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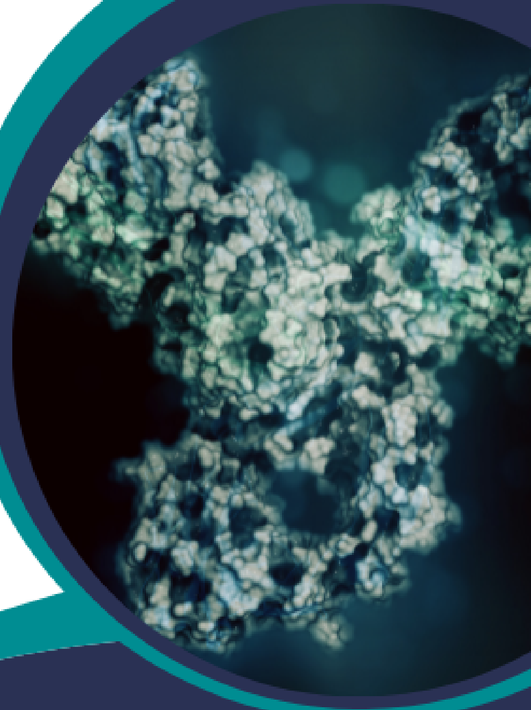
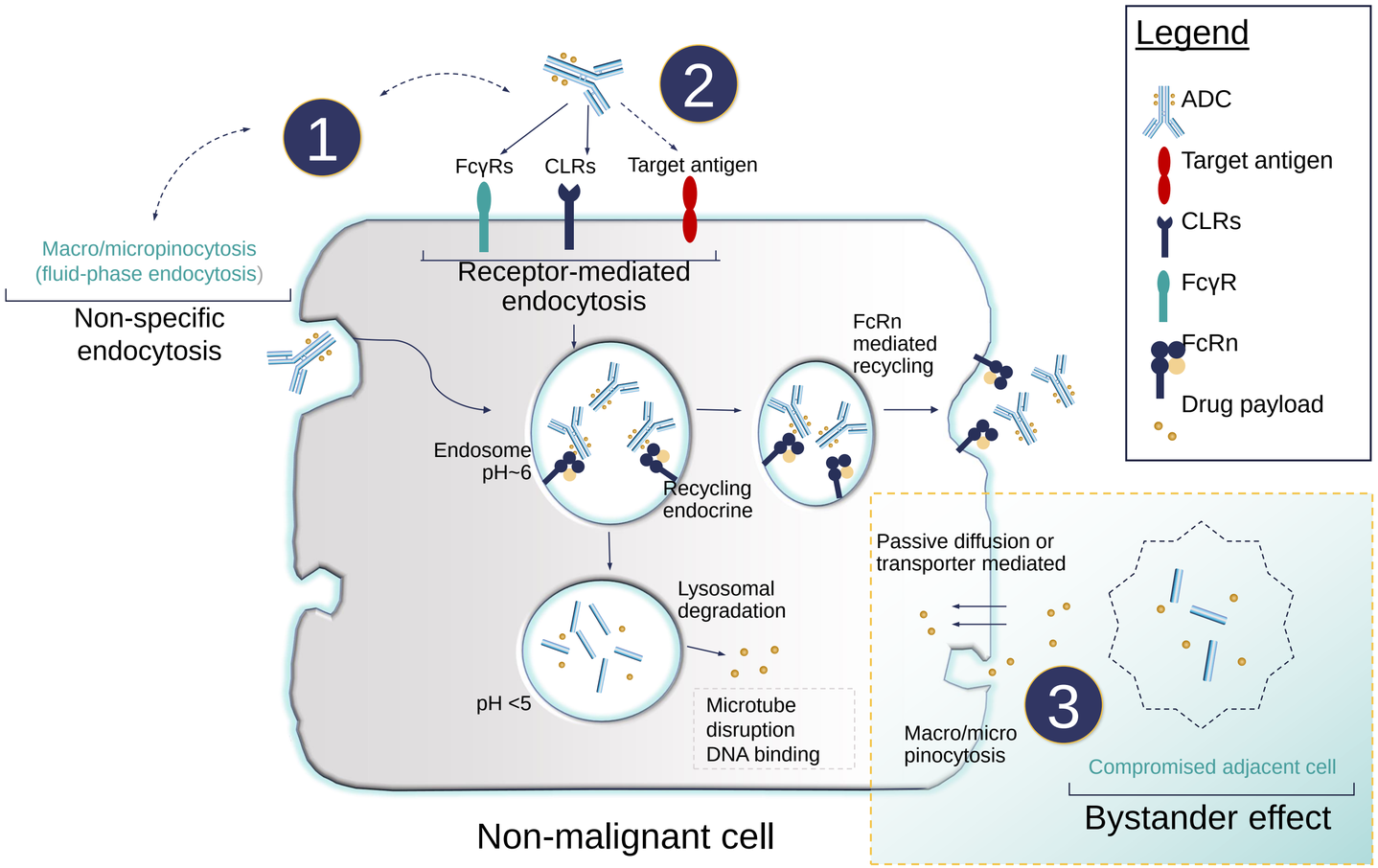
SEOUL IGCS 2023

Patient-Focused Treatment Quality of Life with ADCs: The ABCs of ADCs for Patient Care

Linda Duska, MD, MPH



Potential mechanisms of toxicity associated with ADCs



1. **Target-independent toxicity:** ADC uptake into nonmalignant cells
   - Nonspecific endocytosis
   - Macropinocytosis and micropinocytosis
   - Binding to Fc receptors
2. **On-target, off-tumor toxicity:** target antigen may be expressed on normal cells and contribute to target antigen–dependent uptake of ADCs
3. **Bystander effect (off-target, off-tissue toxicity):** membrane-permeable drug payloads diffuse from target cell into neighboring cells
   - May be beneficial if the neighboring cell is cancerous, or detrimental if neighboring cell is healthy

Microtubule inhibitor	Commonly reported clinical toxicity
MMAE	Anemia, neutropenia, and peripheral neuropathy
DM1	Thrombocytopenia and hepatotoxicity
MMAF and DM4	Ocular toxicity

ADC, antibody-drug conjugate; CLR, C-type leptin receptor; DM1, maytansine 1; DM4, maytansine 4; FcRn, neonatal Fc receptor; FcγR, Fc gamma receptor; MMAE, monomethyl auristatin E; MMAF, monomethyl auristatin F.

Mahalingaiah PK et al. *Pharmacol Ther*. 2019;200:110–125.

Common toxicities observed with select approved ADCs

Hematologic	GI	Peripheral neuropathy	Ocular toxicity	Pulmonary toxicity	Cardiotoxicity
Thrombocytopenia	Nausea	Weakness	Blurred vision	Epistaxis	LVEF decline
Neutropenia	Vomiting	Numbness	Dry eye	Fatigue	
Anemia	Diarrhea	Pain	Decreased visual acuity		
Leukopenia	Decreased appetite		Blurred vision		
Febrile neutropenia	Constipation		Conjunctivitis		
	Abdominal pain				

Overall incidents of TRAEs 91% for all grade events, 46% for great than or equal to Grade 3.

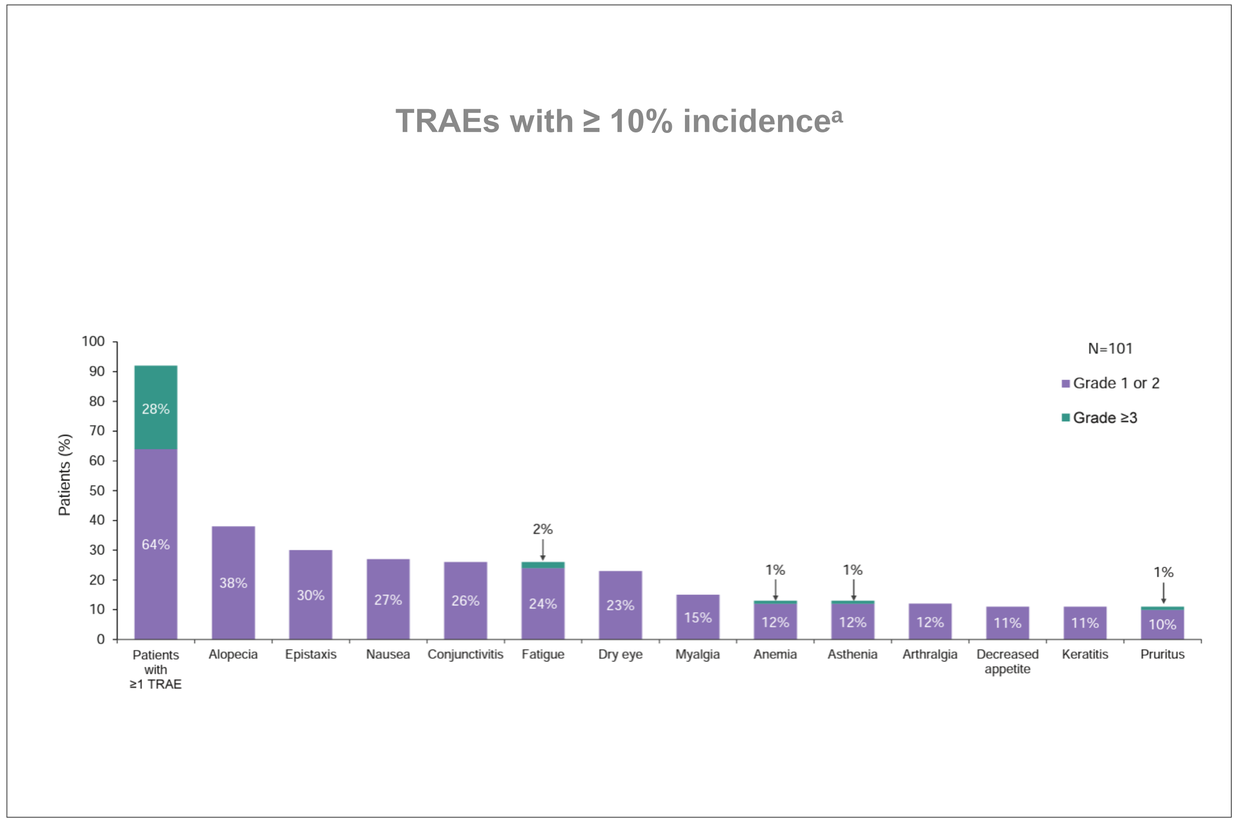
Most common; hematologic, nausea, blurred vision, and peripheral neuropathy.

ADC, antibody-drug conjugate; GI, gastrointestinal; LVEF, left ventricular ejection fraction.

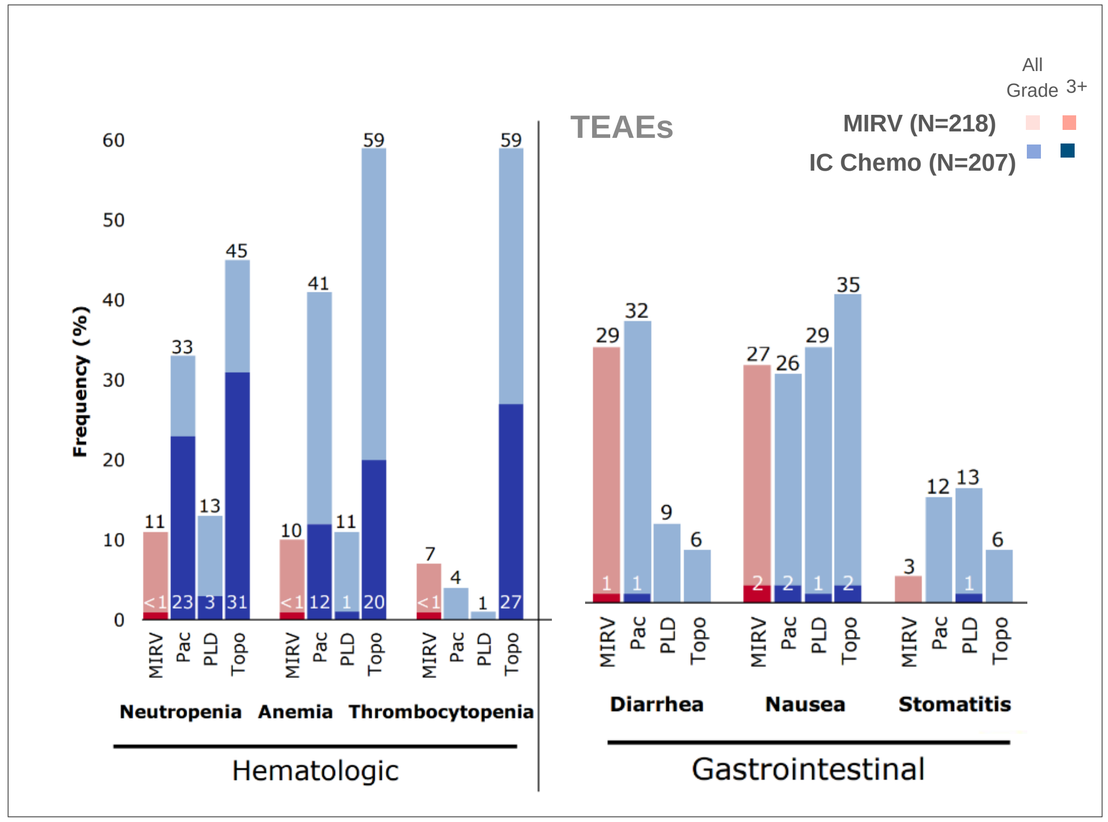
Nguyen TD et al. *Cancers (Basel).* 2023;15(3):713.

Differentiated safety profile observed with approved ADCs

Tisotumab vedotin (InnovaTV 204)[1]



Mirvetuximab soravtansine (MIRASOL)[2]



Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months. Median duration of treatment: 4.2 months (range, 1–16).[1] Data cutoff: March 6, 2023.[2]

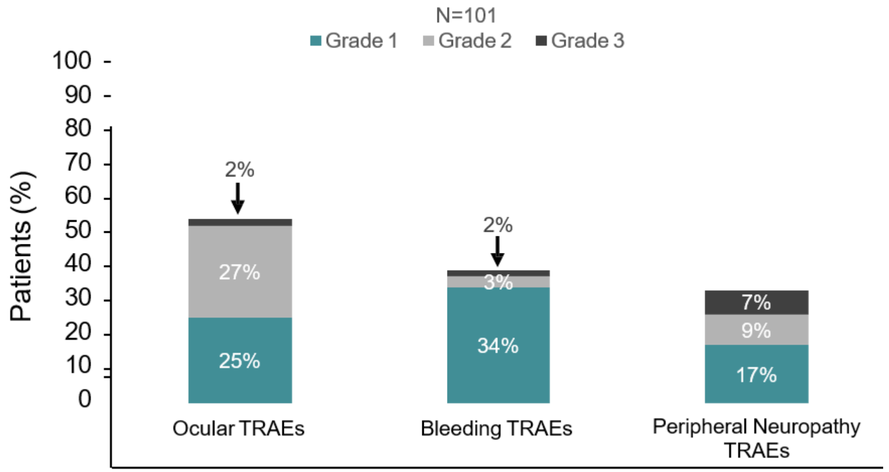
[a]Any-grade AEs included if ≥10%.

ADC, antibody-drug conjugates; IC Chemo: investigator's choice chemotherapy; MIRV, mirvetuximab soravtansine; Pac, paclitaxel; PLD, pegylated liposomal doxorubicin; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; Topo, topotecan.

1. Coleman RL et al. Presented at ESMO 2020. Abstract LBA 32. 2. Gorp TV et al. Poster presented at ESGO 2023. Abstract 1015.

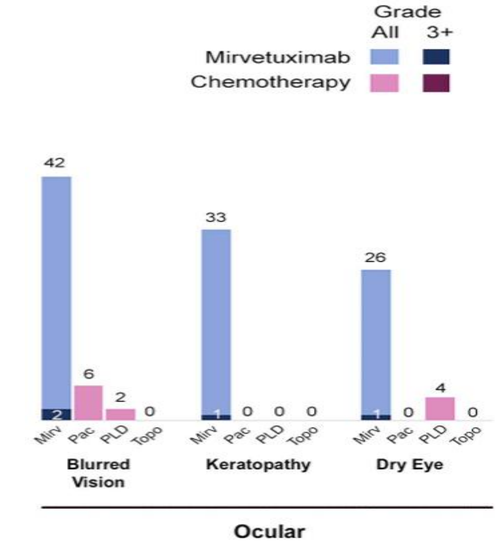
Toxicity observed with approved ADCs in gynecologic oncology

Tisotumab vedotin (InnovaTV 204) – Ocular,[a] bleeding,[b] and peripheral neuropathy[c] TRAEs[1]



	Ocular	Bleeding	Peripheral Neuropathy
Time to onset (median, months)	1.4	0.3	3.1
Events resolved, %	86	90	21
Time to resolution[d] (median, months)	0.7	0.5	0.6

Mirvetuximab soravtansine (SORAYA) - Ocular TRAEs[2,3]



	Integrated Safety Population (N=464)		SORAYA* (N=106)	
Adverse event	All Grade, n (%)	Grade ≥3, n (%)	All Grades, n (%)	Grade ≥3, n (%)
Alopecia	3 (<1)	0	1 (<1)	0
Neuropathy peripheral	64 (14)	4 (<1)	14 (13)	0
Peripheral sensory neuropathy	36 (8)	4 (<1)	4 (4)	2 (2)
Peripheral motor neuropathy	4 (<1)	1 (<1)	2 (2)	1 (<1)
Paresthesia	21 (5)	0	5 (5)	0
Anemia	43 (9)	4 (<1)	8 (8)	1 (<1)
Thrombocytopenia	43 (9)	1 (<1)	10 (9)	2 (2)
Neutropenia	35 (8)	2 (<1)	14 (13)	2 (2)

Data cutoff (tisotumab Vedotin): February 6, 2020. Median duration of follow-up: 10.0 months.[1]

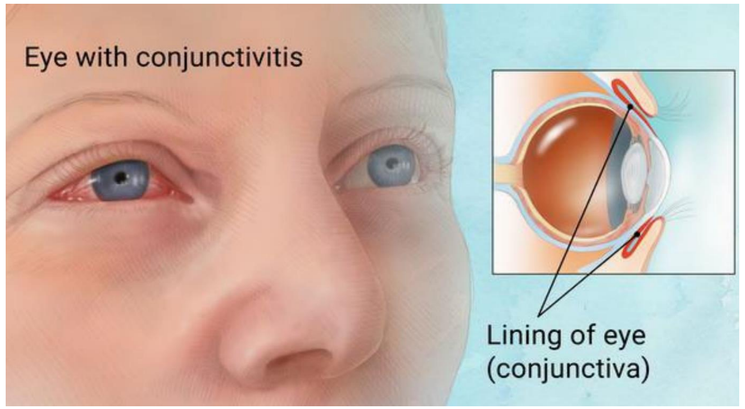
[a]Any ocular SMQ (conjunctival disorders SMQ, corneal disorders SMQ, scleral disorders SMQ, retinal disorders SMQ, periorbital and eyelid disorders SMQ, ocular infections SMQ, optic nerve disorders SMQ, glaucoma SMQ, lacrimal disorders SMQ, and eye disorders SMQ). [b]Hemorrhage SMQ. [C]Peripheral neuropathy SMQ. [d]Assessment limited by the protocol-defined follow-up period for AE of only 30 days after the last dose.

ADC, antibody-drug conjugate; AE, adverse event; Mirv, mirvetuximab soravtansine; Pac, paclitaxel; PLD, pegylated liposomal doxorubicin; Topo, topotecan; TRAE, treatment-related adverse event.

1. Coleman RL et al. Presented at ESMO 2020. Abstract LBA 32. 2. Moore K et al. Poster presented at ASCO Annual Meeting 2022. Abstract 5574; 3. Hendershot A. et al. *Gynecol Oncol Rep.* 2023:47:101155.

Ocular TRAEs – Tisotumab vedotin

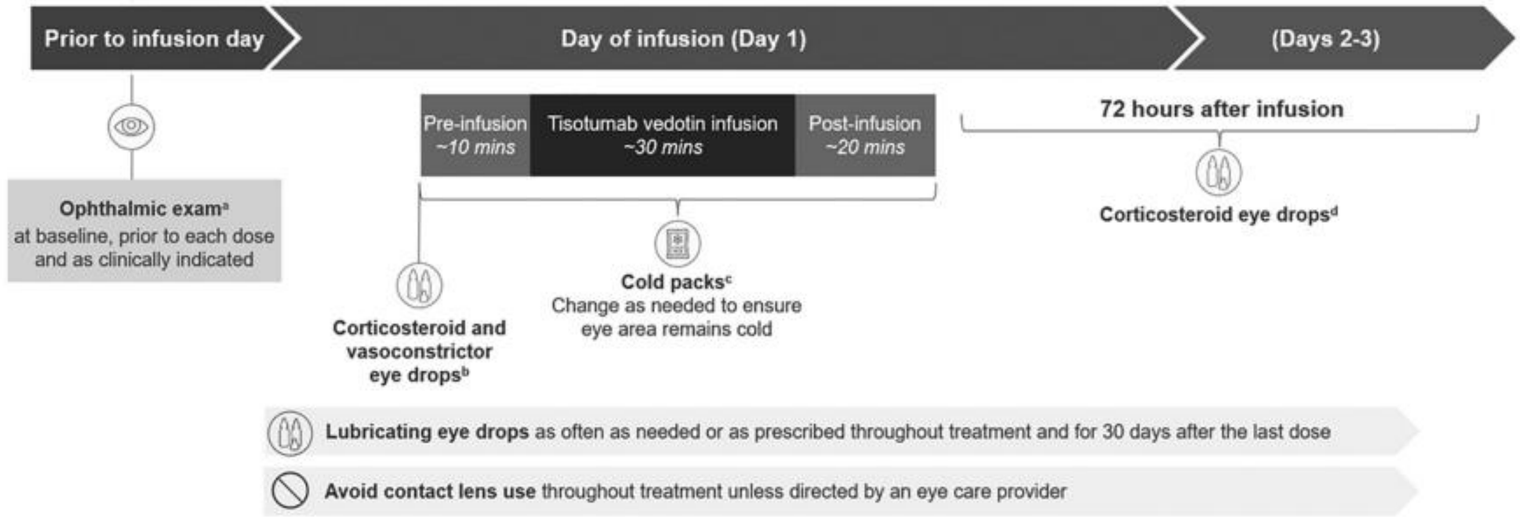
TRAE – conjunctivitis[1]



Ocular adverse events regardless of causality		
Incidence, n (%)	**N=101**	
	Any grade	**Grade 3**
Patients with ≥1 ocular AE	55 (54)	3 (3)
Ocular AE in ≥5 patients		
Conjunctivitis	31 (31)	0
Dry eye	25 (25)	0
Keratitis	11 (11)	0
Blepharitis	7 (7)	0
Punctate keratitis	6 (6)	0

Mitigation strategy[2]

- 5% of patients discontinued treatment due to ocular TEAEs
- 20% of patients required dose reductions due to ocular TEAEs
- The only Grade 3 ocular TEAE was ulcerative keratitis (3%)



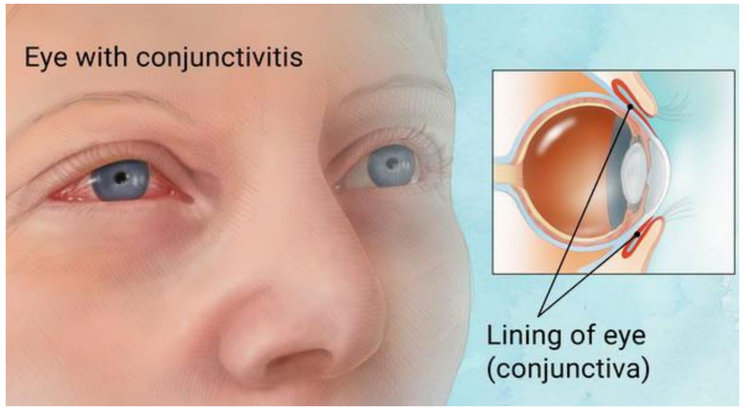
[a]Prior to infusion day, an eye care provider should conduct an ophthalmic exam that includes visual acuity and slit lamp exam. [b]On the day of infusion, prior to the infusion, administer one drop of topical corticosteroid (dexamethasone 0.1% or its equivalent). Immediately before the start of infusion, administer three drops of topical vasoconstrictor (brimonidine tartrate 0.2% or its equivalent) to each eye. [c]Apply cold packs over the eye area and ensure the eye area remains cold both during and approximately 20 min after infusion. [d]For 72 h after each infusion, administer one drop of topical corticosteroid (dexamethasone 0.1% or its equivalent) three times a day, or as prescribed by an eye care provider.

AE, adverse event; TEAE, treatment-emergent adverse event.

1. Coleman RL et al. *Lancet Oncol*. 2021;22(5):609-619. 2. Kim SK et al. *Gynecol Oncol*. 2022;165(2):385-392.

Ocular TRAEs – Tisotumab vedotin mitigation and results

TRAE – conjunctivitis[1]



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Blepharitis	7 (7)	0
Punctate keratitis	6 (6)	0

Mitigation strategies[2]

Key Resources and Materials for Required Eye Care

An eye care plan based on clinical trial experience was developed to help reduce the risk of ocular adverse events with tisotumab vedotin. With these measures, ocular adverse events may be detected early on, and symptoms can be alleviated prior to impacting vision.

Access to eye care providers

- Conduct ophthalmic exam including visual acuity and slit lamp exam at baseline, prior to each dose and as clinically indicated
- Promptly refer patient to an eye care provider if new or worsening ocular symptoms occur

Eye drops ready for use

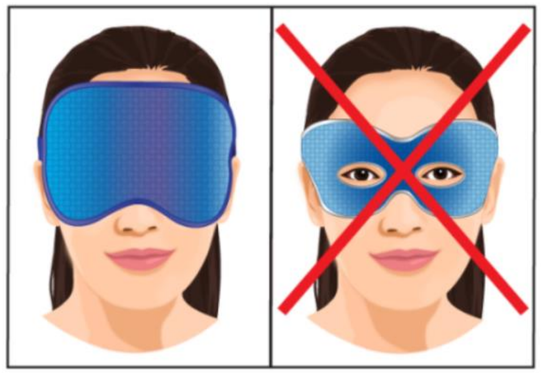
1. Topical steroid (Rx): e.g. dexamethasone 0.1%
2. Topical ocular vasoconstrictor (Rx): e.g. brimonidine tartrate 0.2%
3. Topical lubricating (OTC)

Cold packs during infusion

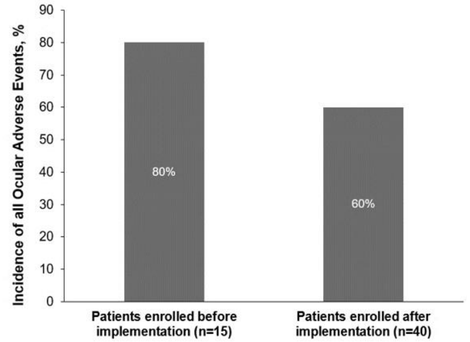
- E.g., standard chemical cold packs which reach approximately 35F
- Apply cold pack fully over eyes following administration of vasoconstrictor eye drops and leave on during the infusion
- Change cold packs as needed throughout infusion to ensure eye area remains cold

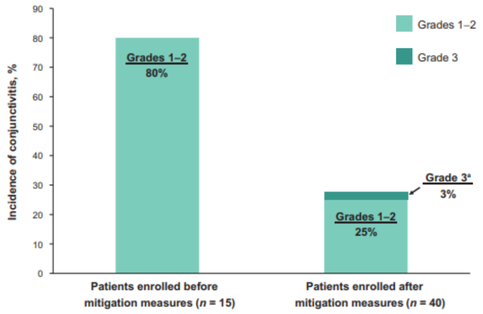
Dose modification guidelines have also been developed to manage potential ocular adverse events.

Required eye care description is based on the tisotumab vedotin US Prescribing Information.



Mitigation results[3,4]





AE, adverse event; OTC, over-the-counter; Rx, medical prescription; TRAE; treatment-related adverse events.

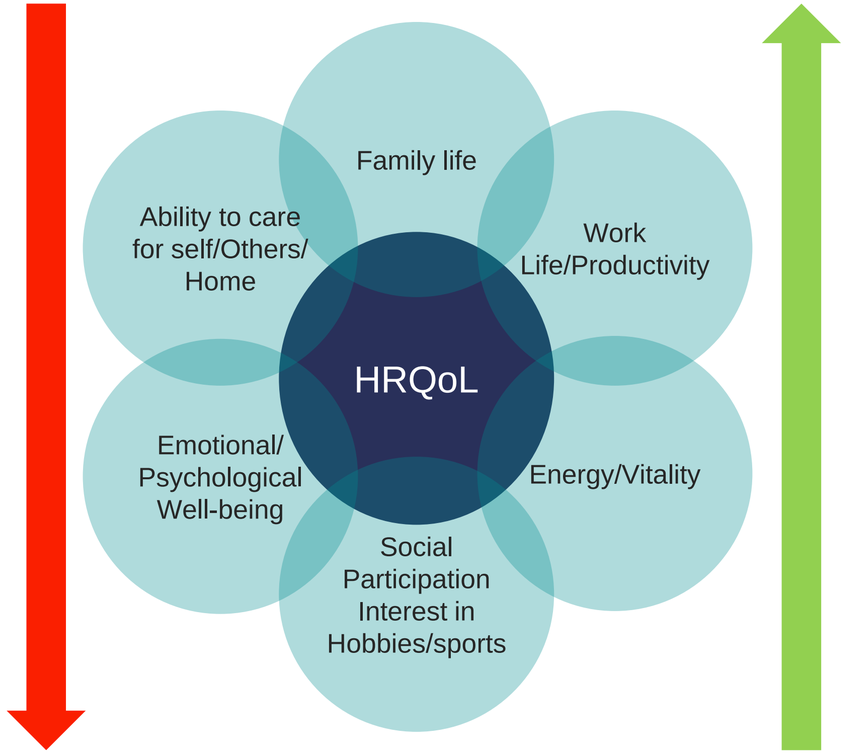
1. Coleman RL et al. *Lancet Oncol*. 2021;22(5):609-619. 2. Kim SK et al.. *Gynecol Oncol*. 2022;165(2):385-392. 3. Martin J et al. *Gynecol Oncol Rep*. 2023;45:101141. 4. Hong DS et al. *Clin Cancer Res*. 2020;26(6):1220-1228.

Importance of HRQoL in oncology

HRQoL combines physical, psychological, and social well-being with patient satisfaction in disease control and functioning

Factors that diminish HRQoL

- Symptom burden/ Progressive symptoms
- Physical impairment
- Medication side effects
- Lack of physical exercise
- Financial impact of disease
- Days off work
- Hospitalization
- Uncertainty of future health status
- Poor clinician knowledge base and poor communication
- Impediments to healthcare access



Factors that augment HRQoL

- Access to healthcare
- Good clinician communication
- Disease knowledge
- Appropriate pharmacological treatment
- Physical training/exercise
- Devices/education to accommodate disability and symptom burden
- Management of medication side effects
- Family/social support
- Development of coping skills

HRQoL, health-related quality of life.

1. Saketkoo LA et al. *Diagnostics (Basel)*. 2021;11(6):1089. 2. Sosnowski R et al. *Cent European J Urol*. 2017;70(2):206-211. 3. Mathai SC et al. *Ann Am Thorac Soc*. 2016;13(1):31-39.

Factors that affect treatment decision-making

Both disease and treatment can negatively affect HRQoL

Physical toxicity

Adverse events associated with treatment (ocular, GI, peripheral neuropathy, cardiotoxicity etc)[1-4]

Financial toxicity

Severe impact of financial burden on patients (eg, skipping medical care [treatments, follow-ups] medication nonadherence, impact on family, finances, etc.)[5]

Factors that put patients at financial risk include high-cost coverage, low socioeconomic patient background, lack of insurance, etc[5]

Time toxicity

Time spent in blood draws, infusion visits, picking up medication, clinic visits and waiting rooms, emergency department visits, hospitalizations, time in nursing/rehabilitation facilities, home-based care[6]

GI, gastrointestinal. HRQoL, health-related quality of life.

1. Masters JC et al. *Invest New Drugs*. 2018;36(1):121–135. 2. Fu Z et al. *Signal Transduct Target Ther*. 2022;7(1):93. 3. Best RL et al. *Toxicol Appl Pharmacol*. 2021;21:115534. 4. Moore KN et al. *Future Oncol*. 2018;14(2):123–136. 5. National Cancer Institute. Financial Toxicity (Financial Distress) and Cancer Treatment PDQ. Published September 2019. Accessed October 12, 2023. https://www.cancer.gov/about-cancer/managing-care/track-care-costs/financial-toxicity-pdq#_273. 6. Gupta et al. *J Clin Oncol*. 2022;40(15):1611-1615.

PROs in clinical practice in gynecologic oncology

Select list of PRO measures in clinical practice[1]

Domain	Measures	Instrument
HRQoL – General	General QoL (physical, social/family, emotional, and functional)	FACT-G SF-36 EORTC-QLQ SF-12
HRQoL – cancer specific	Ovarian specific	EORTC-QLQ-OV28
	Cervical specific	EORTC-QLQ-CX24
	Endometrial specific	FACT-EN EORTC-QLQ-EN24
Sexuality	Sexual function	FSFI SAQ
Symptom assessment	Fatigue	BFI/FAS
	Pain	BPI
Emotional well-being	Depression	CESD
	Emotional coping	Brief COPE
Relationship	Dyadic assessment	DAS
Decisional measures	Decision process	SWD

- **The EORTC-QLQ-C30 consists of multi-item scales and single-item measures as follows[2]:**
  - **5 functional scales** (physical, role, emotional, cognitive, and social functioning)
  - **3 symptom scales** (fatigue, pain, and nausea/vomiting)
  - **6 single questions** (assessing dyspnea, appetite loss, sleep disturbance, constipation, diarrhea, and the perceived financial impact of disease and treatment)
  - **GHS/QoL**
- **EORTC-QLQ-OV28** was designed for patients with local or advanced ovarian cancer who receive treatment by surgery with or without chemotherapy[2] and consists of 7 multi-item scales assessing **abdominal/GI symptoms**, **peripheral neuropathy**, other **chemotherapy side effects**, **hormonal/menopausal symptoms**, **body image, attitude to disease,** and **sexual functioning[3]**

BFI, brief fatigue inventory; BPI, brief pain inventory; CESD, center epidemiology scale depression; COPE, coping orientation to problems experienced; DAS, dyadic adjustment scale; EORTC; European Organisation for Research and Treatment of Cancer; EORTC-QLQ, EORTC quality of life questionnaire; EORTC-QLQ-C30, EORTC quality of life core 30 questionnaire; EORTC-QLQ-CX24; EORTC quality of life questionnaire-cervix module; EORT-QLQ-EN24; EORTC quality of life questionnaire-endometrial module; EORTC-QLQ-OV28, EORTC quality of life questionnaire-ovarian module; FACT-EN, functional assessment of cancer therapy-endometrial cancer subscale; FACT-G, functional assessment of cancer therapy-general; FAS, fatigue assessment scale; FSFI, female sexual function index; GHS, global health status; GI, gastrointestinal; HRQoL, health-related quality of life; PRO, patient-reported outcomes; QoL, quality of life; SAQ, sexual activity questionnaire; SF-12, short-form health survey; SF-36, short-form health survey; SWD, satisfaction with decision scale.

1. Sisodia RC et al. *Gynecol Oncol*. 2020;158(1):194-200. 2. Lenz HJ et al. *Clin Colorectal Cancer*. 2019;18(4):269-279.e5. 3. Greimel E et al. *Expert Rev Pharmacoecon Outcomes Res*. 2010;10(1):63-71.

DESTINY-Breast04, a phase 3 study of T-DXd vs physician's choice in patients with HER2-low, metastatic breast cancer: HEOR endpoints

Questionnaire	Description	Measures of interest	Analyses
EORTC QLQ-C30[a]	Oncology-specific questionnaire	• Global Health Status (GHS)/QoL[c] • Functioning scales: physical, emotional, and social • Symptom scales: pain, fatigue,[d] nausea/vomiting[d]	• Change from baseline • Time to definitive deterioration[e]
EORTC QLQ-BR23[b]	Breast cancer-specific questionnaire	• Symptom scales: arm, breast	• Change from baseline • Time to definitive deterioration[e]
EQ-5D-5L	Generic questionnaire	• Self-rated health status (VAS)[d]	• Time to definitive deterioration[e]

PRO endpoint assessment schedule[f]

Cycle 1 (Baseline)[g]	Cycle 2	Cycle 3	Every 2 cycles (cycle 5, 7, 9, etc.)	End of treatment	40-day follow-up visit	3-month follow-up visit

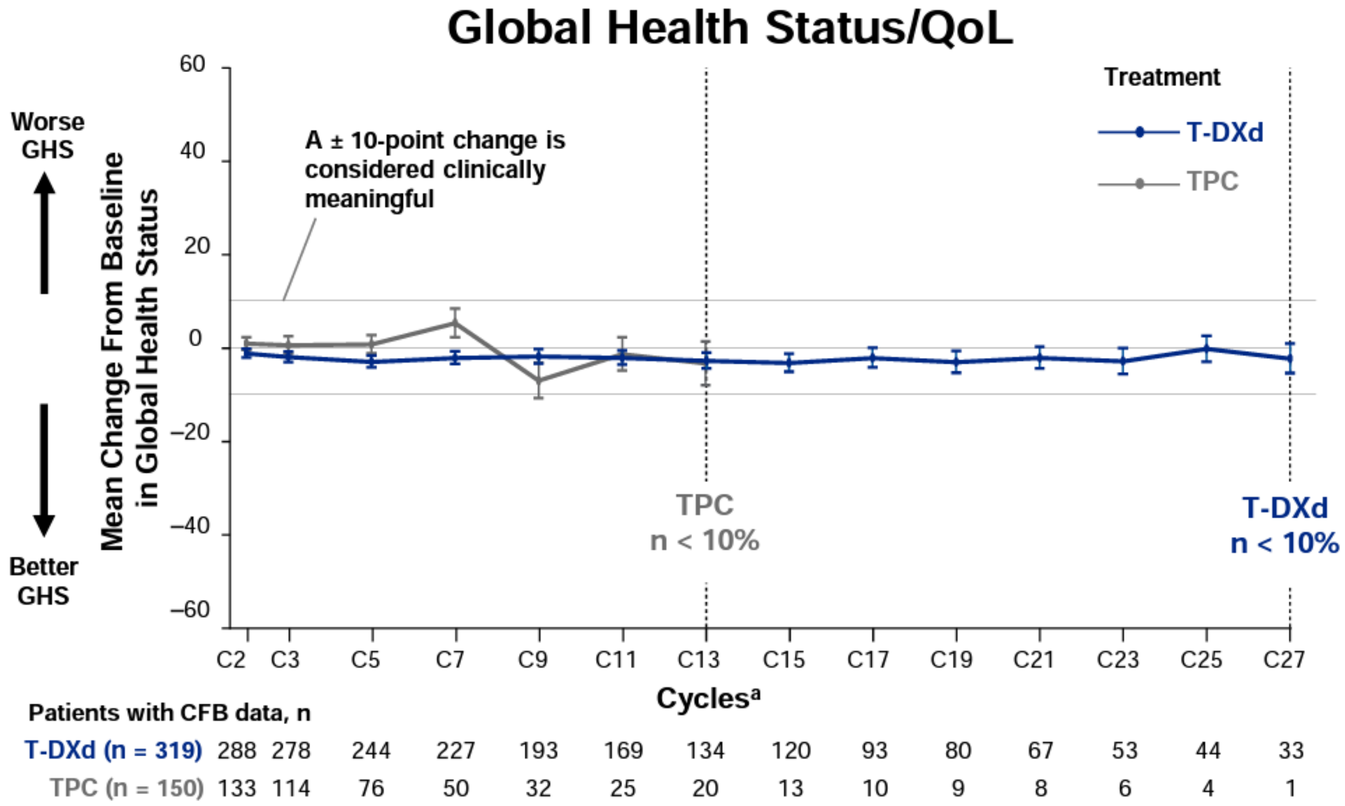
[a]Single-item scales were also assessed: dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, and financial impact. [b]Additional symptom scales assessed: body image, sexual functioning, and systemic therapy side effects. [c]PrimaryPRO variable of interest. [d]TDD of fatigue, nausea/vomiting, and EQ-5D-5L VAS were exploratory analyses. [e]Clinically meaningful definitive deterioration is defined as a change of ≥10 points from baseline at either two or more consecutive time points, last PRO assessment, or death by the first survival follow-up visit. [f]PRO assessments began before infusion on Day 1 of Cycle 1; 1 cycle = 21 days. [g]Baseline PROs were completed after patients were aware of their treatment assignment.

HER2, human epidermal growth factor receptor 2; EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L, EuroQol5-dimension, 5-level questionnaire; GHS, global health status; HEOR, health economics and outcomes research; HR, hormone receptor; PRO, patient-reported outcome; QoL, quality of life; QLQ-BR23, Quality of Life Breast cancer questionnaire; QLQ-C30, Quality of Life Core 30 questionnaire; TDD, time to definitive deterioration; T-DXd, trastuzumab deruxtecan; VAS, visual analog scale.

Ueno NT et al. Presented at ESMO 2022. Abstract 2170

DESTINY-Breast04: GHS/QoL

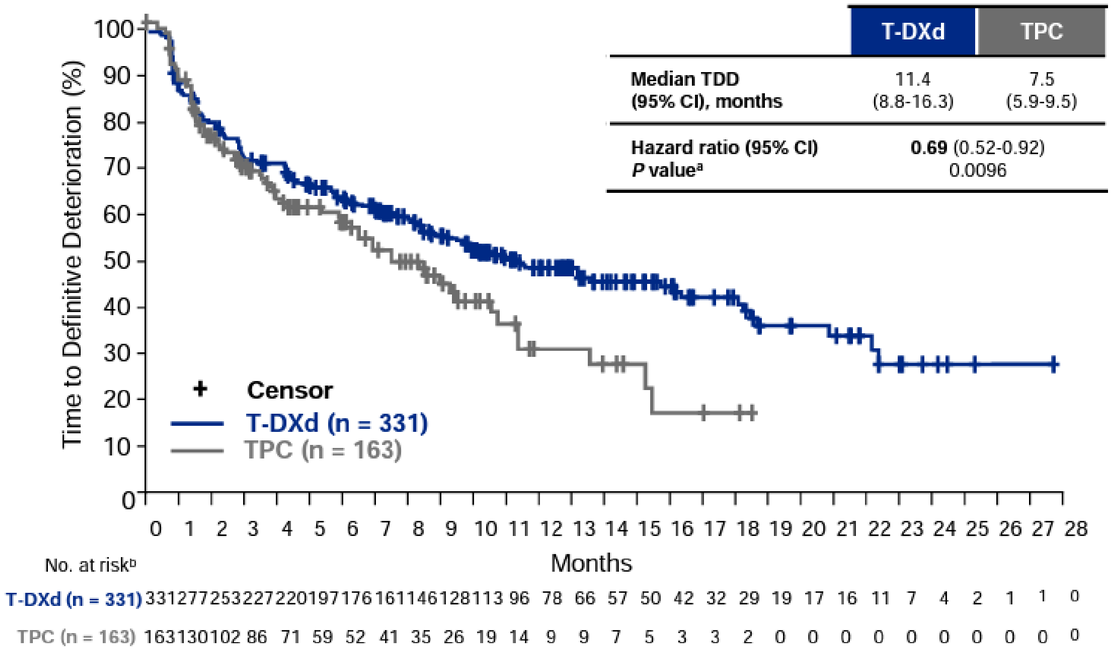
- Patient compliance for HRQoL questionnaires was >92% at baseline and >80% for cycles 2-27
- Mean ± SD baseline GHS score:
  - **T-DXd: 36.3 ± 21.8**
  - **TPC: 37.8 ± 22.5**
- Mean change from baseline for overall **GHS/QoL remained stable** (within ± 10 points) over the course of treatment with **T-DXd up to 27 cycles** and with TPC up to 13 cycles (until n <10%) patients with available CFB data, when results are no longer considered informative)



Scores range from 0 to 100; a linear transformation was applied to the raw GHS score; thus, a higher score represents lower ("worse") GHS/overall QoL.
[a]On Day 1 of Cycle 1.
C, cycle; CFB, change from baseline; GHS, global health scale; QoL, quality of life; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
Ueno NT et al. Presented at ESMO 2022. Abstract 2170

DESTINY-Breast04: GHS/QoL

GHS/QoL

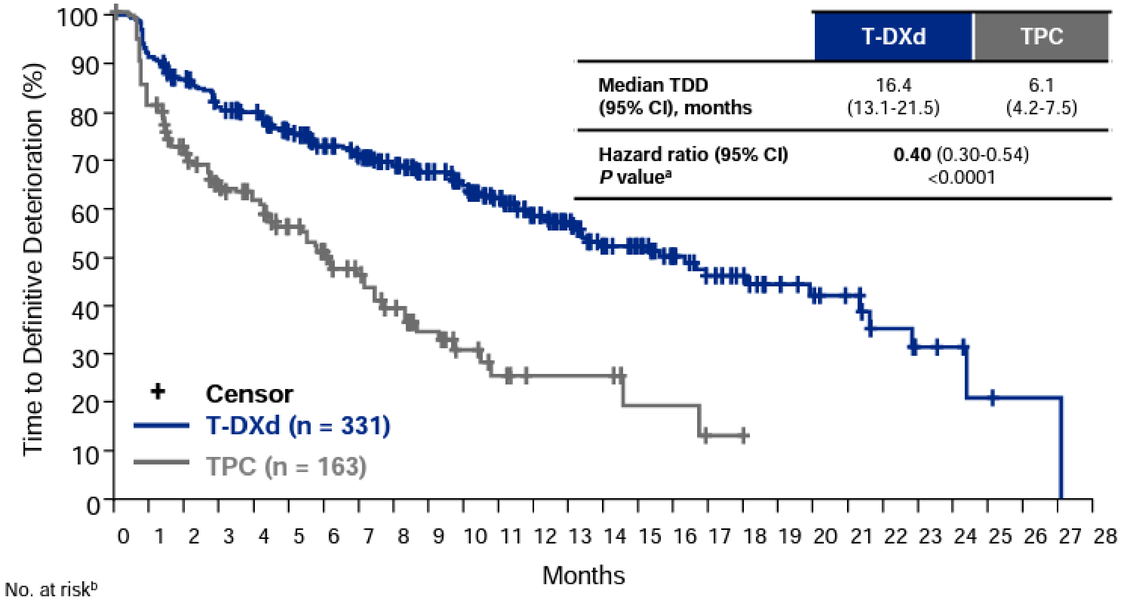


	T-DXd	TPC
Median TDD (95% CI), months	11.4 (8.8-16.3)	7.5 (5.9-9.5)
Hazard ratio (95% CI)	**0.69** (0.52-0.92)	
P value[a]	0.0096	

No. at risk[b]

T-DXd (n = 331)	331	277	253	227	220	197	176	161	146	128	113	96	78	66	57	50	42	32	29	19	17	16	11	7	4	2	1	1	0
TPC (n = 163)	163	130	102	86	71	59	52	41	35	26	19	14	9	9	7	5	3	3	2	0	0	0	0	0	0	0	0	0	0

Pain Symptoms



	T-DXd	TPC
Median TDD (95% CI), months	16.4 (13.1-21.5)	6.1 (4.2-7.5)
Hazard ratio (95% CI)	**0.40** (0.30-0.54)	
P value[a]	<0.0001	

No. at risk[b]

T-DXd (n = 331)	331	291	270	248	239	213	192	179	164	147	132	114	92	76	60	53	43	34	29	20	18	15	9	7	4	2	1	1	0
TPC (n = 163)	163	119	96	79	69	55	46	35	27	19	13	9	6	6	6	3	3	2	1	0	0	0	0	0	0	0	0	0	0

Clinically meaningful definitive deterioration is defined as a change of ≥10 points from baseline at either two or more consecutive time points, last PRO assessment, or death by the first survival follow-up visit.

[a]Nominal *P*-value not adjusted for multiple testing. [b]All patients were included in the analysis; patients without baseline assessments were censored per the statistical analysis plan.

GHS, global health status; PRO, patient-reported outcome; QoL, quality of life; QLQ-C30, Quality of Life Core 30 questionnaire; TDD, time to definitive deterioration; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Ueno NT et al. Presented at ESMO 2022. Abstract 2170

DESTINY-Breast04: Time to definitive deterioration in PRO measures of interest

		Median (95% CI) TDD, months		Hazard Ratio (95% CI)	*P* Value[d]
		T-DXd (n = 331)	TPC (n = 163)		
EORTC QLQ-C30	Global health status/QoL[a]	11.4 (8.8-16.3)	7.5 (5.9-9.5)	0.69 (0.52-0.92)	0.0096
	Pain symptoms	16.4 (13.1-21.5)	6.1 (4.2-7.5)	0.40 (0.30-0.54)	<0.0001
	Physical functioning[b]	16.6 (11.3-21.5)	7.5 (4.9-9.5)	0.53 (0.40-0.70)	<0.0001
	Emotional functioning[b]	19.2 (16.3-24.5)	10.5 (7.1-NE)	0.69 (0.50-0.96)	0.0266
	Social functioning[b]	12.8 (10.4-15.2)	6.0 (4.4-7.7)	0.59 (0.45-0.77)	0.0001
	Fatigue[c]	11.1 (7.2-12.4)	4.5 (3.1-6.2)	0.61 (0.47-0.79)	0.0002
	Nausea and vomiting[c]	5.7 (3.8-8.4)	9.3 (7.5-17.1)	1.46 (1.09-1.96)	0.0128
EORTC QLQ-BR23	Arm symptoms[b]	14.4 (11.9-23.0)	8.7 (5.6-NE)	0.62 (0.45-0.85)	0.0027
	Breast symptoms[b]	NE (24.7-NE)	NE (NE-NE)	0.71 (0.50-1.01)	0.1008
EQ-5D-5L	VAS[b,c]	12.0 (9.9-15.2)	6.8 (4.9-11.4)	0.73 (0.54-0.97)	0.0288

Similar TDD results were observed among all patient cohort in PRO measures of interest

Clinically meaningful definitive deterioration is defined as a change of ≥10 points from baseline at either two or more consecutive time points, last PRO assessment, or death by the first survival follow-up visit.

[a]Primary PRO variable of interest. [b]Secondary PRO variable of interest. [c]TDD of fatigue, nausea/vomiting, and EQ-5D-5L VAS were exploratory analyses; [d]Nominal *P*-value not adjusted for multiple testing.

EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L, EuroQol5-dimension, 5-level questionnaire; NE, not estimable; PRO, patient-reported outcome; QLQ-BR23, Quality of Life Breast cancer questionnaire; QLQ-C30, Quality of Life Core 30 questionnaire; QoL, quality of life; TDD, time to definitive deterioration; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice; VAS, visual analog scale.

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FORWARD I, a phase 3 study of MIRV vs chemotherapy in ovarian cancer (GOG 3011): HEOR endpoints

The phase 3, open-label, randomized trial FORWARD I (N=366; NCT02631876) enrolled patients with platinum-resistant FRα-positive advanced EOC

PRO Assessments

- EORTC QLQ-C30 (C30) – measures functional domains, symptoms, and global QoL/health status
- EORTC QLQ-OV28 (OV28) – Developed to augment the C30
- FOSI – Measure of symptom response to treatment

PRO Analyses

Primary

- MID response in abdominal/GI symptoms at week 8/9 by OV28 Abdominal/GI symptom subscale score:
- ≥15-point increase: Improved
- <15-point increase: Not improved

Secondary

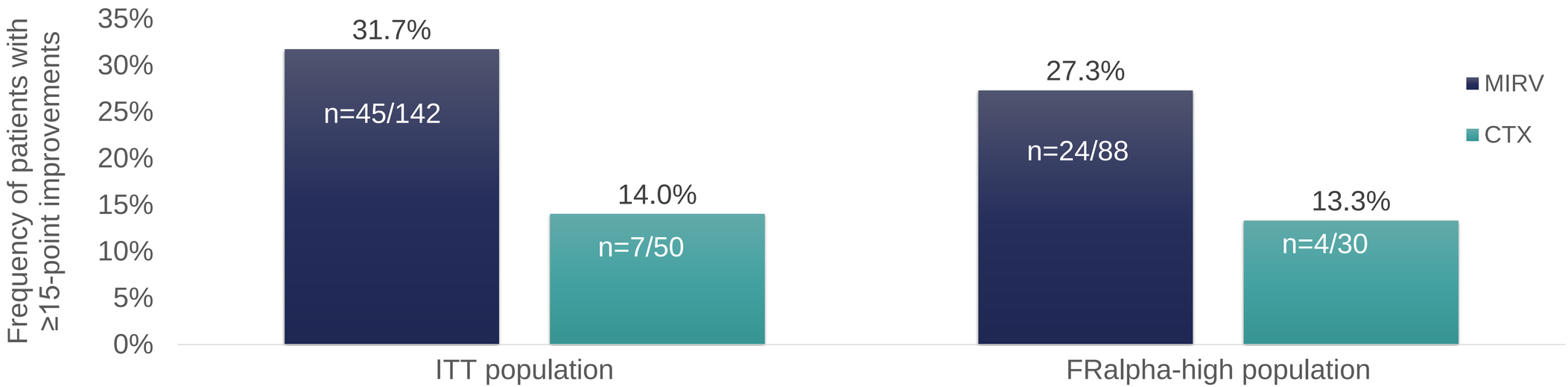
- Time to symptom worsening

C30, EORTC Quality of Life Questionnaire-core 30; EOC, epithelial ovarian cancer; EORTC, European Organisation for Research and Treatment of Cancer; FOSI, Functional Assessment of Cancer Therapy – Ovarian Symptom Index; FRα; folate receptor alpha; GI, gastrointestinal; HEOR, health economics and outcomes research; MID, minimally important difference; MIRV, mirvetuximab soravtansine; OV28, EORTC Quality of Life Questionnaire-Ovarian Cancer Module; PRO, patient-reported outcome; QoL, quality of life.

Moore KN et al. Poster presented at ESMO Congress 2022. Poster 532P.

FORWARD 1 (GOG 3011): patients with ≥15-point improvements in OV28 abdominal/GI scale

Improvement in the OV28 Abdominal/GI Symptom Subscale by Treatment Group at Week 8/9



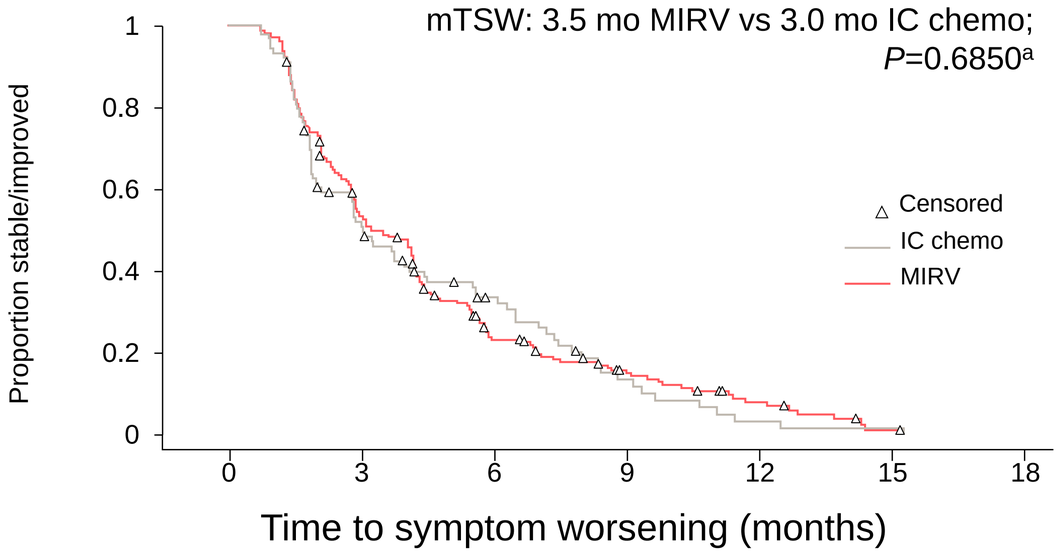
The proportion of patients with a ≥15-point improvement on the OV28 Abdominal/GI scale at week 8/9 was significantly higher in the MIRV ITT group vs IC chemo

CTX, chemotherapy; EORTC, European Organisation for Research and Treatment of Cancer; FR, folate receptor; GI, gastrointestinal; IC chemo, investigator-chosen chemotherapy; MIRV, mirvetuximab soravtansine; OV28, EORTC Quality of Life Questionnaire-Ovarian Cancer Module.

Moore KN et al. Poster presented at ESMO Congress 2022. Poster 532P.

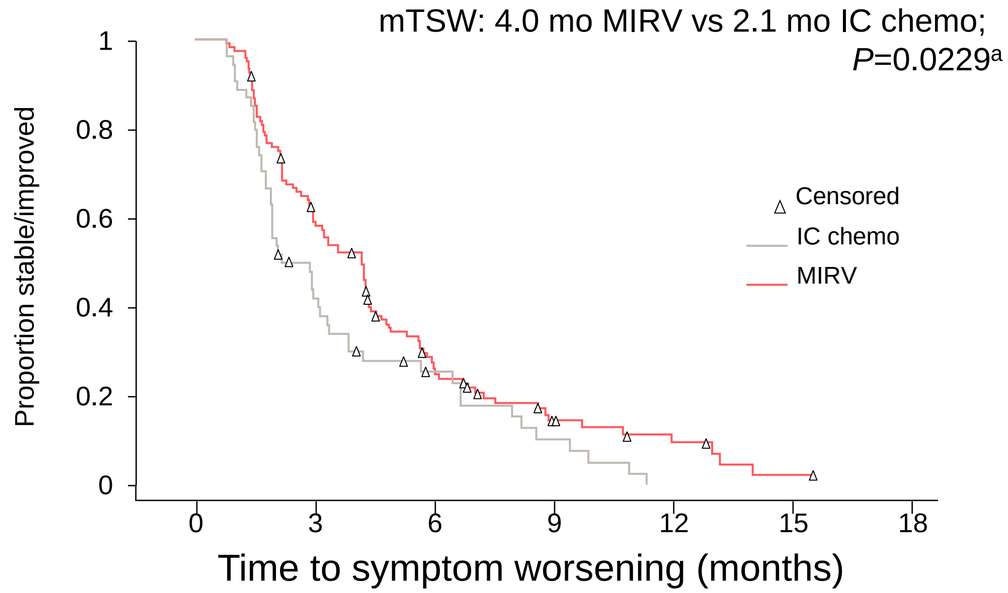
FORWARD 1 (GOG 3011): Time-to-Symptom worsening on OV28 abdominal/GI scale

Time-to-symptom worsening on OV28: ITT population



IC chemo	89	43	23	8	2	1	0
MIRV	205	106	41	21	9	1	0

Time-to-symptom worsening on OV28: FRα population



IC chemo	54	20	10	4	0		
MIRV	121	68	24	9	5	1	0

MIRV showed a nearly 2-month longer median TSW on the OV28 Abdominal/GI Symptom Subscale compared to IC chemo; no significant difference observed between the groups in ITT

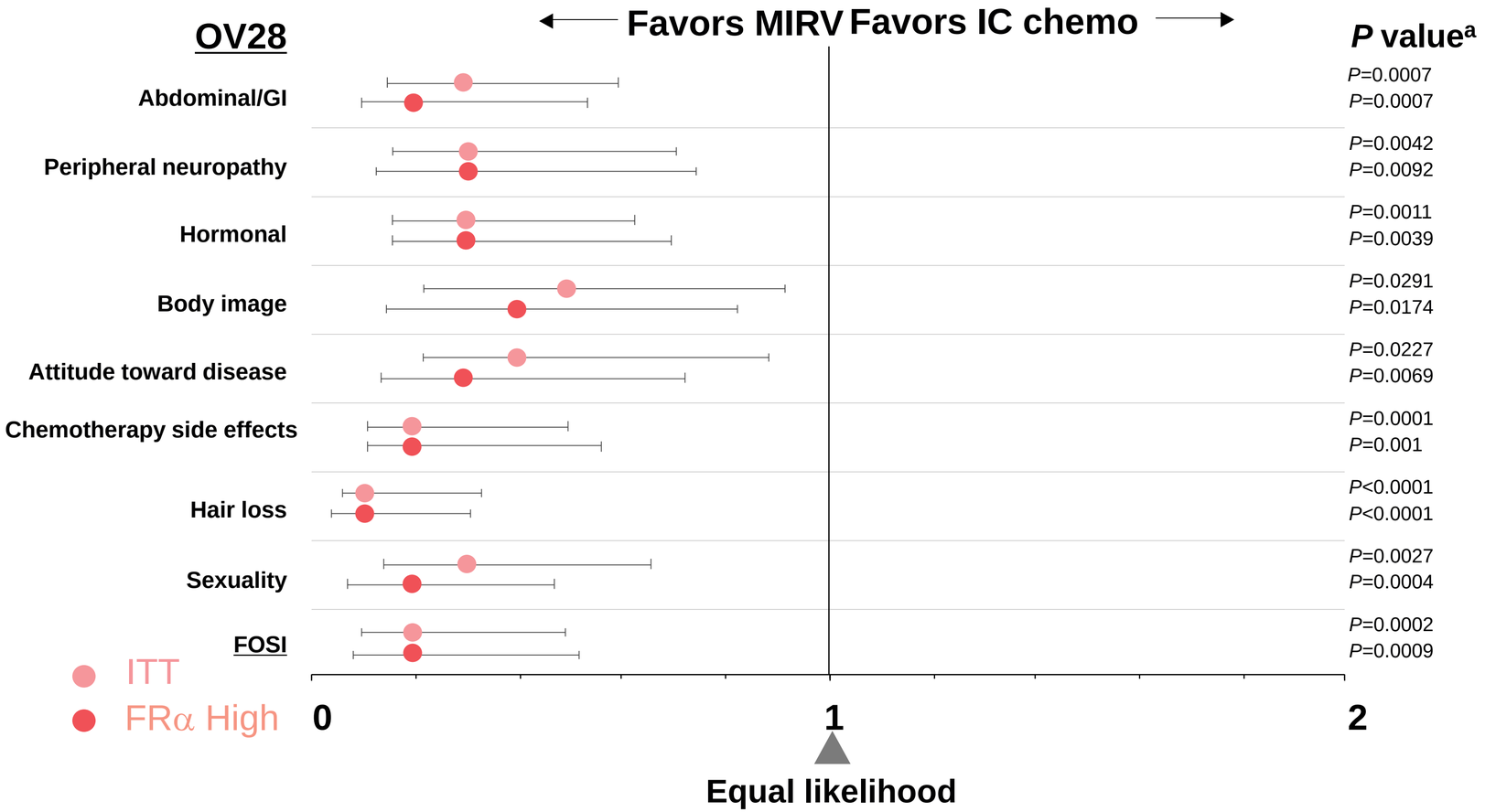
[a]P value based on stratified log-rank test using randomization stratification factors.

EORTC, European Organisation for Research and Treatment of Cancer; FRα, folate receptor alpha; GI, gastrointestinal; IC chemo, investigator's choice of chemotherapy; ITT, intention to treat; MIRV, mirvetuximab soravtansine; mTSW, median time to symptom worsening; OV28, EORTC Quality of Life Questionnaire-Ovarian Cancer Module.

Moore KN et al. Poster presented at ESMO Congress 2022. Poster 532P.

FORWARD 1 (GOG 3011): likelihood of symptom deterioration

Odds ratios for categorical change on the OV28 and FOSI: MIRV vs IC chemo in the longitudinal period population



In comparison to IC chemotherapy, the likelihood of deterioration of abdominal/GI symptoms on the OV28 was

- 70% lower in the MIRV ITT population (95% CI, 0.15–0.60; *P*=0.0007)
- 80% lower in the MIRV FRα-high population (95% CI, 0.10–0.54; *P*=0.0007)

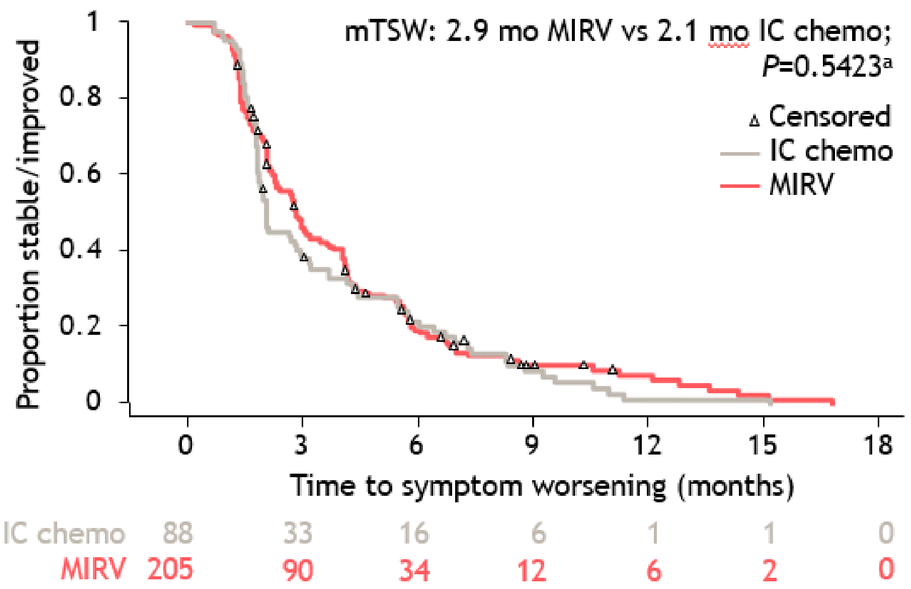
[a]P value for Wald chi-square test associated with mixed model parameter estimate β(treatment)= 0.

EORTC, European Organisation for Research and Treatment of Cancer; FOSI, Functional Assessment of Cancer Therapy – Ovarian Symptom Index; FRα, folate receptor alpha; GI, gastrointestinal; IC chemo, investigator's choice of chemotherapy; ITT, intention to treat; MIRV, mirvetuximab soravtansine; OV28, EORTC Quality of Life Questionnaire-Ovarian Cancer Module.

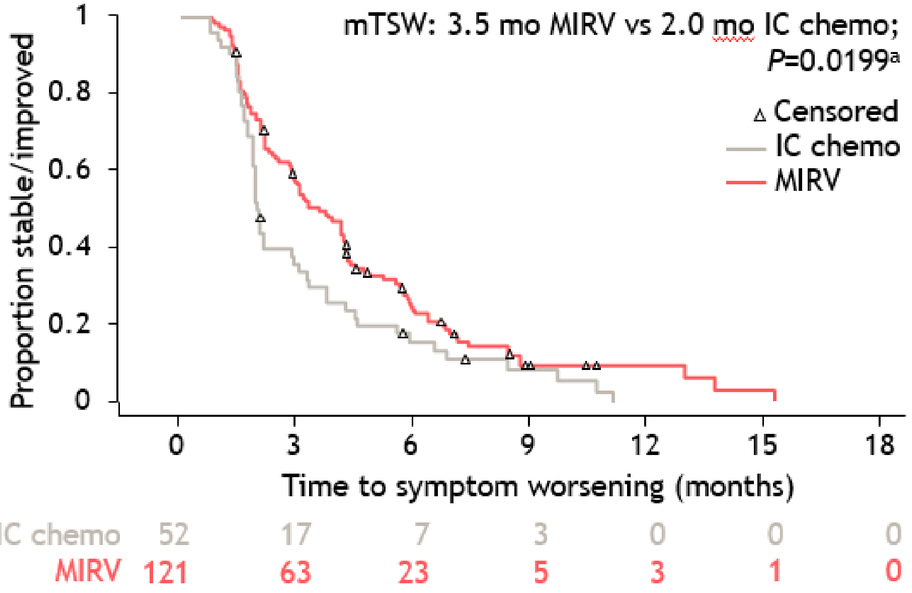
Moore KN et al. Poster presented at ESMO Congress 2022. Poster 532P.

FORWARD 1 (GOG 3011): categorical changes and time-to-symptom worsening on FOSI

Time-to-symptom worsening on FOSI: ITT population



Time-to-symptom worsening on FOSI: FRα population



Categorical change analyses of FOSI scores demonstrated that by cycle 7:
88.9% of ITT population patients on IC chemo had declined vs 70.3% with MIRV
88.1% of FRα-high population patients on IC chemo had declined vs 65.0% with MIRV

[a]P value based on stratified log-rank test using randomization stratification factors.

EORTC, European Organisation for Research and Treatment of Cancer; FOSI, Functional Assessment of Cancer Therapy – Ovarian Symptom Index; FRα, folate receptor a; IC chemo, investigator-chosen chemotherapy; ITT, intention-to-treat; MIRV, mirvetuximab soravtansine; mTSWOV28, EORTC Quality of Life Questionnaire-Ovarian Cancer Module.

Moore KN et al. Poster presented at ESMO Congress 2022. Poster 532P.

Summary

The ADC's mirvetuximab and T-DXd both delayed deterioration of GHS/QoL and showed a QoL benefit; however, this was in a carefully selected clinical trial population with limited prior lines of therapy[1,2]

HRQoL is predictive of mortality independent of objective disease severity measures[3]

- In cancer, symptom distress results in lower HRQoL[3]
- Interventions to decrease symptoms and symptom distress extend survival[3]

ADC, antibody-drug conjugate; GHS, global health scale; HRQoL, health-related quality of life; QOL, quality of life; T-DXd, trastuzumab deruxtecan.

1. Ueno NT et al. Presented at ESMO 2022. 2. Moore KN et al. Poster presented at ESMO Congress 2022. Poster 532P. 3. ACTION study group. *BMC Med*. 2017;15(1):10.