Efficacy and Safety of Tisotumab Vedotin Versus Investigator's Choice of Chemotherapy in 2L or 3L Recurrent or Metastatic Cervical Cancer (innovaTV 301/ENGOT-cx12/GOG-3057): Additional Data From the Global, Randomized, Open-Label, Phase 3 Study

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I have the following financial relationships with ACCME defined ineligible companies to report over the past 24 months:

- Consulting Role: AstraZeneca (ongoing), Clovis (ongoing), Merck (ongoing), Seagen (ongoing), Gilead (ongoing), BioNTech (ongoing), Aadi (ongoing), Novartis (ongoing), GSK (ongoing), Genentech (ongoing), Incyte (ongoing), Regeneron (ongoing), Eisai (ongoing)
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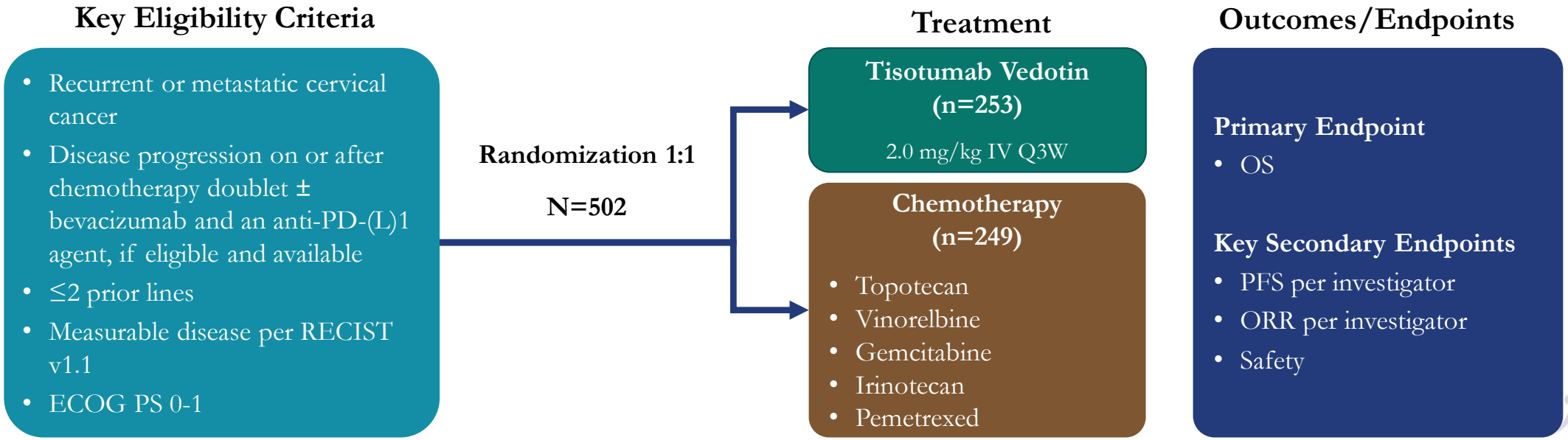
Unlabeled/Investigational Uses

- The safety and effectiveness of tisotumab vedotin have not been established outside of its FDA-approved indication
- Information about potential future uses is intended only for discussion of regulatory review timelines
- Information must not be interpreted as an intent to directly or indirectly promote a product for approved or unapproved uses. Seagen Inc., which was acquired by Pfizer Inc. in Dec 2023, and Genmab prohibit the promotion of unapproved uses and comply with all applicable laws, regulations, and each company's policies

Introduction

- innovaTV 301 is a global, randomized, open-label, phase 3 trial of tisotumab vedotin versus chemotherapy in patients with 2L/3L recurrent or metastatic cervical cancer
  - Tisotumab vedotin reported improved OS versus chemotherapy at pre-planned interim analysis[1]
- Recurrent or metastatic cervical cancer (r/mCC) is a highly symptomatic disease that can progress rapidly; limited treatment options exist to control disease in patients who progress on or after first-line systemic therapy



Data cutoff: 24 July 2023

1. Vergote IB. ESMO 2023: Oral presentation LB9.

Demographics and Disease Characteristics

- Age, ECOG performance status, and regions of enrollment were similar across both arms

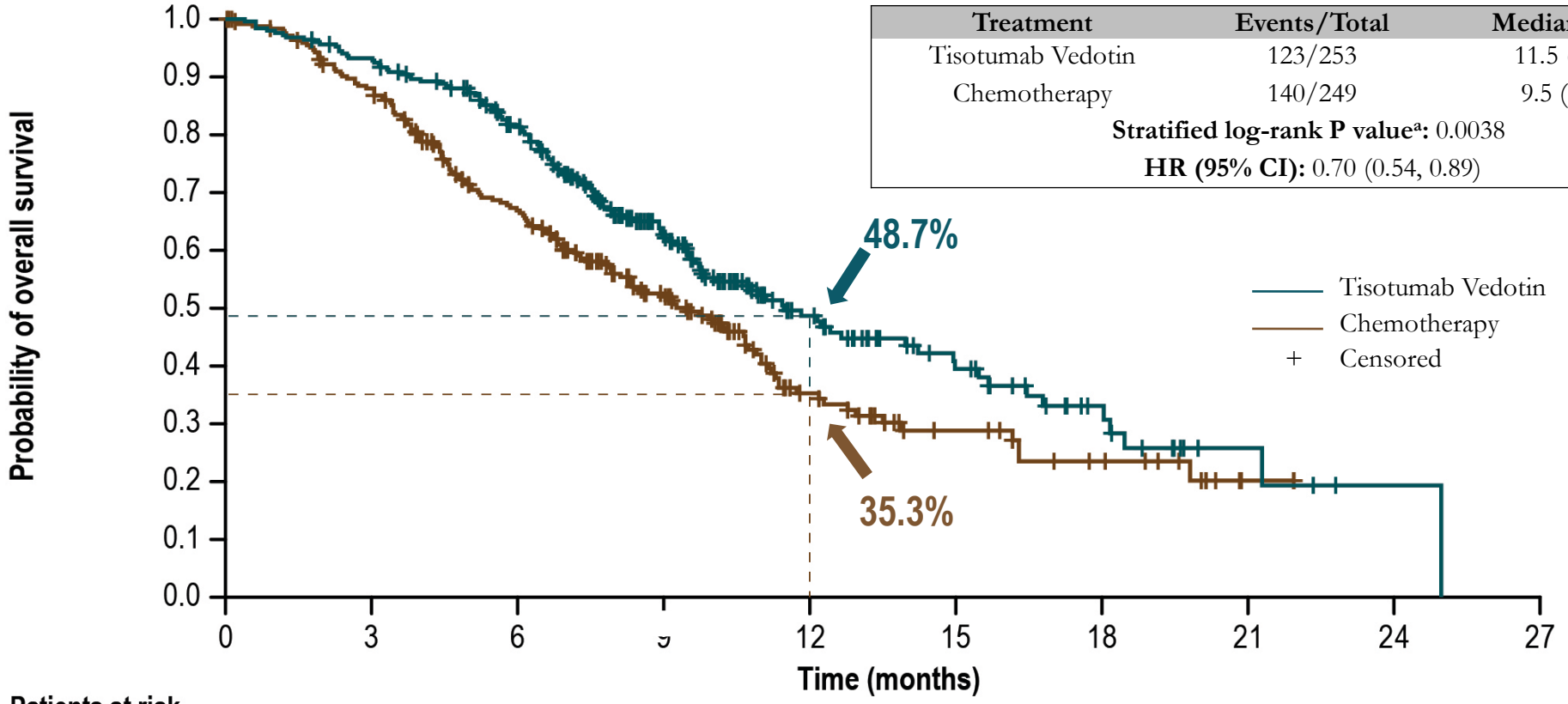
	Tisotumab Vedotin (N=253)	Chemotherapy (N=249)
Disease status at study entry, n (%)		
Pelvic recurrent only	27 (10.7)	24 (9.6)
Extra-pelvic metastatic	226 (89.3)	225 (90.4)
Histology, n (%)		
Squamous cell carcinoma	160 (63.2)	157 (63.1)
Adenocarcinoma	85 (33.6)	75 (30.1)
Adenosquamous carcinoma	8 (3.2)	17 (6.8)
Number of prior r/m systemic regimens, n (%)		
1	159 (62.8)	149 (59.8)
2	93 (36.8)	100 (40.2)
Unknown	1 (0.4)	0
Prior bevacizumab, n (%)	164 (64.8)	157 (63.1)
Prior anti-PD-(L)1 therapy, n (%)	71 (28.1)	67 (26.9)
Prior radiation therapy for cervical cancer, n (%)	205 (81.0)	203 (81.5)
Biopsy evaluable, n (%)	210 (83.0)	194 (77.9)
Positive membrane TF expression[a]	194 (92.4)	183 (94.3)

[a]TF expression is defined as TF membrane expression ≥1% with immunohistochemistry; percentages are calculated based on number of evaluable biopsies.

Overall Survival (Primary Endpoint)

- The study met overall survival statistical significance at the planned interim analysis

Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	123/253	11.5 (9.8, 14.9)
Chemotherapy	140/249	9.5 (7.9, 10.7)
Stratified log-rank P value[a]: 0.0038		
HR (95% CI): 0.70 (0.54, 0.89)		



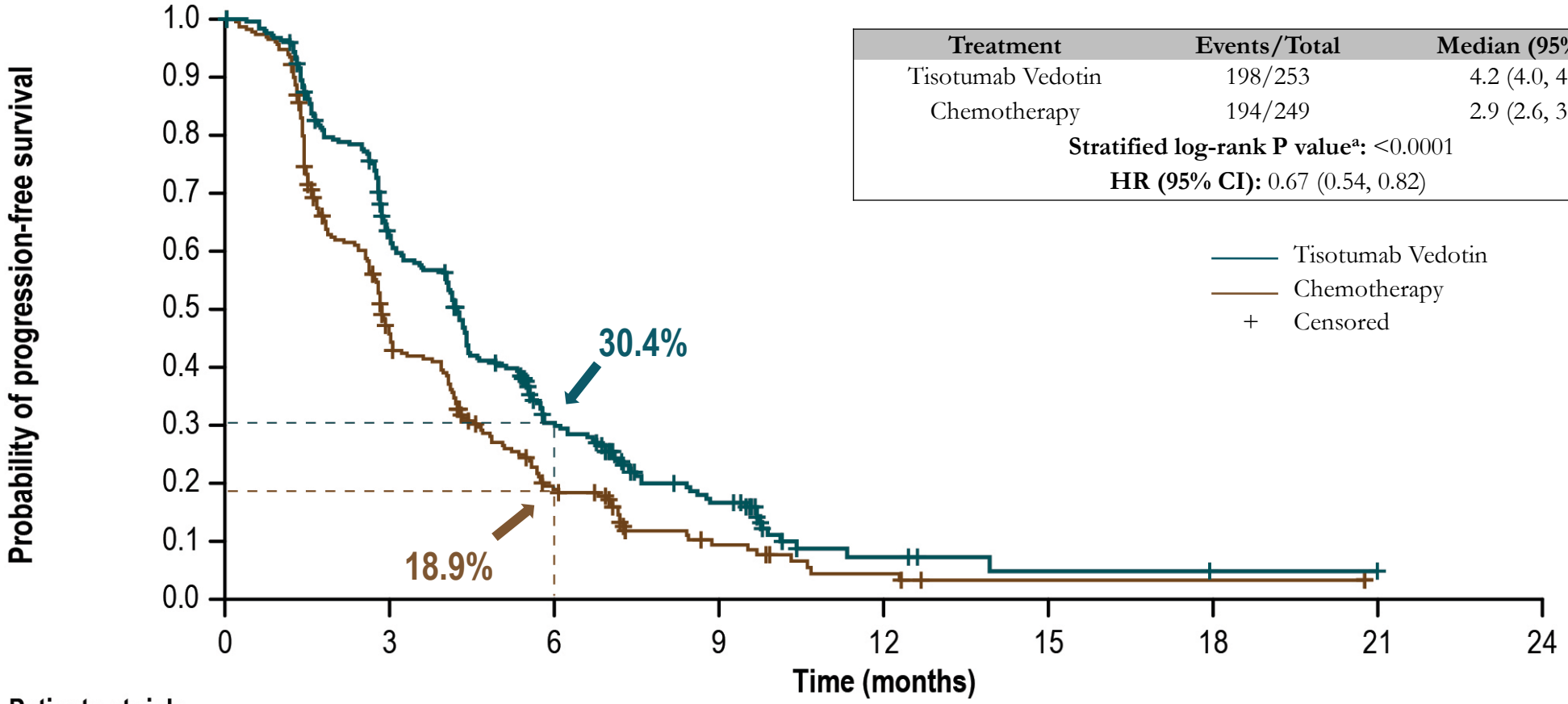
Patients at risk

Tisotumab vedotin	253	234	191	109	52	29	14	4	1	0
Chemotherapy	249	212	150	87	37	19	11	1	0	0

[a]The threshold for statistical significance is 0.0226 (2-sided), based on the actual number of OS events at interim analysis.

Progression-Free Survival Per Investigator

Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	198/253	4.2 (4.0, 4.4)
Chemotherapy	194/249	2.9 (2.6, 3.1)
Stratified log-rank P value[a]: <0.0001		
HR (95% CI): 0.67 (0.54, 0.82)		



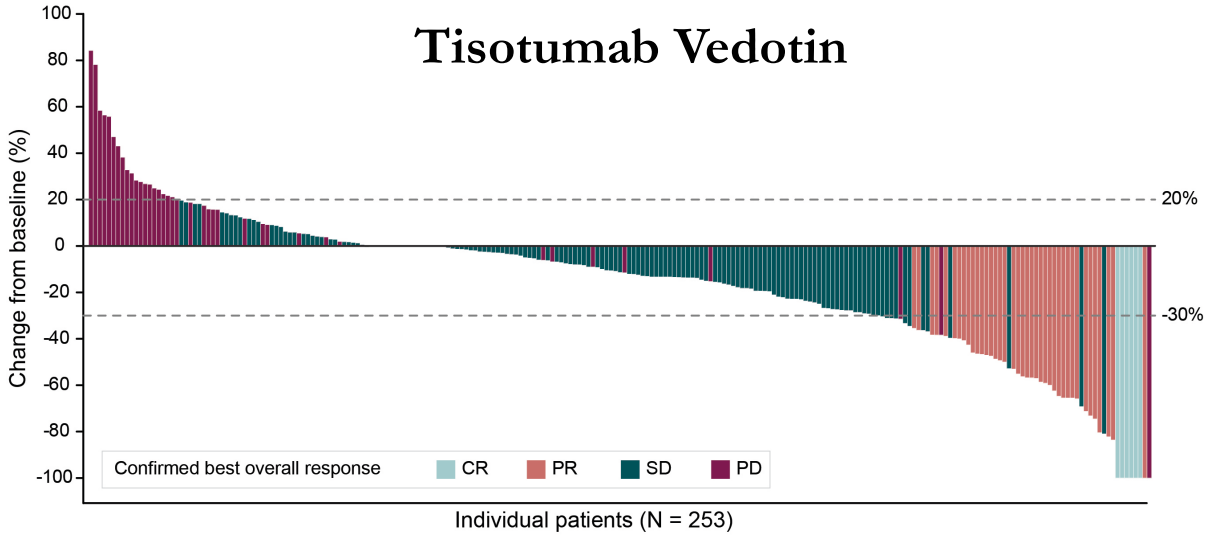
Patients at risk

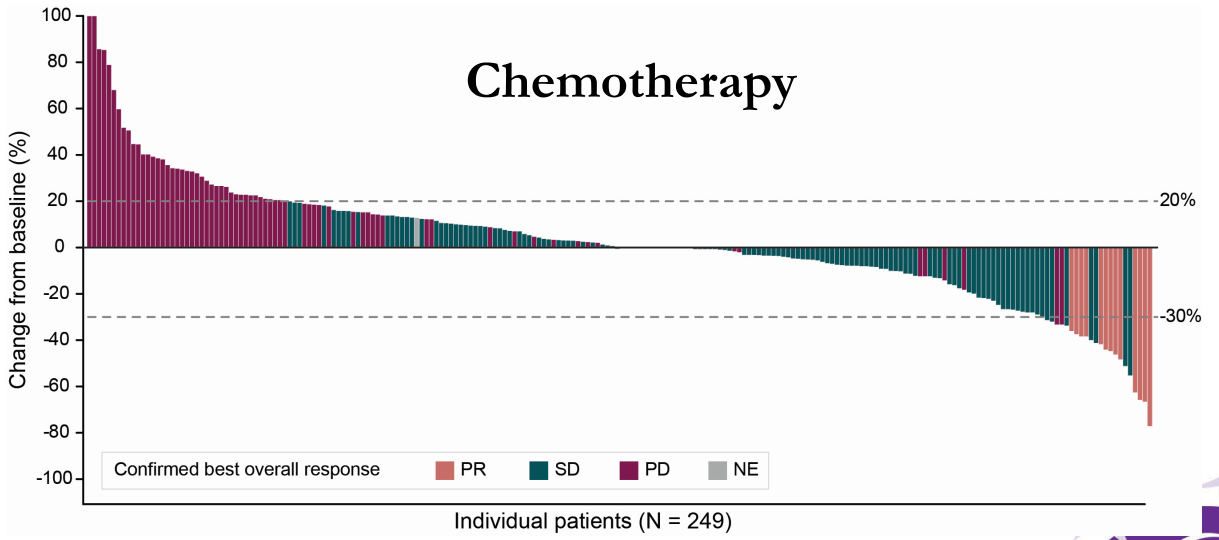
Tisotumab vedotin	253	148	62	25	5	2	1	0	0
Chemotherapy	249	96	34	11	4	1	1	0	0

[a]The threshold for statistical significance is 0.0453 (2-sided), based on the actual number of PFS events at interim analysis.

Antitumor Activity

	Tisotumab Vedotin (N=253)	Chemotherapy (N=249)
ORR, % (95% CI)	17.8 (13.3-23.1)	5.2 (2.8-8.8)
Odds ratio (95% CI)	4.0 (2.1-7.6)	
P value	p<0.0001	
Best Overall Response, n (%)		
CR	6 (2.4)	0
PR	39 (15.4)	13 (5.2)
SD	147 (58.1)	132 (53.0)
PD	46 (18.2)	74 (29.7)
Not evaluable/Not available	15 (5.9)	30 (12.0)
DCR[a], % (95% CI)	75.9 (70.1-81.0)	58.2 (51.8-64.4)
Median DOR (95% CI)	5.3 (4.2-8.3)	5.7 (2.8-NR)





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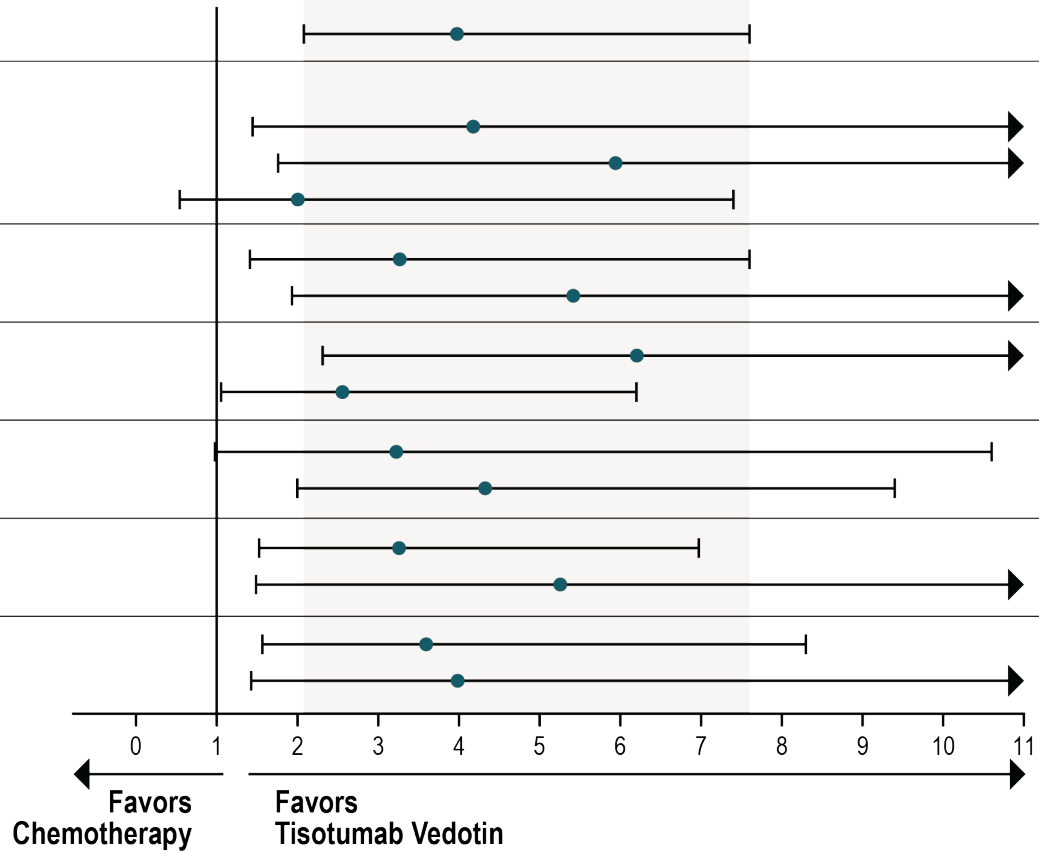
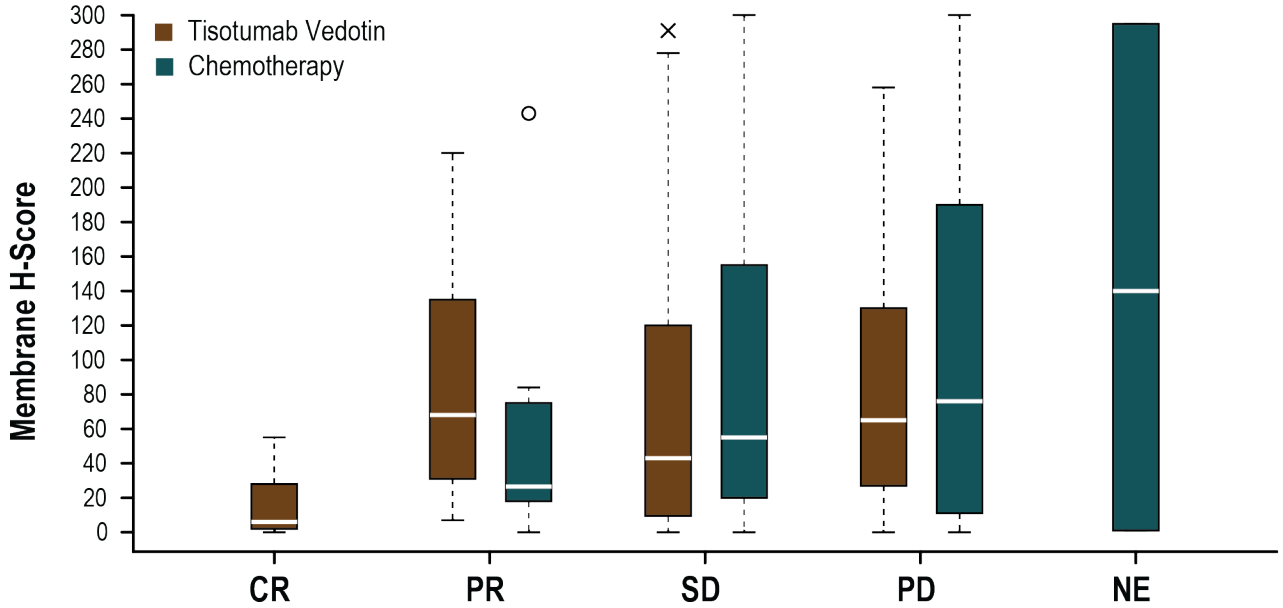
[a]DCR defined as CR+PR+SD; CR and PR were confirmed responses. The minimum criteria for SD duration was ≥5 weeks after the date of randomization.

Key Subgroups: Objective Response Rate

Subgroup	ORR % Tisotumab Vedotin (N=253)	ORR % Chemotherapy (N=249)	Odds Ratio (95% CI)
ITT Population	**17.8**	**5.2**	**4.0 (2.1-7.6)**
United States	18.8	0.0	
Europe	16.0	4.8	4.2 (1.4-12.1)
Asia	20.0	4.5	5.9 (1.8-20.1)
Other	17.4	9.3	2.0 (0.5-7.4)
ECOG 0	16.8	5.9	3.3 (1.4-7.6)
ECOG 1	19.0	4.4	5.4 (1.9-15.2)
Prior bevacizumab	16.5	3.2	6.2 (2.3-16.7)
No prior bevacizumab	20.2	8.7	2.6 (1.1-6.2)
Prior anti-PD-(L)1	16.9	6.0	3.2 (1.0-10.6)
No prior anti-PD-(L)1	18.1	4.9	4.3 (2.0-9.4)
Squamous cell carcinoma	18.8	6.4	3.3 (1.5-7.0)
Adeno- or adenosquamous carcinoma	16.1	3.3	5.3 (1.5-18.6)
1 prior systemic regimen	17.0	5.4	3.6 (1.6-8.3)
2 prior system regimens	18.3	5.0	4.0 (1.4-11.1)



Confirmed Best Overall Response by Membrane Tissue Factor Expression

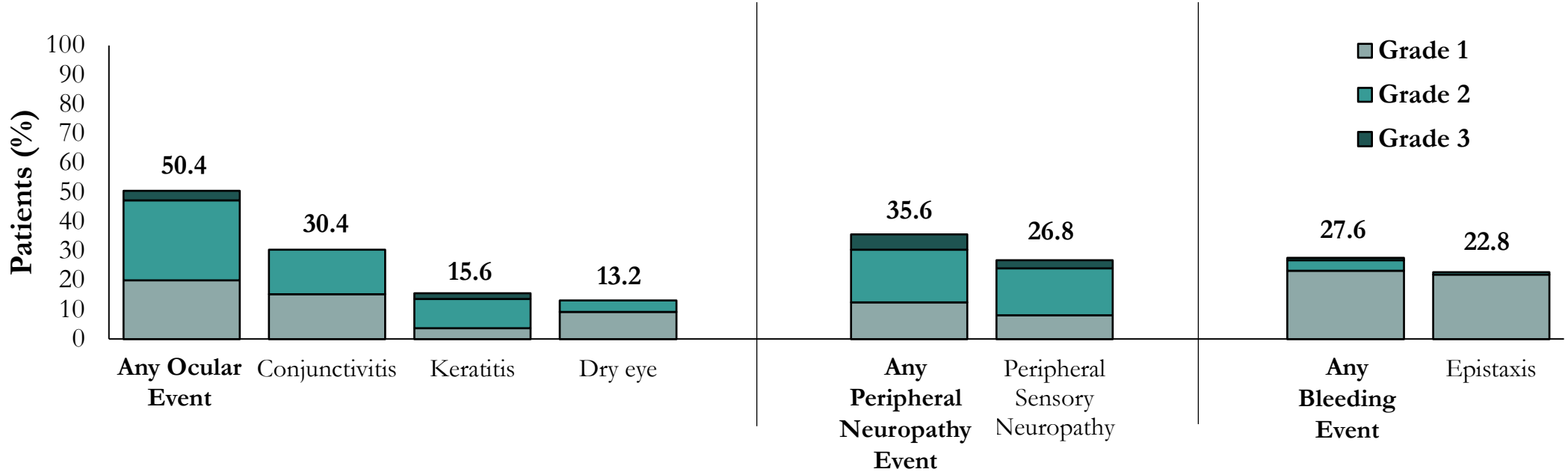


	CR	PR	SD	PD	NE
Tisotumab Vedotin (n)	6	35	120	39	0
Chemotherapy (n)	0	10	107	57	3

- 210 (83.0%) tisotumab vedotin and 194 (77.9%) chemotherapy patients had biopsies evaluable for TF expression
  - Of these, positive membrane TF expression was observed in 194 (92.4%) and 183 (94.3%) patients, respectively
- Comparable distribution of TF expression was observed among different confirmed best overall response groups

Patients whose best overall response was NA (without a valid post-baseline response assessment before new anticancer therapy, end of study, or end of treatment, whichever was earliest) are excluded from the figure.

AESIs in ≥5% of Patients in the Tisotumab Vedotin Arm



- Overall, the incidence of any grade TRAEs was similar across both arms (tisotumab vedotin: 87.6% versus chemotherapy: 85.4%)
  - 58.4% of TRAEs experienced by patients on the tisotumab vedotin arm were Grades 1-2
- Treatment-related AESIs for tisotumab vedotin were consistent with the previous known safety profile, including ocular, peripheral neuropathy, and bleeding events[1]
  - There were no Grade 4-5 AESIs

AESI, adverse event of special interest

1. Coleman RL. Lancet Oncol. 2021:609-619.

Conclusions

- In patients with 2L/3L r/mCC, tisotumab vedotin showed a statistically significant and clinically meaningful improvement in efficacy versus chemotherapy
  - The hazard ratio for OS was 0.70, demonstrating a 30% reduction in the risk of death
  - OS and PFS trends amongst prespecified subgroups had overlapping confidence intervals with the ITT population
- Confirmed ORR trends of tisotumab vedotin were consistent across key prespecified subgroups and the ITT population, regardless of tissue factor expression
- The safety profile of tisotumab vedotin was manageable and consistent with previous experience[1]
- Based on these data, tisotumab vedotin may be considered a potential new standard of care for patients who have progressed after 1L systemic therapy

1. Coleman RL. Lancet Oncol. 2021:609-619.

Acknowledgements

innovaTV 301/ENGOT-cx12/GOG-3057

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