Patient-reported outcomes from the phase 3 ENGOT-cx12/GOG-3057/innovaTV 301 trial of tisotumab vedotin as second-/third-line treatment for recurrent or metastatic cervical cancer

Scott Jordan,[a] Antonio González-Martin,[b] Robert Morlock,[c] Kan Yonemori,[d] Alexandra Leary,[e] Michal Zikan,[f] Hee Seung Kim,[g] Lisa Barraclough,[h] Fernanda Damian,[i] Vanda Salutari,[j] Stéphanie Henry,[k] Michael Kolinsky,[l] Fabian Trillsch,[m] Jacqueline Tromp,[n] Sakari Hietanen,[o] Shin Nishio,[p] Leslie Randall,[q] Alex Mutebi,[r] Devin Abrahami,[s] Ignace Vergote[t]

[a]Broward Health, Fort Lauderdale, FL, USA; [b]Cancer Center Clínica Universidad de Navarra, Madrid, Spain; [c]YourCareChoice, Ann Arbor, MI, USA; [d]National Cancer Center Hospital, Chuo-ku, Japan; [e]Institut Gustave Roussy, Villejuif, France; [f] Bulovka University Hospital, Prague, Czech Republic; [g]Seoul National University, Seoul, Republic of Korea; [h]The Christie NHS Foundation Trust, Manchester, UK; [i]Centro de Pesquisa em Oncologia—HSL-PUCRS, Porto Alegre, Brazil; [j]Fondazione Policlinico Universitario Agostino Gemelli-IRCCS, Rome, Italy; [k]CHU UCL Namur—Site de Sainte-Elisabeth, Namur, Belgium; [l]University of Alberta/Cross Cancer Institute, Edmonton, AB, Canada; [m]Department of Obstetrics and Gynecology, LMU University Hospital, LMU Munich, Munich, Germany.; [n]Amsterdam University Medical Center, Amsterdam, the Netherlands; [o]University of Turku, Turku, Finland; [p]Kurume University Hospital, Kurume, Japan; [q]Virginia Commonwealth University Medical Center, Richmond, VA, USA; [r]Genmab US, Inc. Plainsboro, NJ, USA; [s]Pfizer Inc., Toronto, ON, Canada; [t]Belgium and Luxembourg Gynaecological Oncology Group (BGOG); University Hospitals Leuven, Leuven, Belgium

Conclusions

- This post-hoc PRO analysis (13 cycles) from ENGOT-cx12/GOG-3057/innovaTV 301 suggests that treatment with tisotumab vedotin maintains QoL in patients with r/mCC
- When patients' QoL deteriorated, tisotumab vedotin was associated with slower time to clinically meaningful deterioration compared with chemotherapy across key HRQoL domains
- Taken in context with the clinical outcomes from the ENGOT-cx12/GOG-3057/innovaTV 301 trial, wherein tisotumab vedotin significantly improved OS versus chemotherapy in patients with r/mCC,[4] these findings reinforce tisotumab vedotin as an appropriate therapeutic option for patients with r/mCC
- Limitations of the analysis include its post-hoc nature and the open-label design of the trial; the PRO analyses were not statistically powered. Additionally, the 10-point threshold used to represent clinically meaningful change from baseline was based upon general guidance and may not be appropriate for every subscale, limiting interpretation of the results

Background

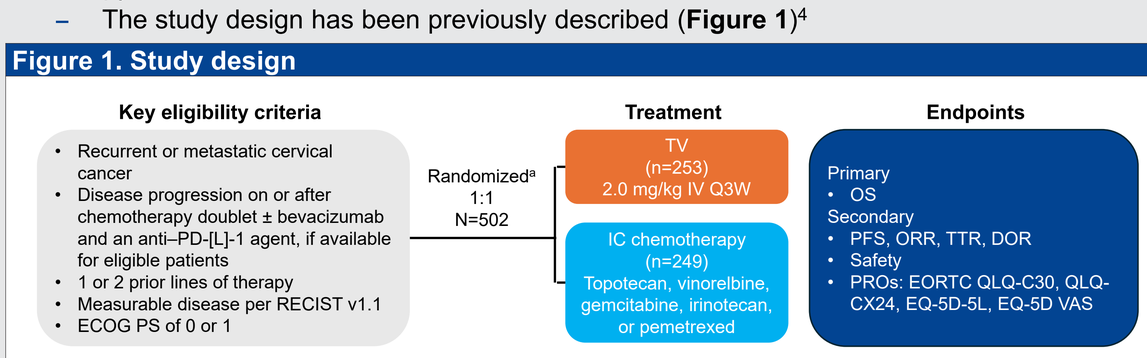
- Tisotumab vedotin is a tissue factor–directed antibody-drug conjugate approved for treating recurrent or metastatic cervical cancer (r/mCC) in multiple regions, including the US, Europe, and Japan[1-3]
- Tisotumab vedotin showed superior efficacy outcomes compared with investigator's choice of chemotherapy, including overall survival (hazard ratio [HR] 0.70; 95% CI, 0.54–0.89; two-sided *P*=0.004), progression-free survival (HR 0.67; 95% CI, 0.54–0.82; two-sided *P*<0.001), and objective response rates in the global phase 3 ENGOT-cx12/GOG-3057/innovaTV 301 trial, and a manageable safety profile[4]
- Previously, we reported that quality of life (QoL) was maintained for patients treated with tisotumab vedotin or chemotherapy up to cycle 5 of treatment in innovaTV 301[4]
- Here, we present post-hoc analyses of patient-reported outcomes (PROs) from ENGOT-cx12/GOG-3057/innovaTV 301

Methods

ENGOT-cx12/GOG-3057/innovaTV 301

- This is a global, randomized, open-label phase 3 study of tisotumab vedotin vs investigator's choice of chemotherapy in patients with r/mCC who had received 1 or 2 prior lines of systemic therapy for their r/mCC
  - The study design has been previously described (**Figure 1**)[4]

Figure 1. Study design

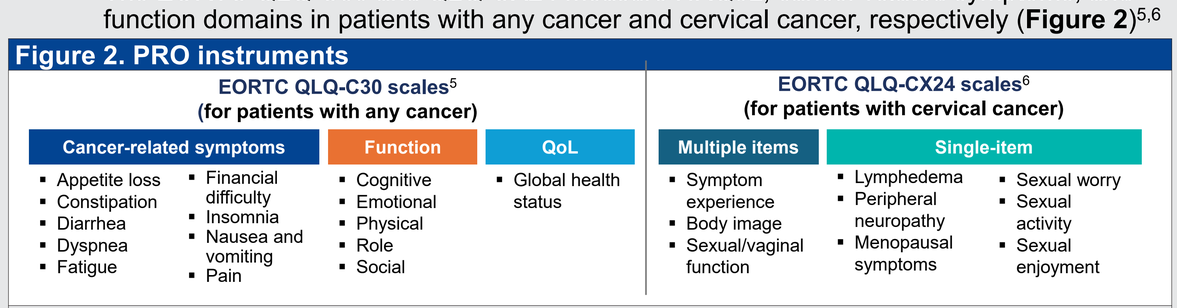


DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, EuroQOL 5-Dimension 5-Level; IC, investigator's choice; IV, intravenous; ORR, overall response rate; OS, overall survival; PD-(L)1, programmed death (ligand) 1; PFS, progression-free survival; PRO, patient-reported outcomes; Q3W, every 3 weeks; QLQ-C30, Quality of Life Questionnaire-C30; QLQ-CX24, Quality of Life Questionnaire-Cervical Cancer Module; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response; TV, tisotumab vedotin; VAS, visual analog scale.
ClinicalTrials.gov ID, NCT04697628.
[a]Randomization was stratified according to ECOG PS score, previous receipt of bevacizumab, geographic region (United States, Europe, Asia, or other), and previous receipt of an anti–PD-[L]-1 agent.

PRO outcomes

- Assessment of PROs was a secondary endpoint in the trial. Patients were administered questionnaires from several PRO instruments, including European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-CX24
  - The EORTC QLQ-C30 and QLQ-CX24 measure HRQoL, cancer-related symptoms, and function domains in patients with any cancer and cervical cancer, respectively (**Figure 2**)[5,6]

Figure 2. PRO instruments



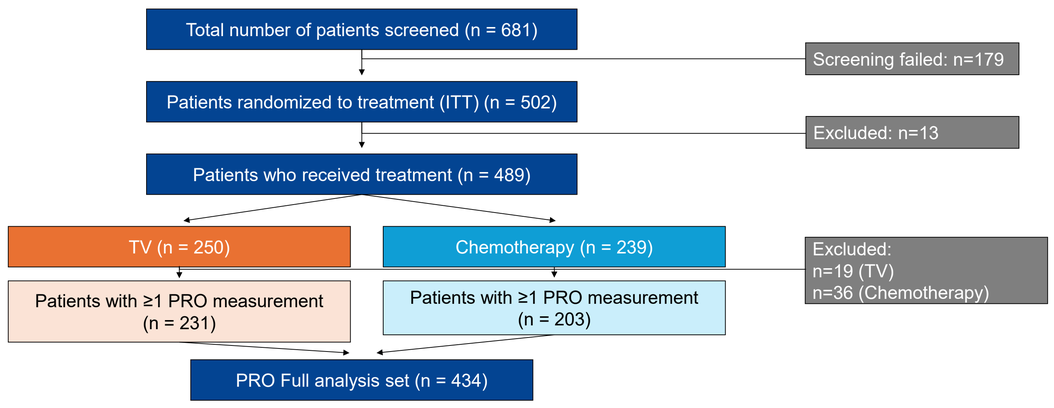
EORTC, European Organisation for Research and Treatment of Cancer; QLQ-C30, Quality of Life Questionnaire-C30; QLQ-CX24, Quality of Life Questionnaire-Cervical Cancer Module; QoL, quality-of-life.

- In this post-hoc analysis, average health-related quality of life (HRQoL) at each cycle and change from baseline (until cycle 13) were assessed using a mixed model for repeated measures
- Time to clinically meaningful deterioration was evaluated using a Cox proportional hazards model
  - Consistent with reported precedents in the literature,[7,8] a >10-point change from baseline was considered to be clinically meaningful
- Analyses were adjusted for baseline ECOG PS, prior bevacizumab, and prior anti–PD-1/PD-L1 therapy

Results

- The PRO full analysis set consisted of 231 patients who received tisotumab vedotin and 203 patients who received chemotherapy (**Figure 3**)
- Patients in the PRO full analysis set were in the study for a median of 250 days

Figure 3. Patient flow diagram



PRO, patient-reported outcomes; ITT, intention-to-treat; TV, tisotumab vedotin.

- The weighted mean compliance rate for the EORTC QLQ-C30 questionnaire from baseline to Cycle 13 was 85.9% (range, 92.0% to 81.3%) for the tisotumab vedotin arm and 83.9% (range, 75.2% to 94.1%) for the chemotherapy arm (**Table 1**)

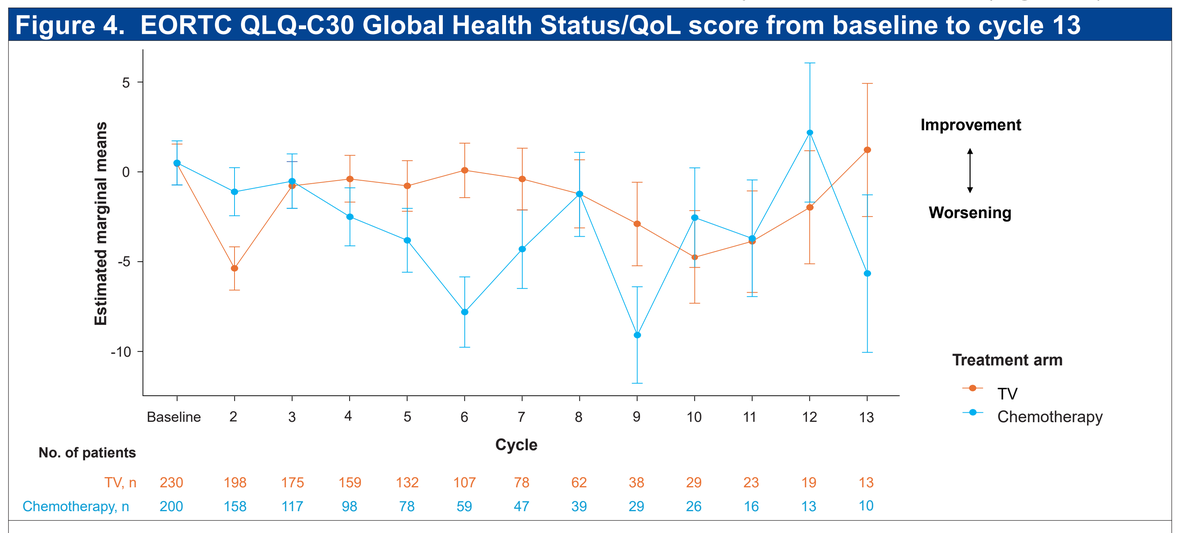
Table 1. EORTC QLQ-C30 assessment rates from baseline to cycle 13

	TV (n=231)			Chemotherapy (n=203)		
	N	Compliance rate[a] (%)	Completion rate[b] (%)	N	Compliance rate[a] (%)	Completion rate[b] (%)
Baseline	230	92.0	92.0	200	83.7	83.7
Cycle 2	198	83.5	79.2	158	75.2	66.1
Cycle 3	175	85.4	70.0	117	78.0	49.0
Cycle 4	159	89.8	63.6	98	79.7	41.0
Cycle 5	132	91.0	52.8	78	80.4	32.6
Cycle 6	107	89.9	42.8	59	80.8	24.7
Cycle 7	78	87.6	31.2	47	79.7	19.7
Cycle 8	62	93.9	24.8	39	84.8	16.3
Cycle 9	38	84.4	15.2	29	85.3	12.1
Cycle 10	29	90.6	11.6	26	92.9	10.9
Cycle 11	23	82.1	9.2	16	94.1	6.7
Cycle 12	19	90.5	7.6	13	92.9	5.4
Cycle 13	13	81.3	5.2	10	83.3	4.2

[a]Defined as the number of completed questionnaires divided by the number of patients at each visit. [b]Defined as the number of completed questionnaires divided by the number of patients in the intention-to-treat population. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30; TV, tisotumab vedotin.

- Global health status/QoL was maintained from baseline to cycle 13 in both arms (**Figure 4**)

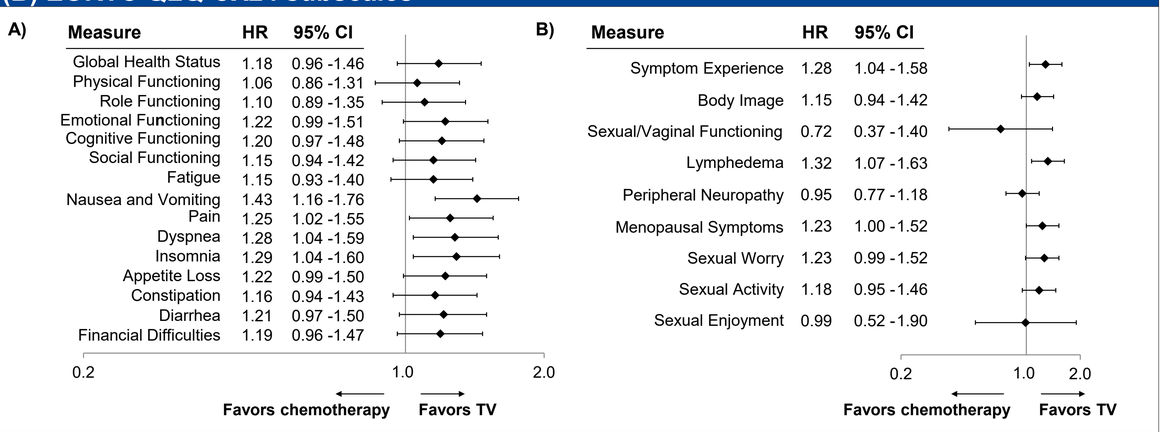
Figure 4. EORTC QLQ-C30 Global Health Status/QoL score from baseline to cycle 13



Higher scores represent a higher quality of life. EORTC, European Organisation for Research and Treatment of Cancer; QLQ-C30, Quality of Life Questionnaire-C30; QoL, quality-of-life; TV, tisotumab vedotin.

- Median time to clinically meaningful deterioration (≥10-point change)[a] was longer with tisotumab vedotin compared with chemotherapy across most of the key domains for QLQ-C30 and QLQ-CX24 (**Figure 5**)

Figure 5. Forest plots for time to deterioration of (A) EORTC QLQ-C30 subscales and (B) EORTC QLQ-CX24 subscales



EORTC, European Organisation for Research and Treatment of Cancer; HR, hazard ratio; QLQ-C30, Quality of Life Questionnaire; QLQ-CX24, Quality of Life Questionnaire-Cervical Cancer Module; QoL, quality-of-life; TV, tisotumab vedotin. [a]Clinically meaningful deterioration was defined as a ≥10-point change from baseline, progression or death.

References: 1. FDA approves tisotumab vedotin-tftv for recurrent or metastatic cervical cancer. FDA. Accessed September 1 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisotumab-vedotin-tftv-recurrent-or-metastatic-cervical-cancer. 2. Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 27-30 January 2025. EMA. Accessed September 1 2025. https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-chmp-27-30-january-2025. 3. TIVDAK® (tisotumab vedotin) approved by Japan Ministry of Health, Labour and Welfare for the treatment of advanced or recurrent cervical cancer that has progressed on or after chemotherapy. Genmab. Accessed September 1 2025. https://ir.genmab.com/news-releases/news-release-details/tivdakr-tisotumab-vedotin-approved-japan-ministry-health-labour. 4. Vergote I, et al. N Engl J Med 2024;391:44-55.5. Kaasa S, et al. Eur J Cancer. 1995;31a: 2260-3. 6. Greimel ER, et al. Cancer. 2006;107: 1812-22. 7. King MT. Qual Life Res. 1996;5: 555-67.8. Osoba D, et al. J Clin Oncol. 1998;16: 139-44.

Acknowledgments: The authors thank all patients who participated in the innovaTV 301 study, their families and caregivers, and the investigators and research staff at all innovaTV 301 clinical sites, the European Network of Gynaecological Oncological Trial Groups (ENGOT) and Gynecologic Oncology Group (GOG). This study was sponsored by Seagen Inc. (acquired by Pfizer in December 2023) and Genmab, the codevelopers of tisotumab vedotin. Medical writing assistance funded by Pfizer according to Good Publication Practice guidelines was provided by Radhika Das Chakraborty, PhD, of Nucleus Global, an Inizio Company.

Disclosures: The presenter (Dr Scott Jordan) has been a speaker for Pfizer/Genmab, GSK, AstraZeneca; an advisor for GSK, AstraZeneca, Karyopharm; and has received medical writing support from Pfizer

Contact: sjordan@browardhealth.org

Copyright © 2025.

Presented at the 2025 ICGS Annual Meeting | November 5- 7, 2025 | Cape Town, South Africa

Electronic Poster
An electronic version of this poster may be obtained by scanning this QR code with your smartphone. If you do not have a smartphone, access the poster via the internet at:
https://scientificpubs.congressposter.com/p/w034gsntb8dj5n7g