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Original Article

Neurotoxic Signals of 14 Chemotherapeutic Agents: Global Real-World Evidence and Nursing Implications Based on FAERS and EudraVigilance Databases

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Abstract:

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating dose-limiting toxicity. Despite its clinical significance, real-world data integrating long-term temporal dynamics with specific nursing care strategies remain limited. This study aims to characterize CIPN signals and onset patterns to provide evidence-based guidance for oncology nursing.

Methods: We performed a retrospective analysis of the US FDA Adverse Event Reporting System (FAERS, 2004–2025), with parallel validation using the EudraVigilance database (EV, 2003–2025). Disproportionality was assessed using Reporting Odds Ratio (ROR), Proportional Reporting Ratio (PRR), and Empirical Bayes Geometric Mean (EBGM) for 14 chemotherapeutic agents. Time-to-Onset (TTO) and clinical severity were evaluated to identify high-risk periods and vulnerable subpopulations.

Results: A total of 9,078 reports were identified in FAERS, with 10,056 reports from EV providing a robust external validation. Both datasets showed a high level of clinical fidelity, with 94.56% of EV reports originating from healthcare professionals. Females and patients aged ≥45 were most affected. In FAERS, the median TTO was 25 days (IQR: 6–78 days), with 54.50% of cases manifesting within the first month. Vincristine showed the highest signal intensity in FAERS (ROR: 12.90), while Paclitaxel (ROR: 7.83) and Vincristine (ROR: 5.04) dominated the EV dataset. Granular PT analysis in EV further confirmed high-intensity signals for peripheral sensory neuropathy (ROR: 9.26) and polyneuropathy (ROR: 20.01). Fatal outcomes in FAERS were associated with a significantly longer TTO (32 days) compared to non-fatal cases (P=0.0288).

Conclusions: CIPN is a predominantly early-onset, severe toxicity requiring immediate vigilance during the first chemotherapy cycle. Nursing interventions must transition from reactive management to proactive, agent-specific monitoring and longitudinal education.

Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) remains one of the most debilitating and prevalent chronic complications of chemotherapeutic therapy123. With the expansion of the cancer survivor population and the widespread use of neurotoxic agents, including taxanes, platinum-based compounds, and vinca alkaloids, CIPN prevalence is reported as high as 68.1% within the first month of treatment, with approximately 30% of patients continuing to experience symptoms six months post-therapy4. Characterized by symmetrical sensory loss,

paresthesia, and neuropathic pain, CIPN can progress to motor dysfunction and autonomic impairment in severe cases5.

As a primary dose-limiting toxicity, severe CIPN often necessitates dose reductions, cycle delays, or the premature termination of life-saving chemotherapy, directly compromising oncological outcomes6. Beyond its clinical implications, the resulting impairment of fine motor skills (e.g., buttoning clothes, writing) and loss of proprioception significantly diminish patient quality of life (QoL)7. Moreover, these deficits markedly increase the risk of falls and permanent functional disability, posing a substantial challenge to long-term patient safety.

Oncology nurses are at the forefront of CIPN management, serving a critical role in early symptom detection, patient education, and the implementation of safety interventions8. However, current nursing practice faces significant hurdles. Neurological assessments are often reactive rather than proactive, frequently lacking standardized, evidence-based tools such as the Total Neuropathy Score (TNS)9. Moreover, the traditional perception of CIPN as a cumulative, late-stage toxicity leads to inadequate surveillance during the early cycles of therapy. Furthermore, there is a lack of agent-specific nursing protocols that account for the distinct neurotoxic profiles and onset patterns, such as the "coasting" effect or the acute cold sensitivity associated with specific regimens.

Despite extensive clinical research, large-scale, real-world evidence spanning multiple decades remains scarce, particularly studies that integrate longitudinal pharmacovigilance data with nursing-oriented outcomes. There is a pressing need to bridge the gap between statistical signal detection and clinical bedside vigilance.

To address this, the present study employs a comprehensive dual-database approach, leveraging both the US FDA Adverse Event Reporting System (FAERS) and the EudraVigilance (EV) database from 2003 through 2025. By performing multi-algorithmic disproportionality analyses across these two global reporting systems, we aim to: (1) quantify the neurotoxic signal intensity of 14 key chemotherapeutic agents; (2) delineate the temporal dynamics (Time-to-Onset) and demographic risk profiles associated with CIPN; and (3) construct an evidence-based framework for nurse-led early warning systems and tailored symptom management strategies.

2. Methods

2.1 Data Source and Study Population

A global, retrospective pharmacovigilance study was conducted to characterize the safety landscape of chemotherapy-induced peripheral neuropathy (CIPN). Primary adverse event (AE) reports were systematically retrieved from the US FDA Adverse Event Reporting System (FAERS), spanning from 2004 through 2025. To provide a parallel validation and ensure the global representativeness of the findings, data were also extracted from the EudraVigilance (EV) database, managed by the European Medicines Agency (EMA), covering the period from 2003 through 2025. For the FAERS dataset, a multi-step deduplication process was performed using SAS software (version 9.4), filtering reports based on overlapping patient age, sex, event dates, and reporting countries.

2.2 Case Definition and MedDRA Mapping

Adverse events were standardized using the Medical Dictionary for Regulatory Activities (MedDRA, version 27.0). CIPN cases were identified through a pre-defined cluster of Preferred Terms (PTs) representing various neurotoxic manifestations, including but not limited to Peripheral sensory neuropathy, Polyneuropathy, Mononeuropathy multiplex, and Polyneuropathy in malignant disease. The analysis focused on 14 neurotoxic

chemotherapeutic agents (Paclitaxel, Carboplatin, Doxorubicin, Docetaxel, Gemcitabine, Irinotecan, Vincristine, Cyclophosphamide, Cisplatin, Etoposide, Bendamustine, Epirubicin, Topotecan, Lurbinectedin), where these drugs were designated as the "primary suspect" (PS) in the AE reports.

2.3 Clinical and Temporal Characterization

Demographic variables (age, sex) and reporter qualifications (physician, pharmacist, etc.) were extracted and analyzed. Clinical outcomes were categorized into "serious" and "non-serious," with serious events further classified into hospitalization, permanent disability, and death.Time-to-Onset (TTO) was defined as the latency period between the initiation of chemotherapy and the first manifestation of neurotoxicity. Due to the non-normal distribution of the temporal data, TTO was expressed as the median with interquartile range (IQR). The Wilcoxon rank-sum test was employed to evaluate statistical disparities in TTO across different clinical cohorts (e.g., fatal vs. non-fatal cases).

2.4 Signal Detection Algorithms (Disproportionality Analysis)

To quantify the association between specific chemotherapeutic agents and CIPN, three distinct disproportionality algorithms were utilized based on 2×2 contingency tables. The specific formulae are as follows.

ROR

$$ROR=\frac{ad}{bc}$$

$$95\%CI=e^{\ln(ROR)\pm1.96\sqrt{\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d}}}$$

If the lower limit of 95% CI>1 and a≥3, the ROR should be considered a signal.

PRR

$$PRR=\frac{a/(a+b)}{c/(c+d)}$$

$$95\%CI=e^{\ln(PRR)\pm1.96\sqrt{\frac{1}{a}+\frac{1}{a+b}+\frac{1}{c}+\frac{1}{c+d}}}$$

If a≥3 and the lower limit of 95% CI > 1, the PRR should be considered a signal.

EBGM

$$EBGM=\frac{a(a+b+c+d)}{(a+c)(a+b)}$$

$$95\%CI=e^{\ln(EBGM)\pm1.96\sqrt{\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d}}}$$

If EBGM05 > 2, it should be considered a signal.

2.5 Statistical Correlation and Subgroup Analysis

Agent-specific neurotoxic profiles were further explored at the PT level to identify unique clinical signatures (e.g., motor vs. sensory deficits). The EudraVigilance cohort served as an independent validation set to verify the robustness of the signals identified in FAERS. Stratified analyses were conducted to pinpoint high-risk subpopulations based on age and gender. All statistical analyses and data visualizations, including TTO density plots and forest plots for signal intensity, were generated using SAS 9.4 and R software (version 4.3.0). A two-sided P-value < 0.05 was considered statistically significant.

3. Results

Descriptive Analysis of CIPN Reports and Baseline Characteristics

Between 2004 and 2025, a total of 9,078 adverse event (AE) reports pertaining to chemotherapy-induced peripheral neuropathy (CIPN) were retrieved from the FAERS database. Data submission was predominantly driven by medical professionals, with physicians (39.93%), pharmacists (23.80%), and other healthcare providers (23.43%) accounting for the bulk of reports (Figure 1). Clinical severity analysis

underscored the significant burden of CIPN, as 97.00% (n=8,806) of cases were classified as serious(Figures 2), including hospitalization (25.85%), death (8.64%), and permanent disability (6.86%) (Figures 3). Demographic trends revealed a female predominance (53.33% vs. 32.71% in males) (Figure 4), with the 45–64 age cohort (33.18%) and patients aged ≥65 (27.87%) (Figure 5)being the most frequently affected. At the agent level, Paclitaxel (N=1,966), Carboplatin (N=1,282), and Docetaxel (N=1,110) were the most common triggers (Figure 6). Notably, the annual report volume exhibited a sustained upward trajectory, peaking in 2019 (n=853) and remaining elevated through 2024 (Figure 7).

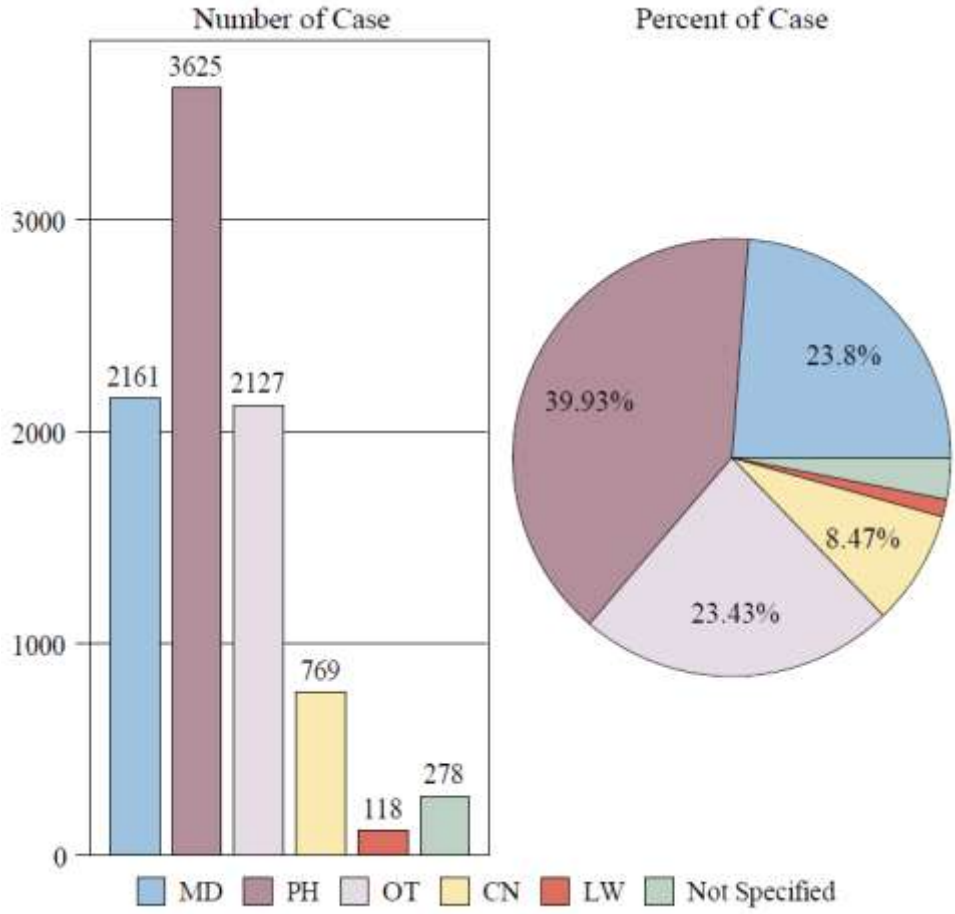


Figure1. Reporter distribution of AE reports (FAERS)

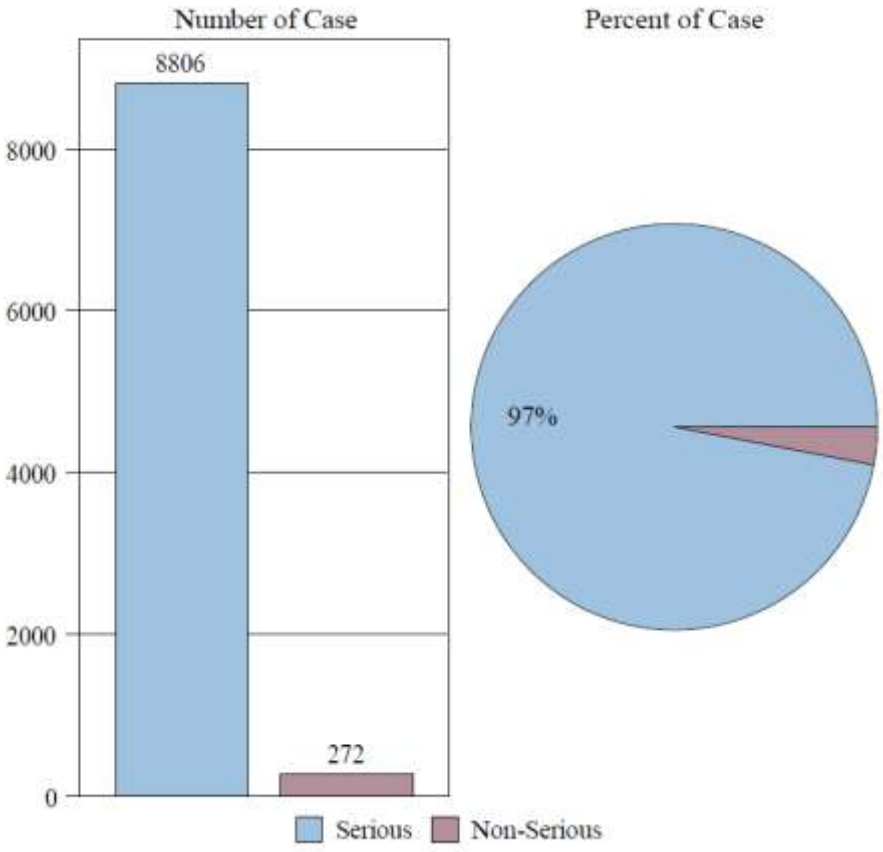


Figure2. Serious Report distribution of AE reports (FAERS)

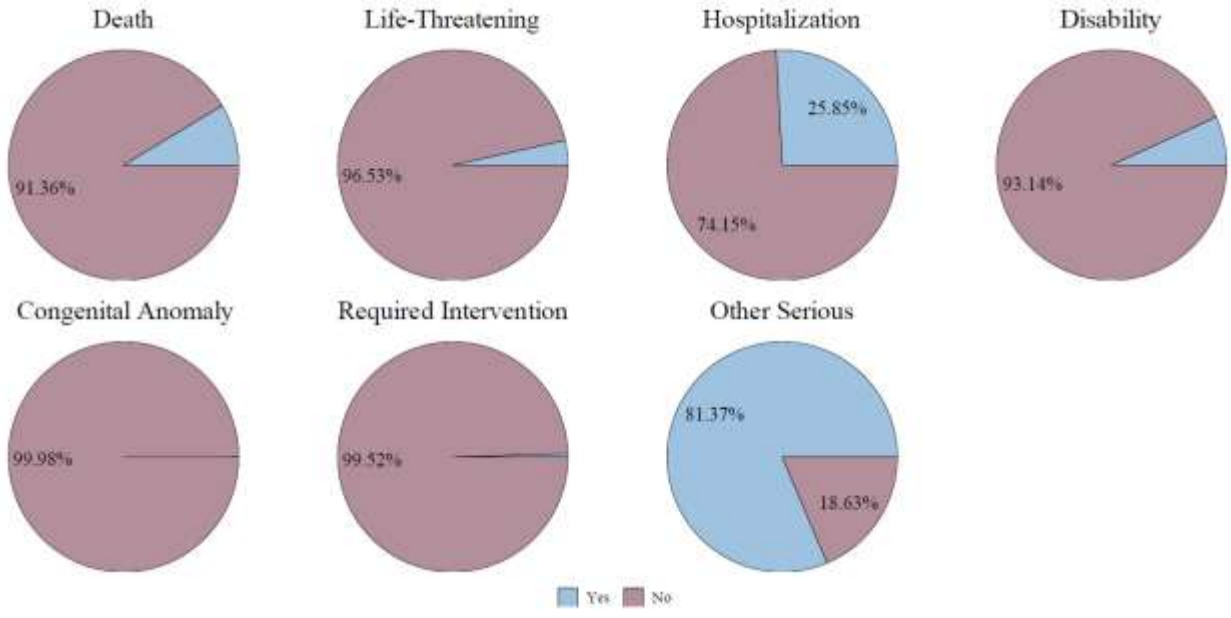


Figure3. Outcomes report distribution of AE reports(FAERS)

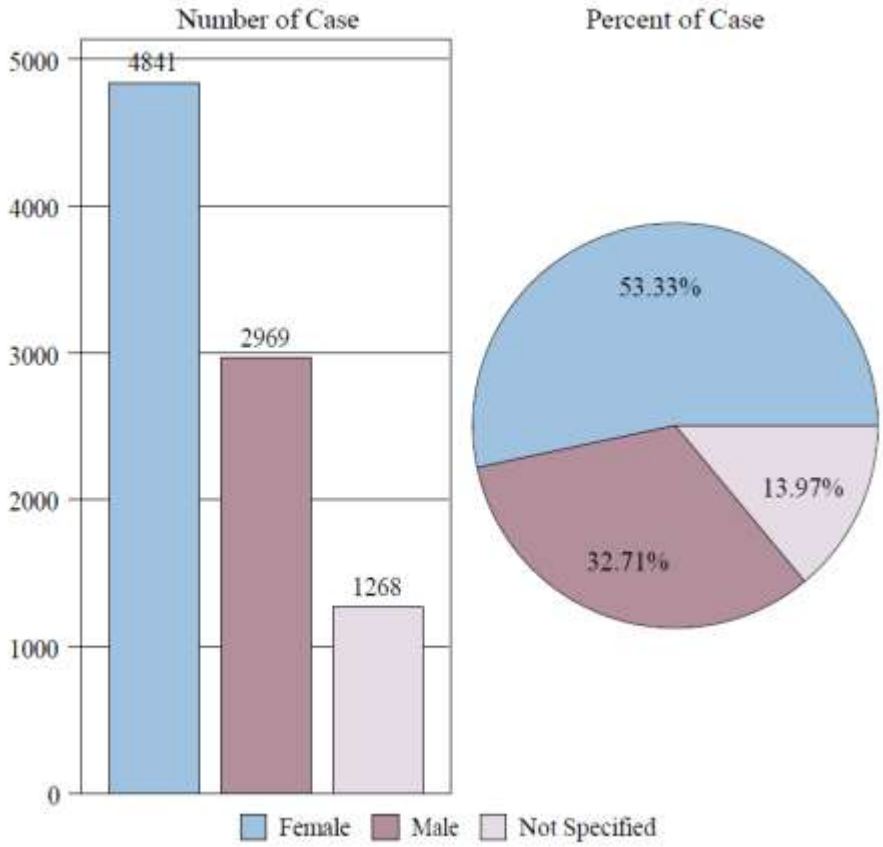


Figure4. Sex distribution of AE reports(FAERS)

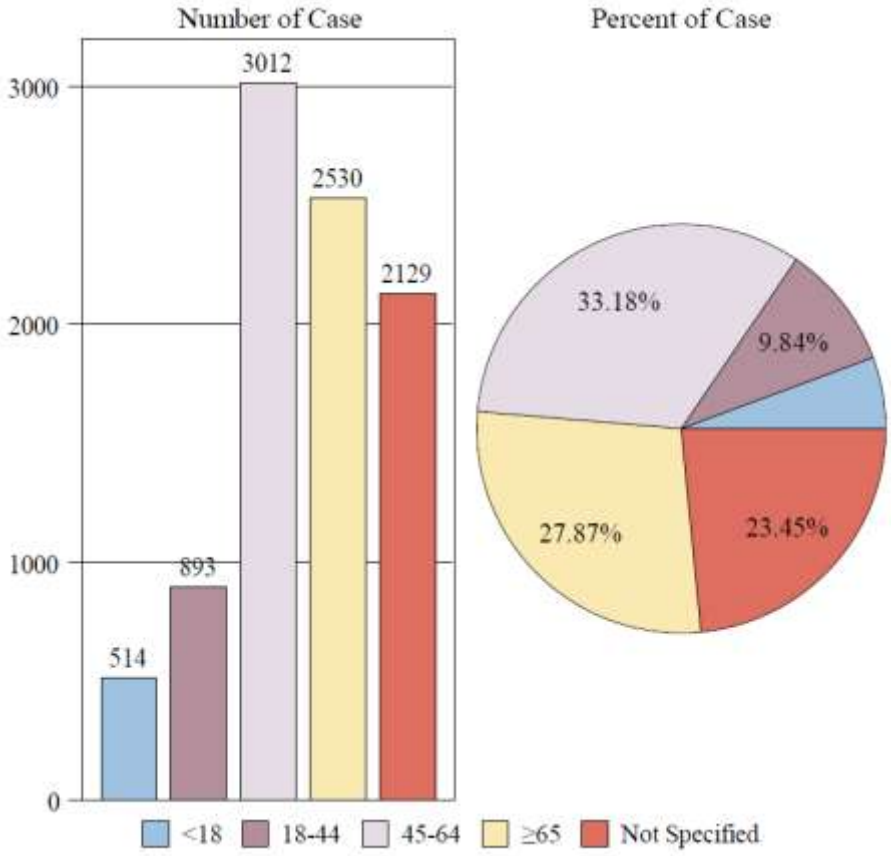


Figure5. Age distribution of AE reports (FAERS)

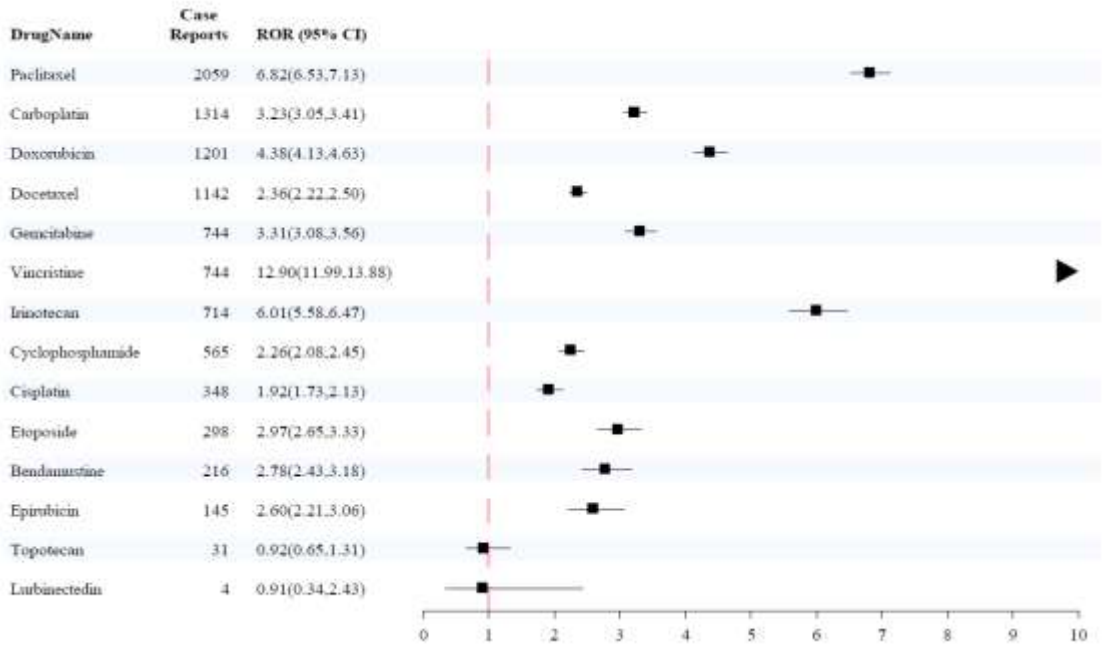


Figure6. Distribution of CIPN reports by chemotherapeutic agent

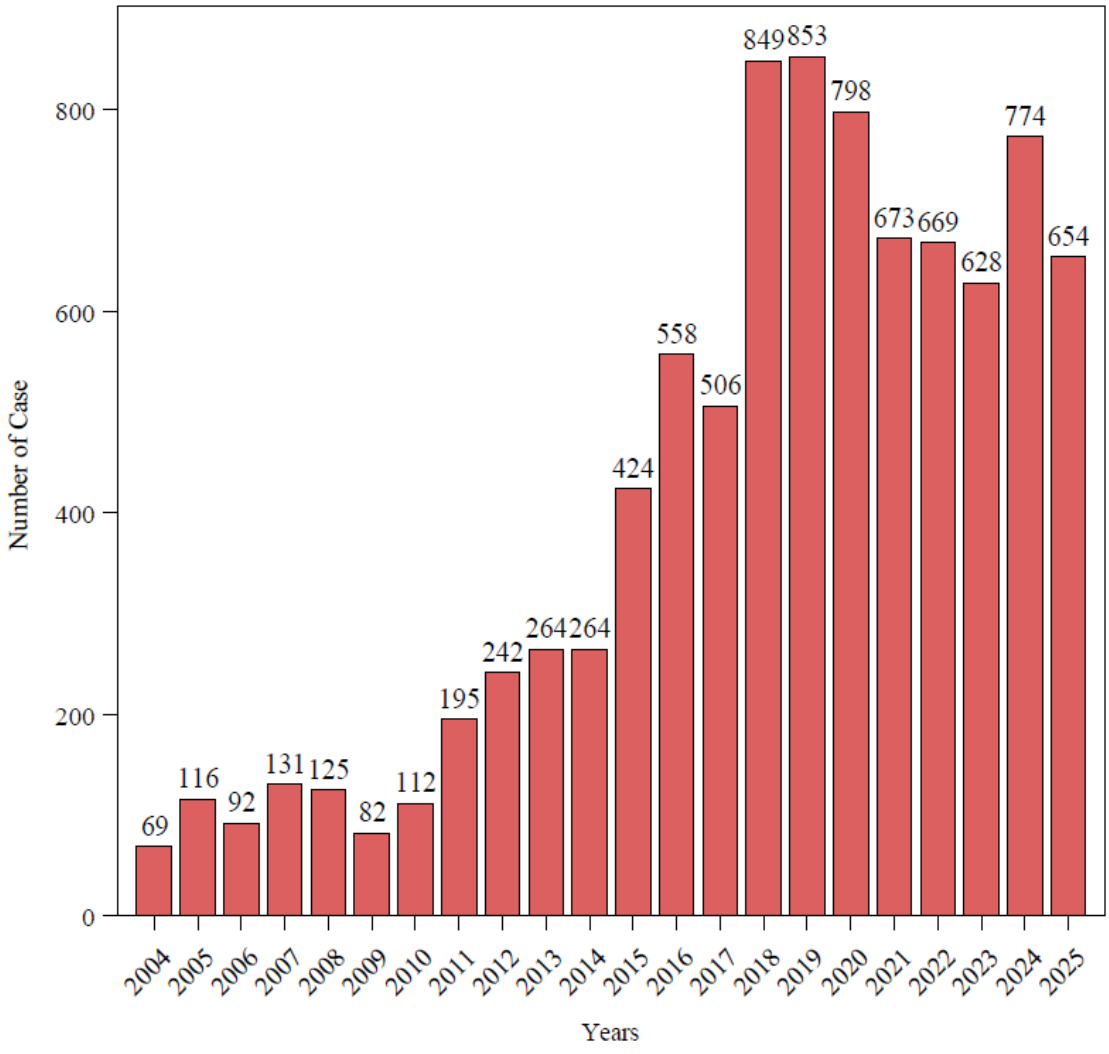


Figure7. Annual distribution of AE reports (FAERS)

Temporal Distribution and Time-to-Onset (TTO) Profile

The temporal analysis of CIPN onset yielded a median TTO of 25.00 days (IQR: 6.00–78.00 days) (Figure 8). A significant proportion of events occurred early in the treatment course, with 54.50% (n=1,180) of timing-specified reports manifesting within the initial 30 days (Figure 9). This "early-peak" pattern waned over time, with only 3.23% of cases emerging after one year of therapy. Subgroup comparisons indicated that TTO was relatively independent of gender (P=0.4575) (Figure 10), age (P=0.2632) (Figure 11), or overall clinical severity (P=0.8171) (Figure 12). However, a distinct temporal shift was observed in fatal outcomes, where the median TTO was significantly longer compared to non-fatal cases (32.00vs.24.00 days; P=0.0288)(Figure 13). Heterogeneity was also observed across different drug classes: Etoposide (12.00 days), Irinotecan (14.00 days), and Cisplatin (18.00 days) showed the shortest latency periods, whereas Docetaxel was characterized by a delayed median onset of 49.50 days (Table 1).

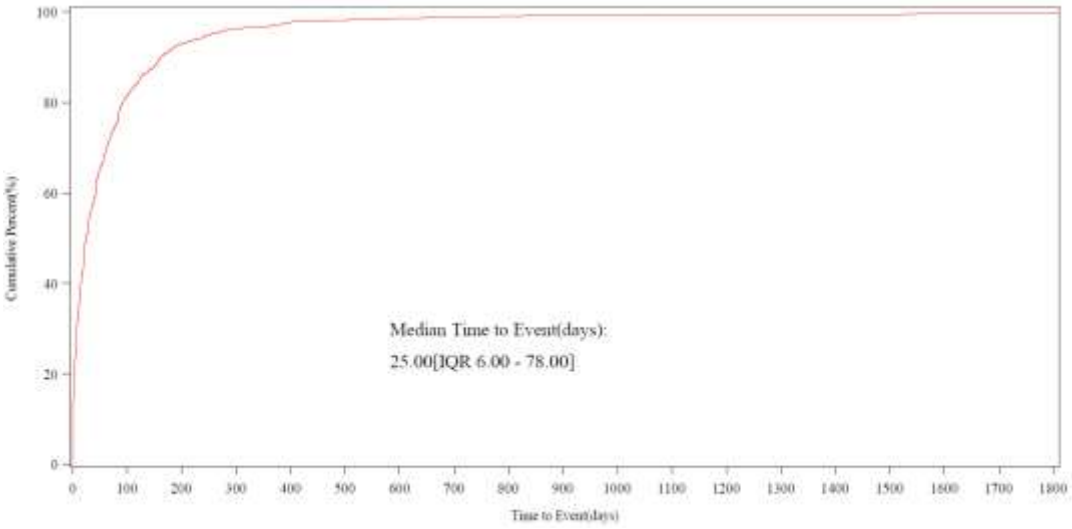


Figure8. Cumulative Distribution of Time-to-Onset(FAERS)

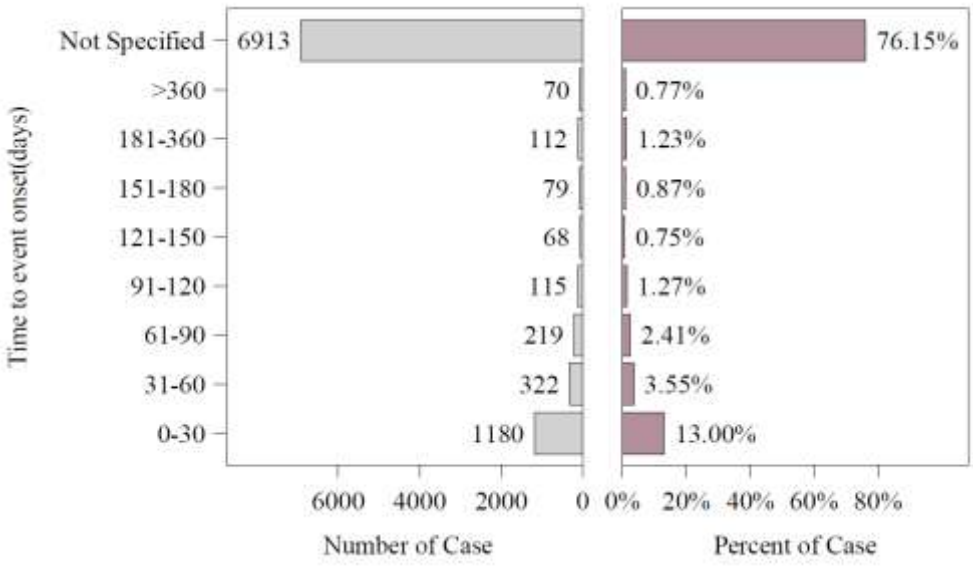


Figure9. Time to event report distribution of AE reports(FAERS)

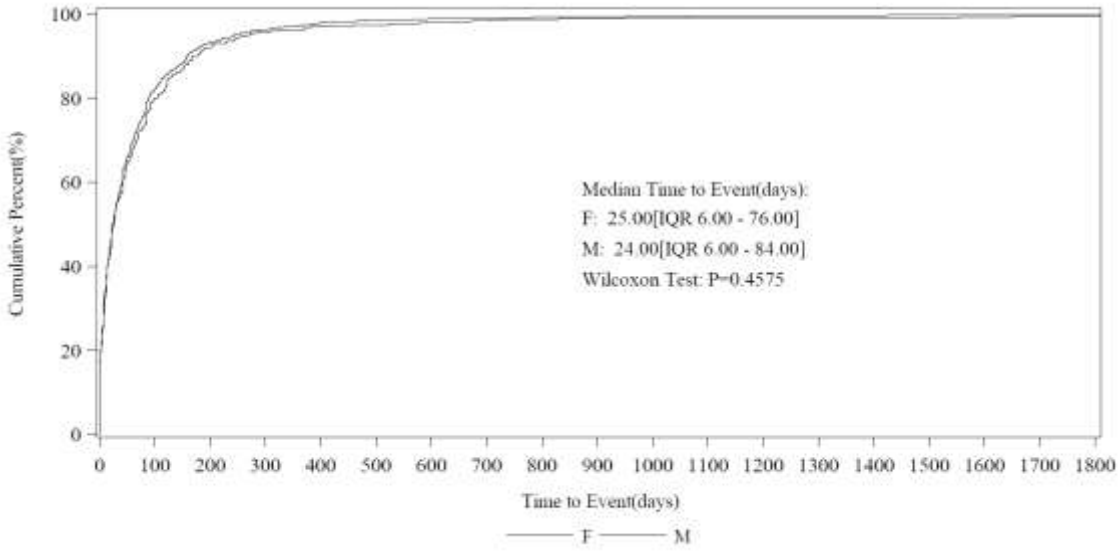


Figure10.Cumulative percentage of time-to-onset across different sex groups(FAERS)

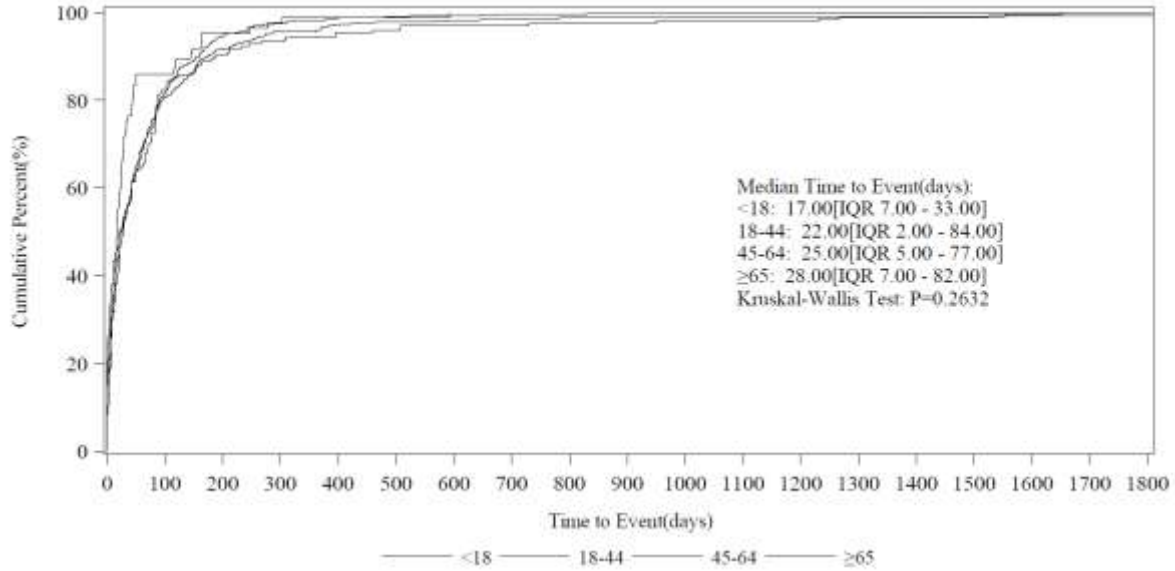


Figure11.Cumulative percentage of time-to-onset across different age groups(FAERS)

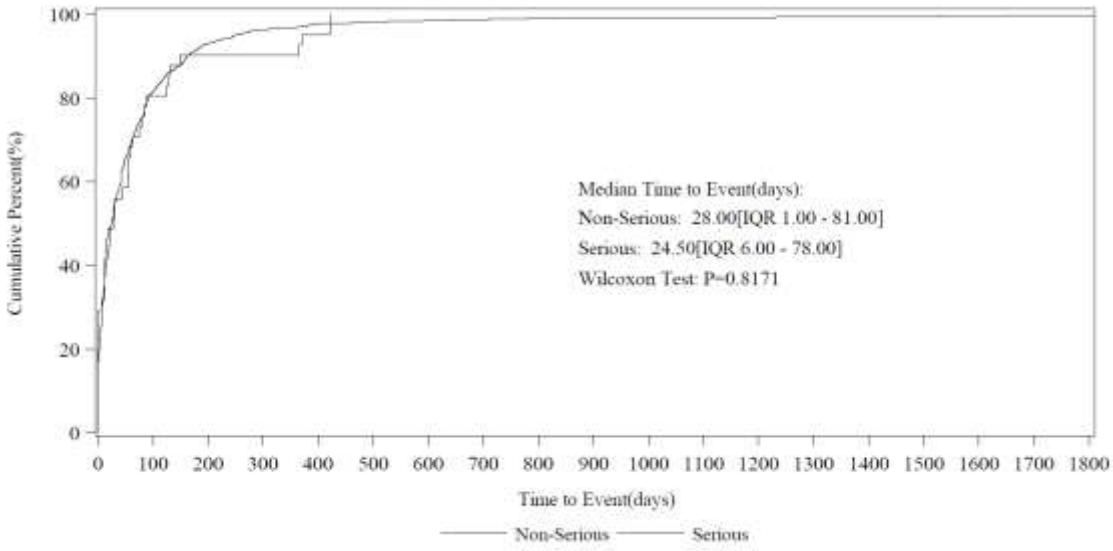


Figure12. Cumulative percentage of time-to-onset across different serious clinical outcomes(FAERS)

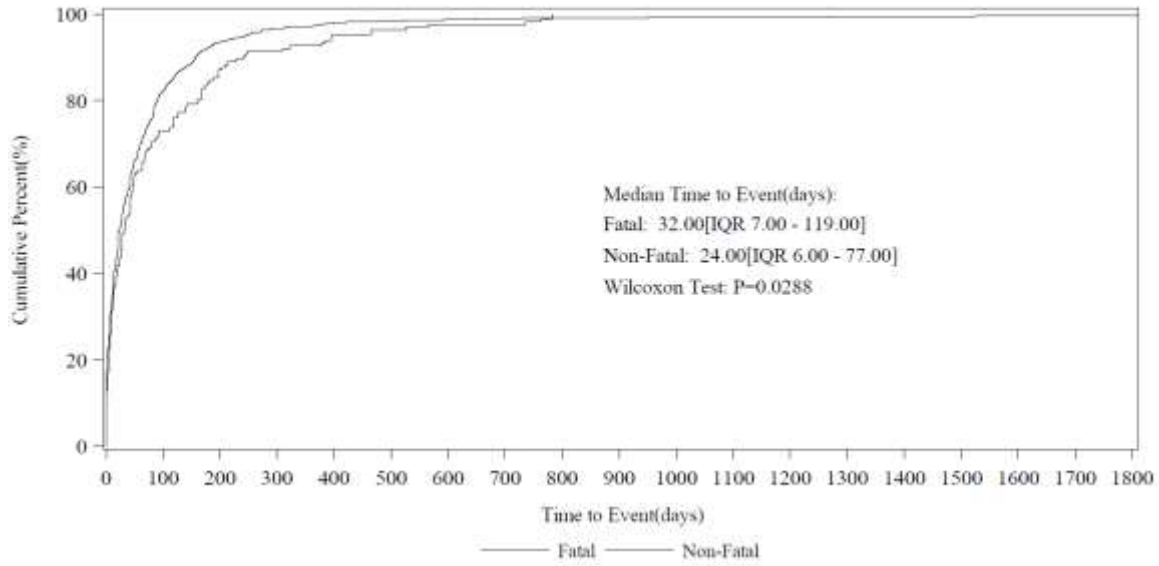


Figure13. Cumulative percentage of time-to-onset for fatal versus non-fatal outcomes(FAERS)

Table 1. TTO Analysis by Agent(FAERS)

Drug/TTO	PACLITAXEL	CARBOPLATIN	DOXORUBICIN	DOCETAXEL	GEMCITABINE	IRINOTECAN	VINCRISTINE	CYCLOPHOSPHAMIDE	CISPLATIN	ETOPOSIDE	BENDAMUSTINE	EPIRUBICIN	TOPOTECAN	LURBINECTEDIN
N(Missing)	596(1370)	377(905)	101(1032)	368(732)	146(586)	172(522)	142(513)	87(440)	44(284)	40(244)	48(152)	34(109)	10(20)	0(4)
Mean(SD)	73.56(134.26)	73.32(240.30)	154.45(512.74)	63.28(128.77)	87.13(131.89)	36.77(68.77)	106.77(555.58)	134.55(488.55)	43.50(56.24)	41.78(118.43)	118.06(308.75)	60.47(162.13)	57.70(123.09)	()
Median(Q1,Q3)	28.00(7.00,89.00)	27.00(7.00,71.00)	21.00(1.00,84.00)	22.50(3.00,68.00)	49.50(7.00,97.00)	14.00(1.00,45.50)	26.50(12.00,70.00)	28.00(9.00,118.00)	18.00(3.00,73.50)	12.00(1.50,22.00)	27.00(0.00,89.00)	21.00(4.00,57.00)	7.00(4.00,28.00)	(,)
Min,Max	0.00,1896.00	0.00,3001.00	0.00,4296.00	0.00,1526.00	0.00,830.00	0.00,644.00	0.00,6574.00	0.00,4296.00	0.00,265.00	0.00,730.00	0.00,1524.00	0.00,950.00	0.00,393.00	,

Disproportionality Assessment and Neurotoxic Signal Strength

Multi-algorithmic disproportionality analysis identified significant neurotoxic signals for 12 of the 14 evaluated chemotherapeutic agents. Vincristine emerged with the highest signal intensity across all metrics (ROR: 12.90, 95% CI: 11.99–13.88; PRR: 12.51; $EBGM_{05}$: 11.57), followed by robust associations for Paclitaxel (ROR: 6.82) and Irinotecan (ROR: 6.01).Granular analysis at the Preferred Term (PT) level

highlighted distinct neurotoxic profiles. Vincristine demonstrated a notably concentrated impact on motor and focal nerves, underscored by extreme risks of peripheral motor neuropathy (ROR: 85.68), sciatic nerve palsy (ROR: 66.88), and mononeuropathy multiplex (ROR: 55.21). In contrast, Paclitaxel signals were predominantly defined by sensory and axonal involvement, particularly classic peripheral sensory neuropathy (ROR: 23.55) and acute motor-sensory axonal neuropathy (ROR: 22.57).Notably, several agents displayed highly specific signatures: Bendamustine showed a potent association with anti-MAG associated polyneuropathy (ROR: 166.03), while Cisplatin exhibited a striking link to alcoholic polyneuropathy (ROR: 100.52). Interestingly, although Cisplatin fulfilled the ROR and PRR thresholds, its $EBGM_{05}$ (1.72) remained below the conservative cutoff of 2.0, suggesting a more moderate association compared to Carboplatin ($EBGM_{05}$: 3.02). No signals were detected for Topotecan or Lurbinectedin. The internal consistency of these findings is underscored by the high degree of algorithmic concordance across ROR, PRR, and EBGM thresholds for core neurotoxic terms (Tables 2–3).

Table 2.Agent-Specific Signal Profiles for Chemotherapy-Induced Peripheral Neuropathy(FAERS)

Drug	ROR(95% CI)	PRR(95% CI)	EBGM(EBGM05)	ROR Signal	PRR Signal	EBGM Signal
PACLITAXEL	6.82(6.53,7.13)	6.72(6.43,7.01)	6.64(6.36)	Y	Y	Y
CARBOPLATIN	3.23(3.05,3.41)	3.21(3.04,3.38)	3.19(3.02)	Y	Y	Y
DOXORUBICIN	4.38(4.13,4.63)	4.34(4.10,4.59)	4.31(4.07)	Y	Y	Y
DOCETAXEL	2.36(2.22,2.50)	2.35(2.21,2.49)	2.34(2.20)	Y	Y	Y
GEMCITABINE	3.31(3.08,3.56)	3.29(3.06,3.53)	3.28(3.05)	Y	Y	Y
VINCRISTINE	12.90(11.99,13.88)	12.51(11.65,13.43)	12.45(11.57)	Y	Y	Y
IRINOTECAN	6.01(5.58,6.47)	5.93(5.51,6.38)	5.91(5.48)	Y	Y	Y
CYCLOPHOSPHAMIDE	2.26(2.08,2.45)	2.25(2.07,2.44)	2.24(2.06)	Y	Y	Y
CISPLATIN	1.92(1.73,2.13)	1.91(1.72,2.12)	1.91(1.72)	Y	Y	N
ETOPOSIDE	2.97(2.65,3.33)	2.96(2.64,3.31)	2.95(2.64)	Y	Y	Y
BENDAMUSTINE	2.78(2.43,3.18)	2.77(2.42,3.16)	2.76(2.42)	Y	Y	Y
EPIRUBICIN	2.60(2.21,3.06)	2.59(2.20,3.04)	2.58(2.20)	Y	Y	Y
TOPOTECAN	0.92(0.65,1.31)	0.92(0.65,1.31)	0.92(0.65)	N	N	N
LURBINECTEDIN	0.91(0.34,2.43)	0.91(0.34,2.42)	0.91(0.34)	N	N	N

Table 3. Neurotoxic Signals of Specific Agents by Preferred Term(FAERS)

Drug	PT	ROR(95% CI)	PRR(95% CI)	EBGM(EBGM05)	ROR Signal	PRR Signal	EBGM Signal
PACLITAXEL	Neuropathy peripheral	7.86(7.45, 8.30)	7.78(7.38, 8.21)	7.68(7.28)	Y	Y	Y
CARBOPLATIN	Neuropathy peripheral	3.29(3.06, 3.53)	3.27(3.05, 3.51)	3.25(3.03)	Y	Y	Y
DOXORUBICIN	Neuropathy peripheral	4.65(4.32, 5.00)	4.63(4.30, 4.97)	4.60(4.27)	Y	Y	Y
DOCETAXEL	Neuropathy peripheral	2.58(2.39, 2.78)	2.57(2.39, 2.77)	2.56(2.38)	Y	Y	Y
GEMCITABI	Neuropathy peripheral	4.07(3.73,	4.05(3.71,	4.03(3.70	Y	Y	Y

NE		4.43)	4.41)	)			
IRINOTECAN	Neuropathy peripheral	7.10(6.49, 7.77)	7.03(6.43, 7.69)	7.00(6.40)	Y	Y	Y
VINCRISTIN E	Neuropathy peripheral	13.91(12. 68,15.26)	13.64(12. 46,14.93)	13.58(12. 38)	Y	Y	Y
CYCLOPHOS PHAMIDE	Neuropathy peripheral	2.03(1.81, 2.28)	2.03(1.80, 2.27)	2.02(1.80)	Y	Y	N
PACLITAXEL	Polyneuropathy	12.21(10. 80,13.81)	12.19(10. 78,13.78)	11.92(10. 54)	Y	Y	Y
PACLITAXEL	Peripheral sensory neuropathy	23.55(20. 71,26.77)	23.50(20. 68,26.71)	22.49(19. 78)	Y	Y	Y
CARBOPLAT IN	Polyneuropathy	8.02(7.03, 9.15)	8.01(7.03, 9.13)	7.86(6.90)	Y	Y	Y
DOCETAXEL	Polyneuropathy	6.07(5.28, 6.97)	6.06(5.28, 6.96)	5.97(5.20)	Y	Y	Y
CISPLATIN	Neuropathy peripheral	1.87(1.62, 2.15)	1.86(1.62, 2.14)	1.86(1.62)	Y	Y	N
DOXORUBIC IN	Peripheral sensory neuropathy	19.13(16. 49,22.19)	19.10(16. 47,22.14)	18.50(15. 95)	Y	Y	Y
DOXORUBIC IN	Polyneuropathy	8.55(7.33, 9.97)	8.54(7.32, 9.96)	8.42(7.22)	Y	Y	Y
ETOPOSIDE	Neuropathy peripheral	2.78(2.38, 3.25)	2.77(2.37, 3.24)	2.77(2.37)	Y	Y	Y
CARBOPLAT IN	Peripheral sensory neuropathy	9.68(8.17, 11.48)	9.68(8.17, 11.46)	9.46(7.98)	Y	Y	Y
BENDAMUS TINE	Neuropathy peripheral	2.75(2.30, 3.29)	2.74(2.30, 3.28)	2.74(2.29)	Y	Y	Y
GEMCITABI NE	Polyneuropathy	7.15(5.94, 8.60)	7.14(5.93, 8.59)	7.08(5.88)	Y	Y	Y
DOCETAXEL	Peripheral sensory neuropathy	6.70(5.56, 8.08)	6.70(5.56, 8.07)	6.58(5.46)	Y	Y	Y
IRINOTECAN	Peripheral sensory neuropathy	24.75(20. 36,30.08)	24.69(20. 32,30.00)	24.25(19. 95)	Y	Y	Y
VINCRISTIN E	Polyneuropathy	23.38(19. 13,28.56)	23.28(19. 07,28.42)	23.08(18. 89)	Y	Y	Y
EPIRUBICIN	Neuropathy peripheral	2.98(2.44, 3.65)	2.98(2.43, 3.64)	2.97(2.43)	Y	Y	Y
CYCLOPHOS PHAMIDE	Polyneuropathy	4.43(3.55, 5.54)	4.43(3.54, 5.53)	4.40(3.52)	Y	Y	Y
IRINOTECAN	Polyneuropathy	8.53(6.76, 10.75)	8.52(6.76, 10.74)	8.47(6.71)	Y	Y	Y
CYCLOPHOS PHAMIDE	Peripheral sensory neuropathy	7.89(6.22, 10.01)	7.88(6.22, 10.00)	7.80(6.15)	Y	Y	Y
CISPLATIN	Polyneuropathy	4.16(3.17, 5.44)	4.15(3.17, 5.44)	4.14(3.16)	Y	Y	Y
GEMCITABI NE	Peripheral sensory neuropathy	6.58(5.00, 8.64)	6.57(5.00, 8.63)	6.52(4.96)	Y	Y	Y
ETOPOSIDE	Peripheral sensory neuropathy	14.25(10. 78,18.83)	14.23(10. 78,18.80)	14.11(10. 68)	Y	Y	Y
VINCRISTIN E	Peripheral sensory neuropathy	22.14(16. 55,29.60)	22.09(16. 53,29.52)	21.91(16. 39)	Y	Y	Y

CISPLATIN	Peripheral sensory neuropathy	7.09(5.28, 9.51)	7.08(5.28, 9.50)	7.03(5.24)	Y	Y	Y
DOXORUBICIN	Peripheral motor neuropathy	19.23(14. 24,25.97)	19.22(14. 23,25.96)	18.62(13. 78)	Y	Y	Y
CYCLOPHOSPHAMIDE	Guillain-Barre syndrome	5.93(4.37, 8.03)	5.93(4.37, 8.03)	5.88(4.34)	Y	Y	Y
VINCRISTINE	Peripheral motor neuropathy	85.68(62. 99,116.54)	85.52(62. 91,116.26)	82.84(60. 90)	Y	Y	Y
PACLITAXEL	Peripheral motor neuropathy	15.25(11. 09,20.97)	15.24(11. 08,20.96)	14.82(10. 78)	Y	Y	Y
CARBOPLATIN	Guillain-Barre syndrome	2.84(2.01, 3.99)	2.84(2.01, 3.99)	2.82(2.00)	Y	Y	Y
BENDAMUSTINE	Polyneuropathy	5.66(3.98, 8.05)	5.65(3.97, 8.04)	5.64(3.96)	Y	Y	Y
ETOPOSIDE	Polyneuropathy	4.10(2.85, 5.90)	4.10(2.85, 5.90)	4.09(2.84)	Y	Y	Y
EPIRUBICIN	Polyneuropathy	6.36(4.29, 9.41)	6.35(4.29, 9.40)	6.34(4.28)	Y	Y	Y
TOPOTECAN	Neuropathy peripheral	1.26(0.84, 1.88)	1.26(0.84, 1.87)	1.26(0.84)	N	N	N
CARBOPLATIN	Peripheral motor neuropathy	6.38(4.19, 9.72)	6.38(4.19, 9.72)	6.29(4.13)	Y	Y	Y
CARBOPLATIN	Peripheral sensorimotor neuropathy	7.31(4.75, 11.26)	7.31(4.75, 11.26)	7.19(4.67)	Y	Y	Y
VINCRISTINE	Peripheral sensorimotor neuropathy	48.13(30. 92,74.92)	48.09(30. 91,74.82)	47.23(30. 35)	Y	Y	Y
VINCRISTINE	Peroneal nerve palsy	9.67(6.23, 15.00)	9.66(6.23, 14.99)	9.63(6.21)	Y	Y	Y
PACLITAXEL	Guillain-Barre syndrome	2.28(1.47, 3.54)	2.28(1.47, 3.54)	2.27(1.47)	Y	Y	N
CYCLOPHOSPHAMIDE	Peripheral motor neuropathy	9.01(5.73, 14.17)	9.00(5.72, 14.16)	8.89(5.65)	Y	Y	Y
IRINOTECAN	Peripheral motor neuropathy	18.78(11. 94,29.54)	18.77(11. 94,29.52)	18.52(11. 77)	Y	Y	Y
PACLITAXEL	Peripheral sensorimotor neuropathy	8.78(5.58, 13.82)	8.78(5.58, 13.82)	8.65(5.49)	Y	Y	Y
CARBOPLATIN	Demyelinating polyneuropathy	7.13(4.48, 11.37)	7.13(4.48, 11.37)	7.02(4.40)	Y	Y	Y
BENDAMUSTINE	Guillain-Barre syndrome	7.70(4.78, 12.40)	7.69(4.78, 12.39)	7.67(4.76)	Y	Y	Y
VINCRISTINE	Guillain-Barre syndrome	10.07(6.2 5,16.22)	10.07(6.2 5,16.20)	10.03(6.2 3)	Y	Y	Y
DOXORUBICIN	Guillain-Barre syndrome	2.16(1.34, 3.47)	2.16(1.34, 3.47)	2.15(1.34)	Y	Y	N
PACLITAXEL	Peroneal nerve palsy	1.58(0.98, 2.54)	1.58(0.98, 2.54)	1.58(0.98)	N	N	N
BENDAMUSTINE	Peripheral sensory neuropathy	5.48(3.30, 9.09)	5.48(3.30, 9.09)	5.46(3.29)	Y	Y	Y
DOCETAXEL	Guillain-Barre syndrome	1.08(0.65, 1.80)	1.08(0.65, 1.80)	1.08(0.65)	N	N	N

DOXORUBICIN	Peripheral sensorimotor neuropathy	7.69(4.62, 12.80)	7.69(4.62, 12.80)	7.60(4.57)	Y	Y	Y
CISPLATIN	Guillain-Barre syndrome	2.91(1.75, 4.83)	2.91(1.75, 4.83)	2.90(1.75)	Y	Y	N
CYCLOPHOSPHAMIDE	Peroneal nerve palsy	1.49(0.86, 2.56)	1.49(0.86, 2.56)	1.48(0.86)	N	N	N
DOCETAXEL	Peripheral motor neuropathy	3.16(1.83, 5.45)	3.16(1.83, 5.45)	3.14(1.82)	Y	Y	N
CISPLATIN	Peripheral sensorimotor neuropathy	10.18(5.89,17.59)	10.18(5.89,17.59)	10.07(5.83)	Y	Y	Y
GEMCITABINE	Guillain-Barre syndrome	1.87(1.06, 3.29)	1.87(1.06, 3.29)	1.86(1.06)	Y	Y	N
EPIRUBICIN	Peripheral sensory neuropathy	6.10(3.46, 10.76)	6.10(3.46, 10.75)	6.09(3.46)	Y	Y	Y
ETOPOSIDE	Guillain-Barre syndrome	3.85(2.13, 6.96)	3.85(2.13, 6.96)	3.85(2.13)	Y	Y	Y
ETOPOSIDE	Peripheral motor neuropathy	12.96(7.16,23.45)	12.95(7.16,23.44)	12.85(7.10)	Y	Y	Y
DOCETAXEL	Peripheral sensorimotor neuropathy	3.20(1.77, 5.79)	3.20(1.77, 5.79)	3.18(1.75)	Y	Y	N
PACLITAXEL	Demyelinating polyneuropathy	5.76(3.18, 10.43)	5.76(3.18, 10.43)	5.70(3.15)	Y	Y	Y
DOCETAXEL	Peroneal nerve palsy	0.59(0.32, 1.09)	0.59(0.32, 1.09)	0.59(0.32)	N	N	N
CARBOPLATIN	Toxic neuropathy	10.03(5.35,18.79)	10.02(5.35,18.78)	9.79(5.22)	Y	Y	Y
CARBOPLATIN	Axonal neuropathy	4.82(2.58, 8.99)	4.82(2.58, 8.99)	4.77(2.56)	Y	Y	Y
PACLITAXEL	Small fibre neuropathy	7.97(4.27, 14.89)	7.97(4.27, 14.89)	7.86(4.21)	Y	Y	Y
BENDAMUSTINE	Demyelinating polyneuropathy	18.68(9.69,36.02)	18.68(9.69,36.00)	18.51(9.60)	Y	Y	Y
CYCLOPHOSPHAMIDE	Peripheral sensorimotor neuropathy	5.08(2.63, 9.78)	5.08(2.63, 9.78)	5.04(2.62)	Y	Y	Y
GEMCITABINE	Peroneal nerve palsy	1.14(0.59, 2.19)	1.14(0.59, 2.19)	1.14(0.59)	N	N	N
VINCRISTINE	Mononeuropathy multiplex	55.21(28.53,106.87)	55.19(28.52,106.80)	54.07(27.94)	Y	Y	Y
VINCRISTINE	Toxic neuropathy	62.24(32.13,120.58)	62.22(32.13,120.50)	60.79(31.38)	Y	Y	Y
DOCETAXEL	Carpal tunnel syndrome	0.22(0.11, 0.42)	0.22(0.11, 0.42)	0.22(0.11)	N	N	N
CARBOPLATIN	Carpal tunnel syndrome	0.26(0.13, 0.50)	0.26(0.13, 0.50)	0.26(0.13)	N	N	N
CARBOPLATIN	Peroneal nerve palsy	0.63(0.33, 1.21)	0.63(0.33, 1.21)	0.63(0.33)	N	N	N
PACLITAXEL	Acute motor-sensory axonal neuropathy	22.57(11.57,44.01)	22.56(11.57,44.00)	21.64(11.09)	Y	Y	Y
ETOPOSIDE	Acute polyneuropathy	48.82(24.	48.81(24.	47.35(23.	Y	Y	Y

		15,98.70)	15,98.66)	42)			
IRINOTECAN	Peripheral sensorimotor neuropathy	9.40(4.69, 18.84)	9.40(4.69, 18.84)	9.34(4.66)	Y	Y	Y
DOXORUBICIN	Peroneal nerve palsy	0.83(0.41, 1.65)	0.83(0.41, 1.65)	0.83(0.41)	N	N	N
CARBOPLATIN	Polyneuropathy in malignant disease	43.70(21.02,90.87)	43.70(21.02,90.87)	39.26(18.88)	Y	Y	Y
CARBOPLATIN	Acute polyneuropathy	11.92(5.90,24.09)	11.92(5.90,24.09)	11.58(5.73)	Y	Y	Y
CISPLATIN	Peripheral motor neuropathy	5.20(2.60, 10.43)	5.20(2.60, 10.42)	5.18(2.58)	Y	Y	Y
PACLITAXEL	Toxic neuropathy	10.61(5.27,21.38)	10.61(5.27,21.38)	10.41(5.17)	Y	Y	Y
GEMCITABINE	Peripheral motor neuropathy	3.65(1.74, 7.67)	3.65(1.74, 7.66)	3.63(1.73)	Y	Y	N
DOCETAXEL	Acute motor-sensory axonal neuropathy	11.01(5.18,23.40)	11.01(5.18,23.40)	10.68(5.03)	Y	Y	Y
DOCETAXEL	Lumbosacral radiculoplexus neuropathy	32.72(15.03,71.24)	32.72(15.03,71.23)	29.76(13.67)	Y	Y	Y
PACLITAXEL	Nerve compression	0.40(0.19, 0.85)	0.41(0.19, 0.85)	0.41(0.19)	N	N	N
PACLITAXEL	Diabetic neuropathy	0.74(0.35, 1.56)	0.74(0.35, 1.56)	0.74(0.35)	N	N	N
PACLITAXEL	Carpal tunnel syndrome	0.27(0.13, 0.56)	0.27(0.13, 0.56)	0.27(0.13)	N	N	N
PACLITAXEL	Axonal neuropathy	4.47(2.12, 9.41)	4.47(2.12, 9.41)	4.44(2.11)	Y	Y	Y
CYCLOPHOSPHAMIDE	Mononeuropathy multiplex	8.66(3.87, 19.38)	8.66(3.87, 19.38)	8.55(3.82)	Y	Y	Y
CYCLOPHOSPHAMIDE	Carpal tunnel syndrome	0.28(0.13, 0.63)	0.28(0.13, 0.63)	0.28(0.13)	N	N	N
GEMCITABINE	Axonal neuropathy	5.23(2.34, 11.68)	5.23(2.34, 11.68)	5.20(2.33)	Y	Y	Y
IRINOTECAN	Nerve compression	0.89(0.40, 1.98)	0.89(0.40, 1.98)	0.89(0.40)	N	N	N
CARBOPLATIN	Axonal and demyelinating polyneuropathy	30.56(13.30,70.23)	30.56(13.30,70.22)	28.34(12.33)	Y	Y	Y
PACLITAXEL	Neuritis	2.14(0.96, 4.77)	2.14(0.96, 4.77)	2.13(0.96)	N	N	N
BENDAMUSTINE	Peripheral motor neuropathy	7.56(3.14, 18.21)	7.56(3.14, 18.20)	7.54(3.13)	Y	Y	Y
CYCLOPHOSPHAMIDE	Lumbosacral radiculoplexus neuropathy	44.11(17.80,109.29)	44.11(17.80,109.28)	41.23(16.64)	Y	Y	Y
GEMCITABINE	Demyelinating polyneuropathy	3.55(1.48, 8.56)	3.55(1.48, 8.56)	3.54(1.47)	Y	Y	N
VINCRISTINE	Axonal neuropathy	16.56(6.87,39.91)	16.56(6.87,39.89)	16.46(6.83)	Y	Y	Y
ETOPOSIDE	Axonal neuropathy	9.81(4.07,	9.81(4.07,	9.75(4.05	Y	Y	Y

		23.63)	23.63)	)			
DOCETAXEL	Small fibre neuropathy	2.51(1.04, 6.04)	2.51(1.04, 6.04)	2.49(1.03)	Y	Y	N
DOCETAXEL	Toxic neuropathy	4.17(1.73, 10.08)	4.17(1.73, 10.08)	4.13(1.71)	Y	Y	N
DOXORUBICIN	Acute polyneuropathy	10.91(4.50,26.43)	10.91(4.50,26.42)	10.72(4.42)	Y	Y	Y
DOXORUBICIN	Toxic neuropathy	7.33(3.03, 17.71)	7.33(3.03, 17.71)	7.25(3.00)	Y	Y	Y
CARBOPLATIN	Miller Fisher syndrome	9.24(3.80, 22.43)	9.24(3.80, 22.43)	9.04(3.72)	Y	Y	Y
CARBOPLATIN	Autoimmune neuropathy	16.39(6.69,40.12)	16.39(6.69,40.12)	15.75(6.43)	Y	Y	Y
PACLITAXEL	Mononeuropathy multiplex	5.84(2.42, 14.11)	5.84(2.42, 14.11)	5.79(2.40)	Y	Y	Y
BENDAMUSTINE	Peroneal nerve palsy	1.47(0.55, 3.93)	1.47(0.55, 3.93)	1.47(0.55)	N	N	N
CYCLOPHOSPHAMIDE	Chronic inflammatory demyelinating polyradiculoneuropathy	2.02(0.76, 5.39)	2.02(0.76, 5.39)	2.01(0.75)	N	N	N
GEMCITABINE	Diabetic neuropathy	0.58(0.22, 1.55)	0.58(0.22, 1.55)	0.58(0.22)	N	N	N
VINCRISTINE	Demyelinating polyneuropathy	10.81(4.05,28.85)	10.80(4.05,28.84)	10.76(4.03)	Y	Y	Y
ETOPOSIDE	Peripheral sensorimotor neuropathy	5.61(2.10, 14.99)	5.61(2.10, 14.98)	5.60(2.10)	Y	Y	Y
DOCETAXEL	Brachial plexopathy	6.23(2.32, 16.77)	6.23(2.32, 16.77)	6.13(2.28)	Y	Y	Y
DOCETAXEL	Miller Fisher syndrome	6.20(2.31, 16.68)	6.20(2.31, 16.68)	6.10(2.27)	Y	Y	Y
TOPOTECAN	Peripheral sensory neuropathy	3.40(1.27, 9.06)	3.40(1.27, 9.05)	3.40(1.27)	Y	Y	N
IRINOTECAN	Ischaemic neuropathy	99.04(35.82,273.84)	99.03(35.82,273.80)	92.03(33.28)	Y	Y	Y
IRINOTECAN	Sciatic nerve palsy	66.88(24.48,182.75)	66.88(24.48,182.72)	63.63(23.29)	Y	Y	Y
EPIRUBICIN	Guillain-Barre syndrome	2.52(0.94, 6.71)	2.52(0.94, 6.70)	2.51(0.94)	N	N	N
EPIRUBICIN	Miller Fisher syndrome	54.18(20.14,145.75)	54.17(20.14,145.69)	53.15(19.76)	Y	Y	Y
DOXORUBICIN	Chronic inflammatory demyelinating polyradiculoneuropathy	1.82(0.68, 4.87)	1.82(0.68, 4.87)	1.82(0.68)	N	N	N
DOXORUBICIN	Demyelinating polyneuropathy	2.31(0.87, 6.18)	2.31(0.87, 6.18)	2.31(0.86)	N	N	N
DOXORUBICIN	Carpal tunnel syndrome	0.17(0.06, 0.45)	0.17(0.06, 0.45)	0.17(0.06)	N	N	N
CISPLATIN	Axonal neuropathy	4.34(1.62,	4.34(1.62,	4.32(1.62	Y	Y	N

		11.59)	11.58)	)			
CISPLATIN	Peroneal nerve palsy	0.63(0.24, 1.68)	0.63(0.24, 1.68)	0.63(0.24)	N	N	N
LURBINECTEDIN	Neuropathy peripheral	1.60(0.60, 4.27)	1.60(0.60, 4.25)	1.60(0.60)	N	N	N
PACLITAXEL	Polyneuropathy in malignant disease	27.48(10.04,75.18)	27.48(10.04,75.17)	26.10(9.54)	Y	Y	Y
PACLITAXEL	Acute polyneuropathy	7.80(2.91, 20.95)	7.80(2.91, 20.95)	7.70(2.87)	Y	Y	Y
PACLITAXEL	Miller Fisher syndrome	9.78(3.64, 26.32)	9.78(3.64, 26.32)	9.62(3.57)	Y	Y	Y
BENDAMUSTINE	Neuritis	4.24(1.37, 13.17)	4.24(1.37, 13.17)	4.23(1.36)	Y	Y	N
CYCLOPHOSPHAMIDE	Polyneuropathy in malignant disease	25.03(7.89,79.41)	25.03(7.89,79.40)	24.10(7.60)	Y	Y	Y
CYCLOPHOSPHAMIDE	Diabetic neuropathy	0.39(0.13, 1.22)	0.39(0.13, 1.22)	0.39(0.13)	N	N	N
CYCLOPHOSPHAMIDE	Toxic neuropathy	4.84(1.55, 15.06)	4.84(1.55, 15.06)	4.81(1.54)	Y	Y	N
CYCLOPHOSPHAMIDE	Axonal neuropathy	2.35(0.76, 7.30)	2.35(0.76, 7.30)	2.34(0.75)	N	N	N
GEMCITABINE	Nerve compression	0.24(0.08, 0.74)	0.24(0.08, 0.74)	0.24(0.08)	N	N	N
VINCRISTINE	Acute motor axonal neuropathy	85.93(27.21,271.45)	85.92(27.21,271.37)	83.21(26.34)	Y	Y	Y
ETOPOSIDE	Polyneuropathy in malignant disease	62.59(19.73,198.52)	62.58(19.73,198.49)	60.18(18.97)	Y	Y	Y
ETOPOSIDE	Demyelinating polyneuropathy	4.79(1.54, 14.89)	4.79(1.54, 14.89)	4.78(1.54)	Y	Y	N
DOCETAXEL	Mononeuritis	6.36(2.03, 19.93)	6.36(2.03, 19.93)	6.25(1.99)	Y	Y	N
DOCETAXEL	Nerve compression	0.11(0.04, 0.34)	0.11(0.04, 0.34)	0.11(0.04)	N	N	N
DOCETAXEL	Neuritis	0.68(0.22, 2.10)	0.68(0.22, 2.10)	0.68(0.22)	N	N	N
DOCETAXEL	Axonal and demyelinating polyneuropathy	12.38(3.91,39.25)	12.38(3.91,39.24)	11.96(3.77)	Y	Y	Y
TOPOTECAN	Polyneuropathy	1.27(0.41, 3.95)	1.27(0.41, 3.94)	1.27(0.41)	N	N	N
IRINOTECAN	Demyelinating polyneuropathy	4.00(1.29, 12.42)	4.00(1.29, 12.42)	3.99(1.28)	Y	Y	N
IRINOTECAN	Peroneal nerve palsy	0.71(0.23, 2.21)	0.71(0.23, 2.21)	0.71(0.23)	N	N	N
DOXORUBICIN	Polyneuropathy in malignant disease	22.64(7.14,71.80)	22.64(7.14,71.80)	21.79(6.87)	Y	Y	Y
DOXORUBICIN	Neuralgic amyotrophy	8.33(2.67, 26.06)	8.33(2.67, 26.06)	8.23(2.63)	Y	Y	Y
DOXORUBIC	Nerve compression	0.19(0.06,	0.19(0.06,	0.19(0.06	N	N	N

IN		0.60)	0.60)	)			
DOXORUBICIN	Neuritis	1.19(0.38, 3.69)	1.19(0.38, 3.69)	1.19(0.38)	N	N	N
CARBOPLATIN	Neuritis	0.80(0.26, 2.49)	0.80(0.26, 2.49)	0.80(0.26)	N	N	N
CISPLATIN	Polyneuropathy in malignant disease	34.64(10.92,109.88)	34.64(10.92,109.87)	33.33(10.51)	Y	Y	Y
CISPLATIN	Toxic neuropathy	6.69(2.15, 20.84)	6.69(2.15, 20.84)	6.65(2.13)	Y	Y	Y
PACLITAXEL	Brachial plexopathy	7.34(2.35, 22.94)	7.34(2.35, 22.94)	7.25(2.32)	Y	Y	Y
PACLITAXEL	Acute motor axonal neuropathy	16.53(5.23,52.21)	16.53(5.23,52.21)	16.03(5.08)	Y	Y	Y
PACLITAXEL	Intensive care unit acquired weakness	3.66(1.18, 11.40)	3.66(1.18, 11.40)	3.64(1.17)	Y	Y	N
PACLITAXEL	Axonal and demyelinating polyneuropathy	19.54(6.16,61.91)	19.54(6.16,61.91)	18.84(5.95)	Y	Y	Y
BENDAMUSTINE	Anti-myelin-associated glycoprotein associated polyneuropathy	166.03(39.24,702.57)	166.02(39.24,702.46)	153.33(36.23)	N	N	Y
BENDAMUSTINE	Diabetic neuropathy	0.84(0.21, 3.38)	0.84(0.21, 3.38)	0.84(0.21)	N	N	N
BENDAMUSTINE	Peripheral sensorimotor neuropathy	3.62(0.90, 14.48)	3.62(0.90, 14.48)	3.61(0.90)	N	N	N
CYCLOPHOSPHAMIDE	Acute polyneuropathy	4.77(1.19, 19.17)	4.77(1.19, 19.17)	4.74(1.18)	N	N	N
CYCLOPHOSPHAMIDE	Nerve compression	0.14(0.04, 0.57)	0.14(0.04, 0.57)	0.14(0.04)	N	N	N
CYCLOPHOSPHAMIDE	Small fibre neuropathy	1.94(0.48, 7.77)	1.94(0.48, 7.77)	1.94(0.48)	N	N	N
GEMCITABINE	Chronic inflammatory demyelinating polyradiculoneuropathy	1.12(0.28, 4.47)	1.12(0.28, 4.47)	1.12(0.28)	N	N	N
GEMCITABINE	Neuritis	0.97(0.24, 3.89)	0.97(0.24, 3.89)	0.97(0.24)	N	N	N
GEMCITABINE	Peripheral sensorimotor neuropathy	1.24(0.31, 4.98)	1.24(0.31, 4.98)	1.24(0.31)	N	N	N
VINCRISTINE	Neuritis	3.70(0.92, 14.80)	3.70(0.92, 14.80)	3.69(0.92)	N	N	N
VINCRISTINE	Diabetic neuropathy	1.10(0.28, 4.42)	1.10(0.28, 4.42)	1.10(0.28)	N	N	N
ETOPOSIDE	Chronic inflammatory demyelinating polyradiculoneuropathy	2.52(0.63, 10.08)	2.52(0.63, 10.08)	2.52(0.63)	N	N	N
ETOPOSIDE	Nerve compression	0.36(0.09, 1.42)	0.36(0.09, 1.42)	0.36(0.09)	N	N	N
ETOPOSIDE	Subacute inflammatory demyelinating polyneuropathy	102.92(24.59,430.66)	102.91(24.59,430.61)	96.54(23.07)	N	N	Y

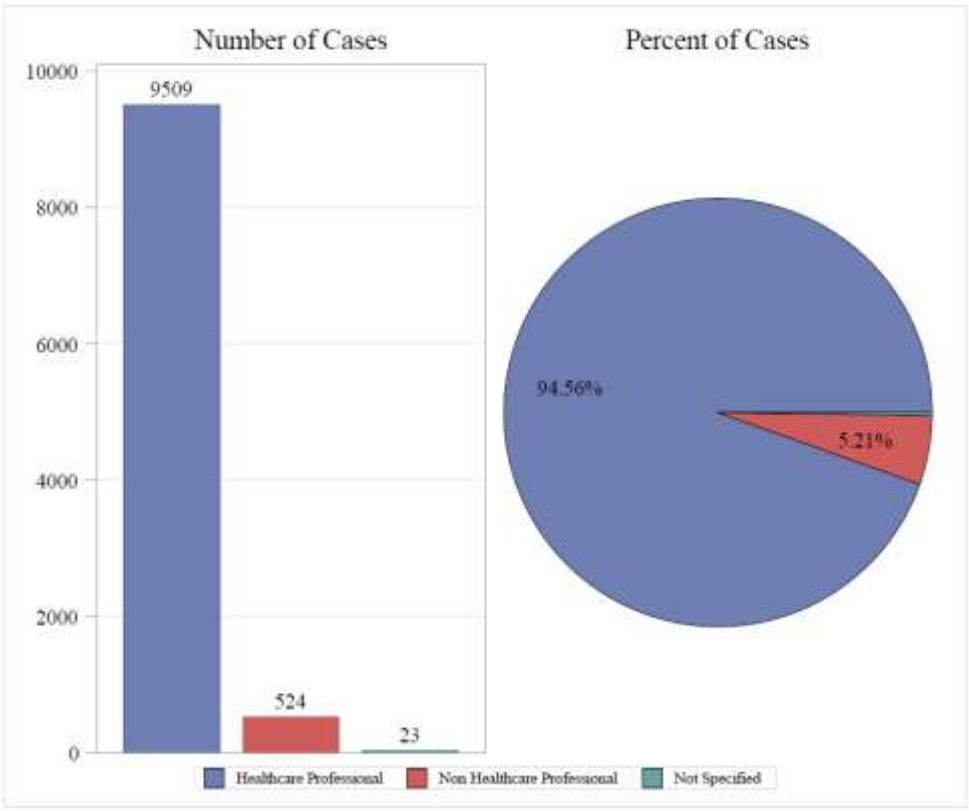
ETOPOSIDE	Toxic neuropathy	8.04(2.00, 32.27)	8.04(2.00, 32.26)	8.00(1.99)	N	N	N
ETOPOSIDE	Intensive care unit acquired weakness	7.49(1.87, 30.07)	7.49(1.87, 30.06)	7.46(1.86)	N	N	N
ETOPOSIDE	Peroneal nerve palsy	0.57(0.14, 2.28)	0.57(0.14, 2.28)	0.57(0.14)	N	N	N
DOCETAXEL	Polyneuropathy in malignant disease	8.48(2.08, 34.52)	8.48(2.08, 34.52)	8.28(2.03)	N	N	Y
DOCETAXEL	Demyelinating polyneuropathy	0.66(0.16, 2.63)	0.66(0.16, 2.63)	0.66(0.16)	N	N	N
IRINOTECAN	Lewis-Sumner syndrome	54.79(13. 31,225.56)	54.78(13. 31,225.53)	52.59(12. 77)	N	N	Y
IRINOTECAN	Guillain-Barre syndrome	0.58(0.15, 2.33)	0.58(0.15, 2.33)	0.58(0.15)	N	N	N
DOXORUBICIN	Lewis-Sumner syndrome	23.76(5.7 7,97.82)	23.76(5.7 7,97.81)	22.83(5.5 5)	N	N	Y
DOXORUBICIN	Acute motor-sensory axonal neuropathy	5.39(1.34, 21.72)	5.39(1.34, 21.71)	5.35(1.33)	N	N	N
CARBOPLATIN	Mononeuropathy multiplex	1.75(0.44, 7.00)	1.74(0.44, 7.00)	1.74(0.43)	N	N	N
CARBOPLATIN	Polyradiculoneuropathy	31.41(7.4 2,132.91)	31.41(7.4 2,132.90)	29.07(6.8 7)	N	N	Y
CARBOPLATIN	Acute motor-sensory axonal neuropathy	3.64(0.90, 14.66)	3.64(0.90, 14.66)	3.62(0.90)	N	N	N
CARBOPLATIN	Immune-mediated neuropathy	6.61(1.63, 26.76)	6.61(1.63, 26.76)	6.52(1.61)	N	N	N
CARBOPLATIN	Nerve compression	0.09(0.02, 0.35)	0.09(0.02, 0.35)	0.09(0.02)	N	N	N
CARBOPLATIN	Diabetic neuropathy	0.16(0.04, 0.64)	0.16(0.04, 0.64)	0.16(0.04)	N	N	N
CARBOPLATIN	Intensive care unit acquired weakness	1.83(0.46, 7.34)	1.83(0.46, 7.34)	1.83(0.46)	N	N	N
CISPLATIN	Polyneuropathy alcoholic	100.52(23 .22,435.12)	100.52(23 .22,435.09)	90.05(20. 80)	N	N	Y
BENDAMUSTINE	Nerve compression	0.23(0.03, 1.63)	0.23(0.03, 1.63)	0.23(0.03)	N	N	N
BENDAMUSTINE	Carpal tunnel syndrome	0.15(0.02, 1.07)	0.15(0.02, 1.07)	0.15(0.02)	N	N	N
BENDAMUSTINE	Axonal and demyelinating polyneuropathy	25.22(3.5 1,181.27)	25.22(3.5 1,181.26)	24.92(3.4 7)	N	N	Y
BENDAMUSTINE	Axonal neuropathy	2.52(0.35, 17.90)	2.52(0.35, 17.90)	2.52(0.35)	N	N	N
CYCLOPHOSPHAMIDE	Mononeuropathy	3.17(0.44, 22.60)	3.17(0.44, 22.59)	3.16(0.44)	N	N	N
CYCLOPHOSPHAMIDE	Mononeuritis	4.06(0.57, 29.03)	4.06(0.57, 29.03)	4.04(0.57)	N	N	N
CYCLOPHOSPHAMIDE	Femoral nerve palsy	10.29(1.4 3,74.26)	10.29(1.4 3,74.26)	10.14(1.4 1)	N	N	N

CYCLOPHOSPHAMIDE	Miller Fisher syndrome	2.97(0.42, 21.18)	2.97(0.42, 21.18)	2.96(0.41)	N	N	N
CYCLOPHOSPHAMIDE	Neuralgic amyotrophy	3.04(0.43, 21.70)	3.04(0.43, 21.70)	3.03(0.43)	N	N	N
CYCLOPHOSPHAMIDE	Neuritis	0.44(0.06, 3.11)	0.44(0.06, 3.11)	0.44(0.06)	N	N	N
GEMCITABINE	Brachial plexopathy	3.31(0.46, 23.61)	3.31(0.46, 23.61)	3.30(0.46)	N	N	N
GEMCITABINE	Acute polyneuropathy	2.63(0.37, 18.78)	2.63(0.37, 18.78)	2.63(0.37)	N	N	N
GEMCITABINE	Miller Fisher syndrome	3.29(0.46, 23.49)	3.29(0.46, 23.49)	3.28(0.46)	N	N	N
GEMCITABINE	Carpal tunnel syndrome	0.05(0.01, 0.37)	0.05(0.01, 0.37)	0.05(0.01)	N	N	N
GEMCITABINE	Toxic neuropathy	1.78(0.25, 12.67)	1.78(0.25, 12.66)	1.78(0.25)	N	N	N
GEMCITABINE	Intensive care unit acquired weakness	1.66(0.23, 11.80)	1.66(0.23, 11.80)	1.66(0.23)	N	N	N
VINCRISTINE	Acute polyneuropathy	10.02(1.41,71.44)	10.02(1.41,71.43)	9.99(1.40)	N	N	N
VINCRISTINE	Acute motor-sensory axonal neuropathy	12.53(1.76,89.39)	12.53(1.76,89.37)	12.48(1.75)	N	N	N
VINCRISTINE	Immune-mediated neuropathy	22.66(3.17,162.29)	22.66(3.17,162.26)	22.48(3.14)	N	N	Y
VINCRISTINE	Small fibre neuropathy	4.09(0.57, 29.05)	4.09(0.57, 29.05)	4.08(0.57)	N	N	N
VINCRISTINE	Intensive care unit acquired weakness	6.31(0.89, 44.91)	6.31(0.89, 44.91)	6.30(0.88)	N	N	N
VINCRISTINE	Radial nerve palsy	7.62(1.07, 54.26)	7.62(1.07, 54.26)	7.60(1.07)	N	N	N
ETOPOSIDE	Mononeuropathy	7.92(1.11, 56.48)	7.92(1.11, 56.48)	7.88(1.10)	N	N	N
ETOPOSIDE	Neuritis	1.09(0.15, 7.77)	1.09(0.15, 7.77)	1.09(0.15)	N	N	N
ETOPOSIDE	Diabetic neuropathy	0.33(0.05, 2.32)	0.33(0.05, 2.32)	0.33(0.05)	N	N	N
DOCETAXEL	Acute polyneuropathy	1.22(0.17, 8.71)	1.22(0.17, 8.71)	1.22(0.17)	N	N	N
DOCETAXEL	Chronic inflammatory demyelinating polyradiculoneuropathy	0.26(0.04, 1.84)	0.26(0.04, 1.84)	0.26(0.04)	N	N	N
DOCETAXEL	Lumbosacral plexopathy	5.21(0.72, 37.59)	5.21(0.72, 37.59)	5.14(0.71)	N	N	N
DOCETAXEL	Axonal neuropathy	0.40(0.06, 2.86)	0.40(0.06, 2.86)	0.40(0.06)	N	N	N
DOCETAXEL	Autoimmune neuropathy	2.67(0.37, 19.12)	2.67(0.37, 19.12)	2.66(0.37)	N	N	N
DOCETAXEL	Radial nerve palsy	0.93(0.13, 6.62)	0.93(0.13, 6.62)	0.93(0.13)	N	N	N
IRINOTECAN	Polyneuropathy in malignant disease	16.94(2.36,121.82)	16.94(2.36,121.81)	16.73(2.33)	N	N	Y

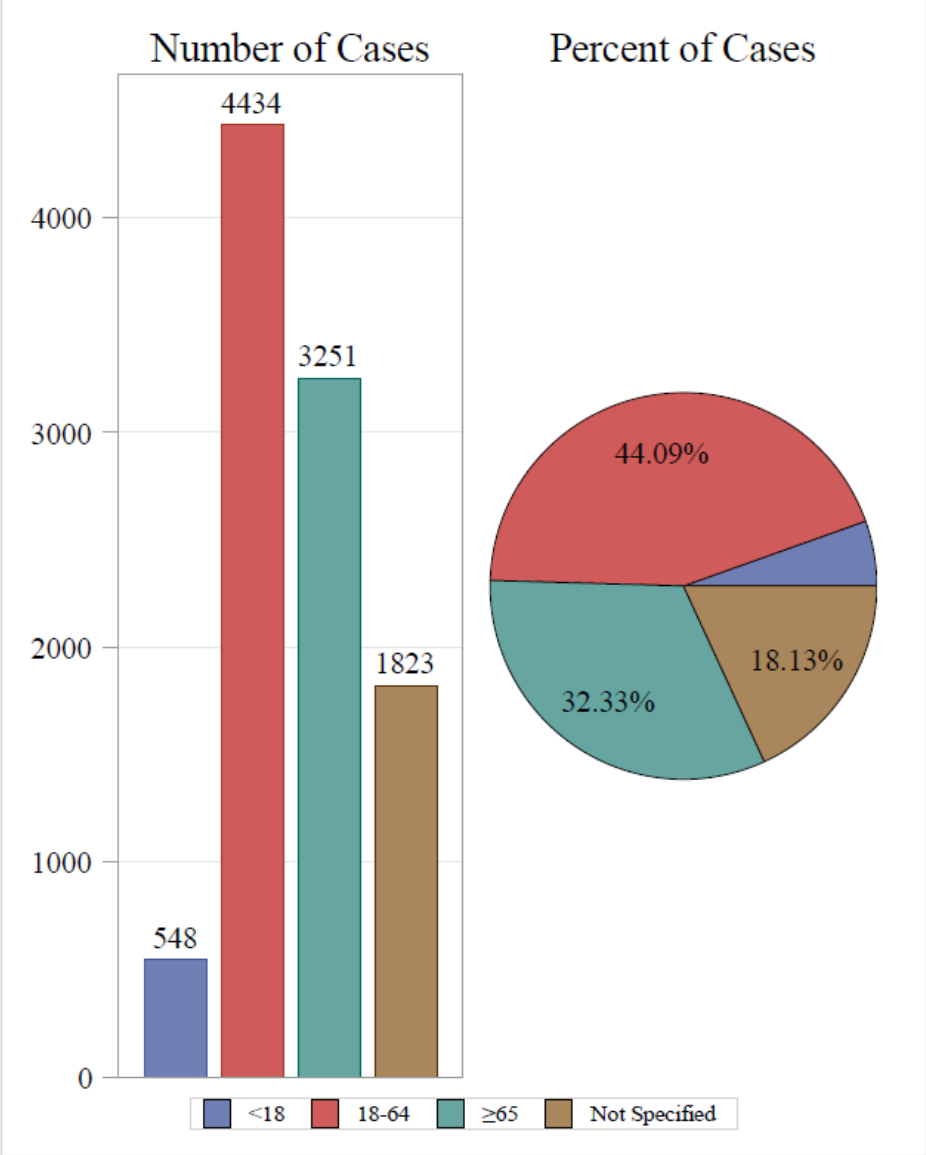
IRINOTECAN	Acute polyneuropathy	4.95(0.69, 35.29)	4.95(0.69, 35.28)	4.94(0.69)	N	N	N
IRINOTECAN	Pancoast's syndrome	99.03(12.95,757.08)	99.03(12.95,757.03)	92.03(12.04)	N	N	Y
IRINOTECAN	Neuritis	0.91(0.13, 6.48)	0.91(0.13, 6.48)	0.91(0.13)	N	N	N
IRINOTECAN	Toxic neuropathy	3.34(0.47, 23.80)	3.34(0.47, 23.80)	3.34(0.47)	N	N	N
IRINOTECAN	Radial nerve palsy	3.76(0.53, 26.80)	3.76(0.53, 26.80)	3.76(0.53)	N	N	N
EPIRUBICIN	Polyneuropathy in malignant disease	36.53(5.08,262.70)	36.53(5.08,262.66)	36.07(5.02)	N	N	Y
EPIRUBICIN	Acute polyneuropathy	10.68(1.50,76.09)	10.68(1.50,76.08)	10.64(1.49)	N	N	N
EPIRUBICIN	Peripheral motor neuropathy	2.10(0.30, 14.93)	2.10(0.30, 14.93)	2.10(0.30)	N	N	N
EPIRUBICIN	Peripheral sensorimotor neuropathy	2.52(0.35, 17.89)	2.52(0.35, 17.88)	2.52(0.35)	N	N	N
EPIRUBICIN	Peroneal nerve palsy	0.51(0.07, 3.64)	0.51(0.07, 3.64)	0.51(0.07)	N	N	N
DOXORUBICIN	Mononeuropathy	2.86(0.40, 20.43)	2.86(0.40, 20.43)	2.85(0.40)	N	N	N
DOXORUBICIN	Mononeuropathy multiplex	1.29(0.18, 9.18)	1.29(0.18, 9.18)	1.29(0.18)	N	N	N
DOXORUBICIN	Axonal neuropathy	0.71(0.10, 5.02)	0.71(0.10, 5.02)	0.71(0.10)	N	N	N
DOXORUBICIN	Autoimmune neuropathy	4.69(0.66, 33.59)	4.69(0.66, 33.58)	4.66(0.65)	N	N	N
CARBOPLATIN	Brachial plexopathy	1.82(0.26, 12.99)	1.82(0.26, 12.99)	1.82(0.25)	N	N	N
CARBOPLATIN	Mononeuritis	2.48(0.35, 17.72)	2.48(0.35, 17.72)	2.47(0.35)	N	N	N
CARBOPLATIN	Pancoast's syndrome	28.99(3.79,221.65)	28.99(3.79,221.64)	26.99(3.53)	N	N	Y
CARBOPLATIN	Thoracic outlet syndrome	1.52(0.21, 10.83)	1.52(0.21, 10.83)	1.52(0.21)	N	N	N
CISPLATIN	Mononeuropathy	4.38(0.61, 31.26)	4.38(0.61, 31.26)	4.36(0.61)	N	N	N
CISPLATIN	Mononeuropathy multiplex	1.97(0.28, 14.04)	1.97(0.28, 14.04)	1.97(0.28)	N	N	N
CISPLATIN	Diabetic neuropathy	0.18(0.03, 1.29)	0.18(0.03, 1.29)	0.18(0.03)	N	N	N
CISPLATIN	Peripheral nerve lesion	2.54(0.36, 18.05)	2.54(0.36, 18.05)	2.53(0.36)	N	N	N
CISPLATIN	Radial nerve palsy	2.50(0.35, 17.79)	2.50(0.35, 17.79)	2.49(0.35)	N	N	N
PACLITAXEL	Immune-mediated neuropathy	4.36(0.61, 31.22)	4.36(0.61, 31.22)	4.33(0.60)	N	N	N
PACLITAXEL	Peripheral nerve lesion	1.49(0.21, 10.59)	1.49(0.21, 10.59)	1.49(0.21)	N	N	N

Validation Analysis Based on the EudraVigilance Database

To ensure the reliability and broader applicability of the initial FAERS findings, we performed a validation analysis using the EudraVigilance database, which yielded a total of 10,056 relevant AE reports. This external dataset demonstrated high clinical diagnostic quality, as evidenced by the fact that 94.56% of reports were documented by healthcare professionals (Figure S1). In terms of patient demographics, the reports were primarily concentrated in the adult (18–64 years, 44.09%) and geriatric (≥65 years, 32.33%) populations, a distribution that closely mirrors the age-related vulnerability observed in the primary study (Figure S2). Signal detection across the 14 agents confirmed the significant neurotoxic potential of these regimens, with Paclitaxel (ROR: 7.83) and Vincristine (ROR: 5.04) emerging as the most prominent triggers(Table S1). Granular analysis at the Preferred Term (PT) level in the EV database further corroborated the distinct clinical phenotypes previously observed in FAERS. Beyond the broad confirmation of "Peripheral sensory neuropathy" (ROR: 9.26) and "Peripheral motor neuropathy" (ROR: 7.98), the EV dataset captured exceptionally potent and specific signals. Notably, Gemcitabine exhibited a striking association with "Acrodynia" (ROR: 76.65), while Bendamustine showed an extreme risk for "Anti-myelin-associated glycoprotein associated polyneuropathy" (ROR: 274.98). Furthermore, the significant signals for "Toxic neuropathy" (ROR: 7.01) and "Axonal neuropathy" (ROR: 3.32) provide additional depth to the neurotoxic profile, pointing toward the structural nerve damage inherent in these t**herapies(Table S2).**



FigureS1. Reporter distribution of AE reports(EV)



FigureS2. Age distribution of AE reports(EV)

TableS1.Agent-Specific Signal Profiles for Chemotherapy-Induced Peripheral Neuropathy(EV)

Drug	ROR(95% CI)	PRR(95% CI)	EBGM(EBGM05)	ROR Signal	PRR Signal	EBGM Signal
PACLITAXEL	7.83(7.60,8.07)	7.67(7.45,7.90)	7.49(7.26)	Y	Y	Y
CYCLOPHOSPHAMIDE	2.34(2.23,2.45)	2.33(2.23,2.44)	2.32(2.21)	Y	Y	Y
CARBOPLATIN	3.58(3.41,3.75)	3.55(3.39,3.72)	3.52(3.36)	Y	Y	Y
VINCRISTINE	5.04(4.79,5.30)	4.98(4.74,5.23)	4.94(4.70)	Y	Y	Y
DOXORUBICIN	3.59(3.40,3.78)	3.56(3.38,3.74)	3.53(3.36)	Y	Y	Y
DOCETAXEL	2.42(2.29,2.55)	2.41(2.28,2.54)	2.40(2.27)	Y	Y	Y
CISPLATIN	2.66(2.48,2.84)	2.64(2.47,2.83)	2.63(2.46)	Y	Y	Y
GEMCITABINE	2.75(2.57,2.95)	2.74(2.56,2.93)	2.73(2.55)	Y	Y	Y
IRINOTECAN	4.47(4.15,4.82)	4.42(4.11,4.76)	4.41(4.09)	Y	Y	Y
ETOPOSIDE	2.11(1.94,2.29)	2.10(1.93,2.28)	2.09(1.93)	Y	Y	N
BENDAMUSTINE	2.06(1.80,2.37)	2.06(1.79,2.36)	2.05(1.79)	Y	Y	N

EPIRUBICIN	0.86(0.74,1.00)	0.86(0.74,1.00)	0.86(0.74)	N	N	N
TOPOTECAN	0.90(0.62,1.30)	0.90(0.62,1.30)	0.90(0.62)	N	N	N

TableS2. Neurotoxic Signals of Specific Agents by Preferred Term(EV)

Drug	PT	ROR(95% CI)	PRR(95% CI)	EBGM(EBGM05)	ROR Signal	PRR Signal	EBGM Signal
PACLITAXEL	Neuropathy peripheral	11.16(10.78,11.54)	10.97(10.61,11.34)	10.58(10.23)	Y	Y	Y
CARBOPLATIN	Neuropathy peripheral	4.52(4.28,4.78)	4.50(4.25,4.75)	4.45(4.20)	Y	Y	Y
CYCLOPHOSPHAMIDE	Neuropathy peripheral	2.81(2.66,2.98)	2.80(2.65,2.97)	2.78(2.63)	Y	Y	Y
DOXORUBICIN	Neuropathy peripheral	4.61(4.34,4.90)	4.58(4.32,4.87)	4.54(4.27)	Y	Y	Y
VINCRISTINE	Neuropathy peripheral	5.73(5.38,6.10)	5.68(5.34,6.04)	5.63(5.29)	Y	Y	Y
DOCETAXEL	Neuropathy peripheral	3.00(2.81,3.19)	2.99(2.80,3.18)	2.96(2.78)	Y	Y	Y
GEMCITABINE	Neuropathy peripheral	3.58(3.31,3.88)	3.57(3.29,3.86)	3.55(3.28)	Y	Y	Y
CISPLATIN	Neuropathy peripheral	3.10(2.85,3.37)	3.09(2.84,3.36)	3.08(2.83)	Y	Y	Y
IRINOTECAN	Neuropathy peripheral	5.24(4.78,5.74)	5.20(4.75,5.70)	5.18(4.73)	Y	Y	Y
PACLITAXEL	Peripheral sensory neuropathy	16.05(14.47,17.80)	16.02(14.45,17.76)	15.19(13.69)	Y	Y	Y
ETOPOSIDE	Neuropathy peripheral	2.24(2.01,2.49)	2.23(2.01,2.49)	2.23(2.00)	Y	Y	Y
PACLITAXEL	Polyneuropathy	6.15(5.50,6.88)	6.14(5.50,6.87)	6.03(5.40)	Y	Y	Y
CYCLOPHOSPHAMIDE	Polyneuropathy	3.07(2.67,3.52)	3.07(2.67,3.52)	3.04(2.65)	Y	Y	Y
DOCETAXEL	Polyneuropathy	3.77(3.27,4.35)	3.76(3.26,4.34)	3.73(3.23)	Y	Y	Y
CARBOPLATIN	Peripheral sensory neuropathy	8.65(7.46,10.04)	8.64(7.45,10.03)	8.45(7.28)	Y	Y	Y
VINCRISTINE	Polyneuropathy	6.32(5.45,7.33)	6.31(5.45,7.32)	6.25(5.39)	Y	Y	Y
IRINOTECAN	Peripheral sensory neuropathy	24.32(20.78,28.45)	24.24(20.73,28.35)	23.70(20.26)	Y	Y	Y
CARBOPLATIN	Polyneuropathy	3.56(3.04,4.16)	3.55(3.03,4.16)	3.52(3.01)	Y	Y	Y
CYCLOPHOSPHAMIDE	Peripheral sensory neuropathy	4.27(3.61,5.07)	4.27(3.61,5.06)	4.21(3.55)	Y	Y	Y
DOXORUBICIN	Polyneuropathy	3.67(3.09,4.35)	3.67(3.09,4.35)	3.64(3.07)	Y	Y	Y
BENDAMUSTINE	Neuropathy peripheral	2.27(1.90,2.71)	2.26(1.90,2.70)	2.26(1.90)	Y	Y	N
DOXORUBIC	Peripheral sensory	7.03(5.87,	7.02(5.87,	6.92(5.7	Y	Y	Y

IN	neuropathy	8.42)	8.41)	8)			
VINCRISTINE	Peripheral sensory neuropathy	8.56(7.12, 10.30)	8.56(7.12, 10.29)	8.43(7.01)	Y	Y	Y
CISPLATIN	Polyneuropathy	3.88(3.22, 4.69)	3.88(3.22, 4.68)	3.86(3.20)	Y	Y	Y
EPIRUBICIN	Neuropathy peripheral	1.00(0.82, 1.21)	1.00(0.82, 1.21)	1.00(0.82)	N	N	N
DOCETAXEL	Peripheral sensory neuropathy	4.10(3.36, 5.00)	4.10(3.36, 5.00)	4.06(3.33)	Y	Y	Y
CISPLATIN	Peripheral sensory neuropathy	6.52(5.28, 8.05)	6.52(5.28, 8.04)	6.45(5.22)	Y	Y	Y
GEMCITABINE	Polyneuropathy	3.15(2.55, 3.91)	3.15(2.54, 3.91)	3.14(2.53)	Y	Y	Y
ETOPOSIDE	Peripheral sensory neuropathy	6.50(5.15, 8.20)	6.50(5.15, 8.20)	6.44(5.11)	Y	Y	Y
GEMCITABINE	Peripheral sensory neuropathy	5.59(4.43, 7.07)	5.59(4.42, 7.06)	5.54(4.39)	Y	Y	Y
CYCLOPHOSPHAMIDE	Guillain-Barre syndrome	1.10(0.85, 1.42)	1.10(0.85, 1.42)	1.10(0.85)	N	N	N
VINCRISTINE	Peripheral motor neuropathy	23.27(17.76,30.50)	23.26(17.75,30.48)	22.28(17.00)	Y	Y	Y
ETOPOSIDE	Polyneuropathy	2.23(1.70, 2.93)	2.23(1.70, 2.93)	2.23(1.70)	Y	Y	N
IRINOTECAN	Polyneuropathy	3.63(2.76, 4.78)	3.63(2.76, 4.78)	3.62(2.75)	Y	Y	Y
CARBOPLATIN	Guillain-Barre syndrome	1.45(1.10, 1.90)	1.45(1.10, 1.90)	1.44(1.10)	Y	Y	N
VINCRISTINE	Peroneal nerve palsy	8.16(6.11, 10.88)	8.15(6.11, 10.88)	8.04(6.03)	Y	Y	Y
PACLITAXEL	Guillain-Barre syndrome	0.93(0.68, 1.28)	0.93(0.68, 1.28)	0.93(0.68)	N	N	N
VINCRISTINE	Peripheral sensorimotor neuropathy	13.25(9.60,18.29)	13.25(9.60,18.28)	12.93(9.37)	Y	Y	Y
PACLITAXEL	Peripheral motor neuropathy	8.14(5.84, 11.34)	8.14(5.84, 11.33)	7.93(5.69)	Y	Y	Y
VINCRISTINE	Guillain-Barre syndrome	1.54(1.11, 2.15)	1.54(1.11, 2.15)	1.54(1.10)	Y	Y	N
VINCRISTINE	Axonal neuropathy	18.05(12.88,25.29)	18.05(12.88,25.28)	17.46(12.46)	Y	Y	Y
BENDAMUSTINE	Polyneuropathy	3.91(2.79, 5.48)	3.91(2.79, 5.47)	3.90(2.79)	Y	Y	Y
CYCLOPHOSPHAMIDE	Peripheral sensorimotor neuropathy	4.53(3.17, 6.46)	4.53(3.17, 6.46)	4.45(3.12)	Y	Y	Y
DOXORUBICIN	Peripheral motor neuropathy	10.02(7.02,14.32)	10.02(7.02,14.31)	9.80(6.86)	Y	Y	Y
DOCETAXEL	Peripheral motor neuropathy	6.70(4.64, 9.68)	6.70(4.64, 9.68)	6.57(4.54)	Y	Y	Y
CYCLOPHOSPHAMIDE	Peroneal nerve palsy	1.89(1.28, 2.77)	1.88(1.28, 2.77)	1.88(1.28)	Y	Y	N
DOXORUBICIN	Guillain-Barre syndrome	0.89(0.61, 1.31)	0.89(0.61, 1.31)	0.89(0.61)	N	N	N

CYCLOPHOSPHAMIDE	Peripheral motor neuropathy	4.34(2.92, 6.45)	4.34(2.92, 6.45)	4.27(2.88)	Y	Y	Y
EPIRUBICIN	Polyneuropathy	1.49(1.01, 2.21)	1.49(1.01, 2.21)	1.49(1.01)	Y	Y	N
CISPLATIN	Guillain-Barre syndrome	1.10(0.74, 1.63)	1.10(0.74, 1.63)	1.10(0.74)	N	N	N
ETOPOSIDE	Guillain-Barre syndrome	1.29(0.86, 1.92)	1.29(0.86, 1.92)	1.29(0.86)	N	N	N
DOXORUBICIN	Peripheral sensorimotor neuropathy	5.37(3.45, 8.35)	5.37(3.45, 8.35)	5.31(3.42)	Y	Y	Y
PACLITAXEL	Peripheral sensorimotor neuropathy	3.74(2.40, 5.81)	3.74(2.40, 5.81)	3.70(2.38)	Y	Y	Y
TOPOTECAN	Neuropathy peripheral	1.03(0.65, 1.64)	1.03(0.65, 1.63)	1.03(0.65)	N	N	N
DOXORUBICIN	Peroneal nerve palsy	2.41(1.52, 3.83)	2.41(1.52, 3.83)	2.40(1.51)	Y	Y	N
CARBOPLATIN	Peripheral motor neuropathy	4.48(2.78, 7.23)	4.48(2.78, 7.23)	4.43(2.75)	Y	Y	Y
PACLITAXEL	Toxic neuropathy	11.40(6.91,18.79)	11.39(6.91,18.79)	10.98(6.66)	Y	Y	Y
PACLITAXEL	Peroneal nerve palsy	1.49(0.91, 2.44)	1.49(0.91, 2.44)	1.49(0.91)	N	N	N
DOCETAXEL	Peroneal nerve palsy	1.44(0.86, 2.39)	1.44(0.86, 2.39)	1.43(0.86)	N	N	N
DOCETAXEL	Guillain-Barre syndrome	0.34(0.20, 0.58)	0.34(0.20, 0.58)	0.34(0.20)	N	N	N
DOCETAXEL	Toxic neuropathy	10.20(5.98,17.38)	10.20(5.98,17.38)	9.88(5.79)	Y	Y	Y
CARBOPLATIN	Peroneal nerve palsy	1.54(0.91, 2.61)	1.54(0.91, 2.61)	1.54(0.91)	N	N	N
GEMCITABINE	Guillain-Barre syndrome	0.61(0.35, 1.05)	0.61(0.35, 1.05)	0.61(0.35)	N	N	N
DOCETAXEL	Peripheral sensorimotor neuropathy	2.49(1.44, 4.29)	2.49(1.44, 4.29)	2.47(1.43)	Y	Y	N
CARBOPLATIN	Peripheral sensorimotor neuropathy	2.86(1.66, 4.95)	2.86(1.66, 4.94)	2.85(1.65)	Y	Y	N
BENDAMUSTINE	Guillain-Barre syndrome	1.73(0.98, 3.04)	1.73(0.98, 3.04)	1.73(0.98)	N	N	N
CYCLOPHOSPHAMIDE	Carpal tunnel syndrome	0.30(0.17, 0.52)	0.30(0.17, 0.52)	0.30(0.17)	N	N	N
GEMCITABINE	Peripheral motor neuropathy	5.22(2.96, 9.21)	5.22(2.96, 9.21)	5.18(2.93)	Y	Y	Y
ETOPOSIDE	Peripheral sensorimotor neuropathy	5.02(2.84, 8.86)	5.02(2.84, 8.85)	4.98(2.82)	Y	Y	Y
EPIRUBICIN	Peripheral sensory neuropathy	1.50(0.85, 2.64)	1.50(0.85, 2.63)	1.49(0.85)	N	N	N
CISPLATIN	Peripheral sensorimotor neuropathy	3.76(2.08, 6.81)	3.76(2.08, 6.81)	3.74(2.07)	Y	Y	Y
PACLITAXEL	Demyelinating polyneuropathy	2.41(1.33, 4.36)	2.41(1.33, 4.36)	2.40(1.32)	Y	Y	N
CYCLOPHOS	Chronic inflammatory	1.62(0.87,	1.62(0.87,	1.62(0.8	N	N	N

PHAMIDE	demyelinating polyradiculoneuropathy	3.03)	3.03)	7)			
ETOPOSIDE	Peripheral motor neuropathy	4.98(2.67, 9.27)	4.98(2.67, 9.27)	4.94(2.65)	Y	Y	Y
CARBOPLATIN	Demyelinating polyneuropathy	2.59(1.39, 4.83)	2.59(1.39, 4.83)	2.58(1.39)	Y	Y	N
CISPLATIN	Peroneal nerve palsy	1.71(0.92, 3.19)	1.71(0.92, 3.18)	1.71(0.92)	N	N	N
CYCLOPHOSPHAMIDE	Axonal neuropathy	1.90(0.99, 3.67)	1.90(0.99, 3.67)	1.89(0.98)	N	N	N
GEMCITABINE	Peroneal nerve palsy	1.64(0.85, 3.16)	1.64(0.85, 3.16)	1.64(0.85)	N	N	N
VINCRISTINE	Toxic neuropathy	11.60(5.99,22.45)	11.60(5.99,22.45)	11.36(5.86)	Y	Y	Y
PACLITAXEL	Diabetic neuropathy	0.59(0.30, 1.13)	0.59(0.30, 1.13)	0.59(0.31)	N	N	N
VINCRISTINE	Mononeuropathy multiplex	9.93(4.93, 19.99)	9.93(4.93, 19.98)	9.75(4.84)	Y	Y	Y
ETOPOSIDE	Peroneal nerve palsy	1.67(0.84, 3.35)	1.67(0.84, 3.35)	1.67(0.83)	N	N	N
CARBOPLATIN	Immune-mediated neuropathy	10.24(5.07,20.71)	10.24(5.07,20.70)	9.96(4.93)	Y	Y	Y
CARBOPLATIN	Toxic neuropathy	6.61(3.28, 13.31)	6.61(3.28, 13.31)	6.50(3.23)	Y	Y	Y
CISPLATIN	Peripheral motor neuropathy	3.25(1.62, 6.52)	3.25(1.62, 6.52)	3.24(1.62)	Y	Y	N
PACLITAXEL	Neuritis	0.92(0.46, 1.84)	0.92(0.46, 1.84)	0.92(0.46)	N	N	N
BENDAMUSTINE	Peripheral sensory neuropathy	1.68(0.80, 3.52)	1.68(0.80, 3.52)	1.68(0.80)	N	N	N
ETOPOSIDE	Axonal neuropathy	4.28(2.04, 9.01)	4.28(2.04, 9.01)	4.26(2.03)	Y	Y	Y
IRINOTECAN	Peripheral motor neuropathy	5.76(2.74, 12.11)	5.76(2.74, 12.10)	5.73(2.73)	Y	Y	Y
DOXORUBICIN	Demyelinating polyneuropathy	2.20(1.04, 4.62)	2.20(1.04, 4.62)	2.19(1.04)	Y	Y	N
CARBOPLATIN	Neuritis	0.95(0.45, 2.00)	0.95(0.45, 2.00)	0.95(0.45)	N	N	N
CISPLATIN	Toxic neuropathy	8.97(4.25, 18.94)	8.97(4.25, 18.93)	8.83(4.18)	Y	Y	Y
PACLITAXEL	Carpal tunnel syndrome	0.22(0.11, 0.47)	0.22(0.11, 0.47)	0.22(0.11)	N	N	N
PACLITAXEL	Axonal neuropathy	1.90(0.91, 4.01)	1.90(0.91, 4.01)	1.90(0.90)	N	N	N
CYCLOPHOSPHAMIDE	Polyneuropathy in malignant disease	16.11(7.02,36.94)	16.11(7.02,36.93)	15.04(6.56)	Y	Y	Y
DOCETAXEL	Carpal tunnel syndrome	0.20(0.09, 0.44)	0.20(0.09, 0.44)	0.20(0.09)	N	N	N
CARBOPLATIN	Polyneuropathy in malignant disease	24.60(10.73,56.42)	24.60(10.73,56.42)	22.93(10.00)	Y	Y	Y
CISPLATIN	Axonal neuropathy	3.00(1.35,	3.00(1.35,	2.99(1.3	Y	Y	N

		6.70)	6.70)	4)			
PACLITAXEL	Immune-mediated neuropathy	6.43(2.86, 14.46)	6.43(2.86, 14.46)	6.31(2.81)	Y	Y	Y
BENDAMUSTINE	Demyelinating polyneuropathy	6.58(2.73, 15.83)	6.58(2.73, 15.83)	6.56(2.72)	Y	Y	Y
CYCLOPHOSPHAMIDE	Acute polyneuropathy	2.13(0.88, 5.15)	2.13(0.88, 5.15)	2.12(0.88)	N	N	N
CYCLOPHOSPHAMIDE	Neuritis	0.44(0.18, 1.07)	0.44(0.18, 1.07)	0.45(0.19)	N	N	N
GEMCITABINE	Demyelinating polyneuropathy	2.14(0.89, 5.15)	2.14(0.89, 5.15)	2.13(0.89)	N	N	N
VINCRISTINE	Acute motor axonal neuropathy	17.61(7.22,42.97)	17.61(7.22,42.96)	17.05(6.99)	Y	Y	Y
VINCRISTINE	Demyelinating polyneuropathy	2.01(0.83, 4.83)	2.01(0.83, 4.83)	2.00(0.83)	N	N	N
VINCRISTINE	Radial nerve palsy	8.29(3.42, 20.05)	8.29(3.42, 20.05)	8.17(3.38)	Y	Y	Y
ETOPOSIDE	Acute polyneuropathy	6.19(2.56, 14.93)	6.19(2.56, 14.93)	6.14(2.54)	Y	Y	Y
DOCETAXEL	Axonal neuropathy	1.40(0.58, 3.36)	1.40(0.58, 3.36)	1.39(0.58)	N	N	N
EPIRUBICIN	Guillain-Barre syndrome	0.37(0.16, 0.90)	0.37(0.16, 0.90)	0.37(0.16)	N	N	N
DOXORUBICIN	Axonal neuropathy	1.95(0.81, 4.70)	1.95(0.81, 4.70)	1.95(0.81)	N	N	N
CARBOPLATIN	Carpal tunnel syndrome	0.19(0.08, 0.45)	0.19(0.08, 0.45)	0.19(0.08)	N	N	N
CARBOPLATIN	Axonal neuropathy	1.61(0.67, 3.87)	1.61(0.67, 3.87)	1.61(0.67)	N	N	N
PACLITAXEL	Polyneuropathy in malignant disease	17.09(6.92,42.19)	17.09(6.92,42.19)	16.15(6.54)	Y	Y	Y
PACLITAXEL	Nerve compression	0.33(0.14, 0.80)	0.33(0.14, 0.80)	0.33(0.14)	N	N	N
BENDAMUSTINE	Anti-myelin-associated glycoprotein associated polyneuropathy	274.98(95.40,792.56)	274.94(95.40,792.37)	235.81(81.81)	Y	Y	Y
CYCLOPHOSPHAMIDE	Mononeuropathy multiplex	2.07(0.77, 5.54)	2.07(0.77, 5.54)	2.06(0.77)	N	N	N
CYCLOPHOSPHAMIDE	Demyelinating polyneuropathy	0.68(0.25, 1.80)	0.68(0.25, 1.80)	0.68(0.25)	N	N	N
CYCLOPHOSPHAMIDE	Toxic neuropathy	2.14(0.80, 5.74)	2.14(0.80, 5.74)	2.13(0.80)	N	N	N
GEMCITABINE	Axonal neuropathy	2.13(0.80, 5.68)	2.13(0.80, 5.68)	2.12(0.80)	N	N	N
VINCRISTINE	Acute motor-sensory axonal neuropathy	10.18(3.78,27.38)	10.18(3.78,27.38)	9.99(3.71)	Y	Y	Y
VINCRISTINE	Nerve compression	0.49(0.18, 1.31)	0.49(0.18, 1.31)	0.49(0.18)	N	N	N
VINCRISTINE	Neuritis	0.84(0.32, 2.25)	0.84(0.32, 2.25)	0.85(0.32)	N	N	N
ETOPOSIDE	Polyneuropathy in	30.37(11.	30.37(11.	28.99(10	Y	Y	Y

	malignant disease	13,82.88)	13,82.87)	.62)			
ETOPOSIDE	Intensive care unit acquired weakness	5.62(2.10, 15.03)	5.62(2.10, 15.03)	5.57(2.08)	Y	Y	Y
DOCETAXEL	Mononeuropathy	4.39(1.64, 11.80)	4.39(1.64, 11.79)	4.34(1.62)	Y	Y	N
TOPOTECAN	Polyneuropathy	1.45(0.54, 3.87)	1.45(0.55, 3.87)	1.45(0.54)	N	N	N
IRINOTECAN	Peripheral sensorimotor neuropathy	2.76(1.03, 7.35)	2.76(1.03, 7.35)	2.75(1.03)	Y	Y	N
DOXORUBICIN	Mononeuropathy	6.14(2.29, 16.48)	6.14(2.29, 16.48)	6.06(2.26)	Y	Y	Y
DOXORUBICIN	Acute polyneuropathy	3.15(1.18, 8.44)	3.15(1.18, 8.44)	3.14(1.17)	Y	Y	N
DOXORUBICIN	Toxic neuropathy	3.97(1.48, 10.62)	3.97(1.48, 10.62)	3.94(1.47)	Y	Y	N
CARBOPLATIN	Diabetic neuropathy	0.31(0.12, 0.82)	0.31(0.12, 0.82)	0.31(0.12)	N	N	N
BENDAMUSTINE	Peripheral sensorimotor neuropathy	3.34(1.08, 10.38)	3.34(1.08, 10.38)	3.34(1.08)	Y	Y	N
CYCLOPHOSPHAMIDE	Mononeuropathy	2.48(0.79, 7.73)	2.48(0.79, 7.73)	2.46(0.79)	N	N	N
CYCLOPHOSPHAMIDE	Acute motor axonal neuropathy	4.39(1.40, 13.76)	4.39(1.40, 13.76)	4.32(1.38)	Y	Y	N
CYCLOPHOSPHAMIDE	Neuralgic amyotrophy	0.50(0.16, 1.56)	0.50(0.16, 1.56)	0.50(0.16)	N	N	N
CYCLOPHOSPHAMIDE	Nerve compression	0.16(0.05, 0.48)	0.16(0.05, 0.48)	0.16(0.05)	N	N	N
CYCLOPHOSPHAMIDE	Diabetic neuropathy	0.15(0.05, 0.47)	0.15(0.05, 0.47)	0.15(0.05)	N	N	N
GEMCITABINE	Nerve compression	0.39(0.13, 1.22)	0.39(0.13, 1.22)	0.39(0.13)	N	N	N
GEMCITABINE	Diabetic neuropathy	0.38(0.12, 1.19)	0.38(0.12, 1.19)	0.38(0.12)	N	N	N
GEMCITABINE	Peripheral sensorimotor neuropathy	1.09(0.35, 3.38)	1.09(0.35, 3.38)	1.09(0.35)	N	N	N
VINCRISTINE	Acute polyneuropathy	3.03(0.97, 9.42)	3.03(0.97, 9.42)	3.02(0.97)	N	N	N
VINCRISTINE	Intensive care unit acquired weakness	3.44(1.11, 10.72)	3.44(1.11, 10.71)	3.43(1.10)	Y	Y	N
ETOPOSIDE	Nerve compression	0.45(0.15, 1.40)	0.45(0.15, 1.40)	0.45(0.15)	N	N	N
ETOPOSIDE	Demyelinating polyneuropathy	1.47(0.47, 4.56)	1.47(0.47, 4.56)	1.47(0.47)	N	N	N
DOCETAXEL	Acute motor-sensory axonal neuropathy	4.24(1.36, 13.25)	4.24(1.36, 13.25)	4.19(1.34)	Y	Y	N
DOCETAXEL	Chronic inflammatory demyelinating polyradiculoneuropathy	0.64(0.21, 2.00)	0.64(0.21, 2.00)	0.64(0.21)	N	N	N
DOCETAXEL	Neuritis	0.35(0.11, 1.10)	0.35(0.11, 1.10)	0.35(0.11)	N	N	N
DOCETAXEL	Small fibre neuropathy	0.79(0.26,	0.79(0.26,	0.79(0.2	N	N	N

		2.47)	2.47)	6)			
TOPOTECAN	Peripheral sensory neuropathy	2.28(0.73, 7.06)	2.27(0.73, 7.05)	2.27(0.73)	N	N	N
IRINOTECAN	Nerve compression	0.75(0.24, 2.31)	0.75(0.24, 2.31)	0.75(0.24)	N	N	N
DOXORUBICIN	Polyneuropathy in malignant disease	14.37(4.54,45.48)	14.37(4.54,45.48)	13.90(4.39)	Y	Y	Y
DOXORUBICIN	Acute motor axonal neuropathy	8.13(2.59, 25.49)	8.13(2.59, 25.49)	7.98(2.54)	Y	Y	Y
DOXORUBICIN	Neuritis	0.49(0.16, 1.53)	0.49(0.16, 1.53)	0.49(0.16)	N	N	N
DOXORUBICIN	Carpal tunnel syndrome	0.14(0.04, 0.42)	0.14(0.04, 0.42)	0.14(0.04)	N	N	N
DOXORUBICIN	Autoimmune neuropathy	6.47(2.07, 20.26)	6.47(2.07, 20.26)	6.39(2.04)	Y	Y	Y
CARBOPLATIN	Acute polyneuropathy	1.95(0.63, 6.06)	1.95(0.63, 6.06)	1.94(0.62)	N	N	N
CARBOPLATIN	Miller Fisher syndrome	2.21(0.71, 6.87)	2.21(0.71, 6.87)	2.20(0.71)	N	N	N
CARBOPLATIN	Intensive care unit acquired weakness	2.21(0.71, 6.89)	2.21(0.71, 6.89)	2.21(0.71)	N	N	N
CISPLATIN	Polyneuropathy chronic	17.36(5.49,54.88)	17.36(5.49,54.88)	16.81(5.32)	Y	Y	Y
CISPLATIN	Neuritis	0.63(0.20, 1.96)	0.63(0.20, 1.96)	0.63(0.20)	N	N	N
PACLITAXEL	Acute polyneuropathy	1.64(0.53, 5.12)	1.64(0.53, 5.12)	1.64(0.53)	N	N	N
PACLITAXEL	Acute motor-sensory axonal neuropathy	4.12(1.32, 12.89)	4.12(1.32, 12.89)	4.08(1.30)	Y	Y	N
PACLITAXEL	Miller Fisher syndrome	1.86(0.60, 5.80)	1.86(0.60, 5.80)	1.86(0.60)	N	N	N
PACLITAXEL	Intensive care unit acquired weakness	1.87(0.60, 5.82)	1.87(0.60, 5.82)	1.86(0.60)	N	N	N
BENDAMUSTINE	Neuritis	1.38(0.35, 5.53)	1.38(0.35, 5.53)	1.38(0.35)	N	N	N
BENDAMUSTINE	Diabetic neuropathy	0.78(0.20, 3.14)	0.78(0.20, 3.14)	0.79(0.20)	N	N	N
BENDAMUSTINE	Axonal neuropathy	3.27(0.82, 13.08)	3.27(0.82, 13.08)	3.26(0.81)	N	N	N
BENDAMUSTINE	Peroneal nerve palsy	1.12(0.28, 4.48)	1.12(0.28, 4.48)	1.12(0.28)	N	N	N
CYCLOPHOSPHAMIDE	Brachial plexopathy	0.93(0.23, 3.72)	0.93(0.23, 3.72)	0.93(0.23)	N	N	N
CYCLOPHOSPHAMIDE	Meralgia paraesthetica	2.26(0.56, 9.09)	2.26(0.56, 9.09)	2.24(0.56)	N	N	N
CYCLOPHOSPHAMIDE	Miller Fisher syndrome	0.96(0.24, 3.86)	0.96(0.24, 3.86)	0.96(0.24)	N	N	N
CYCLOPHOSPHAMIDE	Ischaemic neuropathy	7.19(1.76, 29.42)	7.19(1.76, 29.42)	6.99(1.71)	N	N	N
CYCLOPHOSPHAMIDE	Autoimmune neuropathy	2.32(0.58, 9.34)	2.32(0.58, 9.34)	2.30(0.57)	N	N	N

GEMCITABINE	Acute polyneuropathy	2.15(0.54,8.61)	2.15(0.54,8.61)	2.14(0.53)	N	N	N
GEMCITABINE	Neuritis	0.45(0.11,1.80)	0.45(0.11,1.80)	0.45(0.11)	N	N	N
GEMCITABINE	Carpal tunnel syndrome	0.12(0.03,0.50)	0.12(0.03,0.50)	0.12(0.03)	N	N	N
GEMCITABINE	Intensive care unit acquired weakness	2.44(0.61,9.78)	2.44(0.61,9.78)	2.43(0.61)	N	N	N
GEMCITABINE	Peripheral nerve lesion	3.04(0.76,12.20)	3.04(0.76,12.20)	3.03(0.75)	N	N	N
VINCRISTINE	Polyneuropathy in malignant disease	12.14(2.99,49.35)	12.14(2.99,49.35)	11.88(2.92)	N	N	Y
VINCRISTINE	Meralgia paraesthetica	5.36(1.33,21.59)	5.36(1.33,21.59)	5.31(1.32)	N	N	N
VINCRISTINE	Ischaemic neuropathy	17.08(4.17,69.89)	17.08(4.17,69.89)	16.55(4.04)	N	N	Y
VINCRISTINE	Neuralgic amyotrophy	0.79(0.20,3.18)	0.79(0.20,3.18)	0.79(0.20)	N	N	N
VINCRISTINE	Diabetic neuropathy	0.24(0.06,0.96)	0.24(0.06,0.96)	0.24(0.06)	N	N	N
VINCRISTINE	Carpal tunnel syndrome	0.12(0.03,0.47)	0.12(0.03,0.47)	0.12(0.03)	N	N	N
ETOPOSIDE	Polyneuropathy chronic	13.98(3.44,56.77)	13.98(3.44,56.77)	13.69(3.37)	N	N	Y
ETOPOSIDE	Ischaemic neuropathy	20.85(5.09,85.33)	20.85(5.09,85.32)	20.20(4.93)	N	N	Y
ETOPOSIDE	Neuritis	0.52(0.13,2.06)	0.52(0.13,2.06)	0.52(0.13)	N	N	N
ETOPOSIDE	Toxic neuropathy	3.09(0.77,12.40)	3.09(0.77,12.40)	3.08(0.77)	N	N	N
DOCETAXEL	Mononeuritis	2.07(0.51,8.31)	2.07(0.51,8.31)	2.06(0.51)	N	N	N
DOCETAXEL	Mononeuropathy multiplex	1.36(0.34,5.48)	1.36(0.34,5.48)	1.36(0.34)	N	N	N
DOCETAXEL	Demyelinating polyneuropathy	0.45(0.11,1.79)	0.45(0.11,1.79)	0.45(0.11)	N	N	N
IRINOTECAN	Guillain-Barre syndrome	0.18(0.04,0.71)	0.18(0.04,0.71)	0.18(0.04)	N	N	N
IRINOTECAN	Demyelinating polyneuropathy	1.62(0.41,6.49)	1.62(0.41,6.49)	1.62(0.40)	N	N	N
IRINOTECAN	Toxic neuropathy	5.12(1.28,20.55)	5.12(1.28,20.55)	5.10(1.27)	N	N	N
IRINOTECAN	Peroneal nerve palsy	0.69(0.17,2.77)	0.69(0.17,2.77)	0.69(0.17)	N	N	N
EPIRUBICIN	Polyneuropathy in malignant disease	20.65(5.08,83.94)	20.64(5.08,83.93)	20.18(4.96)	N	N	Y
EPIRUBICIN	Acute polyneuropathy	3.43(0.85,13.74)	3.43(0.85,13.74)	3.42(0.85)	N	N	N
EPIRUBICIN	Carpal tunnel syndrome	0.20(0.05,0.79)	0.20(0.05,0.79)	0.20(0.05)	N	N	N
DOXORUBIC	Brachial plexopathy	1.72(0.43,	1.72(0.43,	1.72(0.4	N	N	N

IN		6.89)	6.89)	3)			
DOXORUBICIN	Chronic inflammatory demyelinating polyradiculoneuropathy	0.60(0.15, 2.39)	0.60(0.15, 2.39)	0.60(0.15)	N	N	N
DOXORUBICIN	Ischaemic neuropathy	13.31(3.25,54.49)	13.31(3.25,54.49)	12.91(3.15)	N	N	Y
DOXORUBICIN	Neuralgic amyotrophy	0.62(0.15, 2.48)	0.62(0.15, 2.48)	0.62(0.15)	N	N	N
DOXORUBICIN	Nerve compression	0.19(0.05, 0.77)	0.19(0.05, 0.77)	0.19(0.05)	N	N	N
DOXORUBICIN	Diabetic neuropathy	0.19(0.05, 0.75)	0.19(0.05, 0.75)	0.19(0.05)	N	N	N
CARBOPLATIN	Mononeuropathy	2.51(0.62, 10.09)	2.51(0.62, 10.09)	2.50(0.62)	N	N	N
CARBOPLATIN	Chronic inflammatory demyelinating polyradiculoneuropathy	0.49(0.12, 1.97)	0.49(0.12, 1.97)	0.49(0.12)	N	N	N
CARBOPLATIN	Nerve compression	0.16(0.04, 0.63)	0.16(0.04, 0.63)	0.16(0.04)	N	N	N
CARBOPLATIN	Axonal and demyelinating polyneuropathy	5.40(1.33, 21.84)	5.40(1.33, 21.84)	5.33(1.32)	N	N	N
CARBOPLATIN	Autoimmune neuropathy	3.54(0.88, 14.26)	3.54(0.88, 14.26)	3.51(0.87)	N	N	N
CISPLATIN	Polyneuropathy in malignant disease	12.13(2.98,49.32)	12.13(2.98,49.32)	11.87(2.92)	N	N	Y
CISPLATIN	Acute polyneuropathy	2.01(0.50, 8.07)	2.01(0.50, 8.07)	2.01(0.50)	N	N	N
CISPLATIN	Acute motor axonal neuropathy	6.90(1.71, 27.84)	6.90(1.71, 27.84)	6.82(1.69)	N	N	N
CISPLATIN	Nerve compression	0.25(0.06, 0.98)	0.25(0.06, 0.98)	0.25(0.06)	N	N	N
CISPLATIN	Intensive care unit acquired weakness	2.29(0.57, 9.18)	2.29(0.57, 9.18)	2.28(0.57)	N	N	N
PACLITAXEL	Mononeuropathy multiplex	1.33(0.33, 5.33)	1.33(0.33, 5.33)	1.33(0.33)	N	N	N
PACLITAXEL	Acute motor axonal neuropathy	3.75(0.93, 15.12)	3.75(0.93, 15.12)	3.71(0.92)	N	N	N
PACLITAXEL	Chronic inflammatory demyelinating polyradiculoneuropathy	0.42(0.10, 1.67)	0.42(0.10, 1.67)	0.42(0.10)	N	N	N
PACLITAXEL	Small fibre neuropathy	0.51(0.13, 2.06)	0.51(0.13, 2.06)	0.52(0.13)	N	N	N
PACLITAXEL	Axonal and demyelinating polyneuropathy	4.56(1.13, 18.44)	4.56(1.13, 18.44)	4.50(1.11)	N	N	N
BENDAMUSTINE	Acute polyneuropathy	3.29(0.46, 23.42)	3.29(0.46, 23.42)	3.29(0.46)	N	N	N
BENDAMUSTINE	Neuralgic amyotrophy	1.30(0.18, 9.22)	1.30(0.18, 9.22)	1.30(0.18)	N	N	N
BENDAMUSTINE	Peripheral motor neuropathy	1.33(0.19, 9.41)	1.33(0.19, 9.41)	1.32(0.19)	N	N	N
BENDAMUS	Peripheral nerve lesion	4.66(0.65,	4.66(0.65,	4.65(0.6	N	N	N

TINE		33.18)	33.17)	5)			
CYCLOPHOSPHAMIDE	Mononeuritis	0.78(0.11, 5.53)	0.78(0.11, 5.53)	0.78(0.11)	N	N	N
CYCLOPHOSPHAMIDE	Multifocal motor neuropathy	1.23(0.17, 8.80)	1.23(0.17, 8.80)	1.23(0.17)	N	N	N
CYCLOPHOSPHAMIDE	Femoral nerve palsy	3.37(0.47, 24.27)	3.37(0.47, 24.27)	3.33(0.46)	N	N	N
CYCLOPHOSPHAMIDE	Acute motor-sensory axonal neuropathy	1.06(0.15, 7.53)	1.06(0.15, 7.53)	1.05(0.15)	N	N	N
CYCLOPHOSPHAMIDE	Polyneuropathy chronic	2.38(0.33, 17.10)	2.38(0.33, 17.10)	2.37(0.33)	N	N	N
CYCLOPHOSPHAMIDE	Immune-mediated neuropathy	0.82(0.11, 5.81)	0.82(0.11, 5.81)	0.82(0.11)	N	N	N
CYCLOPHOSPHAMIDE	Small fibre neuropathy	0.20(0.03, 1.42)	0.20(0.03, 1.42)	0.20(0.03)	N	N	N
CYCLOPHOSPHAMIDE	Lumbosacral plexopathy	3.31(0.46, 23.88)	3.31(0.46, 23.88)	3.28(0.45)	N	N	N
CYCLOPHOSPHAMIDE	Lumbosacral radiculoplexus neuropathy	2.83(0.39, 20.34)	2.83(0.39, 20.34)	2.80(0.39)	N	N	N
CYCLOPHOSPHAMIDE	Peripheral nerve lesion	0.60(0.08, 4.26)	0.60(0.08, 4.26)	0.60(0.08)	N	N	N
GEMCITABINE	Brachial plexopathy	1.17(0.16, 8.33)	1.17(0.16, 8.33)	1.17(0.16)	N	N	N
GEMCITABINE	Mononeuropathy multiplex	1.30(0.18, 9.25)	1.30(0.18, 9.25)	1.30(0.18)	N	N	N
GEMCITABINE	Polyneuropathy chronic	6.03(0.84, 43.27)	6.03(0.84, 43.27)	5.97(0.83)	N	N	N
GEMCITABINE	Acrodynia	76.65(9.43,623.04)	76.65(9.43,623.02)	67.19(8.27)	N	N	Y
GEMCITABINE	Toxic neuropathy	1.34(0.19, 9.57)	1.34(0.19, 9.57)	1.34(0.19)	N	N	N
VINCRISTINE	Lewis-Sumner syndrome	10.07(1.39,72.93)	10.07(1.39,72.93)	9.90(1.37)	N	N	N
VINCRISTINE	Brachial plexopathy	1.10(0.15, 7.83)	1.10(0.15, 7.82)	1.10(0.15)	N	N	N
VINCRISTINE	Polyneuropathy chronic	5.66(0.79, 40.63)	5.66(0.79, 40.63)	5.61(0.78)	N	N	N
VINCRISTINE	Small fibre neuropathy	0.47(0.07, 3.36)	0.47(0.07, 3.36)	0.47(0.07)	N	N	N
VINCRISTINE	Peripheral nerve lesion	1.42(0.20, 10.13)	1.42(0.20, 10.13)	1.42(0.20)	N	N	N
VINCRISTINE	Autoimmune neuropathy	2.74(0.38, 19.54)	2.74(0.38, 19.54)	2.73(0.38)	N	N	N
ETOPOSIDE	Brachial plexopathy	1.34(0.19, 9.55)	1.34(0.19, 9.55)	1.34(0.19)	N	N	N
ETOPOSIDE	Mononeuropathy	2.37(0.33, 16.92)	2.37(0.33, 16.92)	2.37(0.33)	N	N	N
ETOPOSIDE	Acute motor-sensory axonal neuropathy	3.06(0.43, 21.83)	3.06(0.43, 21.83)	3.05(0.43)	N	N	N
ETOPOSIDE	Acute motor axonal neuropathy	4.18(0.59, 29.90)	4.18(0.59, 29.90)	4.16(0.58)	N	N	N

ETOPOSIDE	Pancoast's syndrome	11.83(1.63,85.55)	11.83(1.63,85.55)	11.62(1.61)	N	N	N
ETOPOSIDE	Neuralgic amyotrophy	0.48(0.07,3.44)	0.48(0.07,3.44)	0.48(0.07)	N	N	N
ETOPOSIDE	Peripheral nerve lesion	1.74(0.24,12.37)	1.74(0.24,12.37)	1.74(0.24)	N	N	N
ETOPOSIDE	Axonal and demyelinating polyneuropathy	5.08(0.71,36.38)	5.08(0.71,36.38)	5.05(0.71)	N	N	N
ETOPOSIDE	Autoimmune neuropathy	3.34(0.47,23.86)	3.34(0.47,23.85)	3.33(0.47)	N	N	N
ETOPOSIDE	Radial nerve palsy	2.00(0.28,14.22)	2.00(0.28,14.22)	1.99(0.28)	N	N	N
DOCETAXEL	Brachial plexopathy	0.61(0.09,4.37)	0.61(0.09,4.37)	0.61(0.09)	N	N	N
DOCETAXEL	Polyneuropathy in malignant disease	3.35(0.47,24.04)	3.35(0.47,24.04)	3.32(0.46)	N	N	N
DOCETAXEL	Femoral nerve palsy	4.46(0.62,32.18)	4.46(0.62,32.18)	4.41(0.61)	N	N	N
DOCETAXEL	Acute polyneuropathy	0.56(0.08,3.99)	0.56(0.08,3.99)	0.56(0.08)	N	N	N
DOCETAXEL	Polyneuropathy chronic	3.16(0.44,22.67)	3.16(0.44,22.67)	3.14(0.44)	N	N	N
DOCETAXEL	Miller Fisher syndrome	0.64(0.09,4.53)	0.64(0.09,4.53)	0.64(0.09)	N	N	N
DOCETAXEL	Nerve compression	0.07(0.01,0.49)	0.07(0.01,0.49)	0.07(0.01)	N	N	N
DOCETAXEL	Polyneuropathy idiopathic progressive	3.85(0.54,27.71)	3.85(0.54,27.71)	3.81(0.53)	N	N	N
DOCETAXEL	Lumbosacral plexopathy	4.39(0.61,31.67)	4.39(0.61,31.67)	4.34(0.60)	N	N	N
DOCETAXEL	Lumbosacral radiculoplexus neuropathy	3.75(0.52,26.96)	3.75(0.52,26.96)	3.71(0.52)	N	N	N
DOCETAXEL	Acrodynia	40.17(4.94,326.47)	40.17(4.94,326.46)	35.27(4.34)	N	N	Y
DOCETAXEL	Peripheral nerve lesion	0.79(0.11,5.65)	0.79(0.11,5.65)	0.79(0.11)	N	N	N
DOCETAXEL	Axonal and demyelinating polyneuropathy	2.32(0.32,16.63)	2.32(0.32,16.63)	2.31(0.32)	N	N	N
DOCETAXEL	Autoimmune neuropathy	1.53(0.21,10.91)	1.53(0.21,10.91)	1.53(0.21)	N	N	N
TOPOTECAN	Nerve compression	1.27(0.18,9.04)	1.27(0.18,9.03)	1.27(0.18)	N	N	N
TOPOTECAN	Carpal tunnel syndrome	0.60(0.09,4.29)	0.60(0.09,4.29)	0.60(0.09)	N	N	N
TOPOTECAN	Axonal neuropathy	5.16(0.73,36.69)	5.16(0.73,36.68)	5.16(0.73)	N	N	N
IRINOTECAN	Lewis-Sumner syndrome	20.38(2.82,147.56)	20.38(2.82,147.56)	20.00(2.76)	N	N	Y
IRINOTECAN	Ischaemic neuropathy	16.99(2.35,122.57)	16.99(2.35,122.57)	16.72(2.32)	N	N	Y
IRINOTECAN	Axonal neuropathy	1.01(0.14,	1.01(0.14,	1.01(0.1	N	N	N

		7.16)	7.16)	4)			
IRINOTECAN	Sciatic nerve neuropathy	3.68(0.52, 26.21)	3.68(0.52, 26.21)	3.67(0.52)	N	N	N
IRINOTECAN	Sciatic nerve palsy	11.71(1.63,84.11)	11.71(1.63,84.10)	11.59(1.61)	N	N	N
EPIRUBICIN	Mononeuritis	3.14(0.44, 22.36)	3.14(0.44, 22.36)	3.13(0.44)	N	N	N
EPIRUBICIN	Femoral nerve palsy	13.60(1.89,98.06)	13.60(1.89,98.05)	13.40(1.86)	N	N	N
EPIRUBICIN	Polyneuropathy chronic	9.63(1.34, 69.10)	9.63(1.34, 69.10)	9.53(1.33)	N	N	N
EPIRUBICIN	Miller Fisher syndrome	1.94(0.27, 13.79)	1.94(0.27, 13.79)	1.94(0.27)	N	N	N
EPIRUBICIN	Neuritis	0.36(0.05, 2.55)	0.36(0.05, 2.55)	0.36(0.05)	N	N	N
EPIRUBICIN	Demyelinating polyneuropathy	0.68(0.10, 4.84)	0.68(0.10, 4.84)	0.68(0.10)	N	N	N
EPIRUBICIN	Peripheral motor neuropathy	0.69(0.10, 4.89)	0.69(0.10, 4.89)	0.69(0.10)	N	N	N
EPIRUBICIN	Peripheral sensorimotor neuropathy	0.58(0.08, 4.11)	0.58(0.08, 4.11)	0.58(0.08)	N	N	N
EPIRUBICIN	Axonal neuropathy	0.85(0.12, 6.02)	0.85(0.12, 6.02)	0.85(0.12)	N	N	N
DOXORUBICIN	Lewis-Sumner syndrome	7.86(1.09, 56.86)	7.85(1.09, 56.86)	7.72(1.07)	N	N	N
DOXORUBICIN	Acute motor-sensory axonal neuropathy	1.95(0.27, 13.94)	1.95(0.27, 13.94)	1.95(0.27)	N	N	N
DOXORUBICIN	Immune-mediated neuropathy	1.51(0.21, 10.76)	1.51(0.21, 10.76)	1.51(0.21)	N	N	N
DOXORUBICIN	Peripheral nerve lesion	1.11(0.16, 7.90)	1.11(0.16, 7.90)	1.11(0.16)	N	N	N
DOXORUBICIN	Axonal and demyelinating polyneuropathy	3.25(0.45, 23.23)	3.25(0.45, 23.23)	3.23(0.45)	N	N	N
CARBOPLATIN	Mononeuritis	1.19(0.17, 8.45)	1.19(0.17, 8.45)	1.19(0.17)	N	N	N
CARBOPLATIN	Mononeuropathy multiplex	0.78(0.11, 5.58)	0.78(0.11, 5.58)	0.78(0.11)	N	N	N
CARBOPLATIN	Polyradiculoneuropathy	9.00(1.23, 65.63)	9.00(1.23, 65.63)	8.78(1.20)	N	N	N
CARBOPLATIN	Acute motor-sensory axonal neuropathy	1.61(0.23, 11.50)	1.61(0.23, 11.50)	1.61(0.23)	N	N	N
CARBOPLATIN	Acute motor axonal neuropathy	2.20(0.31, 15.75)	2.20(0.31, 15.75)	2.20(0.31)	N	N	N
CARBOPLATIN	Pancoast's syndrome	6.23(0.86, 45.06)	6.23(0.86, 45.06)	6.13(0.85)	N	N	N
CARBOPLATIN	Ischaemic neuropathy	5.40(0.75, 38.95)	5.40(0.75, 38.95)	5.33(0.74)	N	N	N
CARBOPLATIN	Polyneuropathy idiopathic progressive	4.44(0.62, 31.93)	4.44(0.62, 31.92)	4.39(0.61)	N	N	N
CARBOPLATIN	Peripheral nerve lesion	0.91(0.13, 6.51)	0.91(0.13, 6.51)	0.92(0.13)	N	N	N

CARBOPLATIN	Radial nerve palsy	1.05(0.15, 7.49)	1.05(0.15, 7.49)	1.05(0.15)	N	N	N
CISPLATIN	Brachial plexopathy	1.10(0.15, 7.82)	1.10(0.15, 7.82)	1.10(0.15)	N	N	N
CISPLATIN	Acute motor-sensory axonal neuropathy	2.50(0.35, 17.87)	2.50(0.35, 17.87)	2.50(0.35)	N	N	N
CISPLATIN	Chronic inflammatory demyelinating polyradiculoneuropathy	0.38(0.05, 2.72)	0.38(0.05, 2.72)	0.38(0.05)	N	N	N
CISPLATIN	Ischaemic neuropathy	8.39(1.16, 60.55)	8.39(1.16, 60.55)	8.27(1.15)	N	N	N
CISPLATIN	Neuralgic amyotrophy	0.40(0.06, 2.81)	0.40(0.06, 2.81)	0.40(0.06)	N	N	N
CISPLATIN	Diabetic neuropathy	0.12(0.02, 0.85)	0.12(0.02, 0.85)	0.12(0.02)	N	N	N
CISPLATIN	Demyelinating polyneuropathy	0.40(0.06, 2.84)	0.40(0.06, 2.84)	0.40(0.06)	N	N	N
CISPLATIN	Carpal tunnel syndrome	0.06(0.01, 0.41)	0.06(0.01, 0.41)	0.06(0.01)	N	N	N
CISPLATIN	Small fibre neuropathy	0.47(0.07, 3.36)	0.47(0.07, 3.36)	0.47(0.07)	N	N	N
CISPLATIN	Axonal and demyelinating polyneuropathy	4.16(0.58, 29.78)	4.16(0.58, 29.78)	4.13(0.58)	N	N	N
CISPLATIN	Radial nerve palsy	1.63(0.23, 11.64)	1.63(0.23, 11.64)	1.63(0.23)	N	N	N
PACLITAXEL	Brachial plexopathy	0.60(0.08, 4.25)	0.60(0.08, 4.25)	0.60(0.08)	N	N	N
PACLITAXEL	Mononeuropathy	1.06(0.15, 7.52)	1.06(0.15, 7.52)	1.06(0.15)	N	N	N
PACLITAXEL	Polyradiculoneuropathy	7.60(1.04, 55.41)	7.60(1.04, 55.41)	7.42(1.02)	N	N	N
PACLITAXEL	Polyneuropathy chronic	3.07(0.43, 22.06)	3.07(0.43, 22.05)	3.05(0.42)	N	N	N
PACLITAXEL	Neuronal neuropathy	13.67(1.84,101.89)	13.67(1.84,101.89)	13.07(1.75)	N	N	N
PACLITAXEL	Diabetic mononeuropathy	54.69(6.39,468.18)	54.69(6.39,468.17)	45.75(5.34)	N	N	Y
PACLITAXEL	Polyneuropathy idiopathic progressive	3.75(0.52, 26.95)	3.75(0.52, 26.95)	3.71(0.52)	N	N	N
PACLITAXEL	Peripheral nerve lesion	0.77(0.11, 5.50)	0.77(0.11, 5.50)	0.77(0.11)	N	N	N
PACLITAXEL	Autoimmune neuropathy	1.49(0.21, 10.61)	1.49(0.21, 10.61)	1.48(0.21)	N	N	N

4. Discussion

Our pharmacovigilance analysis of the FAERS database reveals a substantial and increasing burden of chemotherapy-induced peripheral neuropathy (CIPN) over the past two decades, with a striking 97.00% of reported cases classified as serious outcomes10. This high rate of severe adverse events, including hospitalization and permanent disability, underscores that CIPN is not merely a transient side effect but a critical dose-limiting toxicity that significantly

compromises patient quality of life and safety11. The sustained upward trajectory of annual reports peaking in 2019 reflects both the increasing utilization of neurotoxic antineoplastics and heightened awareness among healthcare professionals; however, the dominance of physician reporting (39.93%) compared to other providers suggests an opportunity for nurses to play a more active role in pharmacovigilance and symptom reporting12.

Consistent with previous epidemiological studies, our data identified a female predominance (53.33%) and a higher vulnerability in patients aged 45 and older1314. The heightened risk in older adults may be attributed to age-related physiological changes, such as decreased renal clearance and pre-existing neuronal degeneration, which exacerbate neurotoxicity15. From a nursing perspective, these demographic findings necessitate a tailored assessment approach. For older female patients receiving taxanes or platinum-based therapies, oncology nurses should implement comprehensive baseline neurological assessments—such as the Total Neuropathy Score (TNS)—prior to treatment initiation to establish a reference point for detecting subtle changes16. Furthermore, since older patients are more prone to falls and functional decline, fall-risk screening should be integrated into the routine nursing care plan for this specific subgroup17.

Implications for "Early-Onset" Education A critical finding of this study is the median time-to-onset (TTO) of 25 days, with over half of the cases (54.50%) manifesting within the first month of therapy. This "early-peak" pattern challenges the traditional view of CIPN as solely a cumulative, late-effect toxicity and highlights the urgency of early intervention18. For nursing practice, this implies that patient education regarding neurotoxic symptoms (e.g., numbness, tingling, cold sensitivity) must be intensified during the very first cycle of chemotherapy19. The observation that fatal outcomes were associated with a significantly longer TTO (32 days) compared to non-fatal cases suggests that unchecked, progressive neurotoxicity may contribute to systemic deterioration over time. Therefore, nurses must maintain vigilance not only during the acute infusion phase but also throughout the inter-cycle periods to identify "coasting" phenomena or delayed progression20.

Our disproportionality analysis highlighted distinct neurotoxic profiles that warrant agent-specific nursing interventions. Vincristine exhibited the strongest signal intensity and was uniquely associated with motor and autonomic neuropathies (mononeuropathy multiplex). Consequently, nursing care for patients on Vincristine should focus on assessing motor function, such as fine motor skills (buttoning shirts) and bowel motility (constipation), rather than solely focusing on sensory deficits21. In contrast, Paclitaxel showed strong signals for sensory neuropathy. Given that Docetaxel displayed a significantly delayed onset (median 49.50 days) compared to other agents, nurses should counsel patients that symptoms might emerge or worsen even after treatment cessation, requiring extended follow-up22. The distinct profiles of Carboplatin and Cisplatin also suggest that while Cisplatin is historically more neurotoxic, the higher signal strength of Carboplatin in this dataset may reflect its widespread use in outpatient settings where nurse-led monitoring is pivotal2324.

5.Limitations

While the use of a dual-database validation (FAERS + EV) minimizes geographic bias, this study remains limited by the nature of spontaneous reporting. The lack of denominator data (total patient exposure) means we can assess relative reporting strength but not absolute incidence25. Furthermore, the high serious-event rate suggests a potential "severity bias," where mild, Grade 1 neuropathies may be underreported

despite their negative impact on patient quality of life26.

6.Conclusion

Our study underscores that CIPN is not merely a late-stage cumulative complication but a critical, early-onset toxicity that frequently manifests within the first 30 days of treatment. This "early-peak" pattern, consistently observed across both FAERS and EudraVigilance, creates a defined "window of opportunity" for oncology nurses. By moving toward "cycle-one vigilance" and agent-specific monitoring (e.g., anticipating the motor deficits of Vincristine vs. the delayed sensory onset of Docetaxel), nursing teams can preemptively address functional decline. Ultimately, integrating these real-world insights into bedside practice is essential for reducing long-term disability and preserving the independence of cancer survivors.

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Availability of data and materials

All the data for the present article can be found on the US FDA Adverse Event Reporting System (FAERS) database and the EudraVigilance (EV) database.

Authors' contributions

Li Qing, Wen Mei Hong and Qionglin Huang collected, analyzed, and interpreted the data, wrote the manuscript. Pengkhun Nov, Li Wan Dan and Ling Ling designed, revised, and supervised the study. All authors had reviewed and approved the final manuscript.

Ethics approval and consent to participate.

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Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Clinical trial number

Not applicable.

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