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Neuropathic Pain during Treatment for Childhood Acute Lymphoblastic Leukemia

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Abstract

Background—Improved cure rates for childhood acute lymphoblastic leukemia over the past 2 decades have allowed greater attention to patients' quality of life. Neuropathic pain is an unpleasant side effect of chemotherapeutic agents for leukemia, especially vincristine.

Procedure—We retrospectively reviewed the records of 498 patients treated on a single protocol for acute lymphoblastic leukemia to investigate the risk factors, the incidence, and the use of therapeutic and prophylactic gabapentin treatment for neuropathic pain.

Results—White non-Hispanic race was the only patient variable predictive of neuropathic pain. One hundred seventy-four of 498 patients (34.9%) experienced 207 episodes of neuropathic pain; 16% (28 of 174) patients experienced at least one recurrence of pain after the initial episode. No statistical significance was found in the relation between the severity (grade) of the neuropathic pain episode and the cumulative dose of vincristine ($p=0.45$) or the vincristine dose that immediately preceded the diagnosis (1.5 mg/kg vs. 2.0 mg/kg, $p=0.59$). Of 180 episodes with treatment data, 62.2% (112) and 37.8% (68) were treated with gabapentin or opioids, respectively. The selection of treatment with gabapentin or opioids was not influenced by the pain intensity score at the time of diagnosis of NP ($p=0.91$). The mean gabapentin dose used for 112 episodes was 15.5 mg/kg/day (SD 7.9). We found no evidence that gabapentin prevented recurrence of neuropathic pain.

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Conflict of Interest Statement

The authors of this manuscript have no conflicts of interest to disclose.

Conclusions—Our results highlight the need for prospective randomized studies to elucidate the value of gabapentin regimen for prevention or treatment of vincristine-related pain during treatment of childhood leukemia.

Keywords

acute lymphoblastic leukemia; neuropathic pain; gabapentin; vincristine

Introduction

Now that cure rates for childhood acute lymphoblastic leukemia (ALL) have risen to approximately 90% [1–3], research has begun to focus not only on cure but also on patients' quality of life. Several chemotherapeutic agents used for ALL, especially vincristine, can induce neuropathic pain (NP) [4], which adversely affects patients' quality of life.

Neurotoxicity, the dose-limiting side effect of vincristine, involves both autonomic and sensorimotor neuropathy, either of which can cause NP [5]. Although the incidence of NP in our previous ALL treatment protocol was unknown, the incidence of vincristine-related peripheral neuropathy, including neurosensory and/or neuromotor dysfunction and constipation, was 17.5% (42 of 240) in our previous treatment protocol for childhood ALL [1]. Our subsequent protocol, which was recently completed [3], used a higher dose of vincristine and coincided with the introduction of gabapentin therapy for NP. We reviewed the records of patients treated on this protocol to assess the risk factors and the incidence of NP, as well as to describe the therapeutic and prophylactic use of gabapentin in the context of intensive vincristine treatment.

Patients and Methods

Patients and treatment

We obtained approval for this retrospective review from the St. Jude Institutional Review Board. The study population comprised patients 1 to 18 years old with newly diagnosed ALL treated between June 2000 and October 2007 on the St. Jude Total XV protocol [3].

The Total Therapy XV protocol included four therapy phases: remission induction (7 weeks), consolidation (8 weeks), early continuation/reinduction (14 weeks), and continuation (120 weeks for girls, 146 for males). Three phases included more intensive (weekly) vincristine treatment: remission induction, reinduction I, and reinduction II. The cumulative vincristine dose was 61 mg/m² for the low-risk and 63 mg/m² for the standard- and high-risk groups; both doses were higher than those used in the previous treatment protocol (Total XIII B). All patients received vincristine during remission induction (4 weekly doses of 1.5 mg/m²) and continuation (2 mg/m² monthly), plus doses of 1.5 mg/m² weekly during weeks 7 through 9 and 17 through 19 (reinduction I and II, respectively). Patients in the standard- and high-risk treatment groups received an additional dose of vincristine 2 mg/m² at week 11. Beginning with week 24 of continuation, patients received doses of vincristine 2 mg/m² monthly. Therefore, vincristine exposure was more concentrated around week 4 of remission induction, during reinduction I at week 16, and during reinduction II at week 26. The maximum single dose for vincristine never exceeded 2 mg, as specified by the treatment protocol.

Neuropathic pain was managed with gabapentin or opioids at the discretion of the patient's primary oncologist. At our institution, gabapentin was typically prescribed at a starting dose of at least 5–10 mg/kg/day with optional dose escalation to 50–70 mg/kg/day until relief was obtained. The approach to repetitive episodes of NP associated with subsequent vincristine

doses varied among clinicians. Some prescribed intermittent pulses of gabapentin to start the day prior to each vincristine administration and continuing for 7 days or until any NP resolved; others prescribed gabapentin continuously after the first episode of NP. The prescription, dose regimen, and timing of treatment were decided upon by individual clinicians.

Data collection

Peripheral neurotoxicity was defined and graded by the Total XV study staff according to the NCI Common Toxicity Criteria (CTC), version 2.0 [6]. “Moderate pain” whose severity or treatment interfered with function but not with activities of daily living was defined as Grade 2 peripheral neurotoxicity. “Severe pain” whose intensity or treatment significantly interfered with activities of daily living was defined as Grade 3 peripheral neurotoxicity [6]. The NCI CTC severity grade was used as one measure of the intensity of NP events for this analysis. As prospectively planned in the Total XV protocol, toxicities, including neurotoxicity, were reviewed by Clinical Research Associates for each clinic visit, were collected and compiled in the study database, and were reviewed by the primary attending physicians and the principal investigator of the study every two weeks. To identify the incidence and frequency of NP episodes in this population of ALL patients, we generated from the study database a report of NP adverse events grade 2 or higher that were experienced by any protocol participant.

Events identified in the Total XV study database as peripheral neurotoxicity grades 2 and 3 were then correlated with clinical information and treatment data that were abstracted from the patients’ medical and pharmacy records. At the onset of the event, NP was clinically diagnosed on the basis of subjective descriptors (pain localized in the jaw, back, lower extremities, or abdomen; generalized body pain; or indicators of functional impairment such as refusal to bear weight, walk, open the mouth, or eat). For this retrospective analysis, these NP episodes were reconfirmed in the chart, and the phase of therapy (remission induction, consolidation, early continuation/ reinduction, or continuation therapy) in which the episodes occurred, the temporal relation of each episode to the administration of vincristine, and the cumulative and most recent vincristine dose were recorded, along with other general demographic data. Neuropathic pain was considered to be vincristine-related if vincristine had been administered within the previous 7 days. Recurrent episodes of NP were recorded as new adverse events if the grade of neurotoxicity increased or if a prior episode had been followed by a symptom-free interval.

Pain intensity data expressed as pain scores were retrospectively abstracted from patient records at three time points for this study: the time of diagnosis of NP, the time at which gabapentin treatment was prescribed, and the time of discontinuation of gabapentin treatment. Age-appropriate pain assessment tools specified by institutional standards were used: FLACC for children younger than 3 years [7], FACES for children 4 to 6 years [8], and NPS for those 7 years or older [9]. Descriptors of the quality (e.g., burning, shooting, tingling, “needles and pins,” ache) and location of pain at the time of diagnosis of NP were collected from the study database and the medical records.

Pharmacy records were reviewed to identify gabapentin and opioid prescriptions consistent with the treatment of NP. The medical records were reviewed to determine whether gabapentin was dispensed for the treatment of NP or for prophylaxis of recurrent pain. Patients for whom gabapentin was prescribed for other indications (e.g., seizure control, prevention of migraines) were noted.

The following variables were analyzed to identify risk factors for vincristine-related toxicity: age, sex, race, body mass index (BMI), ALL risk classification, biological ALL risk markers

(t[9;22] [*BCR-ABL1*], t[1;19] [*TCF3-PBX1*], t[12;21] [*ETV6-RUNX1*], t[4;11] [*MLL-AF4*]), and the cumulative dose of vincristine at the onset of neuropathy.

Statistical analysis

The cumulative incidence of vincristine-related NP was calculated by the method of Kalbfleisch and Prentice and compared across groups by Gray's test. The Wilcoxon signed-rank test was used to assess the relation between vincristine dose and NP severity, the relationship between gabapentin dose regimens and indications and severity of toxicity, and gabapentin doses for patients with or without recurrences of NP. We used the exact test based on Pearson's chi square statistic to compare pain scores among treatment categories with opioids or gabapentin.

Results

NP incidence, characteristics and risk factors

Of 498 patients treated on the Total XV protocol, 34.9% (174 patients) experienced 207 episodes of vincristine-related NP; 16% (28 of 174 patients) experienced at least one recurrence of pain after the initial episode. Affected patients experienced a mean of 1.2 episodes (median, 1; range, 1–4). The cumulative incidence was 34.9% (95% CI, 30.5% to 39.2%). Figure 1 illustrates the three periods of increased incidence that corresponded to intense weekly vincristine treatment: week 4 (during remission induction), week 16 (following reinduction I), and week 26 (following reinduction II). The median age at diagnosis of NP was 7.9 years (range, 1.3–19.2 years).

The anatomic sites of NP and the descriptors of pain quality at the onset of NP episodes are presented in Table I. Pain location and quality were documented for 192 and 23, respectively, of the 207 episodes at the time of diagnosis of NP. The most common sites were lower extremity, back, and jaw; some patients reported NP at more than one site.

Among the clinical and biological features analyzed as risk factors, only white (non-Hispanic) race was significantly associated with vincristine-related NP ($p < 0.01$, Table II). The incidence of vincristine-related NP in the 1–5 year-old group was 30.6 compared to 40 for the 16–20 year-old group (Table II). The severity (grade) of the episode of NP was not found to be significantly associated with the cumulative dose of vincristine ($p = 0.45$, Table III) or the vincristine dose that immediately preceded the diagnosis of NP (1.5 mg/kg vs. 2.0 mg/kg, $p = 0.59$).

Therapeutic interventions for NP

Interventions were prescribed by the primary oncologists, with occasional consultation from the pain service. The therapeutic interventions are presented in Figure 2. Treatment data were available for 180 of 207 episodes of NP in 153 of 174 patients; the missing data reflect treatment at a site other than St. Jude. Gabapentin was used to treat 62.2% of episodes (112 of 180) in 65.4% of patients (100 of 153); the remaining 37.8% of episodes (68 of 180) in 34.6% of patients (53 of 153) were treated with opioids. The selection of gabapentin or opioids did not appear to be influenced by the pain intensity score at the time of diagnosis of NP ($p = 0.91$, Table IV).

Table V presents the pain scores associated with 112 episodes for which gabapentin was prescribed, at three time points: the time of diagnosis of vincristine-related NP, the start of gabapentin treatment, and the end of gabapentin treatment. The mean starting dose used for the 112 episodes was 15.5 mg/kg/day (SD 7.9). Gabapentin was prescribed to prevent NP in 20.5% (23 of 112) of the episodes and to treat NP in 69.6% (78 of 112) of the episodes; in 4

cases gabapentin was prescribed to prevent migraines or seizures, and in 7 cases dose information was incomplete. No statistically significant association was observed between the starting dose of gabapentin and the pain severity grade or prescribing indications.

Of 100 patients (112 episodes) treated with gabapentin for various indications, 19 experienced a recurrent NP episode after gabapentin was prescribed. The mean dose of gabapentin (18.1 mg/kg/day [SD 7.6]) received by these 19 patients did not differ significantly from that (15.8 mg/kg/day [SD 8.3]) of the 81 patients who received prophylactic gabapentin and did not experience recurrence ($p=0.13$). Overall, 16% of patients (28 of 174) experienced recurrent episodes of NP. The rate of recurrence of NP was similar (~19%) between the group of patients treated with opioids and those treated with gabapentin; treatment data were not available for 21 patients.

Discussion

The novelty and significance of this study lie in the comprehensive description of all facets of vincristine-related NP: incidence, severity, and treatment; and in the exhaustive investigation of the associated risk factors, in the largest study to date in children treated for ALL. Previous studies of vincristine-induced neurotoxicity in children have been mainly case reports [10–13] and small series [14,15], and only race [16] and BMI [14] have been investigated as risk factors. We found that white non-Hispanic race is significantly predictive of vincristine-related NP, consistent with a previous study showing less neurotoxicity (4.8% vs. 34.8%) and fewer reduced or missed vincristine doses in 21 black children than in 92 white non-Hispanic children with ALL [16]. One mechanism by which Caucasians could have a higher frequency of vincristine neuropathy compared to non-whites is that whites have a higher frequency of the CYP3A5*3 allele (an inactive allele) than do other race groups [17]. Thus, Caucasians may have lower CYP3A-mediated metabolism of vincristine than do other race groups, which has been proposed as a factor that can contribute to vincristine neuropathy [18]. Moreover, many allelic variants differ in frequency between whites and other race/ethnic groups, which could predispose to increase sensitivity to vincristine's neuropathic effects.

The 34.9% cumulative incidence of vincristine-related NP observed in this study is substantially higher than that of vincristine-related peripheral neurotoxicity (17.5%) in our previous study [1], consistent with the higher individual doses (1.5–2.0 mg/m² vs. 1.5 mg/m²) and cumulative doses (61–63 mg/m² vs. 55.5 mg/m²) of vincristine in the Total XV protocol. Greater vigilance in monitoring and treating toxicity may also have played a role in the higher incidence observed in this study. Not surprisingly, the complication was detected more often during periods when vincristine was administered weekly (i.e., week 4 of remission induction and weeks 16 and 26 during reinduction I and II therapy, respectively).

Diagnosis is an important factor in establishing the incidence of NP. Clinical assessment tools have been established for diagnosis of NP in adults [19,20], but the diagnosis of NP in young children is challenging. Adults are able to describe pain characteristics (e.g., burning, tingling, shooting pain, “needles and pins”) that characterize NP, whereas these descriptors are impractical in young children. Despite the availability of diagnostic criteria for adults, the incidence of NP in long-term survivors of ALL is unclear [21]. In this study, we relied mainly on the temporal relation of the onset of pain with vincristine administration to make the diagnosis. However, our finding of the lowest incidence of vincristine-related NP (30.6%) in the youngest age group (1–5 years) and the highest incidence (40%) in the 16–20 year old group may partially reflect these age-related factors in establishing the diagnosis.

We also describe the use of gabapentin as prophylaxis and as treatment of vincristine-related NP in children with ALL and the specific dose regimens used. After an episode of vincristine-related NP was diagnosed, some clinicians prescribed prophylactic gabapentin to accompany subsequent doses of vincristine, while others did not. Eighty-one percent of our patients did not experience recurrent episodes whether the initial episode was treated with gabapentin or not. Most study patients receiving gabapentin had improved pain scores, especially those with NP that was moderate to severe pain at onset; however, the limited documentation of pain scores makes it difficult to draw conclusions.

Three case reports [22–24] and 5 small series [25–29] describe the use of gabapentin as an adjuvant analgesic in children with NP under diverse circumstances: after thoracotomy [23], after multilevel orthopedic surgery [26], and for complex regional pain syndrome [24,28], systemic lupus erythematosus [27], cancer-related pain [22,25], neck pain [25], and phantom limb pain [29]. These studies included 24 children, and the dose regimen of gabapentin was described for only 17 of them [23,25,26,29]. Analgesic efficacy was reported at 22.5 mg/kg/day in a 12-year-old with post-thoracotomy NP [23], 14–40 mg/kg/day in 7 patients 7 to 28 years old with phantom limb pain [29], 19–32.6 mg/kg/day in 4 children 11 to 17 years old with NP after multilevel orthopedic surgery [26], and 10–30 mg/kg/day in 5 children with cancer-related pain (n=4) or neuropathic neck pain (n=1) [25].

Dosing and safety information for the pediatric use of gabapentin has been defined only for anti-seizure therapy [30]. Most pediatric pain specialists recommend the anti-seizure dose regimen for children with NP, starting at 10 mg/kg/day and titrating upward to 50 to 70 mg/kg/day. Gabapentin is currently the first-line therapy for NP at our institution. In this study we found the median starting dose to be 14.2 mg/kg/day, with upward titration to a maximum of 70 mg/kg/day. In the absence of a uniform approach to the use of gabapentin, prospective studies are needed to determine the optimal regimen. There is some evidence that concurrent use of gabapentin and morphine provide better analgesia at doses lower than those used for single-agent therapy [31].

Due to the retrospective nature of this study, inconsistent data were available about the duration of gabapentin therapy, the initiation of gabapentin treatment in relation to the onset of pain, and the time frame of the patient's response to gabapentin, and there was limited documentation of pain scores at the end of gabapentin treatment. Further, we were unable to compare the analgesic efficacy of gabapentin with that of opioids for NP. The lack of consistency in gabapentin prescription, the absence of data on adherence to gabapentin therapy, and the difficulty of retrospectively assessing medication use in the outpatient setting limited useful conclusions. Finally, NP-specific pain scales [19,20] were not used to diagnose NP or measure its intensity; the available assessment tools have yet to be studied in children. The further development of such tools and the conduct of prospective randomized, controlled studies of the analgesic efficacy and safety of treatment regimens for NP will have a major impact on the quality of life of children during and after completion of ALL therapy. Prospective trial designs could include randomized comparisons of gabapentin with other classes of drugs such as tricyclic antidepressants, other anticonvulsants, or opioids. Alternatively, a study design that investigates prophylactic versus therapeutic use of gabapentin could elucidate the prophylactic value for chemotherapy-related NP.

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Figure 1.
Cumulative Incidence of Vincristine-Related Neuropathic Pain in Total Therapy XV.

Figure 2.
Flowchart of VCR-Related Neuropathic Pain Episodes and Treatment Outcomes.
Key: NP: neuropathic pain; VCR: vincristine

Table I

Site and Quality of Vincristine-Related Neuropathic Pain

Location	Episodes (%) (n=207)	Quality	Episodes (%) (n=207)
Lower extremity	130 (62.8)	Aching	6 (2.9)
Back	62 (30)	Burning	4 (1.9)
Jaw	62 (30)	Cramping	3 (1.4)
Abdominal	20 (9.7)	Tingling	3 (1.4)
Upper extremity	16 (7.7)	Numbness	2 (1)
Generalized	14 (6.8)	Soreness	2 (1)
Head	10 (4.8)	Other	2 (1)
Chest	2 (1)	Sharp	1 (0.5)
		Throbbing	1 (0.5)
		Dull	1 (0.5)
		Deep	1 (0.5)
		Stinging	1 (0.5)
		Tender skin	1 (0.5)
Not recorded	15 (7.2%)	Not recorded	184 (88.9)

Note: Patients may have reported more than one location and/or quality per episode.

Table II
Incidence of Vincristine-Related Neuropathic Pain According to Selected Clinical and Biological Characteristics

Variable	No. of Patients	No. (%) of Patients with VCR-related NP	P Value ^d	Cumulative Incidence Estimate + SE (%)			P Value ^d
				Year 1	Year 2	Year 3	
ALL risk group			0.40				0.39
Low	239	88 (36.8)		31.8 (3.0)	35.6 (3.1)	37.1 (3.2)	
Standard or high	259	85 (32.8)		29.3 (2.8)	32.2 (2.9)	33.1 (3.0)	
Age			0.51				0.32
1–5 years old	235	72 (30.6)		26.0 (2.9)	29.4 (3.0)	31.0 (3.1)	
6–10 years old	137	54 (39.4)		35.0 (4.1)	38.8 (4.2)	39.6 (4.2)	
11–15 years old	81	29 (35.8)		32.1 (5.2)	35.0 (5.4)	36.6 (5.5)	
16–20 years old	45	18 (40)		37.8 (7.3)	40.1 (7.4)	40.1 (7.4)	
Sex			0.29				0.20
Male	279	91 (32.6)		28.3 (2.7)	31.7 (2.8)	33.0 (2.8)	
Female	219	82 (37.4)		33.3 (3.2)	36.6 (3.3)	37.7 (3.3)	
Race or ethnic group			<0.01				0.01
White	340	134 (39.5)		34.5 (2.6)	38.8 (2.7)	39.9 (2.7)	
Black	79	23 (29.1)		26.6 (5.0)	27.9 (5.1)	29.5 (5.2)	
Hispanic	60	12 (20.0)		16.7 (4.9)	18.3 (5.0)	24.0 (5.3)	
Asian or other	19	4 (20.0)		20.0 (9.2)	20.0 (9.2)	20.0 (9.2)	
BMI group^b			0.54				
Underweight	14	5 (35.7)		35.7 (13.4)	35.7 (13.4)	35.7 (13.4)	0.56
Healthy weight	245	93 (38.0)		32.7 (3.0)	36.6 (3.1)	38.6 (3.2)	
At risk of overweight	76	22 (29.0)		23.7 (4.9)	27.8 (5.2)	29.3 (5.3)	
Overweight	122	46 (37.7)		34.7 (4.4)	38.2 (4.5)	38.2 (4.5)	
Initial leukocyte count			0.47				0.52
<10×10 ⁹ /L	227	87 (38.3)		33.9 (3.2)	37.6 (3.2)	38.7 (3.3)	
10 – 49×10 ⁹ /L	144	45 (31.3)		27.8 (3.7)	30.6 (3.9)	31.5 (3.9)	
50 – 99×10 ⁹ /L	64	19 (29.7)		23.4 (5.3)	28.2 (5.7)	29.8 (5.8)	

Variable	No. of Patients	No. (%) of Patients with VCR-related NP	P Value ^a	Cumulative Incidence Estimate + SE (%)			P Value ^a
				Year 1	Year 2	Year 3	
100 – 300×10 ⁹ /L	44	17 (38.6)		34.2 (7.2)	36.4 (7.4)	38.9 (7.5)	
≥ 300×10 ⁹ /L	19	5 (26.3)		26.3 (10.4)	26.3 (10.4)	26.3 (10.4)	
ALL immunophenotype			0.70				0.49
B-cell precursor	422	145 (34.4)		30.1 (2.2)	33.5 (2.3)	34.7 (2.3)	
T-cell	76	28 (36.8)		32.9 (5.4)	35.6 (5.5)	37.0 (5.6)	
DNA index			0.28				0.33
≥ 1.16	121	47 (38.8)		33.9 (4.3)	38.0 (4.4)	39.1 (4.5)	
≤ 1.16	377	126 (33.4)		29.4 (2.4)	32.5 (2.4)	33.8 (2.5)	
Genetic abnormality			0.74				0.74
t(9;22) (<i>BCR-ABL1</i>)							
Present	10	4 (40.0)		30.0 (15.5)	30.0 (15.5)	42.0 (17.7)	
Absent	488	169 (34.6)	30.5 (2.1)	33.9 (2.2)	34.9 (2.2)		
t(1;19) (<i>TCF3-PBX1</i>)			0.70				0.68
Present	28	11 (37.9)		37.9 (9.2)	37.9 (9.2)	37.9 (9.2)	
Absent	470	162 (34.5)		37.9 (9.2)	33.6 (2.2)	34.9 (2.2)	
t(12;21) (<i>ETV6-RUNX1</i>)			0.72				0.79
Present	96	35 (36.5)		26.0 (4.5)	33.4 (4.9)	36.9 (5.0)	
Absent	402	138 (34.3)		31.6 (2.3)	33.9 (2.4)	34.5 (2.4)	
t(4;11) (<i>MLL-AF4</i>)			1.00				0.91
Present	3	1 (33.3)		33.3 (33.3)	33.3 (33.3)	33.3 (33.3)	
Absent	495	172 (34.7)		30.5 (2.1)	33.9 (2.1)	35.1 (2.2)	

NP: neuropathic pain; VCR: vincristine; SE: standard error; BMI: body mass index;

^a Gray's Test;

^b BMI data available for 457 patients

Vincristine Dose at Diagnosis and Grade of Neuropathic Pain^a

Table III

	Total	Grade 2	Grade 3
All VCR-related Episodes	207	170	37
Mean (mg/m ²)	13.76	13.6	14.4
Median (mg/m ²)	10	8	11.5
SD (mg/m ²)	13	13.2	12.1
Cumulative Dose of VCR at Diagnosis of NP			p = 0.45 ^c
Not known ^b	6	5	1

NP: neuropathic pain; VCR: vincristine;

^a Graded according to the NCI Common Toxicity Criteria (version 2.0) for peripheral neuropathy;

^b Data were unavailable for some patients who received protocol treatment off-site;

^c Wilcoxon signed-rank test

Table IV
Pain Intensity Scores at Diagnosis and Treatment Choice of Gabapentin or Opioids

Treatment Agent (N=180 episodes)	Pain Score ^a			
	Mild N (%)	Moderate N (%)	Severe N (%)	Not recorded N (%)
Opioids (N=68)	19 (27.9)	17 (25)	14 (20.6)	18 (26.5)
Gabapentin (N=108) ^b	27 (25)	21 (19.4)	21 (19.4)	39 (36.1)

p = 0.91^c

NP: neuropathic pain.

^aPain score: Mild = 0-3; moderate = 4-7; severe = 7-10.

^bPain scores of 4 patients already receiving gabapentin for CNS indications were excluded.

^cPearson chi square test

Table V

Pain Intensity Scores for Events Treated with Gabapentin

Time Point (N = 112)	Pain Score ^a			
	Mild N (%)	Moderate N (%)	Severe N (%)	Not recorded N (%)
Diagnosis of NP	27 (24.1)	19 (17)	26 (23.2)	40 (35.7)
Initiation of gabapentin treatment	38 (33.9)	11 (9.8)	19 (17)	44 (39.2)
End of gabapentin treatment	15 (13.4)	1 (1)	1 (1)	95 ^b (84.8)

NP: neuropathic pain.

^a Pain score: Mild = 0–3; moderate = 4–6; severe = 7–10.

^b Pain scores at end of treatment not available either due to lack of documentation of scores or of treatment end date.