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
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MMAE | Anemia, neutropenia, and peripheral neuropathy
DM1 | Thrombocytopenia and hepatotoxicity
MMAF and DM4 | Ocular toxicity

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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.

## Common toxicities observed with select approved ADCs

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

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.
Differentiated safety profile observed with approved ADCs

Tisotumab vedotin (InnovaTV 204)¹

- Median duration of follow-up: 10.0 months.
- Median duration of treatment: 4.2 months (range, 1–16).

Mirvetuximab soravtansine (MIRASOL)²

- Data cutoff: March 6, 2023.
- Any-grade AEs included if ≥10%.

ADC, antibody-drug conjugate; 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.

## Toxicity observed with approved ADCs in gynecologic oncology

### Tisotumab vedotin (InnovaTV 204) – Ocular,\(^a\) bleeding,\(^b\) and peripheral neuropathy\(^c\) TRAEs\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>Ocular TRAEs</th>
<th>Bleeding TRAEs</th>
<th>Peripheral Neuropathy TRAEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to onset (median, months)</td>
<td>1.4</td>
<td>0.3</td>
<td>3.1</td>
</tr>
<tr>
<td>Events resolved, %</td>
<td>86</td>
<td>90</td>
<td>21</td>
</tr>
<tr>
<td>Time to resolution(^d) (median, months)</td>
<td>0.7</td>
<td>0.5</td>
<td>0.6</td>
</tr>
</tbody>
</table>

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

\(^{1}\)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).

\(^{2}\)Neurotoxicity SMQ.

\(^{3}\)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.

### Mirvetuximab soravtansine (SORAYA) - Ocular TRAEs\(^2,3\)

<table>
<thead>
<tr>
<th></th>
<th>Integrated Safety Population (N=464)</th>
<th>SORAYA* (N=106)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adverse event</strong></td>
<td><strong>All Grade, n (%)</strong></td>
<td><strong>Grade ≥3, n (%)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>All Grade, n (%)</strong></td>
<td><strong>Grade ≥3, n (%)</strong></td>
</tr>
<tr>
<td>Alopecia</td>
<td>3 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>64 (14)</td>
<td>14 (13)</td>
</tr>
<tr>
<td>Peripheral sensory neuropathy</td>
<td>36 (8)</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Peripheral motor neuropathy</td>
<td>4 (1&lt;)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>21 (5)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Anemia</td>
<td>43 (9)</td>
<td>14 (13)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>43 (9)</td>
<td>10 (9)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>35 (8)</td>
<td>12 (10)</td>
</tr>
</tbody>
</table>

Ocular TRAEs – Tisotumab vedotin

TRAE – conjunctivitis

Mitigation strategy

- 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%)

Prior to infusion day:

- An eye care provider should conduct an ophthalmic exam that includes visual acuity and slit lamp exam.

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.
- Apply cold packs over the eye area and ensure the eye area remains cold both during and approximately 20 min after infusion.
- 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.

Ocular adverse events regardless of causality

<table>
<thead>
<tr>
<th>Incidence, n (%)</th>
<th>N=101</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any grade</td>
</tr>
<tr>
<td>Patients with ≥1 ocular AE</td>
<td>55 (54)</td>
</tr>
<tr>
<td>Ocular AE in ≥5 patients</td>
<td></td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>31 (31)</td>
</tr>
<tr>
<td>Dry eye</td>
<td>25 (25)</td>
</tr>
<tr>
<td>Keratitis</td>
<td>11 (11)</td>
</tr>
<tr>
<td>Blepharitis</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Punctate keratitis</td>
<td>6 (6)</td>
</tr>
</tbody>
</table>

Ocular TRAEs – Tisotumab vedotin mitigation and results

TRAE – conjunctivitis

Mitigation strategies

Key Resources and Materials for Required Eye Care

Access to eye care providers
- Contact ophthalmic care including visual acuity and slit lamp exam at baseline, prior to each dose and at clinically indicated
- Promptly refer patient to an eye care provider (e.g., see eye care providers in accessing ocular symptoms early)

Eye drops ready for use
1. Tian triacetate 0.5%
2. Topical ocular vancomycin (5%) and topical calcineurin inhibitor

Cold packs during infusion
- Apply cold pack for 10 minutes during infusion
- Apply cold pack for 20 minutes during infusion

Mitigation results

Ocular adverse events regardless of causality

<table>
<thead>
<tr>
<th>Incidence, n (%)</th>
<th>N=101</th>
<th>Any grade</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≥1 ocular AE</td>
<td></td>
<td>55 (54)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Ocular AE in ≥5 patients</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Punctate keratitis</td>
<td>6 (6)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

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

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.
Factors that affect treatment decision-making

<table>
<thead>
<tr>
<th>Physical toxicity</th>
<th>Adverse events associated with treatment (ocular, GI, peripheral neuropathy, cardiotoxicity etc)(^1)-(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financial toxicity</td>
<td>Severe impact of financial burden on patients (eg, skipping medical care [treatments, follow-ups] medication nonadherence, impact on family, finances, etc.)(^5)</td>
</tr>
<tr>
<td>Time toxicity</td>
<td>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)</td>
</tr>
</tbody>
</table>

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

## PROs in clinical practice in gynecologic oncology

Select list of PRO measures in clinical practice¹

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

- **The EORTC-QLQ-C30** consists of multi-item scales and single-item measures as follows²:
  - **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 chemotherapy² 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 functioning³

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

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Description</th>
<th>Measures of interest</th>
<th>Analyses</th>
</tr>
</thead>
</table>
| EORTC QLQ-C30a        | 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\(^c\) |
| EORTC QLQ-BR23b       | 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**\(^f\)

<table>
<thead>
<tr>
<th>Cycle 1 (Baseline)(^g)</th>
<th>Cycle 2</th>
<th>Cycle 3</th>
<th>Every 2 cycles (cycle 5, 7, 9, etc.)</th>
<th>End of treatment</th>
<th>40-day follow-up visit</th>
<th>3-month follow-up visit</th>
</tr>
</thead>
</table>

\(^a\)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 7179
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.

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
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.

Nominal \( P \)-value not adjusted for multiple testing.

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**

<table>
<thead>
<tr>
<th>EORTC QLQ-C30</th>
<th>Median (95% CI) TDD, months</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value$^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global health status/QoL$^a$</td>
<td>11.4 (8.8-16.3)</td>
<td>7.5 (5.9-9.5)</td>
<td>0.69 (0.52-0.92)</td>
</tr>
<tr>
<td>Pain symptoms</td>
<td>16.4 (13.1-21.5)</td>
<td>6.1 (4.2-7.5)</td>
<td>0.40 (0.30-0.54)</td>
</tr>
<tr>
<td>Physical functioning$^b$</td>
<td>16.6 (11.3-21.5)</td>
<td>7.5 (4.9-9.5)</td>
<td>0.53 (0.40-0.70)</td>
</tr>
<tr>
<td>Emotional functioning$^b$</td>
<td>19.2 (16.3-24.5)</td>
<td>10.5 (7.1-NE)</td>
<td>0.69 (0.50-0.96)</td>
</tr>
<tr>
<td>Social functioning$^b$</td>
<td>12.8 (10.4-15.2)</td>
<td>6.0 (4.4-7.7)</td>
<td>0.59 (0.45-0.77)</td>
</tr>
<tr>
<td>Fatigue$^c$</td>
<td>11.1 (7.2-12.4)</td>
<td>4.5 (3.1-6.2)</td>
<td>0.61 (0.47-0.79)</td>
</tr>
<tr>
<td>Nausea and vomiting$^c$</td>
<td>5.7 (3.8-8.4)</td>
<td>9.3 (7.5-17.1)</td>
<td>1.46 (1.09-1.96)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EORTC QLQ-BR23</th>
<th>Median (95% CI) TDD, months</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value$^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm symptoms$^b$</td>
<td>14.4 (11.9-23.0)</td>
<td>8.7 (5.6-NE)</td>
<td>0.62 (0.45-0.85)</td>
</tr>
<tr>
<td>Breast symptoms$^b$</td>
<td>NE (24.7-NE)</td>
<td>NE (NE-NE)</td>
<td>0.71 (0.50-1.01)</td>
</tr>
<tr>
<td>EQ-SD-5L VAS$^{b,c}$</td>
<td>12.0 (9.9-15.2)</td>
<td>6.8 (4.9-11.4)</td>
<td>0.73 (0.54-0.97)</td>
</tr>
</tbody>
</table>

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-SD-5L VAS were exploratory analyses; $^d$Nominal P-value not adjusted for multiple testing.

EORTC, European Organization for Research and Treatment of Cancer; EQ-SD-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.

Ueno NT et al. Presented at ESMO 2022. Abstract 3179
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

![Graph showing improvement in the OV28 Abdominal/GI Symptom Subscale by Treatment Group at Week 8/9](image)

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.

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

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

**Graph Description:**
- **ITT population:**
  - MIRV: 31.7% (n=45/142)
  - CTX: 14.0% (n=7/50)
- **FRalpha-high population:**
  - MIRV: 27.3% (n=24/88)
  - CTX: 13.3% (n=4/30)

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

**Time-to-symptom worsening on OV28: ITT population**

- mTSW: 3.5 mo MIRV vs 3.0 mo IC chemo; $P=0.6850^{a}$

**Time-to-symptom worsening on OV28: FRα population**

- mTSW: 4.0 mo MIRV vs 2.1 mo IC chemo; $P=0.0229^{a}$

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

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*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 FR\(\alpha\)-high population (95% CI, 0.10–0.54; \(P=0.0007\))
FORWARD 1 (GOG 3011): categorical changes and time-to-symptom worsening on FOSI

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

*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; mTSW028, EORTC Quality of Life Questionnaire-Ovarian Cancer Module.
Moore KN et al. Poster presented at ESMO Congress 2022. Poster 532P.
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\(^3\)