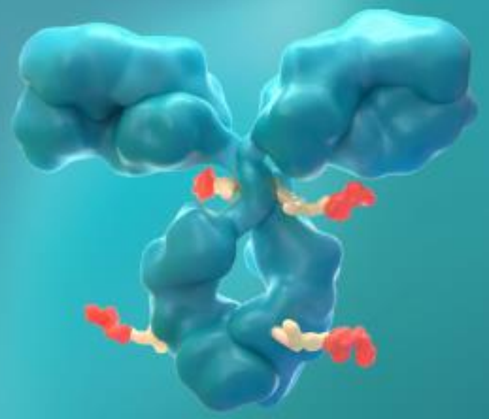
The Changing Landscape of Second-Line Therapies for Recurrent Cervical Cancer

Leslie Randall, MD

Ana Oaknin, MD, PhD

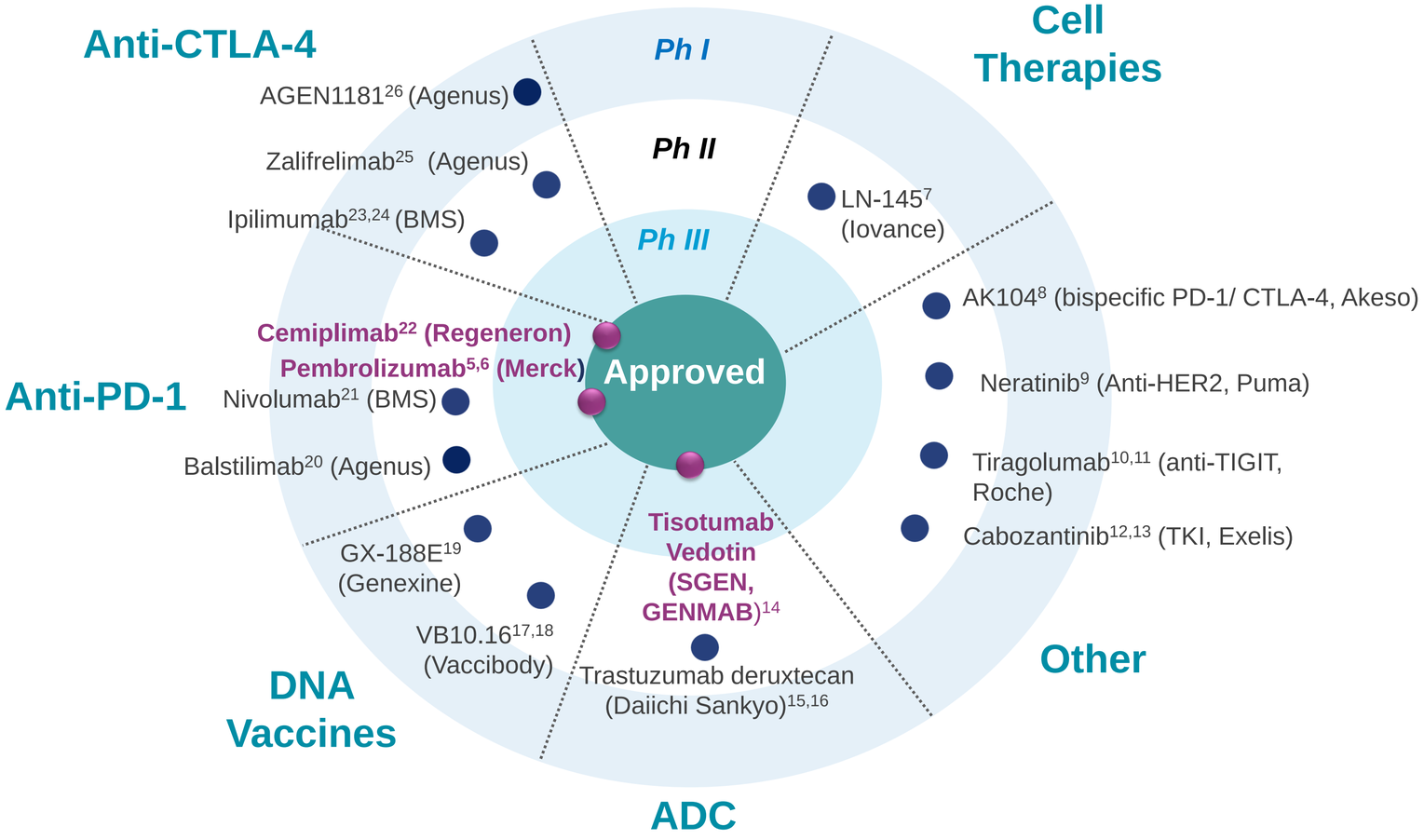


SEOUL IGCS 2023

Current Treatment Regimen for 2L+ R/M CC

Regimen [1-4]	ORR (%)	PFS (months)	OS (months)
Paclitaxel	32	NS	7.3
Cisplatin	23	NS	NS
Irinotecan	21-24	NS	NS
Topotecan	12.5-18	2.1-3.5	4.66-7.0
Capecitabine	2-15.4	2.9-4.1	5.9-9.3
Vinorelbine	7.1-13.7	NS	NS
Pemetrexed	13.9-15	2.5-3.1	7.4-8.8
Bevacizumab	10.9	3.4	7.29
Gemcitabine	4.50	2.1	6.5

Spectrum of Therapies in Different Stages of Development in 2L+ R/M CC



ADC, antibody-drug conjugates; CC, cervical cancer; CPS, combined positive score; CTLA, cytotoxic T-lymphocyte-associated protein; dMMR, DNA mismatch repair; FDA, federal drug administration; GOG, gynecological oncology group; ; MSI, microsatellite instability; NS, not stated; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitors; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; Ph, phase; PFS, progression-free survival; R/M, recurrent/metastatic; TIGIT, T-cell immunoreceptor with Ig and ITIM domain; TKI, tyrosine kinase inhibitor; TMB-H, tumor mutational burden-high; 2L, second-line.

1. Boussios S et al. *Crit Rev Oncol Hematol.* 2016;108:164-174; 2. US FDA Press Release. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-combination-first-line-treatment-cervical-cancer#:~:text=On%20October%2013%2C2021%2C%20the,by%20an%20FDA%2Dapproved%20test. Published October 13, 2021. Accessed September 25, 2023; 3. Le DT. *J Clin Oncol.* 2020;38(1):11-19; 4. Scatchard K et al. Cochrane Database Syst Rev ;2012(10): CD006469. 5. Gennigens C et al. ESMO Open. 2022;7(5):100579. 6. ClinicalTrials.gov. Accessed October 17, 2023. https://clinicaltrials.gov/study/NCT03635567. 7. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT03108495. 8. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT04380805. 9. ClinicalTrials.gov. Accessed October 09, 2023. https://clinicaltrials.gov/study/NCT01953926. 10. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT04300647. 11. Kim TW et al. *JAMA Oncol.* 2023;e233867. 12. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT04205799. 13. CABOMETYX® (cabozantinib) Prescribing Information. Alameda, CA: Exelixis, Inc., September 2023. 14. US FDA. FDA grants accelerated approval to tisotumab vedotin-tftv for recurrent or metastatic cervical cancer. Updated September 21, 2021. Accessed October 9, 2023. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-tisotumab-vedotin-tftv-recurrent-or-metastatic-cervical-cancer. 15. ClinicalTrials.gov. Accessed October 09, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04482309. 16. Indini A et al. *Int J Mol Sci.* 2021;22(9):4774. 17. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT04405349. 18. Nykode Therapeutics Press Release. https://nykode.com/wp-content/uploads/2023/04/230418-Nykode-VB10.16-Data-Update-PR-FINAL.pdf. Published April 18, 2023. Accessed October 17, 2023. 19. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT03444376. 20. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT04943627. 21. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT02488759. 22. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT03257267. 23. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT01693783. 24. YERVOY® (ipilimumab)Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company, February 2023. 25. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT03495882. 26. ClinicalTrials.gov. Accessed September 25, 2023. https://clinicaltrials.gov/study/NCT03860272.

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9: Study Design

An open-label, randomized, phase 3 clinical trial of REGN2810 versus investigator's choice of chemotherapy in recurrent or metastatic cervical carcinoma[1,2]

Key Eligibility Criteria

- Recurrent and metastatic cervical cancer resistant to platinum-based chemotherapy ≥2nd line
- ECOG PS ≤1

N=608: 477 SCC, 131 AC
Randomised 1:1
Stratified by:

- Histology (SCC/AC)
- Geographic region
- Prior bevacizumab (Y/N)
- ECOG PS (0 vs 1)

Previous anti–PD-1 or anti–PD-L1 therapy was not permitted

Cemiplimab 350 mg
Q3W IV

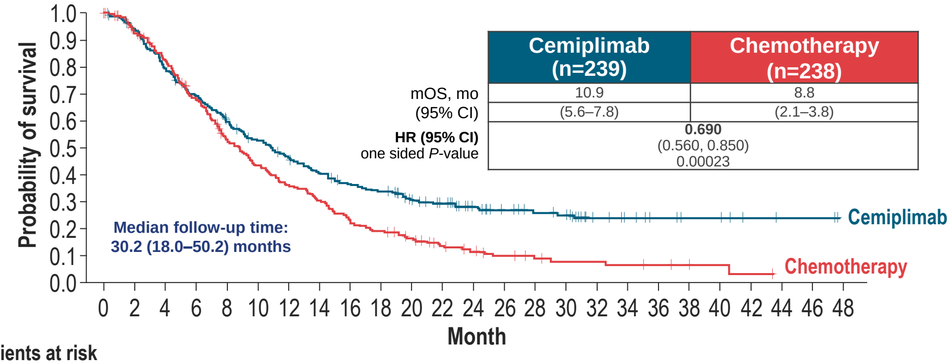
Investigator's choice chemotherapy

Options:

- Pemetrexed 500 mg/m^2 Q3W IV
- Gemcitabine 1,000 mg/m^2 IV on Days 1 and 8 and every 21 days
- Topotecan 1 mg/m^2 daily IV for 5 days, every 21 days
- Irinotecan 100 mg/m^2 IV weekly x 4, followed by 10–14 days rest
- Vinorelbine 30 mg/m^2 IV on Days 1 and 8 and every 21 days

Treat up to 96 weeks with option for re-treatment
Tumour imaging conducted on Day 42 (±7 days) of cycles 1–4, 6, 8, 10, 12, 14, and 16[a]

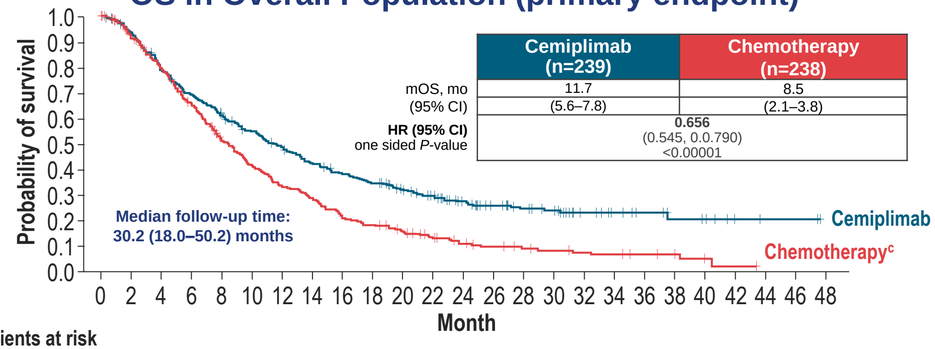
OS in Squamous Cell Histology (primary endpoint)[3,b]



Patients at risk

Cemiplimab	239	223	188	163	140	120	105	91	80	74	60	53	43	35	30	28	17	14	8	6	6	3	2	2	0
Chemotherapy	238	209	182	149	113	92	77	65	50	41	32	22	16	12	9	7	7	6	5	3	2	1	0	0	0

OS in Overall Population (primary endpoint)[3,b]



Patients at risk

Cemiplimab	304	281	236	206	181	158	140	121	108	97	81	69	55	45	37	33	22	18	11	8	7	3	2	2	0
Chemotherapy	304	264	224	183	140	113	92	79	60	50	40	30	21	17	14	12	10	9	7	5	2	1	0	0	0

[a]To account for differences in drug administration schedules, one cycle is defined as 6 weeks.[b]Kaplan–Meier curves of overall survival in the full analysis set. Data cutoff date: January 4, 2022. [c]8/304 chemotherapy patients crossed over to IO, 7 due to PD, 1 due to patient choice.

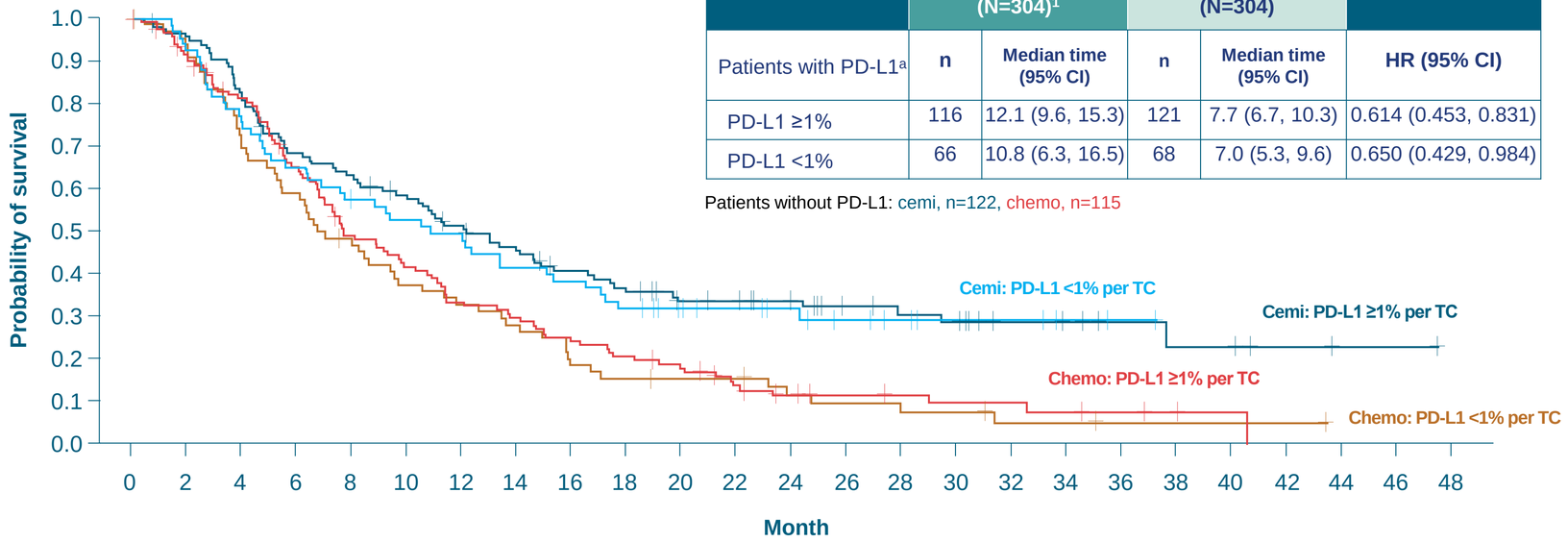
AC, adenocarcinoma; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; IC, investigator's choice; IDMC, independent data monitoring committee; IO, immunotherapy; IV, intravenous; mo, months; mOS, median overall survival; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1; programmed death ligand 1; PS, performance status; SCC, squamous cell carcinoma/adenocarcinoma; Q3W, every 3 weeks; Y/N, yes/no.

1. Tewari KS et al. *N Engl J Med* 2022;386:544-55. 2. Tewari K et al. *N Engl J Med* 2022;386:544-55. [Supplementary Appendix]. 3. Oaknin A et al. Presented at ESMO Congress 2022.

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9: Overall Survival Regardless of PD-L1 Status

	Cemiplimab (N=304)[1]		Chemotherapy (N=304)		
Patients with PD-L1[a]	n	Median time (95% CI)	n	Median time (95% CI)	HR (95% CI)
PD-L1 ≥1%	116	12.1 (9.6, 15.3)	121	7.7 (6.7, 10.3)	0.614 (0.453, 0.831)
PD-L1 <1%	66	10.8 (6.3, 16.5)	68	7.0 (5.3, 9.6)	0.650 (0.429, 0.984)

Patients without PD-L1: cemi, n=122, chemo, n=115



Patients at risk

Cemi: PD-L1 ≥1% per TC	116	110	93	77	71	63	55	48	41	36	30	29	25	20	17	16	10	9	5	4	4	2	1	1	0
Cemi: PD-L1 <1% per TC	66	61	49	43	36	33	30	26	24	20	16	14	12	9	7	5	5	3	1	0	0	0	0	0	0
Chemo: PD-L1 ≥1% per TC	121	107	92	73	54	46	37	33	27	23	19	13	9	7	6	5	5	4	3	2	1	0	0	0	0
Chemo: PD-L1 <1% per TC	68	60	46	39	30	24	21	18	12	10	9	9	6	5	4	4	2	2	1	1	1	1	0	0	0

Kaplan–Meier curves of overall survival in the full analysis set. Data cutoff date: January 4, 2022

[a]For patients without PD-L1, n=122 for cemi, n=115 for chemo. PD-L1 expression was detected with the SP263 monoclonal antibody.

Cemi, cemiplimab; Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1; TC, tumor cell.

Oaknin A et al. Presented at ESMO Congress 2022.

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9: PFS and Safety Summary

mPFS in Overall Population and Squamous Cell carcinoma

	Cemiplimab	IC chemotherapy[2]
mPFS Overall population	**2.8 mon** (95% CI, 2.6 –3.9)	**2.9 mon** (95% CI, 2.7 – 3.4)
HR: 0.75; 95% CI, 0.63-0.89) *P*<0.001		
mPFS Squamous-cell carcinoma	**2.8 mon** (95% CI, 2.6 – 4.0)	**2.9 mon** (95% CI, 2.7 – 3.9)

TEAEs

n (%)	Cemiplimab (n=300)[1]	Chemotherapy (n=290)
Median duration of exposure (range), weeks[1]	15.2 (1.4–107.7)	10.1 (1.1–91.1)
Any treatment-emergent adverse events (TEAEs)		
Overall	269 (89.7)	266 (91.7)
Led to discontinuation	27 (9.0)	15 (5.2)
Led to death	5 (1.7)	2 (0.7)
Any treatment-related AEs		
Overall	172 (57.3)	237 (81.7)
Led to discontinuation	17 (5.7)	10 (3.4)
Led to death	0	2 (0.7)
Any treatment-emergent AEs of special interest (AESI)		
Overall	36 (12.0)	N/A
Led to discontinuation	12 (4.0)	N/A
Led to death	0	N/A

TEAEs in ≥10% Patients

TEAEs in ≥10% of patients, n (%)[1]	Cemiplimab (n=300)		Chemotherapy (n=290)	
	Any grade	Grade 3–5	Any grade	Grade 3–5
Anemia	76 (25.3)	36 (12.0)	128 (44.1)	79 (27.2)
Nausea	57 (19.0)	2 (0.7)	99 (34.1)	6 (2.1)
Vomiting	50 (16.7)	3 (1.0)	68 (23.4)	7 (2.4)
Pyrexia	39 (13.0)	1 (0.3)	62 (21.4)	0
Constipation	45 (15.0)	0	58 (20.0)	1 (0.3)
Decreased appetite	46 (15.3)	1 (0.3)	46 (15.9)	2 (0.7)
Fatigue	51 (17.0)	4 (1.3)	45 (15.5)	4 (1.4)
Neutropenia	6 (2.0)	3 (1.0)	45 (15.5)	27 (9.3)
Asthenia	35 (11.7)	7 (2.3)	44 (15.2)	3 (1.0)
Diarrhea	34 (11.3)	3 (1.0)	39 (13.4)	4 (1.4)
Urinary tract infection	35 (11.7)	15 (5.0)	25 (8.6)	8 (2.8)
Abdominal pain	30 (10.0)	3 (1.0)	33 (11.4)	3 (1.0)
Arthralgia	33 (11.0)	1 (0.3)	8 (2.8)	0
Back pain	32 (10.7)	4 (1.3)	28 (9.7)	2 (0.7)

Cemiplimab was approved by EMA and JAPAN for the 2L treatment of recurrent or metastatic cervical cancer that has progressed on or after platinum-based therapy, regardless of PD-L1 expression status or tumor histology[2]

Data cutoff date: January 4, 2022

AE, adverse events; EMA, European medicines agency; IC, investigator's choice; mon, months; TEAE, treatment-emergent adverse event: N/A, non applicable; PD-L1, programmed death ligand 1; PFS, progression-free survival.

1. Oaknin A et al. Presented at ESMO Congress 2022; 2. Tewari KS et al. *N Engl J Med.* 2022;386(6):544-555. 2. Conroy R. CancerNetwork. https://www.cancernetwork.com/view/european-commission-approves-cemiplimab-for-recurrent-metastatic-cervical-cancer. Accessed September 15, 2023.

DESTINY-PanTumor02: Study Design

A phase 2, multicenter, open-label study to evaluate the efficacy and safety of trastuzumab deruxtecan for the treatment of selected HER2 expressing tumors[1,2]

Key Eligibility Criteria

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
- Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer scoring
- Prior HER-targeting therapy allowed
- ECOG/WHO PS ≤1

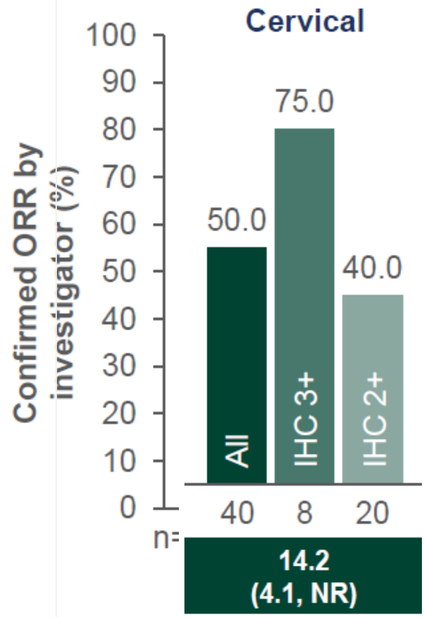
T-DXd
5.4 mg/kg Q3W

40 per cohort[b]

Frequency of HER2 mutations across tumor types

Endometrial cancer	~7%[3]
Cervical cancer	~5%[4]
Ovarian cancer	1–2%[5]
Bladder cancer	9–13%[5]
Other tumors[c]	
Biliary tract cancer	~10%
Pancreatic cancer	~1%[3]

ORR by HER2 status in Cervical Cancer



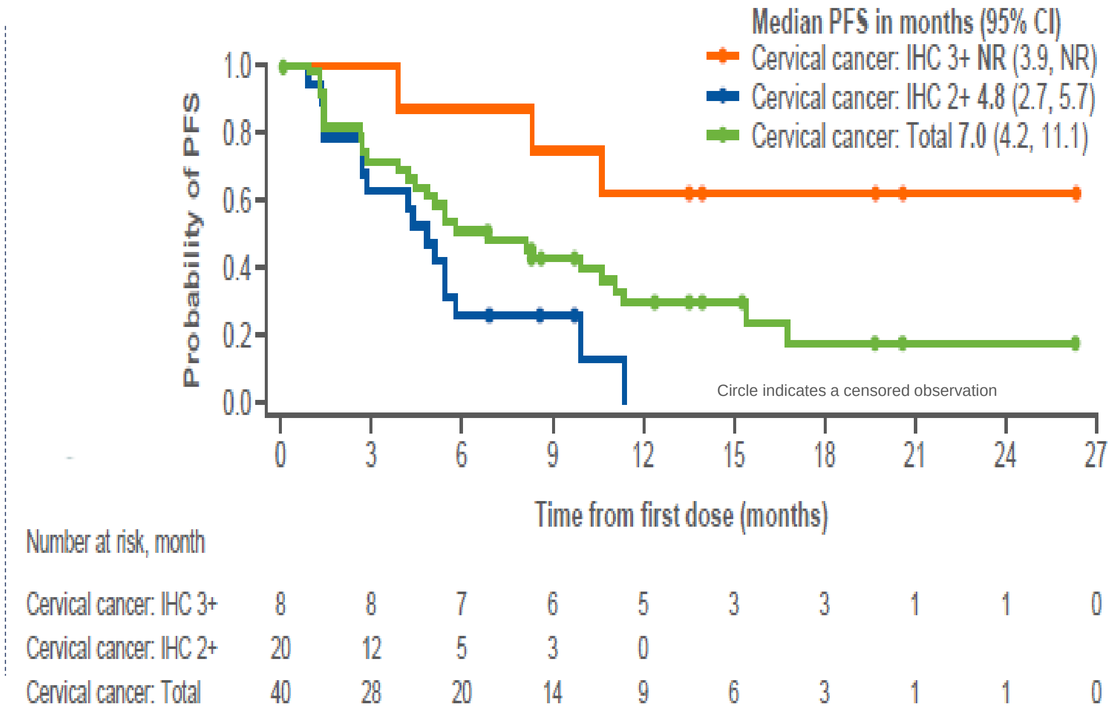
All patients were HER2-positive per local determination

IGCS 2023 SEOUL

Data cutoff: June 8, 2023. Medin f/u: 12.75 months
[a]Patients were eligible for either test. All patients were centrally confirmed. [b]Patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer. [c]Investigator-assessed per Response Evaluation Criteria In Solid Tumors version 1.1.
ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; DCR, disease control rate; DOR, duration of response ECOG; Eastern Cooperative Oncology Group; f/u, follow-up; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression free survival, PS, performance status; T-Dxd; trastuzumab deruxtecan; Q3W, every 3 weeks; WHO, World Health Organization; 2L, second-line.
1. Clinicaltrials.gov.NCT04482309. Accessed October 03, 2023. 2. Funda Meric-Burnstam. Presented at ESMO 2023. Presented orally LBA34. 3. Wang et al. *Front Immunol.* 2022; 13: 799988.4. Oaknin et al. *Gynecol Oncol*. 2020t;159(1):150-156; 5. Li et al. *EBioMedicine*. 2020; 62: 103074; 6. Harding JJ et al. *Nat Commun*. 2023;14(1):630. doi: 10.1038/s41467-023-36399-y.

DESTINY-PanTumor02:

PFS by HER2 status in Cervical Cancer



TEAEs	All patients (N=267); n (%)
Any drug-related TEAEs	226 (84.6)
Drug-related TEAEs Grade ≥3	109 (40.8)
Serious drug-related TEAEs	36 (13.5)
Drug-related TEAEs associated with dose discontinuations	23 (8.6)
Drug-related TEAEs associated with dose interruptions	54 (20.2)
Drug-related TEAEs associated with dose reductions	54 (20.2)
Drug-related TEAEs associated with deaths	4 (1.5)[a]

Most common TEAEs	Any Grade	Grade ≥3
Nausea	55.1	3.7
Fatigue	40.1	7.1
Neutropenia	32.6	19.1
Anemia	27.7	10.9
Diarrhea	25.8	3.7
Vomiting	24.7	1.5
Decreased appetite	17.6	1.5
Thrombocytopenia	17.2	5.6
Alopecia	16.9	
Increased transaminases	10.1	0.4
Leukopenia	10.1	2.6

ILD/pneumonitis adjudicated as T-DXd related, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
All patients (N=267)	7 (2.6)	17 (6.4)	1 (0.4)	0	3 (1.1)	28 (10.5)

Data cutoff: June 8, 2023. Medin f/u: 12.75 months
[a]Patients were eligible for either test. All patients were centrally confirmed. [b]Patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer. [c]Investigator-assessed per Response Evaluation Criteria In Solid Tumors version 1.1.
ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; DCR, disease control rate; DOR, duration of response ECOG; Eastern Cooperative Oncology Group; f/u, follow-up; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression free survival, PS, performance status; T-Dxd; trastuzumab deruxtecan; Q3W, every 3 weeks; WHO, World Health Organization; 2L, second-line.
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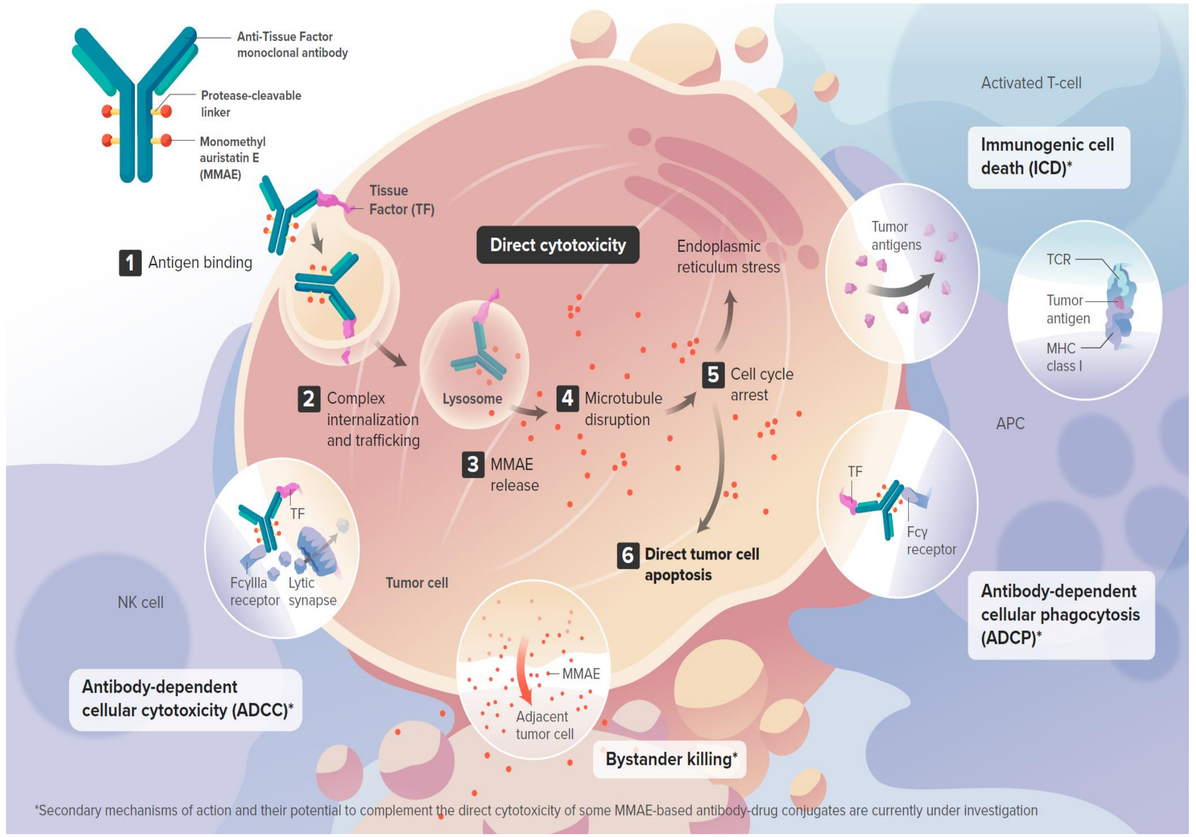
Tisotumab Vedotin: Mechanism of Action

- Tisotumab vedotin is an **ADC directed to tissue factor (TF)** and covalently linked to the microtubule-disrupting agent **MMAE via a protease-cleavable linker**[1]
- **TF is highly prevalent in cervical cancer** and other solid tumors and is associated with cancer pathophysiology and poor prognosis[2-4]
  - TF is co-opted by tumor cells to promote tumor growth, angiogenesis, and metastasis[5]
  - In normal physiology, TF's primary role is to initiate the coagulation cascade after vascular injury[5]
- Tisotumab vedotin has **multiple anti-tumor effects**[6]

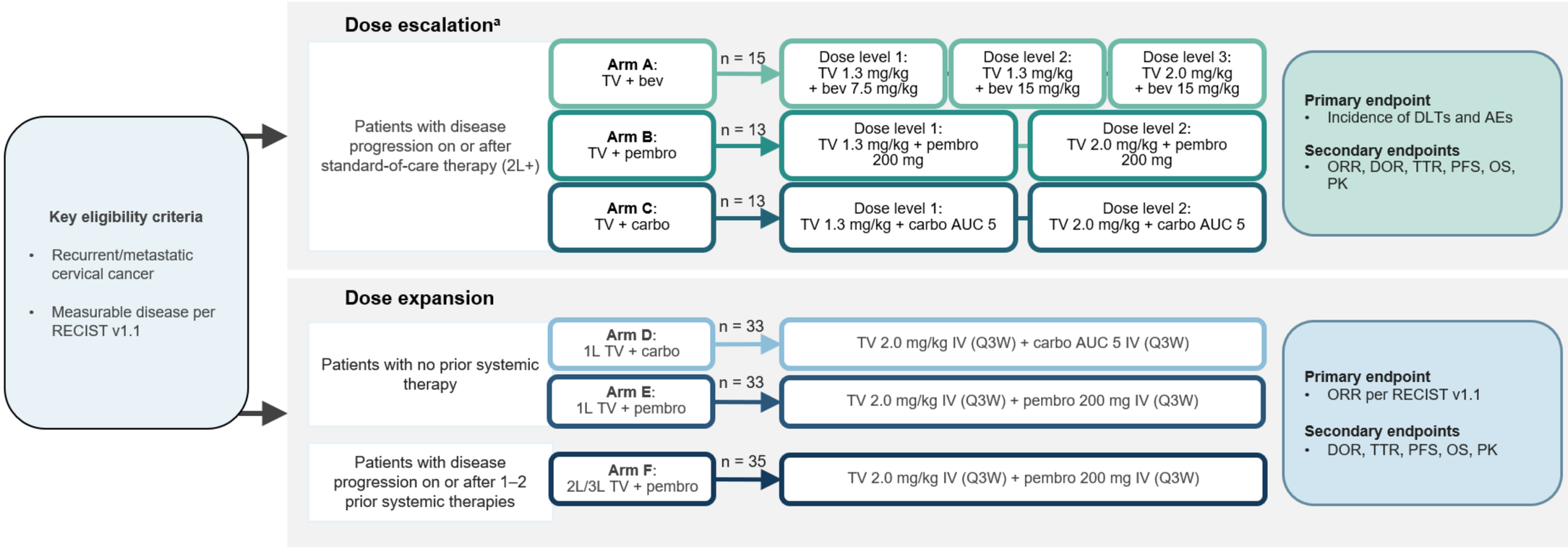


ADC, antibody-drug conjugate; ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; MMAE, monomethyl auristatin E; TF, tissue factor.

1. Vergote I et al. Poster #TPS 5603. Presented at IGCS Annual Meeting 2022. 2. Pan L et al .*Mol Med Rep*. 2019;19:2077-2086. 3. Cocco E et al. *BMC Can*cer. 2011;11:263. 4. Zhao X et al. *Exp Ther Med*. 2018;16:4075-4081. 5. Forster Y et al. *Clin Chim Acta*. 2006;364:12-21. 6. Alley SC et al. American association for Cancer Research Annual Meeting; March 29 – April 3, 2019; Atlanta, GA, USA; Abstract #221; 7. Coleman L. Presented at ESMO 2020.

InnovaTV 205: Study Design

A phase 1b/2 open-label trial of tisotumab vedotin monotherapy and in combination with other agents in subjects with recurrent or stage IVB cervical cancer



[a]TV + bev arm followed a 3 + 3 dose escalation design. TV + pembro and TV + carbo Arms followed a 6 + 6 dose escalation design. Drugs were administered IV on day 1 of each 21-day cycle. Patients were treated for ≥1 cycle to evaluate DLTs and 2 cycles to evaluate RP2D.

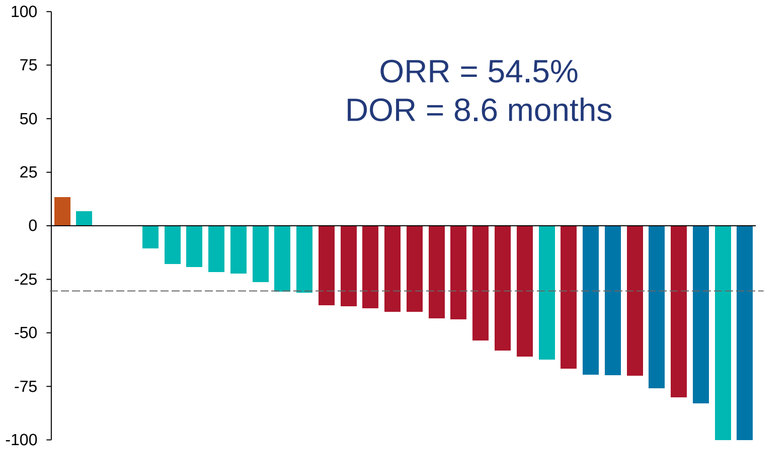
AE, adverse events; AUC, area under the concentration-time curve; bev, bevacizumab; carbo, carboplatin; DLT, dose-limiting toxicity; IV, intravenously; PK, pharmacokinetics; ORR, objective response rate; OS, overall survival; pembro, pembrolizumab; Q3W, every 3 weeks; Progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended phase 2 dose; TTR, time to response; TV, tisotumab vedotin; 1L, first-line; 2L, second-line; 3L, third-line.

Vergote I, et al. *J Clin Oncol*. 2023:JCO2300720.

InnovaTV 205: Best Reduction in Target Lesion Size

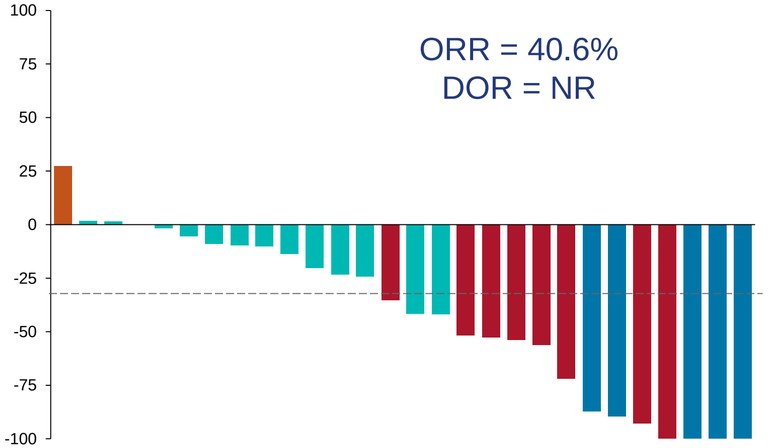
1L TV + Carbo N=33[a]

ORR = 54.5%
DOR = 8.6 months



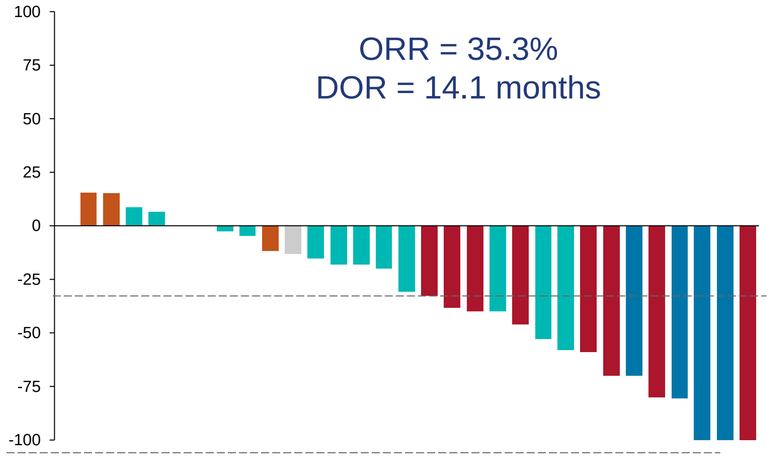
1L TV + Pembro N=32[b]

ORR = 40.6%
DOR = NR



2L/3L TV + Pembro N=34[c]

ORR = 35.3%
DOR = 14.1 months

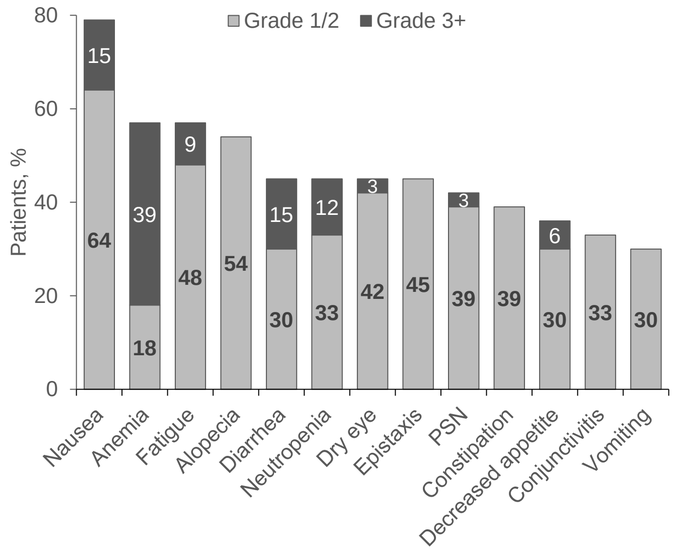


Complete response Partial response Stable disease Progressive disease Not evaluable

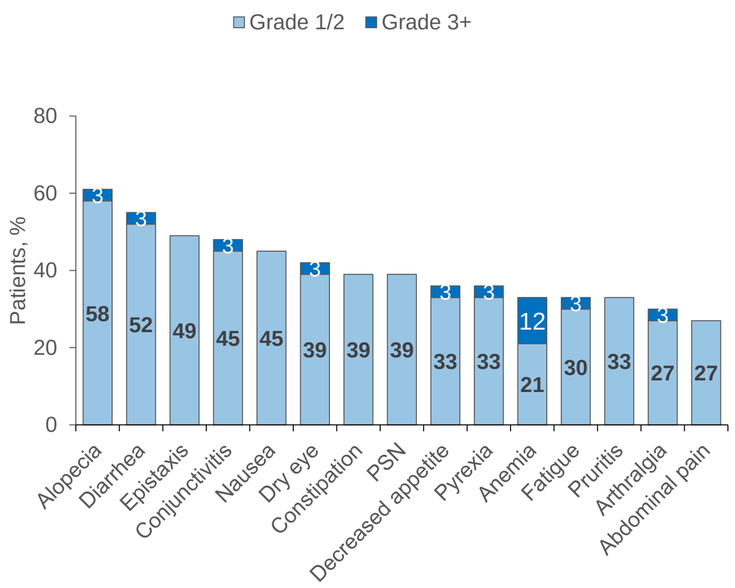
Data cutoff: June 20, 2022.
Median duration of follow-up for 1TV+Carbo: (range):17.8 (1−26) months; for 1 TV+Pembro: 21.7 (1–29) months; for 2L/3L TV + Pembro: 15.0 (1–29) months
The dashed line indicates a 30% reduction from baseline.
Carbo, carboplatin; CBR, clinical benefit rate; CI, confidence interval; DCR, disease control rate; NR, not reached; ORR, objective response rate; pembro, pembrolizumab; TV, tisotumab vedotin; 1L, first-line 2L, second-line; 3L, third-line.
Vergote I, et al. *J Clin Oncol*. 2023:JCO2300720.

InnovaTV 205: Safety Summary of Common AEs Reported in >25% Patients

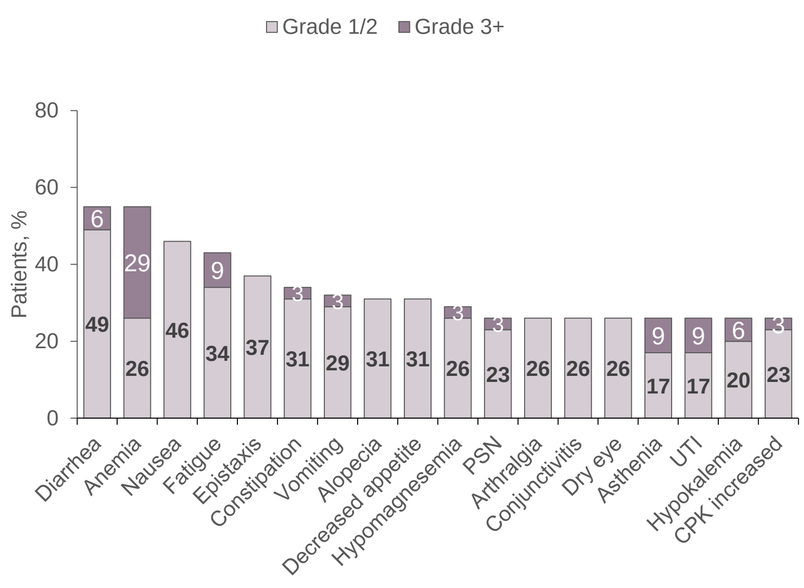
1L TV + Carbo[a] (n=33)



1L TV + Pembro[b] (n=33)



2L/3L TV + Pembro[c] (n=35)



- Most TEAEs were grade 1 or 2
- Observed safety profile was generally consistent with those known for each individual agent
- There was a single grade 5 event with 1L TV + pembro considered by the investigator to be related to trial treatment (due to disseminated intravascular coagulation)
- Immune-mediated AEs observed with TV + pembro were consistent with known safety profile of checkpoint inhibitors

Data cutoff: June 20, 2022

[a]8 (24.2%) patients discontinued TV due to AEs; +b12 (34.3%) patients discontinued TV due to AEs; [c]7 (21.2%) patients discontinued TV due to AEs; AEs leading to discontinuation of TV were mostly related to ocular or neuropathic events.

AE, adverse event; carbo, carboplatin; CPK, blood creatinine phosphokinase; Pembro, pembrolizumab; PSN, peripheral sensory neuropathy; TEAE, treatment emergent adverse event; TV, tisotumab vedotin; UTI, urinary tract infection.

Vergote I, et al. *J Clin Oncol*. 2023:JCO2300720.

InnovaTV 301 (ENGOT cx-12/GOG 3057): Study Design

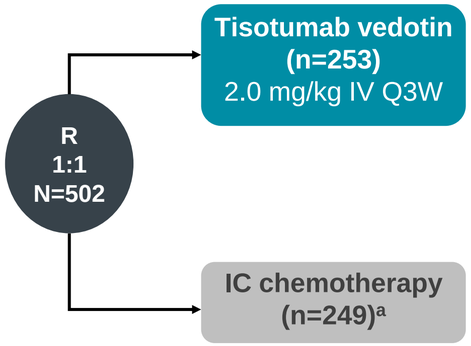
A randomized, open-label, phase 3 confirmatory trial of tisotumab vedotin vs investigator's choice chemotherapy in 2L/3L recurrent or metastatic cervical cancer[1]

Key Eligibility Criteria[2]

- Recurrent or metastatic cervical cancer
- Disease progression on or after chemotherapy doublet ± bevacizumab and an anti-PD-(L)1 agent, if eligible and available
- ≤2 prior lines
- Measurable disease per RECIST v1.1
- ECOG PS 0-1

Stratification Factors

- ECOG PS (0 vs 1)
- Prior bevacizumab (yes vs no)
- Prior anti-PD-(L)1 therapy (yes vs no)
- Geographic region (US, Europe, Other)



IC Chemotherapy

- Topotecan
- Vinorelbine
- Gemcitabine
- Irinotecan
- Pemetrexed

Previous anti–PD-1 or anti–PD-L1 therapy was permitted

Primary endpoint: OS[b]

Secondary endpoints: PFS[c], ORR[c], Safety

Baseline Patient and Disease Characteristics

	Tisotumab Vedotin (N=253)	IC Chemotherapy (N=249)
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)

Baseline patient demographics were balanced across both arms

Data presented herein are a planned interim analysis
End of treatment visit occurred 30 days after the last dose of treatment. Survival follow-up occurred every 60 days after the last dose of treatment.
[a]Chemotherapy regimens were given at the following doses: topotecan 1 or 1.25 mg/m^2 IV on Days 1 to 5 of a 21-day cycle; vinorelbine 30 mg/m^2 IV on Days 1 and 8 of a 21-day cycle; gemcitabine 1000 mg/m^2 IV on Days 1 and 8 of a 21-day cycle; irinotecan 100 or 125 mg/m^2 IV weekly for 28 days every 42 days; pemetrexed 500 mg/m^2 on Day 1 of a 21-day cycle; [b]OS was defined as the time from the date of randomization to the date of death due to any cause; [c]Assessed by investigator.
ECOG PS, eastern cooperative oncology group performance status; IC, investigator's choice; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, response evaluation criteria in solid tumors; 2L, second-line; 3L, third-line.
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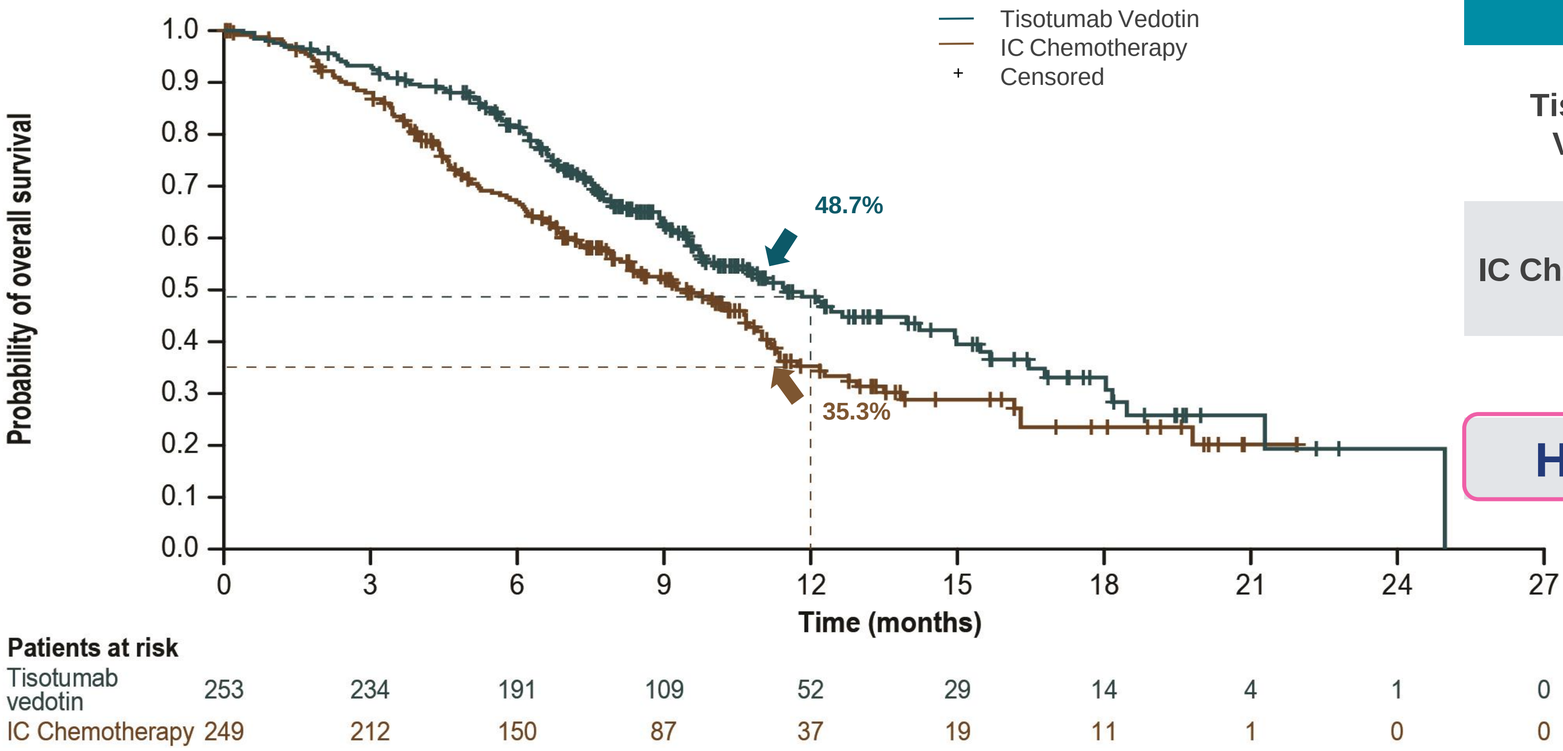
InnovaTV 301 (ENGOT cx-12/GOG 3057): Overall Survival

Overall Survival (Primary endpoint)



Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	123/253	11.5 (9.8, 14.9)
IC 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)

[a]The threshold for statistical significance is 0.0226 (2-sided), based on the actual number of OS events at interim analysis.
IC, investigator choice; PD-L1, Programmed death-ligand 1;
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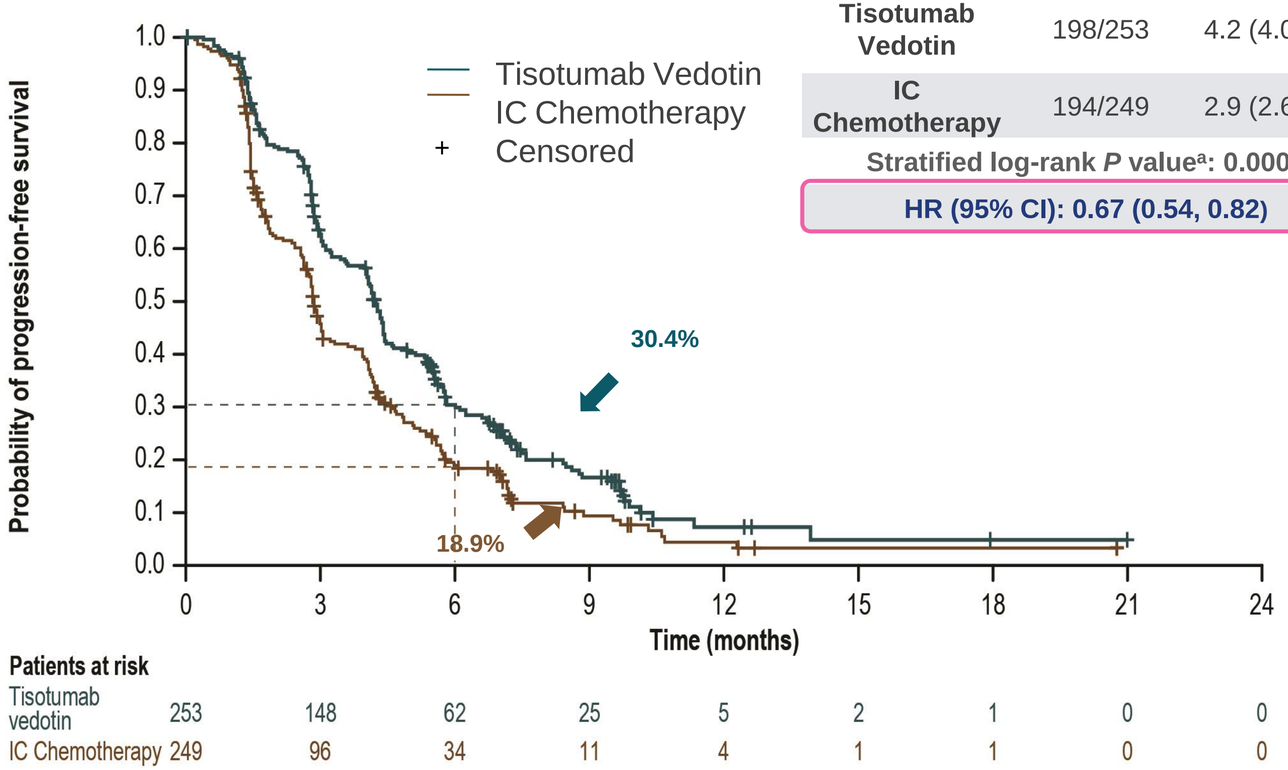
InnovaTV 301 (ENGOT cx-12/GOG 3057): PFS Per Investigator



Treatment	Events/Total	Median (95% CI)
Tisotumab Vedotin	198/253	4.2 (4.0, 4.4)
IC 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)

	Tisotumab Vedotin (N=253)	IC Chemotherapy
ORR, % (95% CI)	**17.8 (13.3 - 23.1)**	**5.2 (2.8-8.8)**
Odds ratio (95% CI) *P* value	4.0 (2.1-7.6) *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[b], % (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)

[a]The threshold for statistical significance is 0.0453 (2-sided), based on the actual number of PFS events at interim analysis. [b]DCR is 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.
CI, confidence interval; CR, complete response; DCR, disease control rate; HR, hazard ratio; IC, investigator choice; ORR, overall response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; SD, stable disease.
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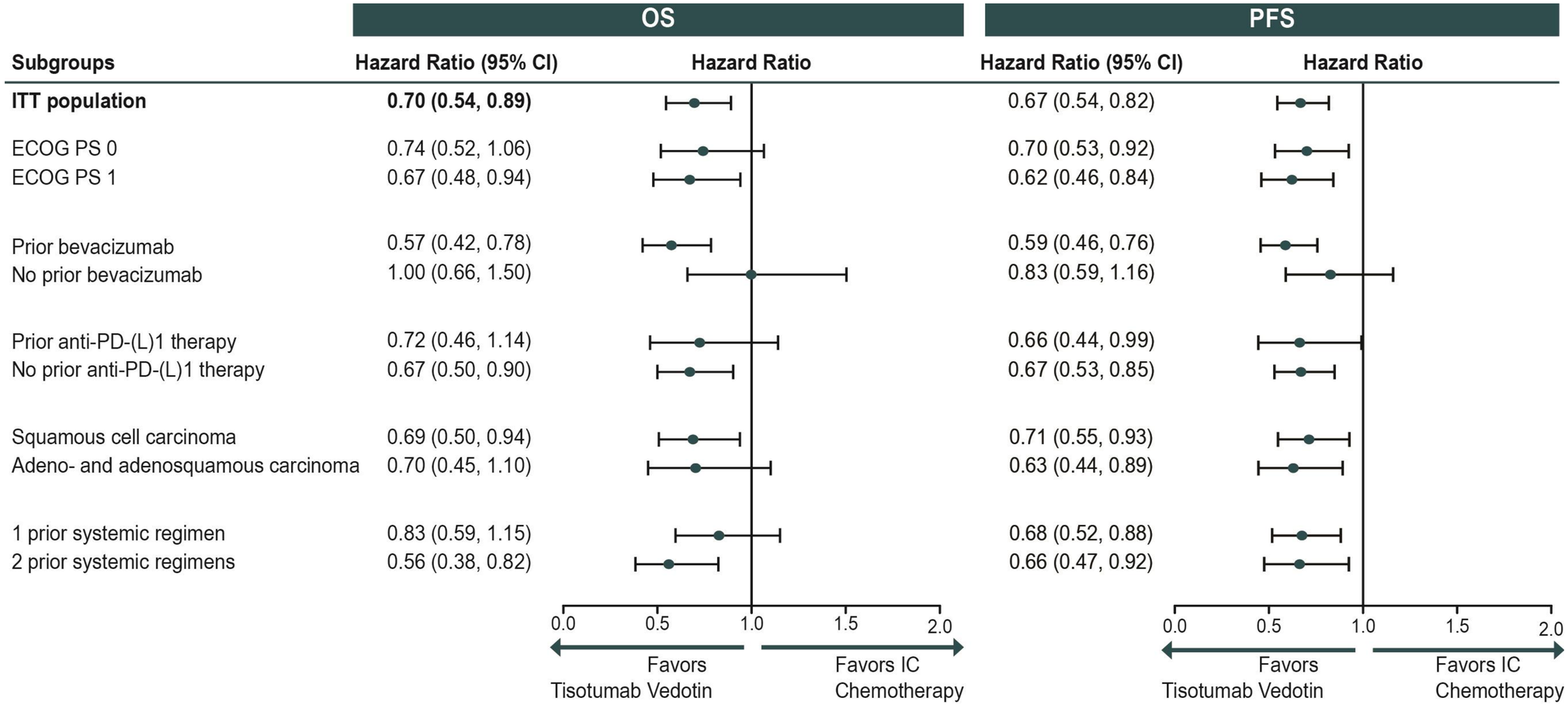
InnovaTV 301 (ENGOT cx-12/GOG 3057): Key Subgroups – OS and PFS



OS and PFS benefit was generally consistent across key subgroups

CI, confidence interval; ECOG PS, eastern cooperative oncology group performance status; IC, investigator choice; ITT, intent-to-treat; OS, overall survival; PFS, progression-free survival; PD-L1, programmed death-ligand 1;
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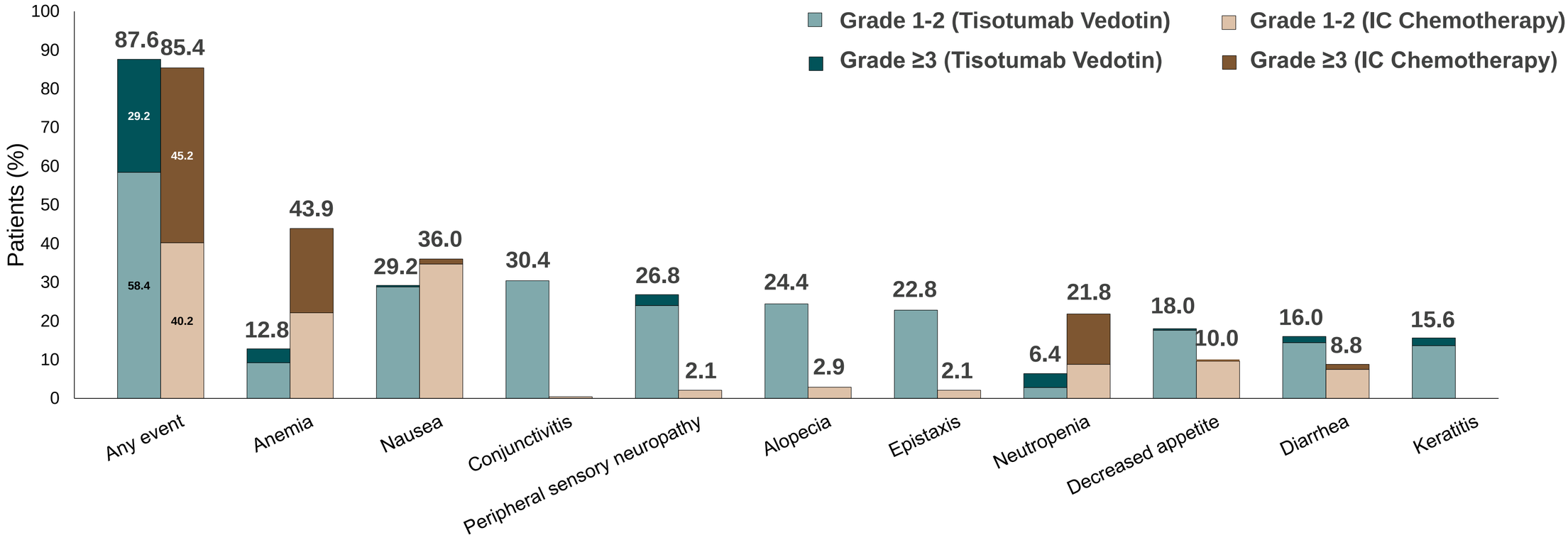
Most Common Treatment-Related Adverse Events



- Grade 5 TRAEs occurred in 2 (0.8%) and 1 (0.4%) patients in the Tisotumab vedotin and IC chemotherapy arms, respectively[a,b]
- Median relative dose intensity was 96.1% and 90.0% in the Tisotumab vedotin and IC chemotherapy arms, respectively

[a]TRAEs listed are those occurring in ≥15% of patients on either arm; [b]Grade 5 TRAEs included acute kidney injury (n=1) and Stevens-Johnson syndrome (n=1) in the tisotumab vedotin arm and pancytopenia (n=1) in the IC chemotherapy arm.
IC, investigator choice; TRAE, treatment-related adverse event.
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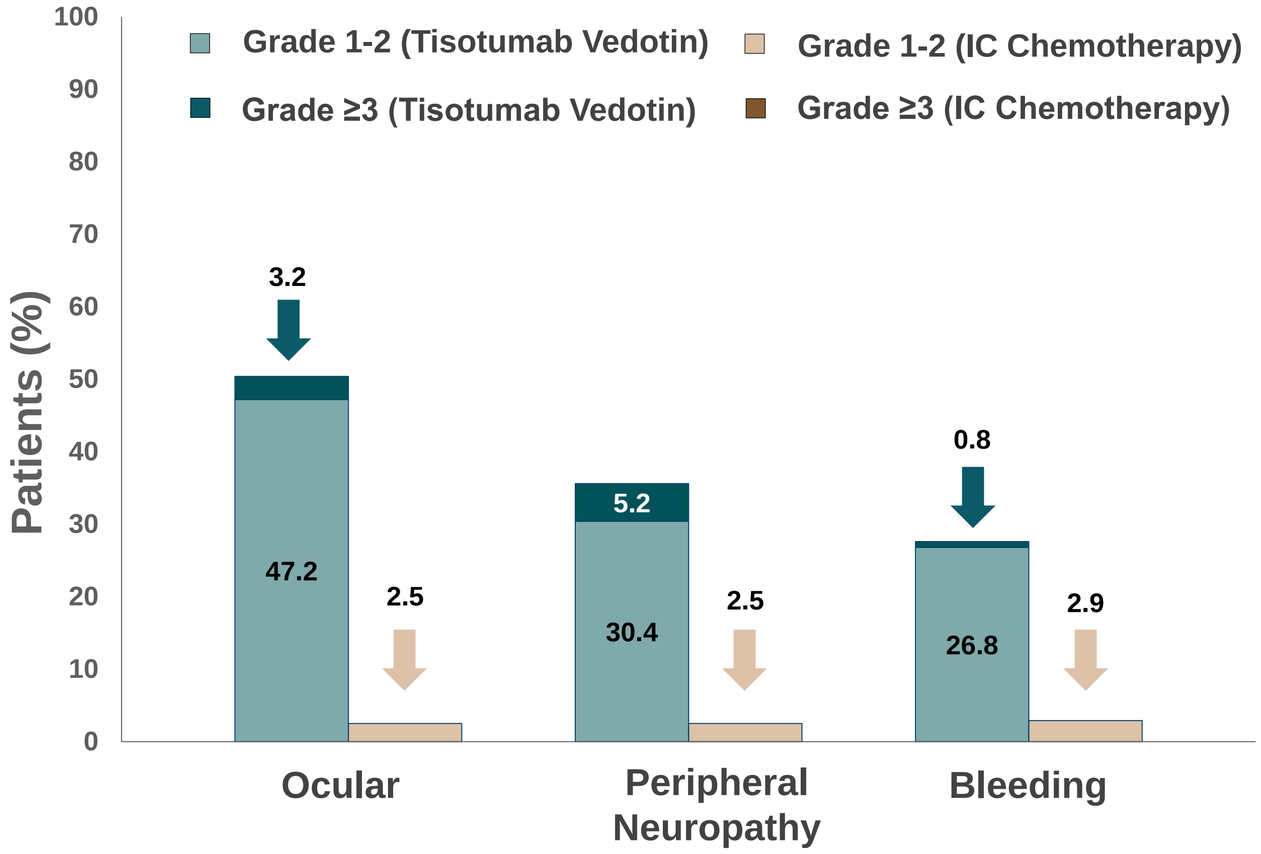
Adverse Events of Special Interest for Tisotumab Vedotin[a]



Three most common preferred terms for each AESI	
Ocular	Conjunctivitis (30.4%), keratitis (15.6%), dry eye (13.2%)
Peripheral neuropathy	Peripheral sensory neuropathy (26.8%), paresthesia (2.8%), muscular weakness (2.4%), peripheral sensorimotor neuropathy (2.4%)
Bleeding	Epistaxis (22.8%), hematuria (3.2%), vaginal hemorrhage (3.2%)

- There were no grade 4 or 5 AESIs
- **Dose discontinuation due to ocular and peripheral neuropathy events occurred in 5.6% of patients for each**

[a]Treatment-related AESIs
AESI, adverse events of special interest; IC, investigator's choice;
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