

**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  $\geq 45$  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 therapy<sup>1,2,3</sup>. 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-therapy<sup>4</sup>. Characterized by symmetrical sensory loss,

paresthesia, and neuropathic pain, CIPN can progress to motor dysfunction and autonomic impairment in severe cases<sup>5</sup>.

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 outcomes<sup>6</sup>. 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)<sup>7</sup>. 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 interventions<sup>8</sup>. 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)<sup>9</sup>. 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

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

$$95\% \text{CI} = e^{\ln(\text{ROR}) \pm 1.96 \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}}$$

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

PRR

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

$$95\% \text{CI} = e^{\ln(\text{PRR}) \pm 1.96 \sqrt{\frac{1}{a} + \frac{1}{a+b} + \frac{1}{c} + \frac{1}{c+d}}}$$

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

EBGM

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

$$95\% \text{CI} = e^{\ln(\text{EBGM}) \pm 1.96 \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}}$$

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.

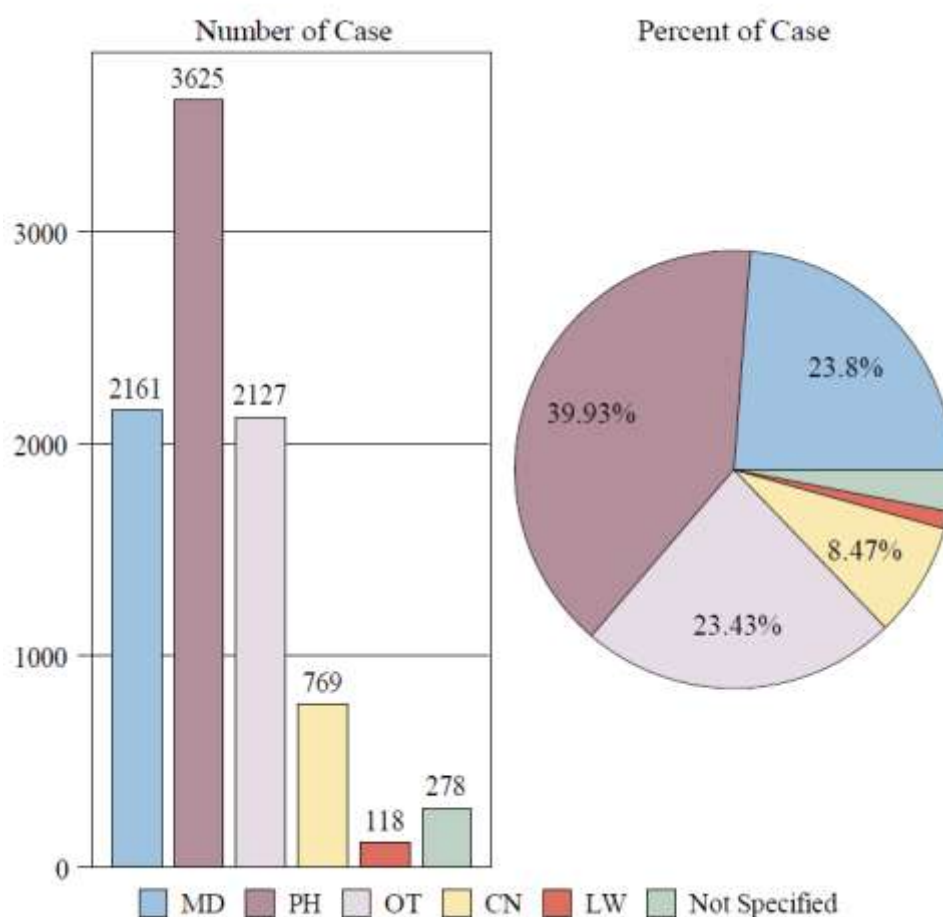
## 3. Results

### Descriptive Analysis of CIPN Reports and Baseline Characteristics

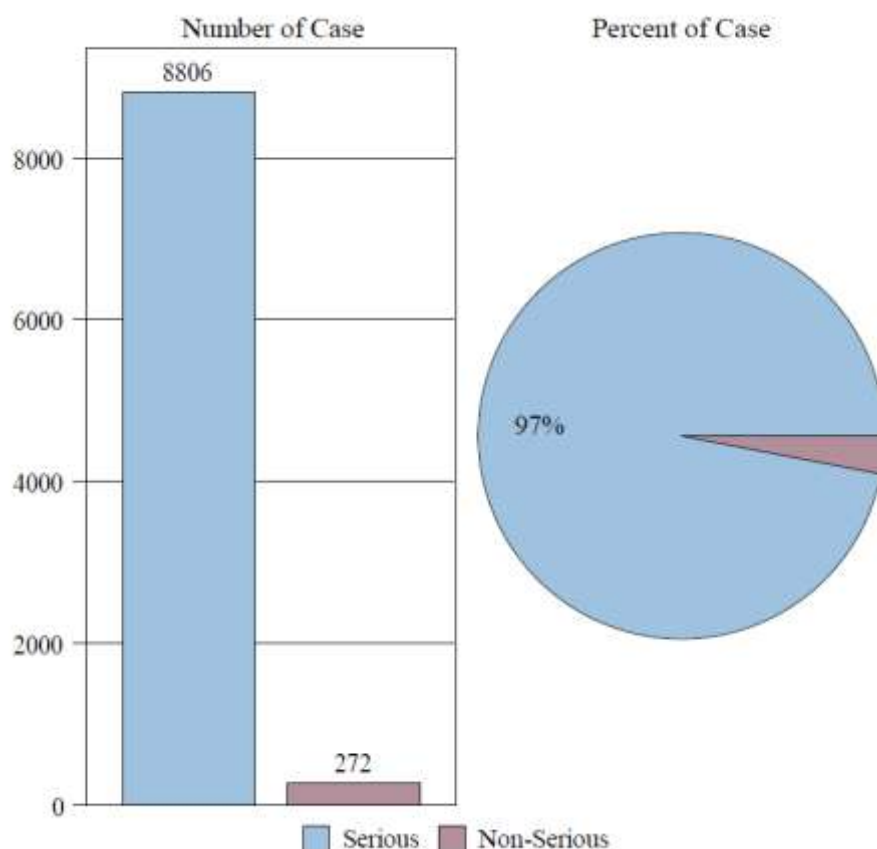
Between 2004 and 2025, a total of 9,078 adverse event (AE) reports pertaining to chemotherapy-induced peripheral neuropathy (CIPN) were retrieved from the FAERS database. Data submission was predominantly driven by medical professionals, with physicians (39.93%), pharmacists (23.80%), and other healthcare 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  $\geq 65$

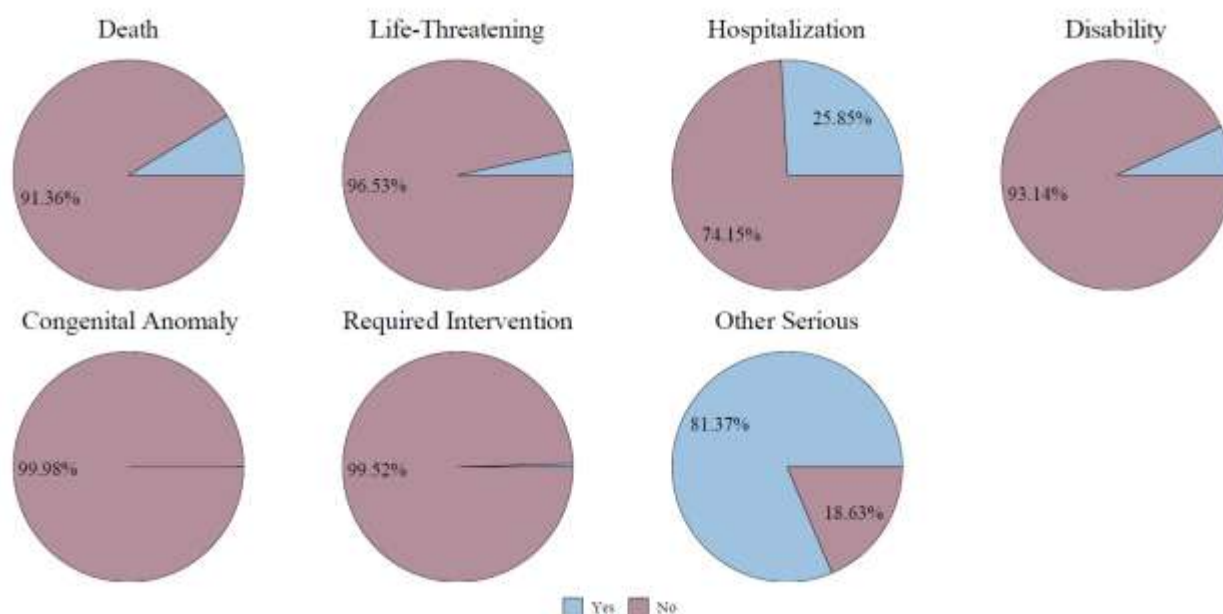
(27.87%) (Figure 5) being the most frequently affected. At the agent level, Paclitaxel (N=1,966), Carboplatin (N=1,282), and Docetaxel (N=1,110) were the most common triggers (Figure 6). Notably, the annual report volume exhibited a sustained upward trajectory, peaking in 2019 (n=853) and remaining elevated through 2024 (Figure 7).



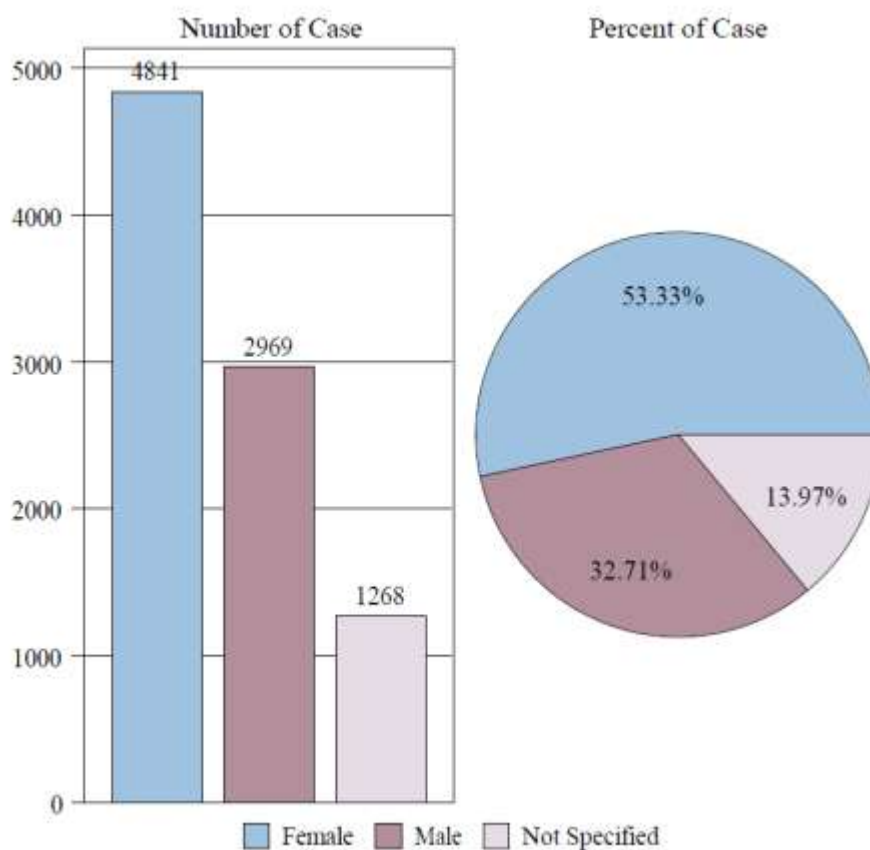
**Figure1. Reporter distribution of AE reports (FAERS)**



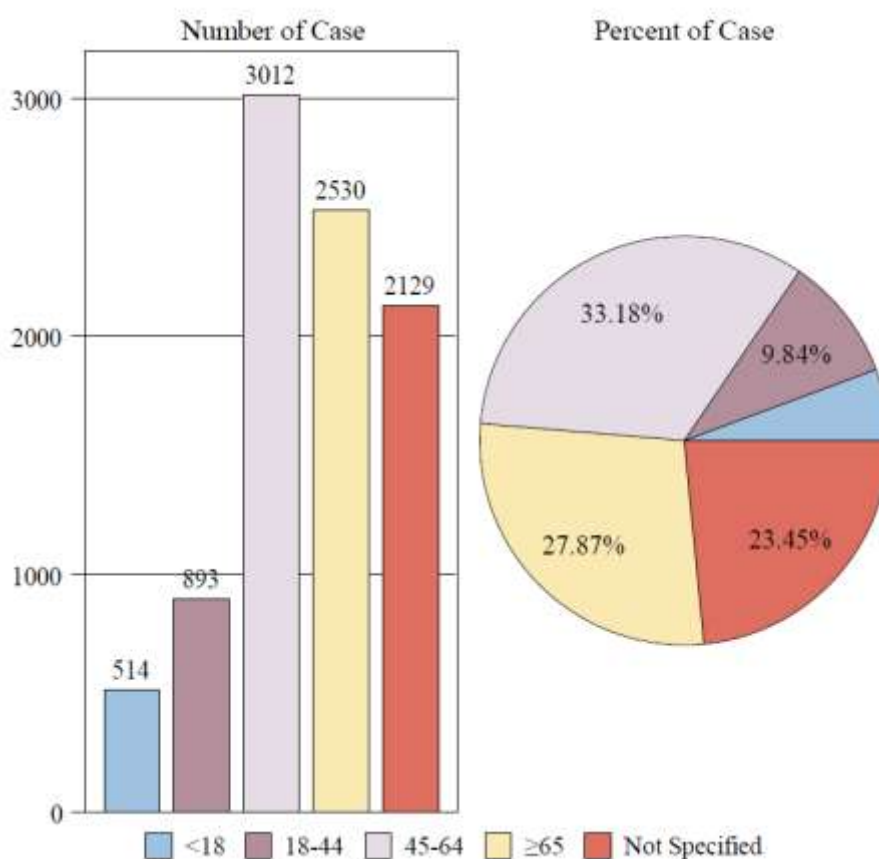
**Figure2. Serious Report distribution of AE reports (FAERS)**



**Figure3. Outcomes report distribution of AE reports(FAERS)**

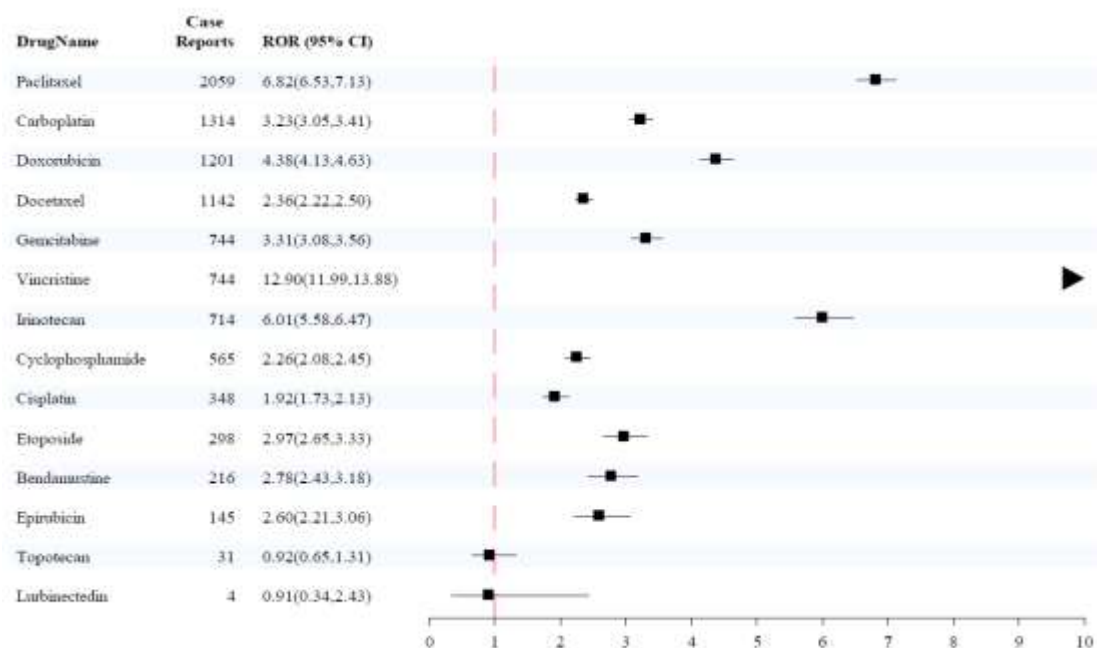


**Figure4. Sex distribution of AE reports(FAERS)**

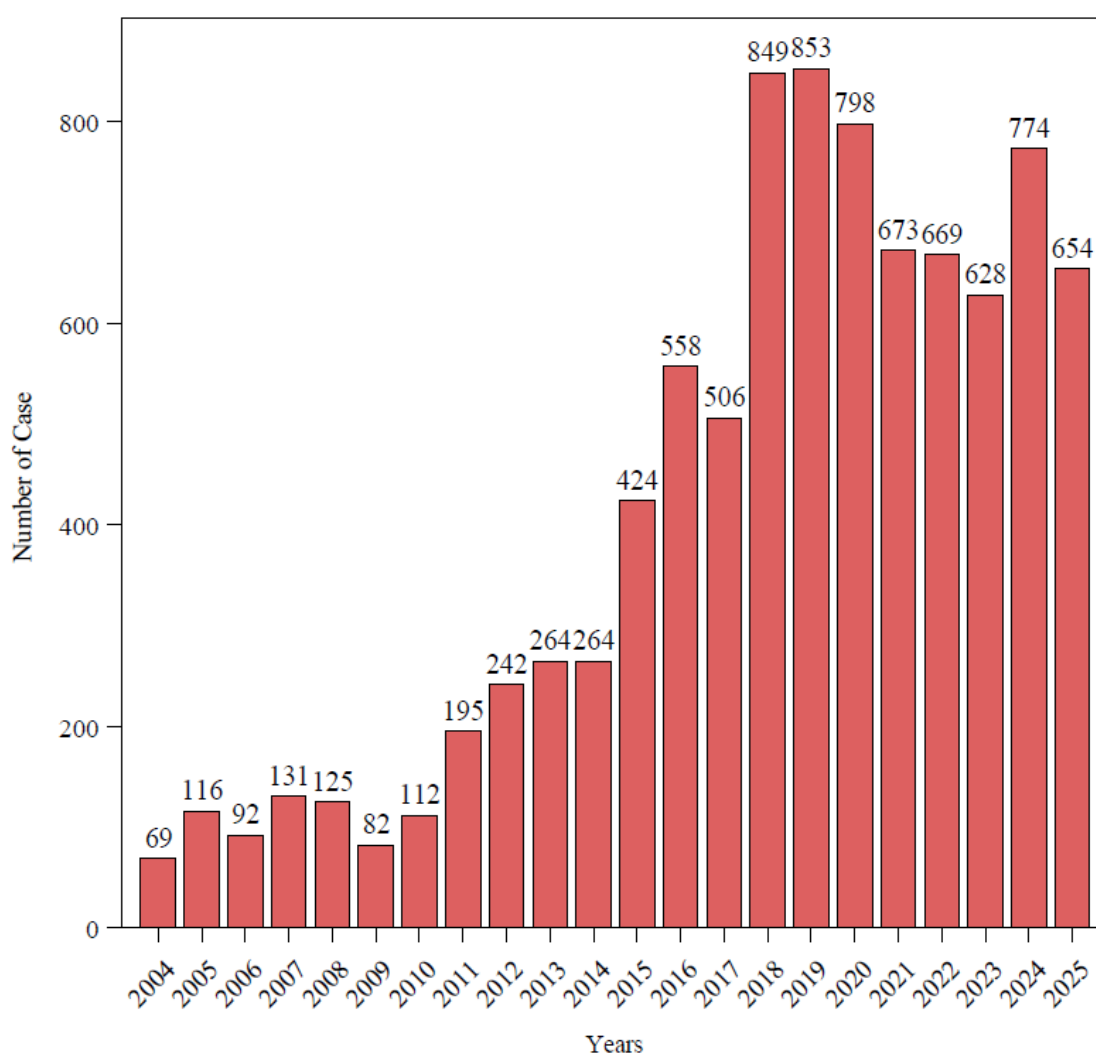


**Figure5. Age distribution of AE reports (FAERS)**





**Figure6. Distribution of CIPN reports by chemotherapeutic agent**

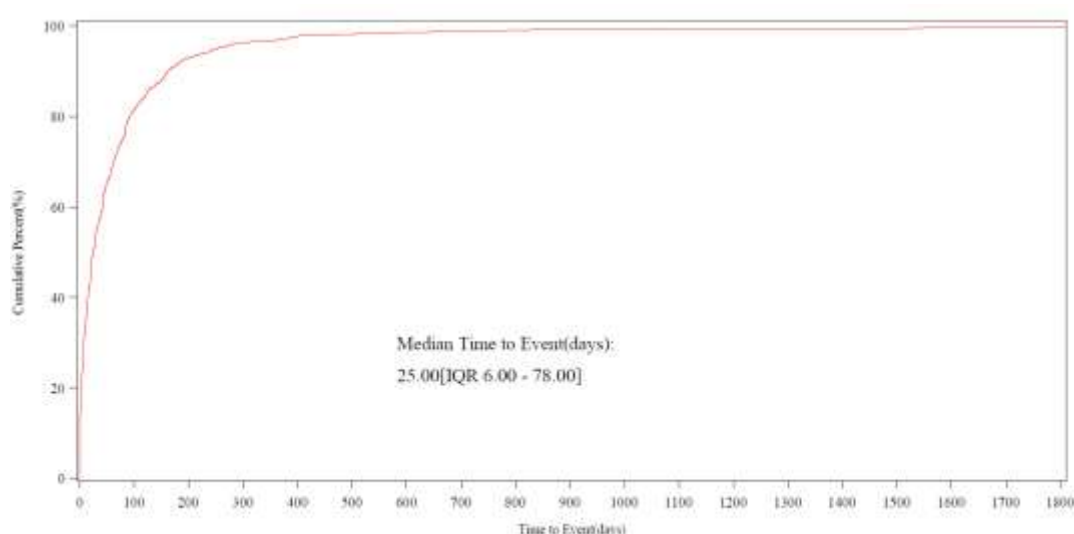


**Figure7. Annual distribution of AE reports (FAERS)**

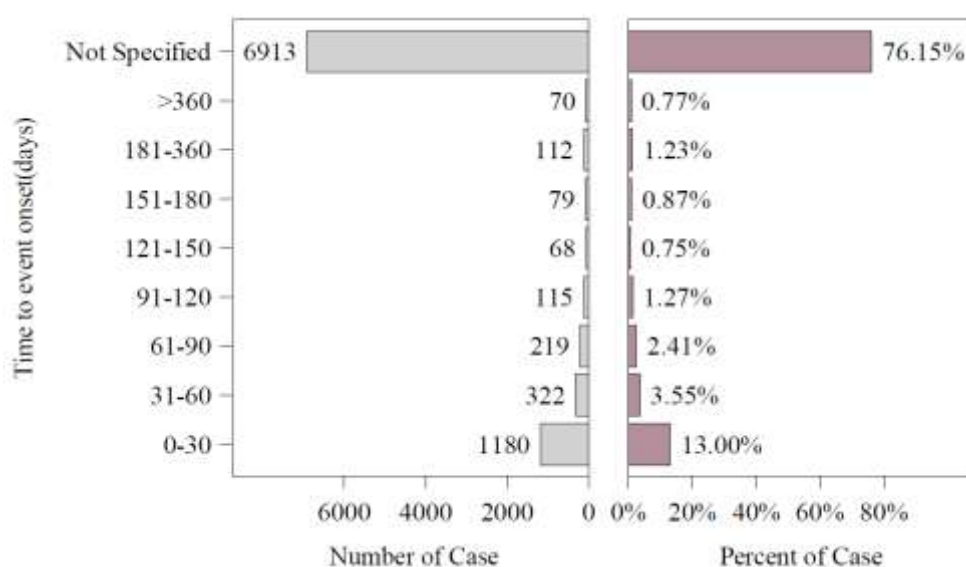
### Temporal Distribution and Time-to-Onset (TTO) Profile

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).

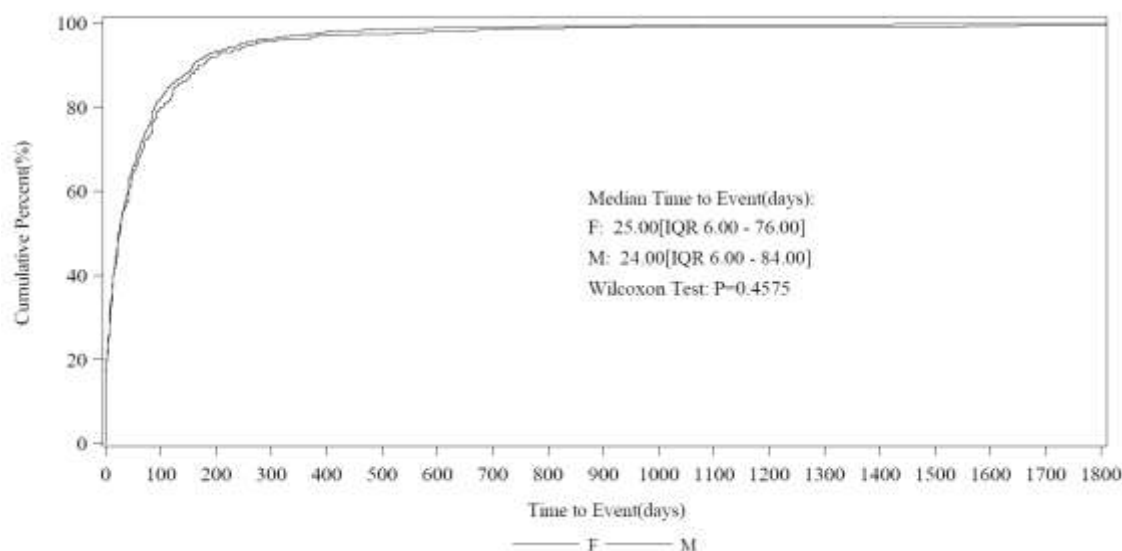


**Figure8. Cumulative Distribution of Time-to-Onset(FAERS)**

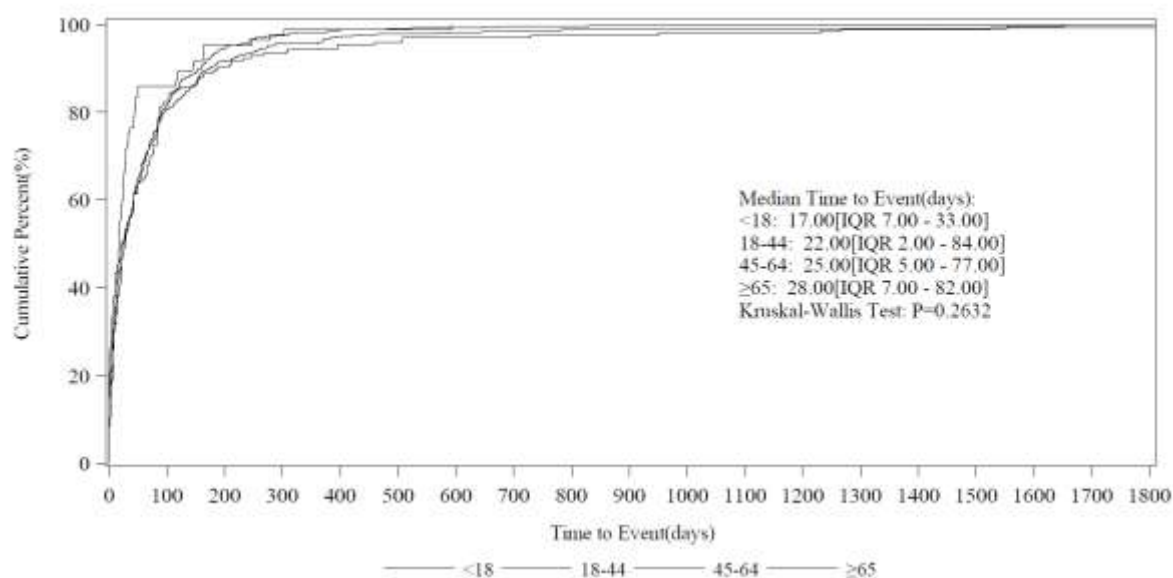


**Figure9. Time to event report distribution of AE reports(FAERS)**

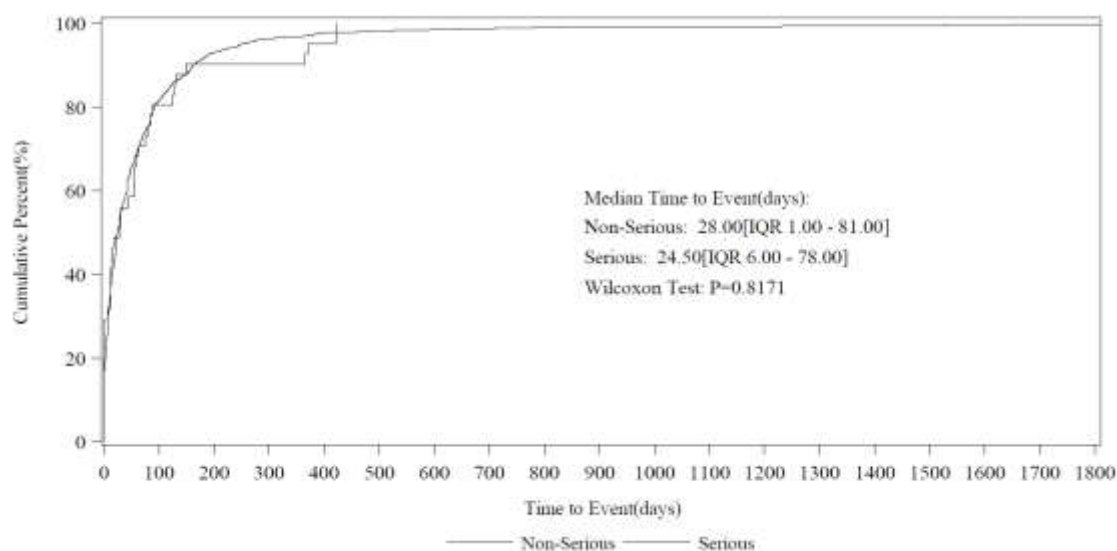




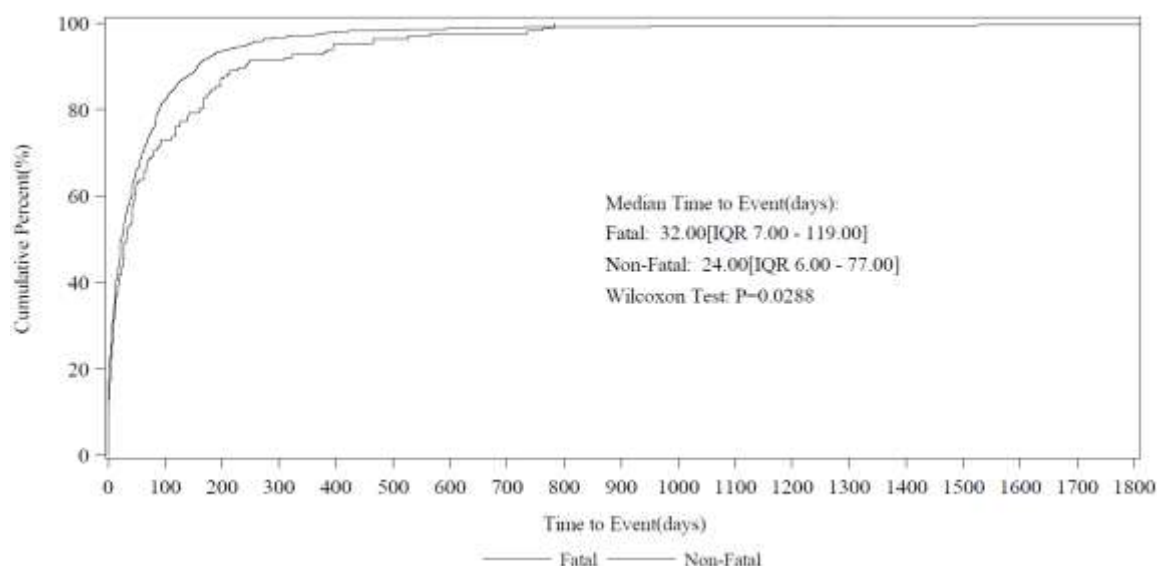
**Figure10.Cumulative percentage of time-to-onset across different sex groups(FAERS)**



**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)**

| Dru<br>g/T<br>TO          | PA<br>CLI<br>TA<br>XE<br>L        | CA<br>RB<br>OP<br>LA<br>TIN       | DO<br>XO<br>RU<br>BIC<br>IN       | DO<br>CE<br>TA<br>XE<br>L         | GE<br>MC<br>ITA<br>BIN<br>E       | IRI<br>NO<br>TE<br>CA<br>N        | VIN<br>CRI<br>STI<br>NE        | CYCL<br>OPHO<br>SPHA<br>MIDE | CIS<br>PL<br>ATI<br>N             | ET<br>OP<br>OSI<br>DE             | BEN<br>DA<br>MU<br>STI<br>NE  | EPI<br>RU<br>BIC<br>IN            | TO<br>PO<br>TE<br>CA<br>N    | LUR<br>BIN<br>ECT<br>EDI<br>N |
|---------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|--------------------------------|------------------------------|-----------------------------------|-----------------------------------|-------------------------------|-----------------------------------|------------------------------|-------------------------------|
| N(<br>Mis<br>sing<br>)    | 596(<br>137<br>0)                 | 377(<br>905)                      | 101(<br>103<br>2)                 | 368(<br>732)                      | 146(<br>586)                      | 172(<br>522)                      | 142(<br>513)                   | 87(440<br>)                  | 44(2<br>84)                       | 40(2<br>44)                       | 48(1<br>52)                   | 34(1<br>09)                       | 10(<br>20)                   | 0(4)                          |
| Mea<br>n(S<br>D)          | 73.5<br>6(13<br>4.26<br>)         | 73.3<br>2(24<br>0.30<br>)         | 154.<br>45(5<br>12.7<br>4)        | 63.2<br>8(12<br>8.77<br>)         | 87.1<br>3(13<br>1.89<br>)         | 36.7<br>7(68<br>.77)              | 106.<br>77(5<br>55.5<br>8)     | 134.55<br>(488.5<br>5)       | 43.5<br>0(56<br>.24)              | 41.7<br>8(11<br>8.43<br>)         | 118.<br>06(3<br>08.7<br>5)    | 60.4<br>7(16<br>2.13<br>)         | 57.7<br>0(1<br>23.0<br>9)    | ()                            |
| Med<br>ian(<br>Q1,<br>Q3) | 28.0<br>0(7.<br>00,8<br>9.00<br>) | 27.0<br>0(7.<br>00,7<br>1.00<br>) | 21.0<br>0(1.<br>00,8<br>4.00<br>) | 22.5<br>0(3.<br>00,6<br>8.00<br>) | 49.5<br>0(7.<br>00,9<br>7.00<br>) | 14.0<br>0(1.<br>00,4<br>5.50<br>) | 26.5<br>0(12.<br>00,7<br>0.00) | 28.00(<br>9.00,11<br>8.00)   | 18.0<br>0(3.<br>00,7<br>3.50<br>) | 12.0<br>0(1.<br>50,2<br>2.00<br>) | 27.0<br>0(0.0<br>0.89.<br>00) | 21.0<br>0(4.<br>00,5<br>7.00<br>) | 7.00<br>(4.0<br>0,28<br>.00) | (,)                           |
| Min<br>,Ma<br>x           | 0.00<br>,189<br>6.00              | 0.00,<br>3001<br>.00              | 0.00<br>,429<br>6.00              | 0.00<br>,152<br>6.00              | 0.00<br>,830<br>.00               | 0.00<br>,644<br>.00               | 0.00,<br>6574<br>.00           | 0.00,42<br>96.00             | 0.00<br>,265<br>.00               | 0.00<br>,730<br>.00               | 0.00,<br>1524<br>.00          | 0.00<br>,950<br>.00               | 0.00<br>,393<br>.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<sub>05</sub>: 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<sub>05</sub> (1.72) remained below the conservative cutoff of 2.0, suggesting a more moderate association compared to Carboplatin (EBGM<sub>05</sub>: 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(EBG M05) | 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           |
| LURBINECTIDIN    | 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           |
| GEMCITABINE | 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(6.25,16.22)    | 10.07(6.25,16.20)    | 10.03(6.23)  | 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 |
| DOXORUBIC IN     | Acute polyneuropathy                                      | 10.91(4.5 0,26.43)    | 10.91(4.5 0,26.42)    | 10.72(4.4 2)  | Y | Y | Y |
| DOXORUBIC IN     | Toxic neuropathy                                          | 7.33(3.03, 17.71)     | 7.33(3.03, 17.71)     | 7.25(3.00 )   | Y | Y | Y |
| CARBOPLAT IN     | Miller Fisher syndrome                                    | 9.24(3.80, 22.43)     | 9.24(3.80, 22.43)     | 9.04(3.72 )   | Y | Y | Y |
| CARBOPLAT IN     | Autoimmune neuropathy                                     | 16.39(6.6 9,40.12)    | 16.39(6.6 9,40.12)    | 15.75(6.4 3)  | 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(4.0 5,28.85)    | 10.80(4.0 5,28.84)    | 10.76(4.0 3)  | 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 |
| DOXORUBIC IN     | Chronic inflammatory demyelinating polyradiculoneuropathy | 1.82(0.68, 4.87)      | 1.82(0.68, 4.87)      | 1.82(0.68 )   | N | N | N |
| DOXORUBIC IN     | Demyelinating polyneuropathy                              | 2.31(0.87, 6.18)      | 2.31(0.87, 6.18)      | 2.31(0.86 )   | N | N | N |
| DOXORUBIC IN     | 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 |
| LURBINECT EDIN   | 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 |
| DOXORUBICIN      | 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(5.77, 97.82)     | 23.76(5.77, 97.81)     | 22.83(5.55)  | 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(7.42, 132.91)    | 31.41(7.42, 132.90)    | 29.07(6.87)  | 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(3.51, 181.27)    | 25.22(3.51, 181.26)    | 24.92(3.47)  | 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(1.43, 74.26)     | 10.29(1.43, 74.26)     | 10.14(1.41)  | 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 |

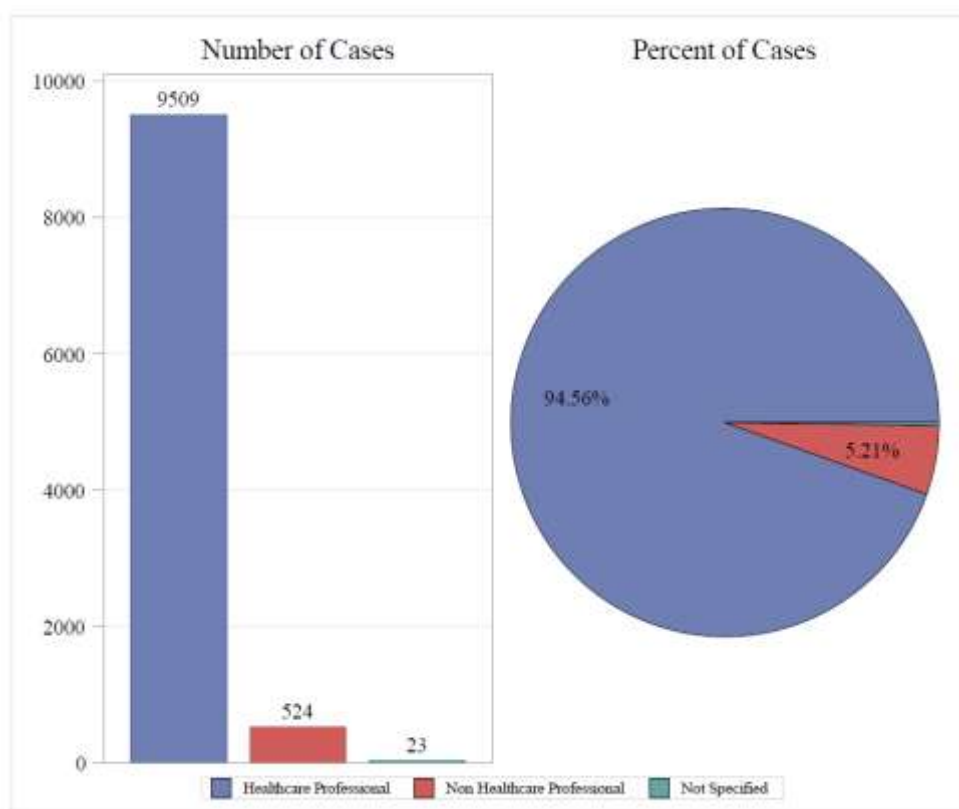


|             |                                     |                       |                       |               |   |   |   |
|-------------|-------------------------------------|-----------------------|-----------------------|---------------|---|---|---|
| IRINOTECAN  | Acute polyneuropathy                | 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(5.0 8,262.70)   | 36.53(5.0 8,262.66)   | 36.07(5.0 2)  | N | N | Y |
| EPIRUBICIN  | Acute polyneuropathy                | 10.68(1.5 0,76.09)    | 10.68(1.5 0,76.08)    | 10.64(1.4 9)  | 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(3.7 9,221.65)   | 28.99(3.7 9,221.64)   | 26.99(3.5 3)  | 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 |

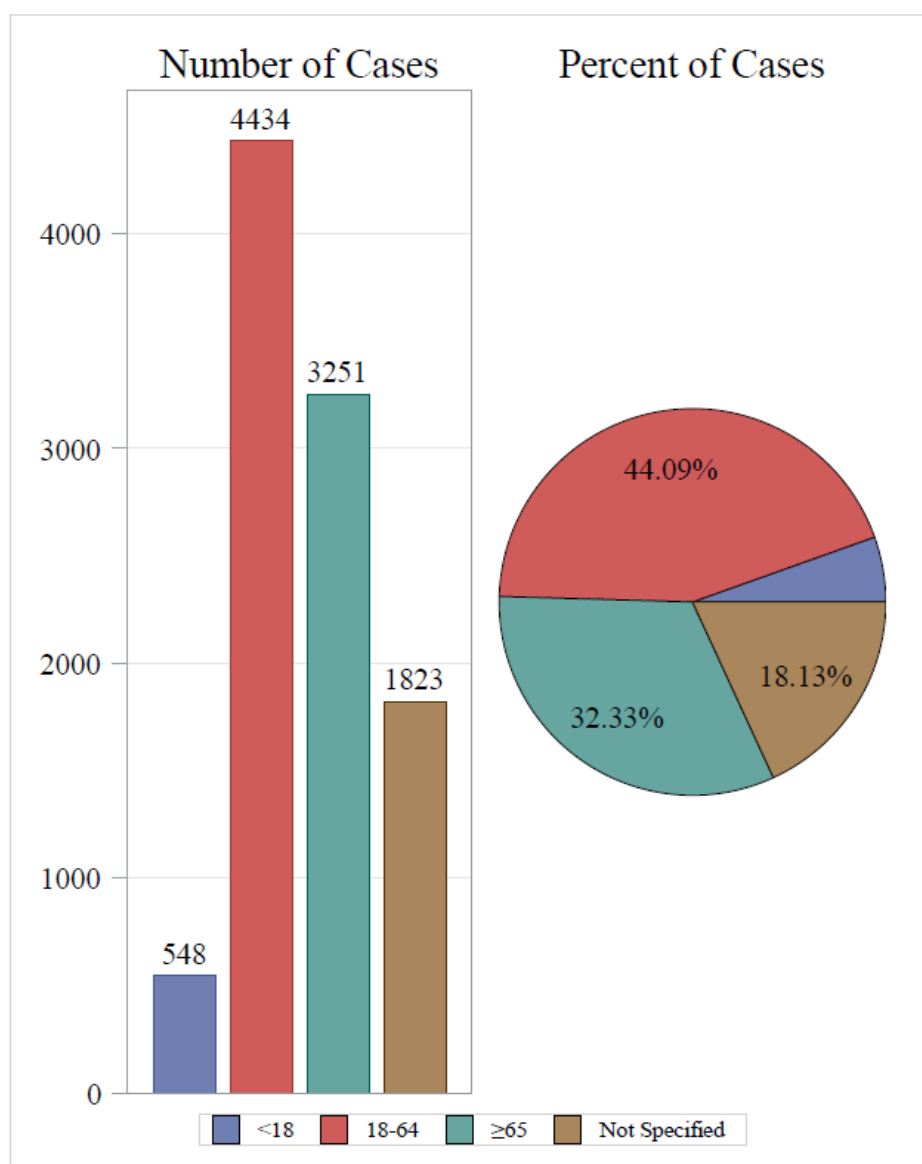
### Validation Analysis Based on the EudraVigilance Database

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 ( $\geq 65$  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 therapies (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(EBG M05) | 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           |
| DOXORUBICIN      | Peripheral sensory neuropathy | 7.03(5.87,         | 7.02(5.87,         | 6.92(5.7     | Y          | Y          | Y           |

|                  |                                    |                     |                     |              |   |   |   |
|------------------|------------------------------------|---------------------|---------------------|--------------|---|---|---|
| IN               | neuropathy                         | 8.42)               | 8.41)               | 8)           |   |   |   |
| VINCRISTIN E     | 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 |
| VINCRISTIN E     | 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 |
| VINCRISTIN E     | 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 |
| VINCRISTIN E     | 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 |
| VINCRISTIN E     | Guillain-Barre syndrome            | 1.54(1.11, 2.15)    | 1.54(1.11, 2.15)    | 1.54(1.10)   | Y | Y | N |
| VINCRISTIN E     | 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 neuropathy motor        | 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 neuropathy sensorimotor | 5.37(3.45, 8.35)   | 5.37(3.45, 8.35)   | 5.31(3.42)  | Y | Y | Y |
| PACLITAXEL       | Peripheral neuropathy sensorimotor | 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 neuropathy motor        | 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 neuropathy sensorimotor | 2.49(1.44, 4.29)   | 2.49(1.44, 4.29)   | 2.47(1.43)  | Y | Y | N |
| CARBOPLATIN      | Peripheral neuropathy sensorimotor | 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 neuropathy motor        | 5.22(2.96, 9.21)   | 5.22(2.96, 9.21)   | 5.18(2.93)  | Y | Y | Y |
| ETOPOSIDE        | Peripheral neuropathy sensorimotor | 5.02(2.84, 8.86)   | 5.02(2.84, 8.85)   | 4.98(2.82)  | Y | Y | Y |
| EPIRUBICIN       | Peripheral neuropathy sensory      | 1.50(0.85, 2.64)   | 1.50(0.85, 2.63)   | 1.49(0.85)  | N | N | N |
| CISPLATIN        | Peripheral neuropathy sensorimotor | 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 |
| CYCLOPHOSPHAMIDE | Chronic inflammatory               | 1.62(0.87, 2.79)   | 1.62(0.87, 2.79)   | 1.62(0.87)  | 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, 6.67)    | 3.00(1.35, 6.67)    | 2.99(1.35)   | 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 |
| VINCRIPTINE      | Acute motor axonal neuropathy                                 | 17.61(7.22, 42.97)    | 17.61(7.22, 42.96)    | 17.05(6.99)         | Y | Y | Y |
| VINCRIPTINE      | Demyelinating polyneuropathy                                  | 2.01(0.83, 4.83)      | 2.01(0.83, 4.83)      | 2.00(0.83)          | N | N | N |
| VINCRIPTINE      | 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 |
| VINCRIPTINE      | Acute motor-sensory axonal neuropathy                         | 10.18(3.78, 27.38)    | 10.18(3.78, 27.38)    | 9.99(3.71)          | Y | Y | Y |
| VINCRIPTINE      | Nerve compression                                             | 0.49(0.18, 1.31)      | 0.49(0.18, 1.31)      | 0.49(0.18)          | N | N | N |
| VINCRIPTINE      | 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(11.00, 79.23)   | 30.37(11.00, 79.23)   | 28.99(10.00, 79.23) | Y | Y | Y |

|                      |                                                                 |                      |                      |                |   |   |   |
|----------------------|-----------------------------------------------------------------|----------------------|----------------------|----------------|---|---|---|
|                      | malignant disease                                               | 13,82.88)            | 13,82.87)            | .62)           |   |   |   |
| ETOPOSIDE            | Intensive care unit<br>acquired weakness                        | 5.62(2.10,<br>15.03) | 5.62(2.10,<br>15.03) | 5.57(2.0<br>8) | Y | Y | Y |
| DOCETAXEL            | Mononeuropathy                                                  | 4.39(1.64,<br>11.80) | 4.39(1.64,<br>11.79) | 4.34(1.6<br>2) | Y | Y | N |
| TOPOTECAN            | Polyneuropathy                                                  | 1.45(0.54,<br>3.87)  | 1.45(0.55,<br>3.87)  | 1.45(0.5<br>4) | N | N | N |
| IRINOTECAN           | Peripheral sensorimotor<br>neuropathy                           | 2.76(1.03,<br>7.35)  | 2.76(1.03,<br>7.35)  | 2.75(1.0<br>3) | Y | Y | N |
| DOXORUBIC<br>IN      | Mononeuropathy                                                  | 6.14(2.29,<br>16.48) | 6.14(2.29,<br>16.48) | 6.06(2.2<br>6) | Y | Y | Y |
| DOXORUBIC<br>IN      | Acute polyneuropathy                                            | 3.15(1.18,<br>8.44)  | 3.15(1.18,<br>8.44)  | 3.14(1.1<br>7) | Y | Y | N |
| DOXORUBIC<br>IN      | Toxic neuropathy                                                | 3.97(1.48,<br>10.62) | 3.97(1.48,<br>10.62) | 3.94(1.4<br>7) | Y | Y | N |
| CARBOPLAT<br>IN      | Diabetic neuropathy                                             | 0.31(0.12,<br>0.82)  | 0.31(0.12,<br>0.82)  | 0.31(0.1<br>2) | N | N | N |
| BENDAMUS<br>TINE     | Peripheral sensorimotor<br>neuropathy                           | 3.34(1.08,<br>10.38) | 3.34(1.08,<br>10.38) | 3.34(1.0<br>8) | Y | Y | N |
| CYCLOPHOS<br>PHAMIDE | Mononeuropathy                                                  | 2.48(0.79,<br>7.73)  | 2.48(0.79,<br>7.73)  | 2.46(0.7<br>9) | N | N | N |
| CYCLOPHOS<br>PHAMIDE | Acute motor axonal<br>neuropathy                                | 4.39(1.40,<br>13.76) | 4.39(1.40,<br>13.76) | 4.32(1.3<br>8) | Y | Y | N |
| CYCLOPHOS<br>PHAMIDE | Neuralgic amyotrophy                                            | 0.50(0.16,<br>1.56)  | 0.50(0.16,<br>1.56)  | 0.50(0.1<br>6) | N | N | N |
| CYCLOPHOS<br>PHAMIDE | Nerve compression                                               | 0.16(0.05,<br>0.48)  | 0.16(0.05,<br>0.48)  | 0.16(0.0<br>5) | N | N | N |
| CYCLOPHOS<br>PHAMIDE | Diabetic neuropathy                                             | 0.15(0.05,<br>0.47)  | 0.15(0.05,<br>0.47)  | 0.15(0.0<br>5) | N | N | N |
| GEMCITABI<br>NE      | Nerve compression                                               | 0.39(0.13,<br>1.22)  | 0.39(0.13,<br>1.22)  | 0.39(0.1<br>3) | N | N | N |
| GEMCITABI<br>NE      | Diabetic neuropathy                                             | 0.38(0.12,<br>1.19)  | 0.38(0.12,<br>1.19)  | 0.38(0.1<br>2) | N | N | N |
| GEMCITABI<br>NE      | Peripheral sensorimotor<br>neuropathy                           | 1.09(0.35,<br>3.38)  | 1.09(0.35,<br>3.38)  | 1.09(0.3<br>5) | N | N | N |
| VINCRISTIN<br>E      | Acute polyneuropathy                                            | 3.03(0.97,<br>9.42)  | 3.03(0.97,<br>9.42)  | 3.02(0.9<br>7) | N | N | N |
| VINCRISTIN<br>E      | Intensive care unit<br>acquired weakness                        | 3.44(1.11,<br>10.72) | 3.44(1.11,<br>10.71) | 3.43(1.1<br>0) | Y | Y | N |
| ETOPOSIDE            | Nerve compression                                               | 0.45(0.15,<br>1.40)  | 0.45(0.15,<br>1.40)  | 0.45(0.1<br>5) | N | N | N |
| ETOPOSIDE            | Demyelinating<br>polyneuropathy                                 | 1.47(0.47,<br>4.56)  | 1.47(0.47,<br>4.56)  | 1.47(0.4<br>7) | N | N | N |
| DOCETAXEL            | Acute motor-sensory<br>axonal neuropathy                        | 4.24(1.36,<br>13.25) | 4.24(1.36,<br>13.25) | 4.19(1.3<br>4) | Y | Y | N |
| DOCETAXEL            | Chronic inflammatory<br>demyelinating<br>polyradiculoneuropathy | 0.64(0.21,<br>2.00)  | 0.64(0.21,<br>2.00)  | 0.64(0.2<br>1) | N | N | N |
| DOCETAXEL            | Neuritis                                                        | 0.35(0.11,<br>1.10)  | 0.35(0.11,<br>1.10)  | 0.35(0.1<br>1) | N | N | N |
| DOCETAXEL            | Small fibre neuropathy                                          | 0.79(0.26,<br>       | 0.79(0.26,<br>       | 0.79(0.2<br>   | 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(2.9, 49.35)  | 12.14(2.9, 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(3.4, 45.67)  | 13.98(3.4, 45.67)  | 13.69(3.37) | N | N | Y |
| ETOPOSIDE   | Ischaemic neuropathy                  | 20.85(5.0, 98.53)  | 20.85(5.0, 98.53)  | 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(0.41)  | 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(5.0, 88.94)  | 20.64(5.0, 88.93)  | 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 |
| DOXORUBICIN | Brachial plexopathy                   | 1.72(0.43, 8.61)   | 1.72(0.43, 8.61)   | 1.72(0.43)  | N | N | N |

|              |                                                           |                    |                    |             |   |   |   |
|--------------|-----------------------------------------------------------|--------------------|--------------------|-------------|---|---|---|
| IN           |                                                           | 6.89)              | 6.89)              | 3)          |   |   |   |
| DOXORUBIC IN | Chronic inflammatory demyelinating polyradiculoneuropathy | 0.60(0.15, 2.39)   | 0.60(0.15, 2.39)   | 0.60(0.15)  | N | N | N |
| DOXORUBIC IN | Ischaemic neuropathy                                      | 13.31(3.25, 54.49) | 13.31(3.25, 54.49) | 12.91(3.15) | N | N | Y |
| DOXORUBIC IN | Neuralgic amyotrophy                                      | 0.62(0.15, 2.48)   | 0.62(0.15, 2.48)   | 0.62(0.15)  | N | N | N |
| DOXORUBIC IN | Nerve compression                                         | 0.19(0.05, 0.77)   | 0.19(0.05, 0.77)   | 0.19(0.05)  | N | N | N |
| DOXORUBIC IN | Diabetic neuropathy                                       | 0.19(0.05, 0.75)   | 0.19(0.05, 0.75)   | 0.19(0.05)  | N | N | N |
| CARBOPLAT IN | Mononeuropathy                                            | 2.51(0.62, 10.09)  | 2.51(0.62, 10.09)  | 2.50(0.62)  | N | N | N |
| CARBOPLAT IN | Chronic inflammatory demyelinating polyradiculoneuropathy | 0.49(0.12, 1.97)   | 0.49(0.12, 1.97)   | 0.49(0.12)  | N | N | N |
| CARBOPLAT IN | Nerve compression                                         | 0.16(0.04, 0.63)   | 0.16(0.04, 0.63)   | 0.16(0.04)  | N | N | N |
| CARBOPLAT IN | Axonal and demyelinating polyneuropathy                   | 5.40(1.33, 21.84)  | 5.40(1.33, 21.84)  | 5.33(1.32)  | N | N | N |
| CARBOPLAT IN | 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 |
| BENDAMUSTINE | Peripheral nerve lesion                                   | 4.66(0.65, 31.1)   | 4.66(0.65, 31.1)   | 4.65(0.65)  | 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(1.6<br>3,85.55)  | 11.83(1.6<br>3,85.55)  | 11.62(1.<br>61) | N | N | N |
| ETOPOSIDE  | Neuralgic amyotrophy                       | 0.48(0.07,<br>3.44)    | 0.48(0.07,<br>3.44)    | 0.48(0.0<br>7)  | N | N | N |
| ETOPOSIDE  | Peripheral nerve lesion                    | 1.74(0.24,<br>12.37)   | 1.74(0.24,<br>12.37)   | 1.74(0.2<br>4)  | N | N | N |
| ETOPOSIDE  | Axonal and demyelinating<br>polyneuropathy | 5.08(0.71,<br>36.38)   | 5.08(0.71,<br>36.38)   | 5.05(0.7<br>1)  | N | N | N |
| ETOPOSIDE  | Autoimmune neuropathy                      | 3.34(0.47,<br>23.86)   | 3.34(0.47,<br>23.85)   | 3.33(0.4<br>7)  | N | N | N |
| ETOPOSIDE  | Radial nerve palsy                         | 2.00(0.28,<br>14.22)   | 2.00(0.28,<br>14.22)   | 1.99(0.2<br>8)  | N | N | N |
| DOCETAXEL  | Brachial plexopathy                        | 0.61(0.09,<br>4.37)    | 0.61(0.09,<br>4.37)    | 0.61(0.0<br>9)  | N | N | N |
| DOCETAXEL  | Polyneuropathy in<br>malignant disease     | 3.35(0.47,<br>24.04)   | 3.35(0.47,<br>24.04)   | 3.32(0.4<br>6)  | N | N | N |
| DOCETAXEL  | Femoral nerve palsy                        | 4.46(0.62,<br>32.18)   | 4.46(0.62,<br>32.18)   | 4.41(0.6<br>1)  | N | N | N |
| DOCETAXEL  | Acute polyneuropathy                       | 0.56(0.08,<br>3.99)    | 0.56(0.08,<br>3.99)    | 0.56(0.0<br>8)  | N | N | N |
| DOCETAXEL  | Polyneuropathy chronic                     | 3.16(0.44,<br>22.67)   | 3.16(0.44,<br>22.67)   | 3.14(0.4<br>4)  | N | N | N |
| DOCETAXEL  | Miller Fisher syndrome                     | 0.64(0.09,<br>4.53)    | 0.64(0.09,<br>4.53)    | 0.64(0.0<br>9)  | N | N | N |
| DOCETAXEL  | Nerve compression                          | 0.07(0.01,<br>0.49)    | 0.07(0.01,<br>0.49)    | 0.07(0.0<br>1)  | N | N | N |
| DOCETAXEL  | Polyneuropathy idiopathic<br>progressive   | 3.85(0.54,<br>27.71)   | 3.85(0.54,<br>27.71)   | 3.81(0.5<br>3)  | N | N | N |
| DOCETAXEL  | Lumbosacral plexopathy                     | 4.39(0.61,<br>31.67)   | 4.39(0.61,<br>31.67)   | 4.34(0.6<br>0)  | N | N | N |
| DOCETAXEL  | Lumbosacral<br>radiculoplexus neuropathy   | 3.75(0.52,<br>26.96)   | 3.75(0.52,<br>26.96)   | 3.71(0.5<br>2)  | N | N | N |
| DOCETAXEL  | Acrodynia                                  | 40.17(4.9<br>4,326.47) | 40.17(4.9<br>4,326.46) | 35.27(4.<br>34) | N | N | Y |
| DOCETAXEL  | Peripheral nerve lesion                    | 0.79(0.11,<br>5.65)    | 0.79(0.11,<br>5.65)    | 0.79(0.1<br>1)  | N | N | N |
| DOCETAXEL  | Axonal and demyelinating<br>polyneuropathy | 2.32(0.32,<br>16.63)   | 2.32(0.32,<br>16.63)   | 2.31(0.3<br>2)  | N | N | N |
| DOCETAXEL  | Autoimmune neuropathy                      | 1.53(0.21,<br>10.91)   | 1.53(0.21,<br>10.91)   | 1.53(0.2<br>1)  | N | N | N |
| TOPOTECAN  | Nerve compression                          | 1.27(0.18,<br>9.04)    | 1.27(0.18,<br>9.03)    | 1.27(0.1<br>8)  | N | N | N |
| TOPOTECAN  | Carpal tunnel syndrome                     | 0.60(0.09,<br>4.29)    | 0.60(0.09,<br>4.29)    | 0.60(0.0<br>9)  | N | N | N |
| TOPOTECAN  | Axonal neuropathy                          | 5.16(0.73,<br>36.69)   | 5.16(0.73,<br>36.68)   | 5.16(0.7<br>3)  | N | N | N |
| IRINOTECAN | Lewis-Sumner syndrome                      | 20.38(2.8<br>2,147.56) | 20.38(2.8<br>2,147.56) | 20.00(2.<br>76) | N | N | Y |
| IRINOTECAN | Ischaemic neuropathy                       | 16.99(2.3<br>5,122.57) | 16.99(2.3<br>5,122.57) | 16.72(2.<br>32) | N | N | Y |
| IRINOTECAN | Axonal neuropathy                          | 1.01(0.14,<br>3.44)    | 1.01(0.14,<br>3.44)    | 1.01(0.1<br>4)  | 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(0.5 2)  | N | N | N |
| IRINOTECAN   | Sciatic nerve palsy                     | 11.71(1.6 3,84.11) | 11.71(1.6 3,84.10) | 11.59(1. 61) | N | N | N |
| EPIRUBICIN   | Mononeuritis                            | 3.14(0.44, 22.36)  | 3.14(0.44, 22.36)  | 3.13(0.4 4)  | N | N | N |
| EPIRUBICIN   | Femoral nerve palsy                     | 13.60(1.8 9,98.06) | 13.60(1.8 9,98.05) | 13.40(1. 86) | N | N | N |
| EPIRUBICIN   | Polyneuropathy chronic                  | 9.63(1.34, 69.10)  | 9.63(1.34, 69.10)  | 9.53(1.3 3)  | N | N | N |
| EPIRUBICIN   | Miller Fisher syndrome                  | 1.94(0.27, 13.79)  | 1.94(0.27, 13.79)  | 1.94(0.2 7)  | N | N | N |
| EPIRUBICIN   | Neuritis                                | 0.36(0.05, 2.55)   | 0.36(0.05, 2.55)   | 0.36(0.0 5)  | N | N | N |
| EPIRUBICIN   | Demyelinating polyneuropathy            | 0.68(0.10, 4.84)   | 0.68(0.10, 4.84)   | 0.68(0.1 0)  | N | N | N |
| EPIRUBICIN   | Peripheral motor neuropathy             | 0.69(0.10, 4.89)   | 0.69(0.10, 4.89)   | 0.69(0.1 0)  | N | N | N |
| EPIRUBICIN   | Peripheral sensorimotor neuropathy      | 0.58(0.08, 4.11)   | 0.58(0.08, 4.11)   | 0.58(0.0 8)  | N | N | N |
| EPIRUBICIN   | Axonal neuropathy                       | 0.85(0.12, 6.02)   | 0.85(0.12, 6.02)   | 0.85(0.1 2)  | N | N | N |
| DOXORUBIC IN | Lewis-Sumner syndrome                   | 7.86(1.09, 56.86)  | 7.85(1.09, 56.86)  | 7.72(1.0 7)  | N | N | N |
| DOXORUBIC IN | Acute motor-sensory axonal neuropathy   | 1.95(0.27, 13.94)  | 1.95(0.27, 13.94)  | 1.95(0.2 7)  | N | N | N |
| DOXORUBIC IN | Immune-mediated neuropathy              | 1.51(0.21, 10.76)  | 1.51(0.21, 10.76)  | 1.51(0.2 1)  | N | N | N |
| DOXORUBIC IN | Peripheral nerve lesion                 | 1.11(0.16, 7.90)   | 1.11(0.16, 7.90)   | 1.11(0.1 6)  | N | N | N |
| DOXORUBIC IN | Axonal and demyelinating polyneuropathy | 3.25(0.45, 23.23)  | 3.25(0.45, 23.23)  | 3.23(0.4 5)  | N | N | N |
| CARBOPLAT IN | Mononeuritis                            | 1.19(0.17, 8.45)   | 1.19(0.17, 8.45)   | 1.19(0.1 7)  | N | N | N |
| CARBOPLAT IN | Mononeuropathy multiplex                | 0.78(0.11, 5.58)   | 0.78(0.11, 5.58)   | 0.78(0.1 1)  | N | N | N |
| CARBOPLAT IN | Polyradiculoneuropathy                  | 9.00(1.23, 65.63)  | 9.00(1.23, 65.63)  | 8.78(1.2 0)  | N | N | N |
| CARBOPLAT IN | Acute motor-sensory axonal neuropathy   | 1.61(0.23, 11.50)  | 1.61(0.23, 11.50)  | 1.61(0.2 3)  | N | N | N |
| CARBOPLAT IN | Acute motor axonal neuropathy           | 2.20(0.31, 15.75)  | 2.20(0.31, 15.75)  | 2.20(0.3 1)  | N | N | N |
| CARBOPLAT IN | Pancoast's syndrome                     | 6.23(0.86, 45.06)  | 6.23(0.86, 45.06)  | 6.13(0.8 5)  | N | N | N |
| CARBOPLAT IN | Ischaemic neuropathy                    | 5.40(0.75, 38.95)  | 5.40(0.75, 38.95)  | 5.33(0.7 4)  | N | N | N |
| CARBOPLAT IN | Polyneuropathy idiopathic progressive   | 4.44(0.62, 31.93)  | 4.44(0.62, 31.92)  | 4.39(0.6 1)  | N | N | N |
| CARBOPLAT IN | Peripheral nerve lesion                 | 0.91(0.13, 6.51)   | 0.91(0.13, 6.51)   | 0.92(0.1 3)  | N | N | N |

|             |                                                           |                     |                     |                 |   |   |   |
|-------------|-----------------------------------------------------------|---------------------|---------------------|-----------------|---|---|---|
| CARBOPLATIN | Radial nerve palsy                                        | 1.05(0.15, 7.49)    | 1.05(0.15, 7.49)    | 1.05(0.15, 5)   | N | N | N |
| CISPLATIN   | Brachial plexopathy                                       | 1.10(0.15, 7.82)    | 1.10(0.15, 7.82)    | 1.10(0.15, 5)   | 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, 5)   | N | N | N |
| CISPLATIN   | Chronic inflammatory demyelinating polyradiculoneuropathy | 0.38(0.05, 2.72)    | 0.38(0.05, 2.72)    | 0.38(0.05, 5)   | N | N | N |
| CISPLATIN   | Ischaemic neuropathy                                      | 8.39(1.16, 60.55)   | 8.39(1.16, 60.55)   | 8.27(1.16, 5)   | N | N | N |
| CISPLATIN   | Neuralgic amyotrophy                                      | 0.40(0.06, 2.81)    | 0.40(0.06, 2.81)    | 0.40(0.06, 6)   | N | N | N |
| CISPLATIN   | Diabetic neuropathy                                       | 0.12(0.02, 0.85)    | 0.12(0.02, 0.85)    | 0.12(0.02, 2)   | N | N | N |
| CISPLATIN   | Demyelinating polyneuropathy                              | 0.40(0.06, 2.84)    | 0.40(0.06, 2.84)    | 0.40(0.06, 6)   | N | N | N |
| CISPLATIN   | Carpal tunnel syndrome                                    | 0.06(0.01, 0.41)    | 0.06(0.01, 0.41)    | 0.06(0.01, 1)   | N | N | N |
| CISPLATIN   | Small fibre neuropathy                                    | 0.47(0.07, 3.36)    | 0.47(0.07, 3.36)    | 0.47(0.07, 7)   | N | N | N |
| CISPLATIN   | Axonal and demyelinating polyneuropathy                   | 4.16(0.58, 29.78)   | 4.16(0.58, 29.78)   | 4.13(0.58, 8)   | N | N | N |
| CISPLATIN   | Radial nerve palsy                                        | 1.63(0.23, 11.64)   | 1.63(0.23, 11.64)   | 1.63(0.23, 3)   | N | N | N |
| PACLITAXEL  | Brachial plexopathy                                       | 0.60(0.08, 4.25)    | 0.60(0.08, 4.25)    | 0.60(0.08, 8)   | N | N | N |
| PACLITAXEL  | Mononeuropathy                                            | 1.06(0.15, 7.52)    | 1.06(0.15, 7.52)    | 1.06(0.15, 5)   | N | N | N |
| PACLITAXEL  | Polyradiculoneuropathy                                    | 7.60(1.04, 55.41)   | 7.60(1.04, 55.41)   | 7.42(1.04, 2)   | N | N | N |
| PACLITAXEL  | Polyneuropathy chronic                                    | 3.07(0.43, 22.06)   | 3.07(0.43, 22.05)   | 3.05(0.43, 2)   | N | N | N |
| PACLITAXEL  | Neuronal neuropathy                                       | 13.67(1.84, 101.89) | 13.67(1.84, 101.89) | 13.07(1.84, 75) | N | N | N |
| PACLITAXEL  | Diabetic mononeuropathy                                   | 54.69(6.39, 468.18) | 54.69(6.39, 468.17) | 45.75(6.39, 34) | N | N | Y |
| PACLITAXEL  | Polyneuropathy idiopathic progressive                     | 3.75(0.52, 26.95)   | 3.75(0.52, 26.95)   | 3.71(0.52, 2)   | N | N | N |
| PACLITAXEL  | Peripheral nerve lesion                                   | 0.77(0.11, 5.50)    | 0.77(0.11, 5.50)    | 0.77(0.11, 1)   | N | N | N |
| PACLITAXEL  | Autoimmune neuropathy                                     | 1.49(0.21, 10.61)   | 1.49(0.21, 10.61)   | 1.48(0.21, 1)   | 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 outcomes<sup>10</sup>. 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 safety<sup>11</sup>. 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 reporting<sup>12</sup>.

Consistent with previous epidemiological studies, our data identified a female predominance (53.33%) and a higher vulnerability in patients aged 45 and older<sup>13,14</sup>. 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 neurotoxicity<sup>15</sup>. 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 changes<sup>16</sup>. 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 subgroup<sup>17</sup>.

**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 intervention<sup>18</sup>. 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 chemotherapy<sup>19</sup>. 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 progression<sup>20</sup>.

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 deficits<sup>21</sup>. 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-up<sup>22</sup>. 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 pivotal<sup>23,24</sup>.

## 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 incidence<sup>25</sup>. 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 life<sup>26</sup>.

## 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.

Not applicable.

## 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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