original article

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A phase III randomized, double-blind, placebo-controlled trial of gabapentin in the management of hot flashes in men (N00CB)

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Introduction: Hot flashes represent a significant problem in men undergoing androgen deprivation therapy.
Materials and methods: Via a prospective, double-blind, placebo-controlled clinical trial, men with hot flashes, on a stable androgen deprivation therapy program for prostate cancer, received a placebo or gabapentin at target doses of 300, 600, or 900 mg/day. Hot flash frequencies and severities were recorded daily during a baseline week and for 4 weeks while the patients took the study medication.
Results: In the 214 eligible patients who began the study drug on this trial, comparing the fourth treatment week to the baseline week, mean hot flash scores decreased in the placebo group by 4.1 units and in the three increasing dose gabapentin groups by, 3.2, 4.6, and 7.0 units. Comparing the three combined gabapentin arms to the placebo arm did not result in significant hot flash differences. Wilcoxon rank-sum *P* values for change in hot flash scores and frequencies after 4 weeks of treatment were 0.10 and 0.02, comparing the highest dose gabapentin arm to the placebo arm, respectively. The gabapentin was well tolerated in this trial.
Conclusion: These results support that gabapentin decreases hot flashes, to a moderate degree, in men with androgen ablation-related vasomotor dysfunction.
Key words: hot flashes, men, prostate cancer

introduction

Hot flashes can be a prominent problem in men with prostate cancer undergoing androgen deprivation therapy. Whether androgen deprivation therapy is carried out by medical or surgical means, hot flashes affect up to 75% of patients [1, 2].

There are limited therapeutic options for treating men with hot flashes. While clonidine moderately helps hot flashes in women, a randomized, placebo-controlled, double-blind trial demonstrated no significant benefit in men [3]. Placebo-controlled trials evaluating estrogen or progestational agents have demonstrated efficacy in treating male hot flashes, with about a 75% reduction seen with hormones versus a 25% reduction with a placebo [4, 5]. Nonetheless, these hormonal treatments can have side-effects. Estrogen can cause breast tenderness and enlargement. Progestational agents have been associated with rising prostate-specific antigen levels in some men with prostate cancer [6].

Gabapentin is an antiseizure agent which has been utilized for the treatment of a number of pain syndromes. Anecdotal experience reported a reduction of hot flashes in five women and one man [7]. Subsequent pilot trials also suggested efficacy [8, 9].

Given this promising evidence and the similar treatment benefits of some drugs for hot flashes in men and women, it was hypothesized that gabapentin would be effective against hot flashes in men receiving androgen ablation therapy. This current clinical trial was developed to study the efficacy and side-effects of three relatively low gabapentin doses in this patient population.

materials and methods

patient eligibility characteristics

Men with a history of prostate cancer, who were on a stable program of androgen ablation hormone therapy for the prior 4 weeks and who were not planning on discontinuing hormone therapy for 5 weeks, were eligible for this trial if they had bothersome hot flashes. Bothersome hot flashes were defined by their occurrence of at least 14 times per week and of sufficient severity to make the patient desire therapeutic intervention, with the hot flashes being present for at least 1 month before study entry. Patients were required to have an estimated life expectancy of at least 6 months and a good performance status.

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Eligible patients could not have had a history of any significant renal insufficiency (defined as a serum creatinine of 1.5 times normal in the prior 2 years) nor could they have any of the following concurrent (≤4 weeks) or planned therapies: antineoplastic chemotherapy, androgens, estrogens, or progestational agents. They could not have used gabapentin previously. Antidepressant use was allowed if the patient had been on a stable dose for at least 1 month and did not plan to modify this treatment during the ensuing 5 weeks.

All patients provided written informed consent for participating in this trial, monitored by local Internal Review Boards as mandated by United States Federal regulations. Patients were stratified before randomization on the basis of the patient's reported number of hot flashes per day (2–3 versus 4–9 versus ≥10) and the reported duration of hot flash symptoms (<9 versus ≥9 months). Patients were then randomized, using a dynamic allocation method that balances the marginal distributions of the stratification factors [10], to receive one of four treatment schedules: gabapentin 300 mg at bedtime for 28 days, versus gabapentin 300 mg at bedtime for 7 days and then 300 mg twice daily for 21 days, versus gabapentin 300 mg at bedtime for 7 days then 300 mg twice daily for 7 days and then 300 mg three times daily for 14 days, versus a placebo for 28 days. Patients receiving placebo were divided into three groups so that one group received one tablet at bedtime for 28 days, a second group received one tablet at bedtime for 7 days then one tablet b.i.d. for 21 days, and a third group received one tablet at bedtime for 7 days then one tablet b.i.d. for 7 days then one tablet t.i.d. for 14 days. The assigned treatment was administered following the completion of a 1-week period to collect baseline hot flash data. All treatment assignments were blinded to the patients and clinical investigators, with only the North Central Cancer Treatment Group (NCCTG) randomization office, the pharmacists, and the study statisticians having access to the drug assignments for individual patients. Gabapentin and matching placebo tablets were provided by Pfizer Corporation, New York.

At study entry, the patient was given a booklet that contained patient instructions, hot flash definitions, hot flash diary questionnaires to be completed daily for 5 weeks, symptom experience diaries to be completed weekly for 5 weeks, and the 30-item Profile of Mood States-Brief (POMS-B) [11] form to be completed at the end of the baseline week and then at the end of 4 weeks of treatment. Hot flash definitions were provided to each patient, derived from other men who had participated in a previous hot flash trial [12]. The hot flash diary was similar to a validated diary that has been utilized in a series of clinical trials which have now involved >1500 subjects [13]. This diary questionnaire inquired regarding the numbers of mild, moderate, severe, and very severe hot flashes per 24-hour period. The weekly symptom experience diaries asked about the severity of potential side-effects of gabapentin on a 0–10 scale including appetite loss, undesirable appetite increase, nausea, mouth dryness, fatigue, dizziness, trouble walking/balance problems, muscle pain, trouble concentrating, constipation, sleepiness, sleeping troubles, blurry vision, nervousness, and mood changes. It also inquired about hot flash distress, satisfaction with hot flash control, quality of life (QoL), and how much hot flashes affected QoL, each on a 0–10 scale. The POMS-B asked about the severity of weekly mood changes. Throughout the presented results, all patient-reported outcomes have been transformed onto a 0–100 scale with 0 indicating the most negative outcome and 100 indicating the most positive outcome, for ease of comparability. On the last day of each treatment week, patients were asked about their compliance with taking the study medication by asking them how many tablets they were taking per day.

Each patient was to be contacted by telephone weekly for the first 5 weeks to document compliance, encourage completion of the questionnaires, and address questions.

On the last scheduled day of the randomized double-blind treatment, each patient, after assuring that he had completed his questionnaires, was allowed to be told which dose of gabapentin he received and was subsequently given the choice of whether he would like to continue with gabapentin or to start active drug if he was on the placebo.

Table 1. Baseline eligible patient characteristics

	Placebo ($n = 53$)	300 mg/day ($n = 54$)	600 mg/day ($n = 53$)	900 mg/day ($n = 54$)	P value[a]
Age					0.89
Mean (standard deviation)	70 (8.89)	69 (8.53)	70 (7.02)	69 (7.69)	
Median	71	69	69	72	
Range	(47-87)	(50-89)	(58-86)	(52-85)	
Race/ethnicity					0.66
White	49 (93%)	49 (91%)	49 (93%)	50 (93%)	
Black or African-American	3 (6%)	5 (9%)	3 (6%)	4 (7%)	
Asian	1 (2%)	0 (0%)	0 (0%)	0 (0%)	
Hispanic	0 (0%)	0 (0%)	1 (2%)	0 (0%)	
ECOG performance score					0.39
0	41 (77%)	47 (87%)	42 (79%)	40 (74%)	
1	12 (23%)	7 (13%)	11 (21%)	14 (26%)	
No. of hot flashes per day					0.62
1: 2–3	7 (13%)	5 (9%)	4 (7%)	10 (19%)	
2: 4–9	22 (42%)	26 (48%)	28 (53%)	23 (43%)	
3: ≥10	24 (45%)	23 (43%)	21 (40%)	21 (39%)	
Duration of hot flashes (months)					0.99
1: <9	31 (58%)	33 (61%)	31 (58%)	32 (59%)	
2: ≥9	22 (42%)	21 (39%)	22 (42%)	22 (41%)	

[a]P values for Kruskal–Wallis test for age and chi-squared test for all other variables.
ECOG, Eastern Cooperative Oncology Group.

statistical methods

Methods used to analyze the data were similar to those used for a previous dose-finding hot flash study of venlafaxine [14]. The primary end point in this current study was change from baseline in hot flash score after 4 weeks of treatment. The hot flash score was computed for each patient using data provided on the hot flash diary by assigning points (1 = mild, 2 = moderate, 3 = severe, and 4 = very severe) to each hot flash based on reported severity, summing the points for each day, and averaging the daily scores across each week of the study.

A sample size of 50 patients per arm was required to provide at least 80% power to detect a clinically meaningful difference in the primary end point between the collective gabapentin arm (150 patients) and the placebo arm (50 patients) with a two-sided 5% type I error rate using the Wilcoxon rank-sum test. For comparisons between any pair of arms, the power was 66% for detecting the same clinically meaningful difference in the primary end point using a Wilcoxon rank-sum test with a two-sided 5% type I error rate. For this study, a clinically meaningful difference in the primary end point was defined as 0.5 standard deviations, which, based on previous data, equates to 2.5 units of hot flash score. Cohen identifies such an effect as being of moderate size [15]. For each Wilcoxon rank-sum comparison, the Hodges–Lehmann (HL) shift estimator (median of all pairwise differences) with 95% confidence interval (CI) is reported herein. Additional analyses included Kruskal–Wallis testing of the primary end point across the three gabapentin arms (i.e. dose levels) followed by pairwise comparisons using Wilcoxon rank-sum tests among the three gabapentin arms. Additionally, the primary end point for each gabapentin arm was compared with the placebo arm, using Wilcoxon rank-sum tests.

Secondary analyses included analysis of hot flash frequency similar to that carried out using hot flash score, where a clinically meaningful difference equates to 1 hot flash per day. CIs were constructed for the median reductions in hot flash score and frequency by arm, and plots were created of average hot flash scores and frequencies (as percent of baseline) during this double-blind study by treatment arm. Additionally, changes at week 4, from baseline values, in side-effects as measured by the symptom experience diary, mood (POMS-B), hot flash distress, satisfaction with hot flash control, QoL, and hot flash effect on QoL tools were

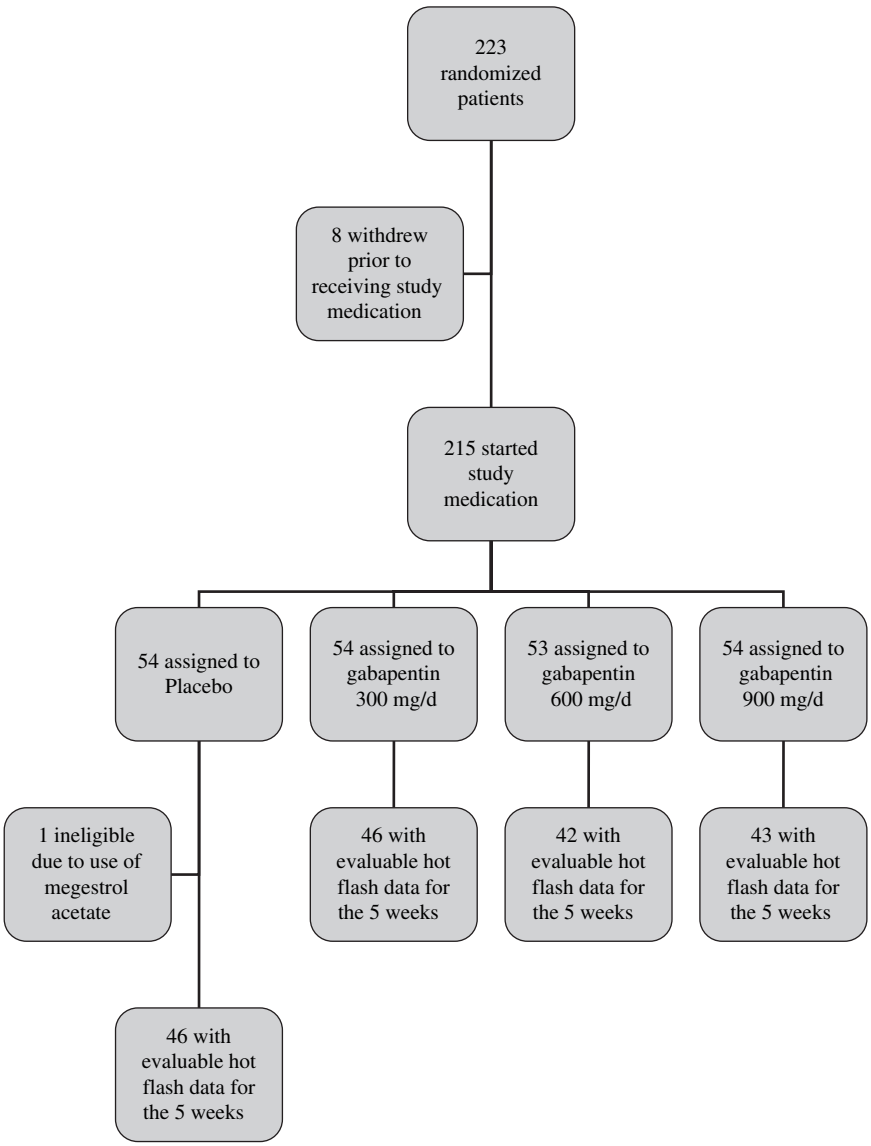

Figure 1. Consort diagram of patient flow in this trial.

compared between the gabapentin arms and the placebo arm using Wilcoxon rank-sum tests. Two-sided P values ≤0.05 were considered statistically significant throughout.

The impact of the missing data on conclusions was investigated using imputation. Analyses were first carried out using all available data and then carried out on datasets with missing values imputed using the last value carried forward and the average value carried forward. Conclusions were consistent throughout. Results of the analyses using all available data are presented in the following section.

As confirmatory analyses to the prespecified primary and secondary analyses, hot flash scores (and frequencies) at week 4 were compared using analysis of covariance with baseline scores (frequencies) as the covariate. Results of these analyses were very similar to those of our primary and secondary analyses (results not shown).

results

From 12 February 2002 to 9 November 2006, 223 patients were entered on this clinical trial from 45 institutions in the United States. Eight patients canceled before receiving study treatment and one patient, on the placebo arm, was deemed ineligible due to concomitant treatment with megestrol acetate, leaving 214 eligible patients. Baseline characteristics (Table 1) were well balanced across the treatment arms. The flow of patients on this trial is illustrated in Figure 1.

Changes from baseline hot flash scores and frequencies during the fourth treatment week were available for 177 of 214 (83%) patients—46 of 54 (85%), 46 of 54 (85%), 42 of 53 (79%), and 43 of 54 (80%) patients for the placebo arm and the 300, 600, and 900 mg/day gabapentin arms, respectively. Changes in hot flash score from the baseline week over the four treatment weeks are illustrated in Figure 2 and Table 2. The primary comparison of change from baseline in hot flash score after 4 weeks of treatment between the collective gabapentin arm and the placebo arm was not statistically significant [HL (95% CI) = −0.6 (−2.3, 1.0); Wilcoxon $P = 0.48$]. However, the comparisons of changes from baseline hot flash score and frequency at week 4 between the 900 mg/day gabapentin arm (the highest gabapentin dose arm) and the placebo were associated with Wilcoxon rank-sum P values of 0.10 and 0.02 [HL (95% CI) of −1.9 (−4.1, 0.3) and −1.4 (−2.7, −0.3)], respectively. P values for all pairwise Wilcoxon rank-sum comparisons among the four treatment arms appear in Table 3. There was no apparent difference in efficacy between sets of patients grouped by whether they had 10 or more baseline hot flashes per day, versus less.

With regard to side-effects, the only statistically significant differences between the combined gabapentin arms and the placebo arm were appetite loss and constipation [change during week 4, from baseline; appetite loss HL (95% CI) = 0 (0, 0), Wilcoxon $P = 0.002$; constipation HL (95% CI) = 0 (0, 0), Wilcoxon $P = 0.02$], with the significant differences favoring the gabapentin arms (i.e. patients on the placebo arm reported more trouble with both appetite loss and constipation). In comparing the highest gabapentin dose arm to the placebo arm, the significant differences included appetite loss [HL (95% CI) = 0 (0, 0), Wilcoxon $P = 0.02$), fatigue [HL (95% CI) = 10 (0, 20), Wilcoxon $P = 0.05$), and indigestion/belching [HL (95% CI) = 0 (0, 10), Wilcoxon $P = 0.02$), each, again favoring the gabapentin arm. The proportion of patients ending active treatment early due to side-effects was not significantly different in any of the four study arms or in the combined gabapentin arms as compared with the placebo arm (Fisher's exact test; 5.9% versus 4.3%, $P = 0.69$).

Hot flash distress changes are illustrated in Figure 3. The difference between the combined gabapentin arms and the placebo arm in change from baseline at week 4 was significant for satisfaction with hot flash control [HL (95% CI) = 10 (0, 20), Wilcoxon $P = 0.03$) and the effect of hot flashes on QoL [HL (95% CI) = 10 (0, 20), Wilcoxon $P = 0.01$), with the

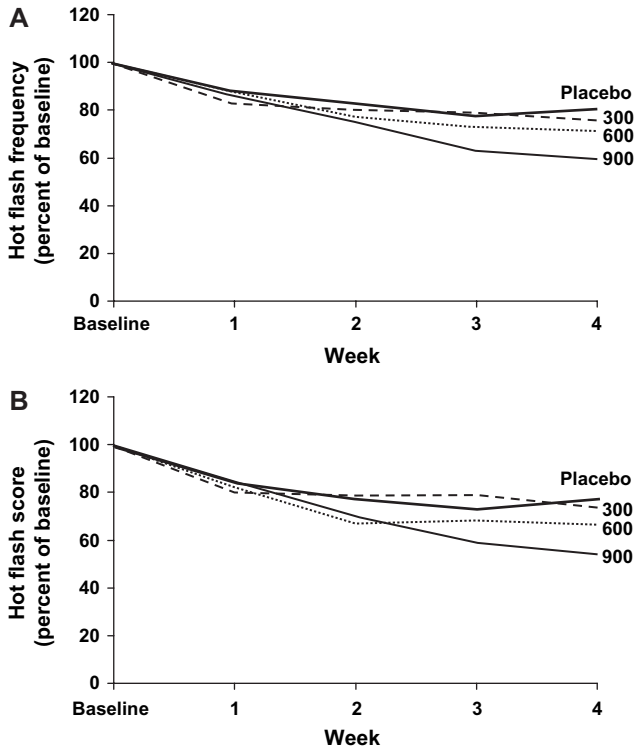

Figure 2. Mean changes from baseline for hot flash scores (A) and frequencies (B) for all study arms.

Table 2. Median percent decreases in hot flash score and frequency during treatment week 4, from baseline

Measure	Median % change from baseline to week 4 (95% confidence interval)			
	Placebo	300 mg/day	600 mg/day	900 mg/day
Hot flash frequency	21.5 (11.3–30.9)	22.8 (12.1–33.0)	31.8 (16.5–40.5)	45.5 (31.1–50.6)
Hot flash score	27.0 (12.1–36.1)	29.7 (13.1–36.9)	33.8 (22.2–47.1)	44.4 (35.2–56.3)

Table 3. Wilcoxon rank-sum comparisons of change from baseline at week 4 for hot flash score and frequency

		Placebo ($n = 46$)	300 mg/day ($n = 46$)	600 mg/day ($n = 42$)	900 mg/day ($n = 43$)	Collective gabapentin ($n = 131$)	Hodges–Lehmann shift estimator (95% confidence interval)	Wilcoxon P value
		Table values are median changes from baseline at week 4						
Hot flash score	Collective gabapentin versus placebo[a]	−2.8				−3.3	−0.6 (−2.3, 1.0)	0.48
	300 mg/day versus placebo	−2.8	−2.4				0.1 (−1.7, 2.2)	0.80
	600 mg/day versus placebo	−2.8		−3.1			−0.3 (−2.6, 1.6)	0.72
	900 mg/day versus placebo	−2.8			−4.3		−1.9 (−4.1, 0.3)	0.10
	300 mg/day versus 600 mg/day		−2.4	−3.1			0.7 (−1.3, 2.9)	0.44
	300 mg/day versus 900 mg/day		−2.4		−4.3		2.1 (0.0, 4.1)	0.05
	600 mg/day versus 900 mg/day			−3.1	−4.3		1.4 (−0.9, 3.4)	0.19
Hot flash frequency	Collective gabapentin versus placebo	−1.6				−2.1	−0.6 (−1.6, 0.3)	0.19
	300 mg/day versus placebo	−1.6	−1.8				−0.1 (−1.3, 1.0)	0.75
	600 mg/day versus placebo	−1.6		−2.0			−0.3 (−1.6, 1.0)	0.60
	900 mg/day versus placebo	−1.6			−2.6		−1.4 (−2.7, −0.3)	0.02
	300 mg/day versus 600 mg/day		−1.8	−2.0			0.3 (−1.0, 1.6)	0.73
	300 mg/day versus 900 mg/day		−1.8		−2.6		1.3 (0.1, 2.7)	0.03
	600 mg/day versus 900 mg/day			−2.0	−2.6		1.1 (−0.3, 2.5)	0.10

[a]Primary comparison.

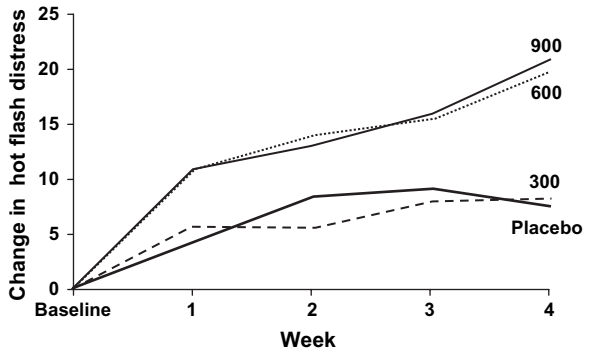

Figure 3. Median changes from baseline in hot flash distress, for each study arm (higher scores are better, on a total scale of 100 points).

significant differences favoring the gabapentin arms. The differences between the highest gabapentin dose arm and the placebo arm in changes in the week 4 values, from the baseline week, were significant for hot flash distress [HL (95% CI) = 10 (0, 20), Wilcoxon $P = 0.04$), satisfaction with hot flash control [HL (95% CI) = 10 (0, 30), Wilcoxon $P = 0.03$), and the effect of hot flashes on QoL [(95% CI) = 10 (0, 20), Wilcoxon $P = 0.003$], with the significant differences again favoring the gabapentin arm. Overall QoL (as changes during week 4, from baseline) was not significantly different between the gabapentin arm and the placebo arm [HL (95% CI) = 0 (0, 10), Wilcoxon $P = 0.49$] or between the highest dose of gabapentin and the placebo arm [HL (95% CI) = 0 (0, 10), Wilcoxon $P = 0.42$).

The differences between the combined gabapentin arms and the placebo arm in changes during week 4, from the baseline week, were insignificant (all Wilcoxon $P > 0.05$) for the POMS-B Total Mood Disturbance and all subscale scores (tension/anxiety, depression/dejection, confusion/bewilderment, fatigue/inertia, and anger/hostility) except for vigor/activity [HL (95% CI) = 5 (0, 10), Wilcoxon $P = 0.03$], with the significant difference in favor of the combined gabapentin arms. The difference between the highest gabapentin dose arm and the placebo arm in change during week 4, from the baseline week, was insignificant (all Wilcoxon $P > 0.05$) for the POMS-B Total Mood Disturbance and all subscale scores except for depression/dejection [HL (95% CI) = 5 (0, 10), Wilcoxon $P = 0.02$), with the significant difference again favoring the gabapentin arm.

Compliance information, obtained from patient self-reports, appears in Table 4. During each week of treatment, compliance rates for patients who did not drop out of the study were high (≥89% for each of the individual treatment regimens and ≥95% for the combination of all study arms) during this double-blind study. There were no significant differences in compliance rates across the gabapentin arms and matching placebo regimens at each treatment week.

The proportion of patients choosing to continue on with gabapentin (or start taking gabapentin if initially on the placebo arm) at the end of the double-blind study was 78%, 77%, 56%, and 62% in the placebo and three increasing gabapentin dose arms.

The placebo arm was broken up into three subsets, based on whether the target dose was 1, 2, or 3 tablets per day. When comparing these three arms to each other, there were no substantial differences between them in terms of hot flash scores (which, during the fourth treatment week were 78%, 80%, and 72% of the baseline week in the three subsets, respectively), toxicity, or compliance (Table 4).

discussion

The efficacy of gabapentin seen in this current trial parallels the efficacy seen with similar doses in women with hot flashes, with each of these revealing an ∼50% reduction in hot flashes at a gabapentin dose of 300 mg given three times daily [16, 17]. A cross study comparison of the results from this current trial and the results of the two trials in women with 900 mg of gabapentin per day is illustrated in Figure 4, demonstrating similarities among the three different trials. Recent data from another trial in women also revealed very similar results, with a 51% reduction of hot flashes with gabapentin, compared with a 26% reduction with a placebo ($P < 0.0001$) [18].

The gabapentin was extremely well tolerated in this trial, without any evidence of side-effects being observed more than what was seen in the placebo group. Similar results were seen in a placebo-controlled trial looking at gabapentin for treatment of chemotherapy neuropathy, with this trial utilizing up to 2700 mg/day in divided doses [19].

The mechanism of action of gabapentin's effect against hot flashes is not clear. It has been hypothesized that modulation of calcium currents may be involved [17]. Nonetheless, there is not definitive information regarding the mechanism for its efficacy.

It is worth providing a few words with regards to the methodology of this trial. The utilized methodology has been validated [13] and has been used in a series of Mayo Clinic/NCCTG clinical trials involving both women and men with hot flashes [14, 20–25]. A similar methodology has also been used by investigators in other hot flash trials [16, 26, 27].

With regards to trial length, it might be argued that the duration of treatment in this trial (4 weeks) is shorter than what has been utilized in other trials evaluating hot flash treatment regimens. Nonetheless, trials that investigated nonhormonal agents for hot flashes over 8–12 weeks nicely demonstrate that there is a plateau effect on the curves from 4 weeks on to 6–12 weeks [16, 17, 25–27].

Another methodology question deals with the placebo program that was utilized in this trial. The placebo arm could be broken up into three subsets, based on whether the target dose was 1, 2, or 3 tablets per day. One might argue that the patients getting more tablets per day might demonstrate greater placebo or nocebo effects or be less compliant. Nonetheless, the results of this trial did not illustrate a difference in efficacy,

Table 4. Patient-reported compliance: the placebo arms are designated as those that had target doses of 1, 2, or 3 tablets per day to correspond to gabapentin doses of 300, 600, and 900 mg/day, respectively

	Placebo (1/day)	Placebo (2/day)	Placebo (3/day)	300 mg/day	600 mg/day	900 mg/day	Total	*P* value[a]
Compliance week 1								0.21
Missing	0	0	0	2	1	3	6	
Yes	17 (100%)	15 (94%)	16 (94%)	49 (100%)	42 (89%)	43 (96%)	182 (95%)	
No	0 (0%)	1 (6%)	1 (6%)	0 (0%)	5 (11%)	2 (4%)	9 (5%)	
Compliance week 2								0.31
Missing	0	0	0	1	1	2	4	
Yes	16 (100%)	15 (94%)	17 (100%)	49 (100%)	44 (98%)	44 (100%)	185 (99%)	
No	0 (0%)	1 (6%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)	2 (1%)	
Compliance week 3								0.33
Missing	0	0	0	2	0	3	5	
Yes	16 (100%)	14 (93%)	17 (100%)	48 (98%)	42 (93%)	43 (100%)	180 (97%)	
No	0 (0%)	1 (7%)	0 (0%)	1 (2%)	3 (7%)	0 (0%)	5 (3%)	
Compliance week 4								0.16
Missing	0	1	0	6	2	3	12	
Yes	15 (100%)	13 (93%)	17 (100%)	44 (100%)	39 (91%)	41 (98%)	169 (97%)	
No	0 (0%)	1 (7%)	0 (0%)	0 (0%)	4 (9%)	1 (2%)	6 (3%)	

Compliant patient status was defined by the patient stating that he took the correct number of daily pills, with the given percentage applying to all patients that answered that question.

[a]Each week is a 2 × 6 two-way table [compliance (yes, no) versus arm (placebo 1/day, placebo 2/day, placebo 3/day, 300 mg/day, 600 mg/day, 900 mg/day)] and each *P* value is for a chi-squared test with 5 degrees of freedom (for the week).

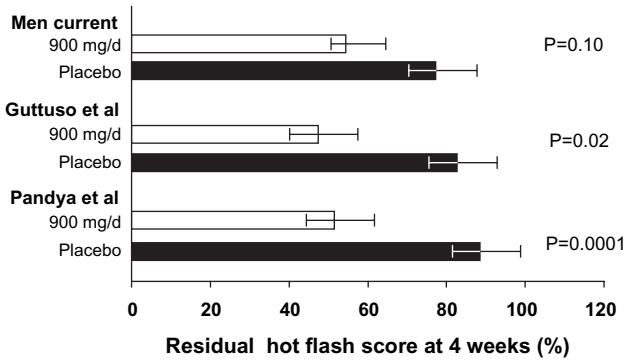

Figure 4. Cross study comparisons of data from two studies of gabapentin in women [16, 17] and the current one in men. Error bars represent 95% confidence intervals.

presumed toxicity, or compliance among the three subsets of the placebo arm (Figure 4).

It is reasonable to ask whether this current project should be considered as a positive clinical study. On the one hand, it could be argued that the primary analysis written in the statistical section of this protocol, that being a comparison of the combined gabapentin arms to the placebo arm, did not reveal a statistically significant difference, and thus this is a negative clinical study. On the other hand, it can easily be argued that this is not the best analytical means to look at a study such as this. It was expected that there was likely to be a dose–response effect for the chosen low doses of gabapentin and that only the higher doses might have shown a positive result, as was seen in another similarly designed clinical trial conducted by the NCCTG [14] and in a placebo-controlled double-blind, randomized trial in women examining gabapentin at 300 and 900 mg/day [16]. This was, in fact, what was observed.

Facts that support that gabapentin moderately decreases hot flashes in men include a statistically significant comparison of hot flash frequencies and a trend for improvement in hot flash scores between the 900 mg/day and placebo arms; statistically significant improvements of hot flash frequencies and scores between the 900 mg/day and 300 mg/day arms; that dose–response relationships are apparent in Figures 1 and 2; that the results in men look so similar to what was seen in three trials in women [16–18]; that there were significant differences for satisfaction with hot flash control and the effect of hot flashes on QoL for the combined gabapentin arms compared with the placebo arm, and that there were significant differences between the highest gabapentin dose arm and the placebo arm in changes in the week 4 values, from the baseline week, for hot flash distress, satisfaction with hot flash control, and the effect of hot flashes on QoL.

Thus, it appears reasonable to utilize gabapentin in clinical practice for hot flashes in men, noting that it would be ideal to have further data to substantiate its benefit. Nonetheless, the magnitude of benefit with this therapy appears to be relatively moderate. More information about gabapentin's ability to relieve hot flashes in men is desirable. Better therapies for alleviating hot flashes in men on androgen deprivation therapy are still needed.

funding

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