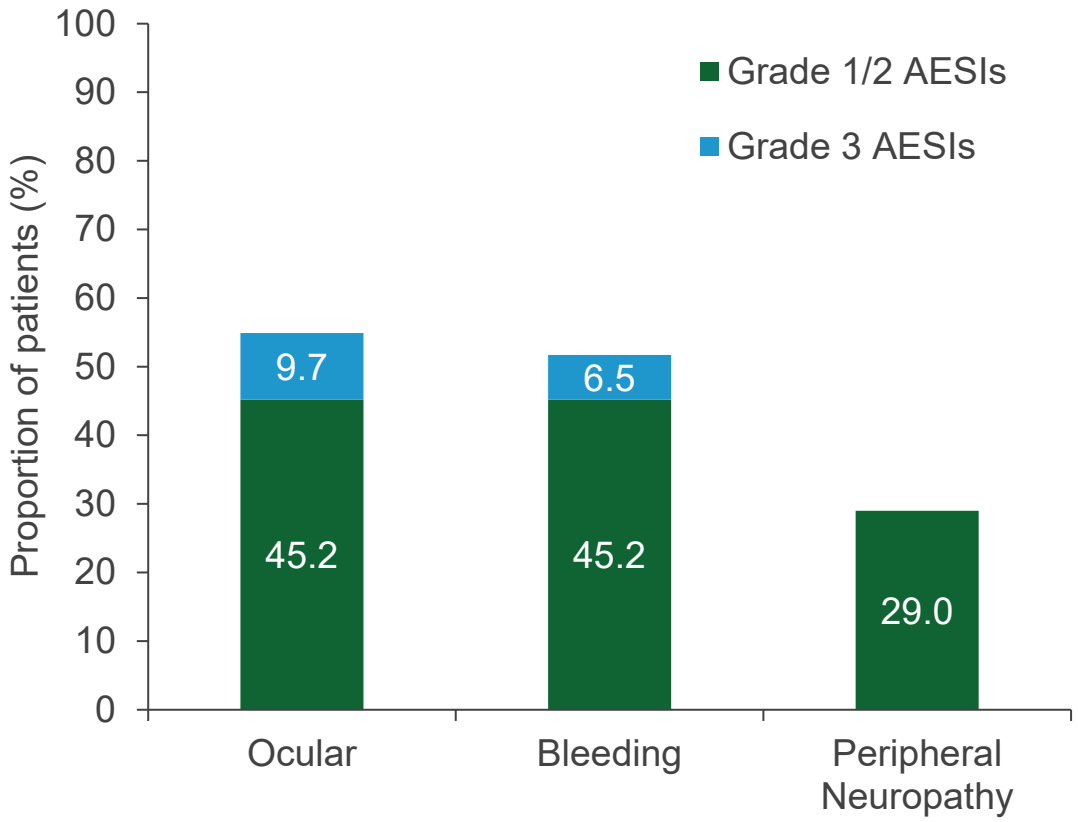
Prespecified AEs of Interest with Tisotumab Vedotin

Adverse Events of Special Interest in ≥10% of Patients

	N=31	
	Grade 1-2	Grade ≥3[a]
Ocular event		
Dry eye	8 (25.8)	1 (3.2)
Conjunctivitis	4 (12.9)	1 (3.2)
Blepharitis	5 (16.1)	0
Keratitis	3 (9.7)	1 (3.2)
Bleeding event		
Epistaxis	10 (32.3)	0
Hemoptysis	6 (19.4)	1 (3.2)
Peripheral neuropathy event		
Peripheral sensory neuropathy	8 (25.8)	0

[a] No Grade 4 or 5 events were observed.
Data cutoff Oct 15, 2020. All datapoints displayed as "n (%)" except where otherwise indicated.

Rates of Ocular, Bleeding, and Peripheral Neuropathy TEAEs



Author's Conclusions

- For SCCHN patients that have progressed after a platinum-containing regimen (and checkpoint inhibitor and cetuximab, if eligible), tisotumab vedotin administered at 2.0 mg/kg IV Q3W demonstrated encouraging preliminary evidence of antitumor activity
  - Confirmed ORR of 16%
  - Disease control rate of 58%
- Tisotumab vedotin had a tolerable safety profile with no new safety signals among SCCHN patients
  - The most common adverse events related to tisotumab vedotin were nausea (29%), myalgia (29%), and epistaxis (29%)
- These data support additional research with tisotumab vedotin in recurrent or metastatic SCCHN:
  - Treatment naïve patients in combinations with pembrolizumab and carboplatin or cisplatin, at a dose of 2.0 mg/kg IV Q3W (innovaTV 207 Part D)
  - As 2L+ treatment, 1.7mg/kg IV given on Day 1 and 15 of a 28-day cycle (innovaTV 207 Part C)

SCCHN, squamous cell carcinoma of the head and neck; IV, intravenous; ORR, objective response rate; Q3W, every 3 weeks.

Acknowledgements

- We thank the patients, their families, and their caregivers for participating in this study
- This study is funded by Seagen Inc. and Genmab A/S