

ORIGINAL RESEARCH ARTICLE

Reported adverse events with mirvetuximab soravtansine: A disproportionality analysis of the Food and Drug Administration Adverse Event Reporting System

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Abstract

Introduction: Mirvetuximab soravtansine (MIRV) is a first-in-class antibody–drug conjugate (ADC) targeting folate receptor alpha, approved for platinum-resistant ovarian cancer. However, real-world safety data remain limited.

Objective: To characterize the real-world adverse event reporting profile of mirvetuximab soravtansine, including disproportionality safety signals, time-to-onset patterns, severity and clinical outcomes, and reporting proportions relative to other ADCs.

Methods: Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) data from 2022Q4 through 2025Q4 were analyzed. Disproportionality signals were detected using four algorithms: reporting odds ratio (ROR), proportional reporting ratio, information component, and empirical Bayesian geometric mean. Time-to-onset, severity, subgroup, and comparative analyses with four other FDA-approved ADCs were performed.

Results: We identified 1,252 reports with MIRV containing 2,617 adverse event records (median age 65 years, 99.7% female). Strong reporting signals emerged for keratopathy (ROR: 318.6, 95% confidence interval [CI]: 232.6–436.3), keratitis (ROR: 255.8, 95% CI: 191.3–342.0), blurred vision (ROR: 12.7, 95% CI: 10.3–15.7), peripheral neuropathy (ROR: 14.1, 95% CI: 11.4–17.4), and pneumonitis (ROR: 37.0, 95% CI: 29.1–46.9). Gastrointestinal events occurred early (median <7 days), while ocular and neurological events showed delayed onset (median >30 days). Death was reported in 9.2% of all reports and 19.4% of pneumonitis reports. MIRV showed the highest reporting proportion for ocular toxicity among ADCs (24.4% vs. <3% for most comparators), while trastuzumab deruxtecan showed a higher reporting proportion for pneumonitis (13.5% vs. 6.8%).

Conclusion: This disproportionality analysis characterizes the adverse event reporting profile of MIRV in FAERS, identifying strong reporting signals for ocular toxicity, peripheral neuropathy, and pneumonitis. The observed temporal patterns, based on a subset with available onset data, suggest early vigilance for gastrointestinal symptoms and sustained ophthalmologic surveillance. These hypothesis-generating findings may inform monitoring strategies and patient counseling.

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Keywords: Mirvetuximab soravtansine; Antibody–drug conjugate; Adverse events; Food and Drug Administration Adverse Event Reporting System; Pharmacovigilance; Real-world study; Drug safety; Ovarian cancer

1. Introduction

Antibody–drug conjugates (ADCs) represent one of the fastest-growing classes of targeted cancer therapeutics, ingeniously combining the specificity of monoclonal antibodies with the cytotoxic potency of small-molecule payloads. Mirvetuximab soravtansine (MIRV, Elahere®) is a first-in-class ADC targeting folate receptor alpha (FR α), comprising a humanized anti-FR α antibody conjugated to the maytansinoid payload DM4 via a cleavable disulfide linker.^{1,2} This design enables targeted delivery of the cytotoxic agent to FR α -expressing tumor cells, predominantly in epithelial ovarian cancer.

In November 2022, the Food and Drug Administration (FDA) granted accelerated approval to MIRV for adult patients with FR α -positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic regimens.¹ The approval was based on the SORAYA trial (NCT04296890), which demonstrated an objective response rate of 32.4% with a median duration of response of 6.9 months.² Subsequently, the confirmatory MIRASOL trial (NCT04209855) showed significant improvements in both progression-free survival (5.62 vs. 3.98 months) and overall survival (16.46 vs. 12.75 months) compared to investigator's choice chemotherapy,³ solidifying its role in the treatment landscape. On March 22, 2024, the FDA granted full approval to MIRV–gynx for the same indication based on the MIRASOL trial; the FDA communication noted that the product had previously received accelerated approval in November 2022.

The clinical development program identified several class-related adverse events, including ocular adverse events (blurred vision, keratopathy, dry eye), peripheral neuropathy, and gastrointestinal disturbances.^{2–5} These toxicities are attributed to the DM4 payload and its effects on rapidly dividing cells, such as the corneal epithelium and peripheral neurons.^{6,7} An integrated safety analysis across four clinical studies confirmed that MIRV monotherapy is generally well-tolerated, with most adverse events being low-grade and manageable.³ However, clinical trials are limited by relatively small sample sizes, stringent eligibility criteria, and controlled settings that may not fully reflect the diversity of real-world patient populations.

Post-marketing pharmacovigilance offers essential complementary insights through access to broader

patient populations, longer follow-up duration, and the ability to detect rare or delayed adverse events. The FDA Adverse Event Reporting System (FAERS) is an invaluable resource for such analyses, containing millions of spontaneous adverse event reports from healthcare professionals, consumers, and manufacturers.^{8–10} Recent pharmacovigilance studies have successfully characterized the safety profiles of other ADCs, including their ocular toxicity,^{11,12} neurotoxicity,^{13,14} and hematologic effects,^{15,16} providing both a methodological framework and a basis for descriptive comparative analysis.

This study was therefore designed to address this gap by: (i) characterizing the reporting profile of adverse events with MIRV using FAERS data; (ii) identifying significant safety signals through multiple disproportionality algorithms; (iii) analyzing temporal patterns of adverse event onset; (iv) evaluating adverse event severity and clinical outcomes; (v) descriptively comparing reporting proportions for MIRV with other FDA-approved ADCs; and (vi) conducting subgroup and sensitivity analyses to assess signal robustness. To our knowledge, a MIRV-focused real-world pharmacovigilance analysis integrating disproportionality signals, temporal patterns, severity assessment, and descriptive comparison of reporting proportions with other ADCs remains lacking.

2. Methods

The study flow diagram is depicted in [Figure 1](#).

2.1. Data sources

Data were extracted from FAERS quarterly data files covering the period from 2022Q4 (the quarter of MIRV approval, November 14, 2022) through 2025Q4. The database was downloaded on January 15, 2026. The exact first date included was November 14, 2022 (the FDA approval date), and the last date included was December 31, 2025. The entire 2022Q4 quarter was analyzed; however, reports submitted before the approval date within 2022Q4 were excluded as they could not plausibly involve MIRV. The number of reports by calendar quarter is provided in Table S5. FAERS is a publicly available database containing spontaneous adverse event reports submitted by healthcare professionals, consumers, and pharmaceutical manufacturers. Each report includes demographic information, drug exposure details, adverse events coded using the Medical Dictionary for Regulatory

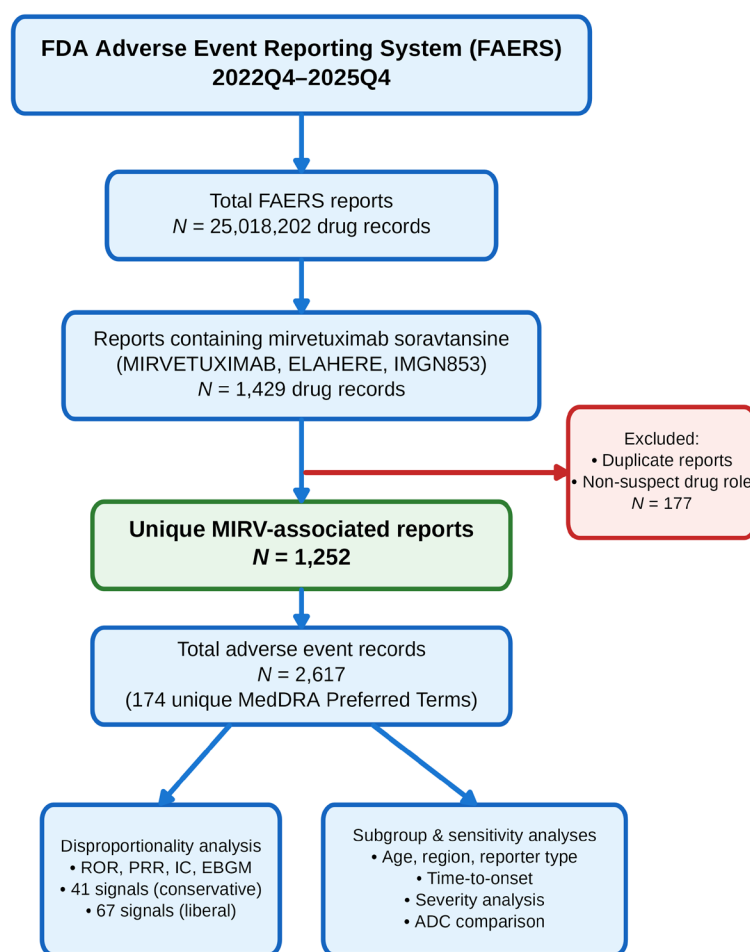


Figure 1. Study flow diagram. A total of 25,018,202 drug records from FAERS (2022Q4 –2025Q4) were screened. After deduplication at the case level, the background denominator consisted of unique FAERS cases, and each case contributed no more than once to a given drug–Preferred Term combination. After identifying 1,429 MIRV-associated drug records and excluding 177 duplicate or non-suspect reports, 1,252 unique MIRV-associated reports containing 2,617 adverse event records (174 unique MedDRA Preferred Terms) were retained for disproportionality analysis and subgroup/sensitivity analyses.

Abbreviations: ADC: Antibody–drug conjugate; EBGM: Empirical Bayes geometric mean; FAERS: FDA Adverse Event Reporting System; FDA: Food and Drug Administration; IC: Information component; MedDRA: Medical Dictionary for Regulatory Activities; MIRV: Mirvetuximab soravtansine; PRR: Proportional reporting ratio; ROR: Reporting odds ratio.

Activities (MedDRA) Preferred Terms (MedDRA version 27.0), and documented outcomes.⁸

2.2. Case identification

Reports with MIRV were identified by searching the DRUG file for records containing the following drug names: “MIRVETUXIMAB,” “MIRVETUXIMAB SORAVTANSINE,” “MIRVETUXIMAB SORAVTANSINE–GYNX,” “ELAHERE,” “IMG853,” and “MIRVETUXIMAB SORAVTANSINE–GYNX” (including common spelling and hyphenation variants such as “mirvetuximab–soravtansine” and “mirvetuximab soravtansine gynx”). Capitalization and punctuation were

normalized by converting all drug names to uppercase and removing leading/trailing spaces. Equivalent name dictionaries were constructed for every comparator ADC, including generic names, brand names, and developmental-code names. Duplicate reports were removed by retaining only the most recent FDA_DT (FDA date received) for each unique CASEID. When reports shared the same CASEID and FDA_DT but had different PRIMARYIDs, the report with the highest PRIMARYID was retained as the most recent version. Follow-up versions and duplicate manufacturer/consumer submissions were handled by this CASEID-based deduplication. Duplicate drug–event combinations within a single report were collapsed so that

each Preferred Term contributed no more than once per case. Combination products and misspelled product names were considered during the name-matching process. The primary analysis included reports where MIRV was listed as the primary suspect (role_cod = "PS") or secondary suspect (role_cod = "SS") drug. A sensitivity analysis restricted to primary suspect reports was also conducted to assess the potential confounding by concomitant treatment. The frequency of co-suspect and concomitant drugs was reported. In heavily pretreated oncology populations, pneumonitis, neuropathy, cytopenias, and gastrointestinal symptoms may be attributable to previous or concomitant therapies, disease progression, infection, or comorbidity.

2.3. Disproportionality analysis

We employed four established disproportionality algorithms to detect reporting signals, consistent with pharmacovigilance best practices.^{8,9} The background denominator consisted of unique FAERS cases (after CASEID-based deduplication), and each case contributed no more than once to a given drug–Preferred Term combination. Specifically, for each drug–Preferred Term combination, the four cells of the 2×2 contingency table were constructed as follows: a = unique cases with both the drug and the Preferred Term; b = unique cases with the drug but not the Preferred Term; c = unique cases with the Preferred Term but not the drug; and d = unique cases with neither. Drug rows from the DRUG file and reaction rows from the REAC file were linked at the PRIMARYID level and then deduplicated so that each case contributed at most once per drug–Preferred Term pair, avoiding multiple contributions from a single polypharmacy report.

- (i) Reporting odds ratio (ROR): Calculated as $(a/b)/(c/d)$, where a = reports with both MIRV and the adverse event, b = reports with MIRV but not the adverse event, c = reports with the adverse event but not MIRV, and d = reports with neither. A reporting signal was defined as ROR lower 95% confidence interval (CI) >1 .⁹
- (ii) Proportional reporting ratio (PRR): Calculated as $[a/(a + b)]/[c/(c + d)]$. A reporting signal was defined as $PRR \geq 2$, chi-square ≥ 4 , and $a \geq 3$. The PRR chi-square statistic and minimum-count criterion are reported in Table S1.¹³
- (iii) Information component (IC): A Bayesian measure calculated as $\log_2(\text{observed/expected})$ using a Bayesian shrinkage approach with a normal approximation for the information component. A reporting signal was defined as IC025 (lower 95% credible interval) >0 .⁹ IC025 is the lower 2.5th percentile of the posterior distribution.
- (iv) Empirical Bayesian geometric mean (EBGM):

Calculated using a gamma–Poisson shrinker model. The prior distribution was a two-parameter gamma distribution whose shape and scale parameters were estimated from the observed data using the method of moments. The EBGM is the ratio of the observed count to the expected count under the null model, shrunk toward the prior. EBGM05 is the 5th percentile of the posterior distribution. Zero cells were handled by adding a continuity correction of 0.5. All Bayesian calculations were implemented using the PhViD package in R (version 4.3.2). A signal was defined as EBGM05 (lower 90% confidence bound) ≥ 2 .⁹

2.4. Subgroup analyses

Subgroup analyses were performed stratified by age (<65 vs. ≥ 65 years; reference category: <65 years), geographic region (United States vs. non-United States; reference category: non-United States), reporter type (healthcare professional vs. consumer; reference category: healthcare professional), and reporting period (early $\leq 2023Q2$ vs. late $>2023Q2$; reference category: early $\leq 2023Q2$). The cut-off at 2023Q2 was prespecified to separate the early post-approval period (approximately the first eight months after approval) from the later period. For each adverse event, odds ratios with 95% CIs were calculated using Fisher's exact test. All subgroup analyses were exploratory and a false discovery rate correction (Benjamini–Hochberg method) was applied to account for multiple testing; however, given the exploratory nature, nominal p -values are also reported and isolated nominal p -values should not be interpreted as established differences.

2.5. Time-to-onset analysis

For reports with available therapy start dates and event onset dates, time-to-onset was calculated as the interval between MIRV initiation and adverse event occurrence. Time-to-onset was available for only 174 of 1,252 reports (13.9%); the characteristics of reports with versus without calculable onset were compared. Incomplete dates (missing day or month) were excluded from time-to-onset calculation. Negative or implausible intervals were excluded. Same-day events (interval = 0 days) were retained. Onset referred to the date of the first reported event. Treatment interruptions, rechallenge, and multiple therapy periods could not be distinguished in FAERS data. Adverse events were categorized as early-onset (<7 days), intermediate-onset (7–30 days), or late-onset (≥ 30 days).

2.6. Severity analysis

Serious outcomes were classified according to FAERS outcome codes: death (DE), life-threatening (LT), hospitalization (HO), disability (DS), congenital anomaly

(CA), required intervention (RI), and other serious (OT). Fatality proportions were calculated for each adverse event category as the proportion of reports with a DE outcome among all reports for that AE. Serious-outcome categories may overlap, as a single report can include DE, HO, and OT outcomes simultaneously; denominators and overlapping categories are explicitly described in Table S7.

2.7. Comparative analysis with other antibody–drug conjugates

Reporting proportions for each toxicity category (ocular toxicity, peripheral neuropathy, pneumonitis/interstitial lung disease, gastrointestinal toxicity, hematologic toxicity, and skin toxicity) were calculated as the number of reports with the adverse event divided by the total number of reports for that drug, expressed as a percentage. The Preferred Terms included within each grouped toxicity category are listed in Table S1. Overlapping terms (e.g., “ocular toxicity,” “keratopathy,” “keratitis,” “dry eye,” and “vision blurred” may occur within the same report) were not treated as independent patients or mutually exclusive outcomes; one report can contribute to multiple categories. The total number of reports for every ADC is reported alongside each percentage. We extracted FAERS data for four other FDA-approved ADCs: trastuzumab deruxtecan,¹⁷ sacituzumab govitecan,¹⁸ enfortumab vedotin,¹⁹ and tisotumab vedotin. These four comparators were selected because they represent the major FDA-approved ADCs with sufficient FAERS reporting volume during the study period. The comparative analysis is strictly descriptive and does not constitute a valid head-to-head safety comparison, as these products differ substantially in cancer indication, patient demographics, previous and concomitant treatments, duration of marketing, overall number and source of reports, labeled warnings, and manufacturer reporting practices. The FDA specifically advises against using FAERS data alone for drug-to-drug safety comparisons.

2.8. Sensitivity analysis

The primary signal rule was prespecified as: ROR lower 95% CI > 1, PRR ≥ 2 with chi-square ≥ 4 and a ≥ 3, IC025 > 0, and EBGM05 ≥ 2. To evaluate the robustness of signals, we also applied three threshold levels for all four algorithms: (i) conservative: ROR lower CI ≥ 2.0, IC025 ≥ 0.5, EBGM05 ≥ 2.0, PRR ≥ 2.0; (ii) standard: ROR lower CI ≥ 1.5, IC025 ≥ 0.0, EBGM05 ≥ 1.5, PRR ≥ 1.5; and (iii) liberal: ROR lower CI ≥ 1.0, IC025 ≥ -0.5, EBGM05 ≥ 1.0, PRR ≥ 1.0. The consistency of key signals across thresholds was assessed.

2.9. Statistical analysis

All analyses were performed using R version 4.3.2 (R Foundation for Statistical Computing, Austria) with the dplyr, tidyr, and ggplot2 packages for data processing and visualization, and the PhViD package for disproportionality signal detection (ROR, PRR, IC, and EBGM). Two-sided *p*-values < 0.05 were considered statistically significant. In accordance with standard pharmacovigilance practice for signal detection,⁸ no adjustment for multiple comparisons was made in the primary disproportionality analysis.

3. Results

3.1. Patient characteristics

From 2022Q4 to 2025Q4, we identified 1,252 unique reports with MIRV containing 2,617 adverse event records (Table 1). Among reports with available demographic data (sex was available for 901 of 1,252 reports, 71.9%; age was available for 293 of 1,252 reports, 23.4%; reporter type was available for 1,245 of 1,252 reports, 99.4%), 99.7% (898/901) were female, consistent with the ovarian cancer indication. The median age was 65 years (interquartile range: 57–72 years), with 49.5% of patients aged <65 years and 50.5% aged ≥65 years. The term “patient characteristics” was used cautiously because the unit of analysis is an adverse event report, not necessarily a unique, clinically verified patient. Most reports originated in the United States (85.2%), and healthcare professionals submitted 69.9% of reports. Regarding serious outcomes, 47.3% (592/1,252) of reports documented at least one serious outcome, including DE in 9.2% (115/1,252), HO in 12.2% (153/1,252), and life-threatening events in 1.2% (15/1,252).

3.2. Disproportionality, temporal, and comparative analyses

Multi-algorithm disproportionality analysis identified 174 unique Preferred Terms in reports with MIRV, of which 41 met all four prespecified primary signal criteria (Table 2, Figure 2). The strongest reporting signals were observed for ocular toxicities, including keratopathy (ROR: 318.6, 95% CI: 232.6–436.3), keratitis (ROR: 255.8, 95% CI: 191.3–342.0), and blurred vision (ROR: 12.7, 95% CI: 10.3–15.7), consistent with known ADC-associated effects.^{2,3,11,12} Neurological toxicity also showed a robust reporting signal, with peripheral neuropathy yielding an ROR of 14.1 (95% CI: 11.4–17.4),¹³ while pulmonary toxicity manifested as pneumonitis (ROR: 37.0, 95% CI: 29.1–46.9) and interstitial lung disease (ROR: 4.6, 95% CI: 2.7–7.6). Gastrointestinal adverse events, including abdominal pain (ROR: 4.6, 95% CI: 3.6–5.8) and diarrhea (ROR: 1.6, 95% CI: 1.3–2.0),

were also significantly associated. Disease progression was excluded from the primary toxicity signal analysis as it represents an outcome of the underlying malignancy rather than a drug toxicity. Time-to-onset analysis among 174 reports with available data (13.9% of the total 1,252 reports; this severe missingness should be considered when interpreting these findings) (Table S6, Figure S1). Gastrointestinal events typically presented early, with a median onset of 0 days for abdominal pain (interquartile range [IQR]: 0–2 days) and 1 day for diarrhea (IQR: 0–8 days). The median of zero days for abdominal pain raises the possibility that symptoms were pre-existing, recorded at treatment initiation, or affected by date imprecision; such findings should not automatically be interpreted as treatment-emergent early toxicity. Blurred vision (the MedDRA Preferred Term “Vision blurred”) emerged with intermediate onset (median: 18.5 days, IQR: 9–30 days), representing an early subjective visual symptom distinct from later diagnosed corneal pathology, while late-onset adverse events included keratitis (median: 33 days, IQR: 30–39 days), peripheral neuropathy (median: 33 days, IQR: 15–62 days), pneumonitis (median: 74 days, IQR: 33–100 days), and cataract (median: 128 days, IQR: 63–130 days), reflecting the cumulative toxicity of repeated ADC dosing. The range of onset for ocular events was 18–128 days, and early subjective visual symptoms should be distinguished from later-diagnosed corneal pathology.⁷ Severity analysis demonstrated differential proportions of DE outcomes across adverse event categories (Table S7, Figure S2). Among reports containing pneumonitis, 19.4% (14/72) also contained a DE outcome; this does not prove that pneumonitis caused the DE, followed by ascites (16.7%), anemia (16.7%), and neutropenia (12.5%). Gastrointestinal adverse events showed intermediate proportions of DE outcomes, while ocular adverse events and peripheral neuropathy demonstrated low or no DE outcomes, consistent with their generally reversible nature.^{3,6} Descriptive comparative analysis with four other FDA-approved ADCs revealed distinct reporting patterns (Figure 3). MIRV showed the highest rate of ocular toxicity (24.4%), followed by tisotumab vedotin (12.8%), with other ADCs below 3%, consistent with maytansinoid-associated ocular effects.^{11,12} Peripheral neuropathy had the highest reporting proportion with enfortumab vedotin (13.9%),¹⁹ while trastuzumab deruxtecan exhibited the highest pneumonitis rate (13.5%),¹⁷ substantially exceeding MIRV (6.8%). Sacituzumab govitecan demonstrated the highest hematologic toxicity reporting proportion (19.0%),^{14,18} and enfortumab vedotin led in skin toxicity reporting proportion (22.2%),¹⁹ whereas MIRV showed the lowest reporting proportion in these categories (4.8% and 1.7%, respectively).

Table 1. Baseline characteristics of patients with mirvetuximab soravtansine-associated adverse event reports in the Food and Drug Administration Adverse Event Reporting System

Characteristic	N (%)
Total reports	1,252
Sex	
Data available	901
Female	898 (99.7%)
Male	3 (0.3%)
Age (years)	
Data available	293
<65	145 (49.5%)
≥65	148 (50.5%)
Median (interquartile range), years	65 (57–72)
Reporter country	
United States	1,067 (85.2%)
Non-United States	185 (14.8%)
Reporter type	
Data available	1,245
Healthcare professional	870 (69.9%)
Consumer	375 (30.1%)
Serious outcomes	
Any serious outcome	592 (47.3%)
Death	115 (9.2%)
Hospitalization	153 (12.2%)
Life-threatening	15 (1.2%)
Disability	8 (0.6%)

Note: Missing-data percentages relative to all 1,252 reports are shown for age, sex, and reporter type.

3.3. Subgroup and sensitivity analyses

Exploratory subgroup analyses revealed several associations (Tables S2–S5). Diarrhea was more common in patients ≥65 years (8.1% vs. 2.1%; odds ratio [OR]: 0.24, 95% CI: 0.07–0.87, $p = 0.031$; reference category: ≥65 years), while blurred vision showed a trend toward higher reporting proportions in patients <65 years (10.3% vs. 4.7%; OR: 2.32, 95% CI: 0.92–5.88, $p = 0.078$). Cataract was significantly more frequent in United States reports (6.7% vs. 1.6%; OR: 4.39, 95% CI: 1.37–14.08, $p = 0.004$; reference category: non-United States), possibly reflecting differences in ophthalmologic surveillance. Keratopathy was more

Table 2. Disproportionality analysis results for adverse events with strong reporting signals in reports with mirvetuximab soravtansine

Adverse event	N	ROR (95% CI)	PRR	IC (IC025)	EBGM (EBGM05)
Vision blurred	97	12.7 (10.3–15.7)	11.8	3.48 (3.28)	11.2 (9.5)
Neuropathy peripheral	95	14.1 (11.4–17.4)	13.1	3.62 (3.42)	12.3 (10.4)
Cataract	75	16.3 (12.9–20.6)	15.4	3.81 (3.58)	14.0 (11.6)
Abdominal pain	72	4.6 (3.6–5.8)	4.4	2.10 (1.87)	4.3 (3.5)
Pneumonitis	72	37.0 (29.1–46.9)	34.9	4.81 (4.58)	28.1 (23.2)
Dry eye	50	10.5 (7.9–14.0)	10.1	3.21 (2.94)	9.3 (7.4)
Keratopathy	43	318.6 (232.6–436.3)	307.7	6.07 (5.77)	67.0 (52.2)
Ocular toxicity	30	339.5 (233.2–494.2)	331.4	5.67 (5.32)	51.0 (37.9)
Keratitis	50	255.8 (191.3–342.0)	245.6	6.14 (5.87)	70.6 (56.0)
Infusion-related reaction	44	6.7 (5.0–9.1)	6.5	2.62 (2.32)	6.1 (4.8)
Interstitial lung disease	15	4.6 (2.7–7.6)	4.5	2.02 (1.52)	4.0 (2.7)

Notes: Events meeting all four prespecified primary signal criteria (ROR lower 95% CI > 1, PRR ≥ 2 with chi-square ≥ 4 and a ≥ 3, IC025 > 0, EBGM05 ≥ 2) are shown. The PRR chi-square statistic is reported in Table S1. Disease progression has been excluded as it represents an outcome of the underlying malignancy rather than a drug toxicity.

Abbreviations: CI: Confidence interval; EBGM: Empirical Bayes geometric mean; IC: Information component; PRR: Proportional reporting ratio; ROR: Reporting odds ratio.

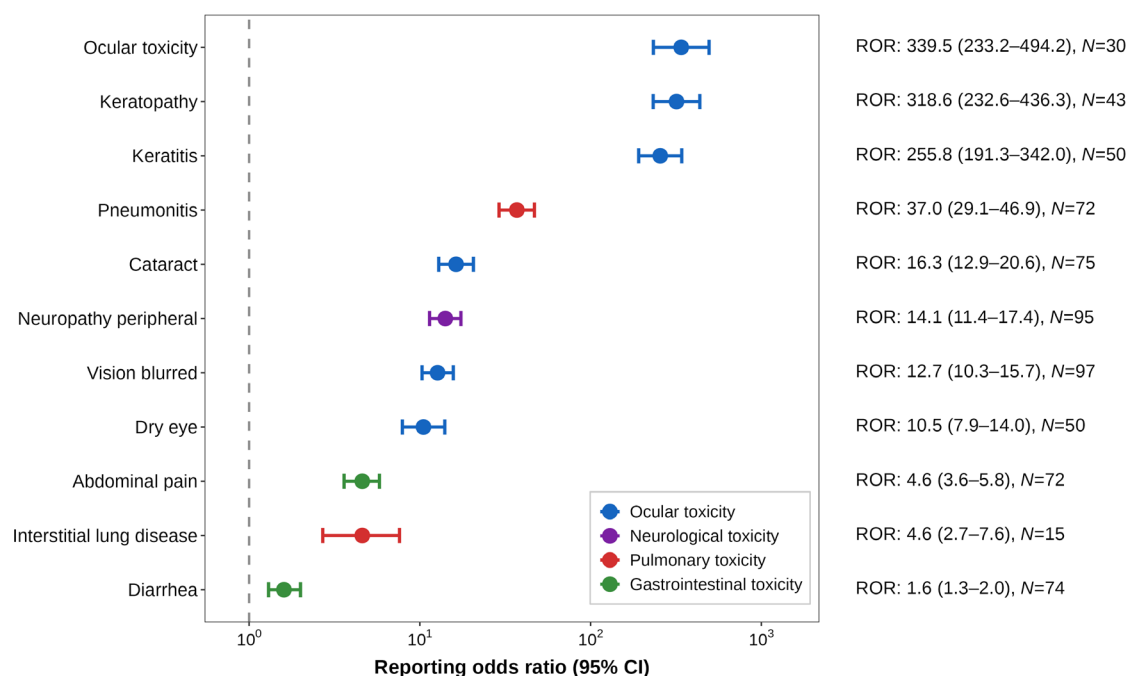


Figure 2. Forest plot of key adverse events associated with mirvetuximab soravtansine. Forest plot displaying reporting odds ratios (ROR) with 95% confidence intervals (CIs) for selected adverse events meeting prespecified primary signal criteria (all four algorithms positive). The x-axis is displayed on a logarithmic scale because of the extreme range of ROR values. Events are grouped by toxicity category: ocular toxicity (blue), neurological toxicity (purple), pulmonary toxicity (red), and gastrointestinal toxicity (green). The dashed vertical line at ROR = 1 represents the null hypothesis of no disproportionate reporting. *N* indicates the number of reports for each adverse event.

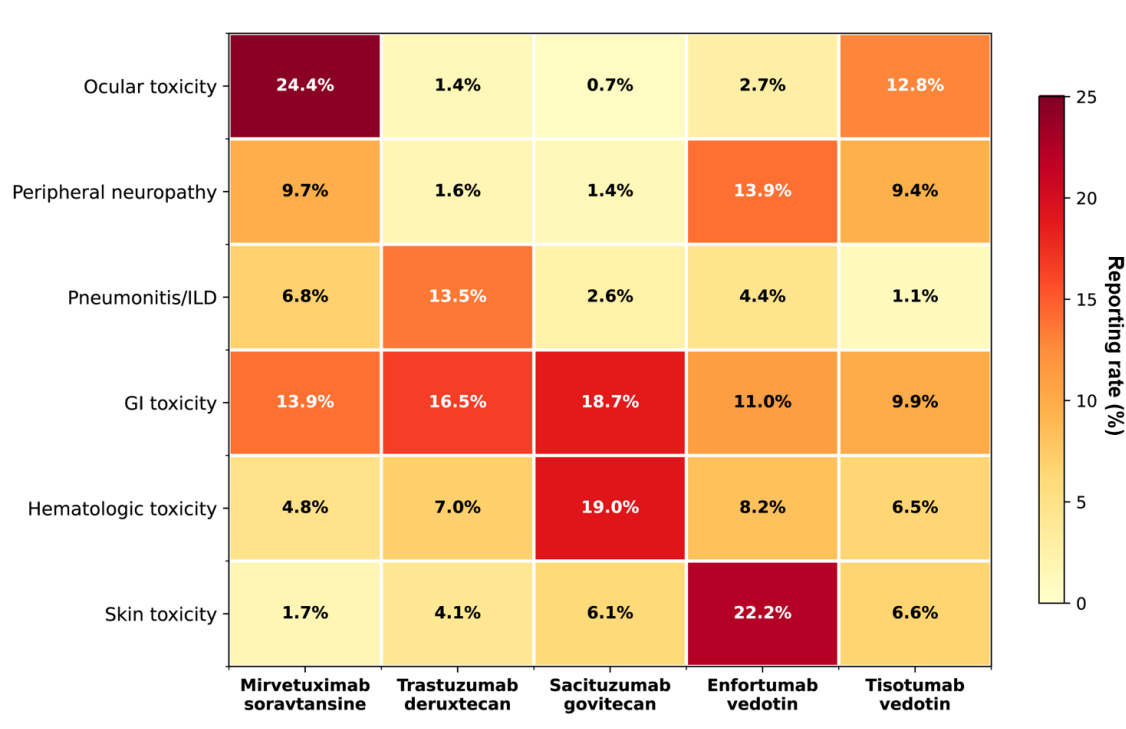


Figure 3. Comparative safety profile of Food and Drug Administration (FDA)-approved antibody–drug conjugates (ADCs) (FDA Adverse Event Reporting System 2022Q4–2025Q4). Heatmap showing the reporting proportions (%) of six major toxicity categories across five FDA-approved ADCs. Color intensity reflects the reporting proportion, with darker red indicating higher proportions. The total number of reports for every ADC is displayed alongside each percentage. One report can contribute to multiple toxicity categories, as categories are not mutually exclusive. Abbreviations: GI: Gastrointestinal; ILD: Interstitial lung disease.

commonly reported by healthcare professionals (4.7% vs. 0.5%; OR: 9.22, 95% CI: 2.22–38.34, $p < 0.001$ reference category: healthcare professional), whereas blurred vision (14.9% vs. 4.6%; OR: 0.27, 95% CI: 0.18–0.42, $p < 0.001$), peripheral neuropathy (13.3% vs. 5.2%; OR: 0.35, 95% CI: 0.23–0.54, $p < 0.001$), and fatigue (7.7% vs. 1.8%; OR: 0.22, 95% CI: 0.12–0.42, $p < 0.001$) were more frequently reported by consumers. No significant temporal trends were observed between early and late reporting periods. All subgroup results should be interpreted as exploratory given the small denominators and missing demographic information. Sensitivity analysis confirmed the robustness of the reporting signal across thresholds (Table S8), with key safety signals (ocular toxicity, peripheral neuropathy, pneumonitis) remaining significant under all criteria.

4. Discussion

This pharmacovigilance analysis of MIRV using FAERS provides a large-scale, real-world characterization of its adverse event reporting profile over a post-marketing period of more than three years (November 2022 through December 2025). By analyzing 1,252 reports and employing multiple disproportionality algorithms, we not

only corroborate the reporting signals consistent with adverse events observed in pivotal clinical trials but also provide descriptive insights into the temporal patterns, severity, and comparative reporting proportions of MIRV, offering hypothesis-generating intelligence for its safe use.

The most distinctive finding is the exceptionally high and specific signal for ocular toxicity, with disproportionality statistics (e.g., keratopathy ROR: 318.6, 95% CI: 232.6–436.3) that are among the highest reported for any approved ADC. However, this estimate is based on only 43 reports, and the wide CI and potential effects of known-event and stimulated-reporting bias should be acknowledged. This finding is consistent with the mechanism of action of the DM4 payload, a maytansinoid that disrupts microtubule dynamics in rapidly dividing cells, such as the corneal epithelium.^{6,7} While clinical trials^{2,3} and other real-world studies^{11,12} have noted these events, our analysis provides a more granular descriptive view. The time-to-onset data (available for only 13.9% of reports) reveal a crucial clinical nuance: while subjective symptoms like blurred vision (the MedDRA Preferred Term “Vision blurred”) can appear early (median: 18 days), objective, more severe pathologies like keratitis and cataract develop later (median: 33 and

128 days, respectively). This delayed onset underscores the necessity for proactive and sustained ophthalmologic surveillance that extends well beyond the initial treatment cycles, as recommended in the prescribing information.²⁰ Importantly, the low proportion of DE outcomes associated with these events suggests that with rigorous monitoring and timely dose modifications,^{3,21} the risk of irreversible vision impairment can be effectively managed.

In contrast to the high-frequency events with low proportions of DE outcomes, pneumonitis, though less commonly reported, emerged as the most clinically concerning toxicity due to its high proportion of DE outcomes (19.4%; i.e., among reports containing pneumonitis, 19.4% also contained a DE outcome, which does not prove causality). This finding elevates pneumonitis from a known adverse event to a critical safety priority. The delayed median onset of 74 days indicates that respiratory vigilance cannot be confined to the early treatment phase. While the overall reporting proportion of pneumonitis with MIRV (6.8%) is lower than that reported for trastuzumab deruxtecan (13.5%),¹⁷ its severe consequences demand immediate and thorough diagnostic evaluation for any new or worsening respiratory symptoms. This pattern, a lower reporting proportion but higher severity for a particular toxicity, highlights the importance of looking beyond simple reporting rates to fully characterize a drug's risk profile.

The reporting profile of MIRV is further contextualized by our descriptive comparative analysis with other ADCs, which reveals a distinct reporting pattern for each agent. This comparison is strictly descriptive and does not establish comparative safety, as the products differ in indication, patient population, marketing duration, and reporting practices. MIRV's predominant ocular reporting proportion stands in stark contrast to the higher reporting proportions of pneumonitis with trastuzumab deruxtecan,¹⁷ hematologic toxicity with sacituzumab govitecan,¹⁸ and skin toxicity with enfortumab vedotin.¹⁹ This descriptive comparative landscape may inform clinicians' treatment decisions, especially when sequencing therapies or managing patients with pre-existing conditions. It also underscores that the ADC class is highly heterogeneous, and toxicity management must be drug-specific. Peripheral neuropathy, a class effect for tubulin-binding payloads,¹³ showed comparable reporting signals across MIRV, enfortumab vedotin, and tisotumab vedotin, but with differing severity.

Subgroup analyses, while exploratory and based on small denominators with substantial missing demographic data, offer additional practical insights. The higher reporting of keratopathy by healthcare professionals, versus subjective

symptoms such as neuropathy by consumers, reflects the nature of these events and suggests that patient-reported outcomes are critical for capturing the full toxicity burden. Geographic variation in cataract reporting may reflect differences in surveillance practices, reinforcing the value of standardized ophthalmologic monitoring protocols.

This study has limitations inherent to spontaneous reporting databases, including potential underreporting, reporting biases, and the inability to calculate true incidence rates. Additional limitations include: confounding by indication and disease severity; the potential contribution of concomitant and prior anticancer therapies to reported events; lack of exposure denominators; duplicate or linked reports that may remain after automated deduplication; stimulated reporting following boxed warnings or regulatory communications; missing clinical narratives; inability to validate diagnoses or grades; absence of causality assessment; lack of dosage and cumulative-exposure information; incomplete onset and demographic data; non-independence of multiple Preferred Terms within a report; instability of very large ROR estimates based on relatively small counts; and limitations of cross-product comparisons. However, FAERS remains a powerful tool for detecting rare events, characterizing real-world safety, and generating hypotheses that can be tested in controlled settings. The consistency of our signals across multiple algorithms and sensitivity analyses supports our findings, although ROR, PRR, IC, and EBGM are calculated from essentially the same underlying contingency table and therefore do not constitute independent confirmation.

In summary, this real-world analysis confirms MIRV's unique safety profile and characterizes the reporting profile of adverse events with MIRV, showing a predominant pattern of ocular reporting signals and a lower but clinically critical proportion of DE outcomes associated with pneumonitis. The observed temporal patterns of adverse events (based on the subset with available data) provide a roadmap for targeted monitoring: early vigilance for gastrointestinal symptoms, sustained ophthalmologic surveillance for late-onset ocular toxicity, and continuous awareness of respiratory symptoms throughout treatment. The descriptive comparative toxicity fingerprinting across ADCs reinforces the need for drug-specific risk management strategies. These findings provide clinicians with hypothesis-generating evidence to optimize patient selection, enhance monitoring protocols, and ultimately improve the safe use of MIRV in clinical practice. Beyond treatment-related determinants, the ovarian cancer population is heterogeneous with respect to inherited susceptibility and potentially modifiable environmental or metabolic factors. For example, a prospective cohort

study of *BRCA1* carriers reported an association between elevated blood molybdenum levels and ovarian cancer risk, underscoring the broader need to consider host-level factors in individualized oncological care; these findings require independent confirmation.²²

5. Conclusion

This real-world pharmacovigilance analysis of MIRV using the FAERS database characterizes and substantially expands our understanding of its distinctive adverse-event reporting profile. The study shows that MIRV has a distinct reporting pattern dominated by exceptionally strong signals for ocular adverse events, particularly keratopathy, keratitis, and blurred vision, followed by peripheral neuropathy and pneumonitis. These findings align with the DM4 payload mechanism and are consistent with, but more granular than, clinical trial observations. The analysis provides clinically actionable temporal insights: gastrointestinal toxicities manifest early within days, while ocular and neurological events exhibit delayed onset over weeks to months, mandating differentiated monitoring strategies throughout treatment. Severity analysis reveals a critical safety hierarchy: ocular events are most common but carry low mortality, whereas pneumonitis, though less frequent, demonstrates the highest fatality rate and warrants heightened vigilance. Comparative analysis across five FDA-approved ADCs positions MIRV as the agent with the most pronounced ocular toxicity profile, providing valuable guidance for treatment selection, patient counseling, and toxicity management. These findings empower clinicians to implement proactive, temporally appropriate monitoring protocols, optimize risk-benefit assessment, and enhance patient safety during MIRV therapy. Future research should focus on elucidating risk factors for severe toxicity and developing preventive strategies for high-risk populations.

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Conflict of interest

All authors have declared no conflicts of interest.

Author contributions

Conceptualization: All authors

Formal analysis: All authors

Investigation: Ming-Zhu Jin

Methodology: Ming-Zhu Jin

Writing–original draft: Ming-Zhu Jin

Writing–review & editing: All authors

Ethics approval and consent to participate

This study used publicly available, de-identified data from FAERS and did not require institutional review board approval.

Consent for publication

Not applicable.

Availability of data

This study is based on the FAERS database, which is publicly accessible at <https://fis.fda.gov/extensions/FPD-QDE-FAERS/FPD-QDE-FAERS.html> without requiring prior applications. The R code used for analysis is available from the corresponding author upon reasonable request.

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