Nebivolol Efficacy and Safety in Patients with Stage I-II Hypertension

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ABSTRACT

Background: Nebivolol is a novel, β_1-adrenergic receptor blocker with vasodilatory properties mediated through activation of the L-arginine/nitric oxide pathway.

Hypothesis: This multicenter, double-blind, parallel-group, placebo-controlled study investigated the antihypertensive efficacy and safety of nebivolol in patients with stage I through stage II hypertension (sitting diastolic blood pressure [SiDBP] $\geq$95 mm Hg and $\leq$109 mm Hg).

Methods: A total of 811 patients were randomized to placebo or nebivolol 5 mg, 10 mg, or 20 mg once daily for 12 weeks. The primary efficacy endpoint was the reduction in mean trough SiDBP from baseline.

Results: At study end, the least squares mean reductions in trough SiDBP from baseline with nebivolol 5 mg, 10 mg, and 20 mg were −7.8 mm Hg, −8.5 mm Hg, and −9.1 mm Hg, respectively, compared with −4.6 mm Hg for placebo ($P = .002$ for nebivolol 5 mg, $P < .001$ for nebivolol 10 mg and 20 mg, vs placebo). Nebivolol treatment also produced reductions in trough sitting systolic blood pressure; however, only the 20 mg dose was statistically significant compared with placebo (−6.7 mm Hg vs −0.4 mm Hg; $P < .001$). Response rates (defined as an average trough SiDBP <90 mm Hg or a decrease by $\geq$10 mm Hg from baseline at the end of the study) ranged from 66.0% to 68.9% with nebivolol 5–20 mg, compared with 49.3% with placebo ($P \leq .009$). Nebivolol 5 mg and 10 mg doses were well tolerated, with an overall adverse event incidence comparable to placebo.

Conclusions: Once-daily nebivolol is an effective antihypertensive agent in patients with stage I-II hypertension.

Key words: nebivolol, β-blockers, hypertension, tolerability, nitric oxide

Introduction

β-Blockers differ with regard to their degree of selectivity for the β_1-adrenergic receptor, duration of action, degree of lipophilicity, and presence or absence of intrinsic sympathomimetic activity.[1,2] Some newer β-blockers have vasodilating properties, which are mediated via different pathways and provide distinct pharmacodynamic and hemodynamic profiles, and may have improved safety and tolerability, with less risk of metabolic adverse events (AEs), compared with conventional nonvasodilating β-blockers.[2–4]

Nebivolol is a novel β-blocker that combines highly selective β_1-adrenoceptor blockade with endothelium-dependent vasodilation, which occurs through stimulation of the L-arginine/nitric oxide (NO) pathway.[5,6] The vasodilatory activity of nebivolol results in a reduction in peripheral vascular resistance and an improvement in stroke volume, with a neutral impact on cardiac output.[4–6]

In previous clinical studies, nebivolol 2.5–40 mg effectively lowered blood pressure (BP) in patients with stage I-II hypertension and was also well tolerated.[7,8] The present study further investigated the antihypertensive efficacy, tolerability, and safety of nebivolol monotherapy in patients with stage I-II hypertension.

Methods

Study Population

Eligible patients were men and women $\geq$18 years with stage I-II hypertension (average SiDBP $\geq$95 mm Hg and $\leq$109 mm Hg).

Study Design

This was a double-blind, randomized, parallel-group, placebo-controlled, dose-ranging study conducted at 82 sites (59 in the United States and 23 in the European Union). The protocol and written informed consents were reviewed and approved by a central Institutional Review Board/Independent Ethics Committee prior to the enrollment of any patients.

The study consisted of 2 phases: a screening/washout/single-blind, placebo run-in period (4–6 wks), followed by randomization and double-blind treatment (12 wks). At screening and end of study (Week 12), each patient had a physical examination; clinical laboratory evaluations were performed at screening, randomization (Day 0), and end of study. At randomization (Day 0), baseline and demographic characteristics were recorded, and eligible patients were randomized to placebo or nebivolol 5 mg, 10 mg, or 20 mg once daily in a double-blind manner for 12 weeks. At Weeks 2, 4, 8, and 12 of the double-blind treatment period, BP and

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heart rate (HR) were measured. Patients were monitored for AEs, and concomitant medications and compliance with study medication were recorded. Treatment compliance was assessed by pill count at each study visit.

Endpoints and Objectives

The primary efficacy endpoint was the change in mean SiDBP at trough drug concentration (24±2 h after the previous morning's dose) at Week 12 compared with baseline. Secondary endpoints included mean changes from baseline to Week 12 in trough sitting systolic BP (SiSBP). A responder analysis was conducted (defined as mean trough SiDBP <90 mm Hg or a decrease of ≥10 mm Hg from baseline at end of study). Additional objectives assessed nebivolol safety and tolerability.

Efficacy and Safety Assessments

Blood pressure was measured in the sitting, supine, and standing positions at peak and trough. Blood pressure measurements at trough were taken at baseline (Day 0) and Weeks 2, 4, 8, and 12. Peak BP was measured at baseline and on Weeks 4 and 12. All measurements were taken in triplicate at 2-minute intervals, and the mean value was calculated.

Safety was assessed by monitoring AEs, HR, and the results of physical examination, 12-lead electrocardiograms, and clinical laboratory evaluations (chemistry panel, hematology profile, and urinalysis). All AEs from screening until the end of the study were recorded. The severity of an AE and its relationship to study medication was defined based on a qualitative evaluation by the study investigator.

Trough-to-peak ratio was computed by dividing BP reduction at trough by BP at peak.

Statistical Analysis

The primary population for the efficacy and safety analysis was the intent-to-treat (ITT) population. This included all randomized patients who received at least 1 dose of study medication. Missing data were imputed using the last-observation-carried-forward approach.

Sample Size Determination: It was estimated that a sample size of 122 patients receiving nebivolol 5 mg, 10 mg, and 20 mg once daily would give 90% power to detect a 3 mm Hg difference among doses. A 20% dropout rate was considered yielding minimum enrollment of 74 patients in the placebo group and 242 in each nebivolol dose group.

Statistical Tests: Demographics and baseline parameters were summarized using descriptive statistics. The *P* value was based on the analysis of variance overall F-test for continuous variables and on the χ^2 test for categorical variables.

The primary statistical method of treatment comparison for continuous variables was a step-down, dose-response trend test utilizing linear contrast in an analysis of covariance (ANCOVA) model up to and including the nebivolol 20 mg dose group.

Response rates of treatment groups were analyzed using a logistic regression model with responder as the response variable and baseline DBP and dichotomous variables as covariates. Response rates were compared using the Wald χ^2 test.

The analyses for categoric safety variables were assessed using the Cochran-Mantel-Haenszel test adjusted for baseline dichotomous covariates. All other safety parameters were summarized.

Results

A total of 811 patients completed the single-blind treatment placebo run-in period and were randomized to double-blind treatment. Four randomized patients did not receive study medication; therefore, the ITT population comprised 807 patients. Of these, 75 patients received placebo treatment, and 3 groups of 244 patients received nebivolol 5 mg, 10 mg, or 20 mg. A total of 702 patients (87.0%) completed the study, 61/75 placebo-treated patients (81.3%) and 641/732 patients in the combined nebivolol group (87.6%), with discontinuation rates ranging from 10.7% to 15.6% across the nebivolol dose groups. The main reasons for discontinuation were "other" (3.1%), AEs (3.0%), and withdrawal of consent (2.9%).

Treatment groups were comparable with respect to demographic and baseline clinical characteristics (Table 1), with no statistically significant differences among treatment groups. For the ITT population, the majority of patients were male (53.5%), nonblack (87.0%) and <65 years (81.8%); 4.6% of patients had diabetes. Of note, 40.1% of randomized patients were obese (body mass index [BMI] ≥30 kg/m^2). The average baseline SiDBP and SiSBP were similar across treatment groups, ranging from 98.7 mm Hg to 99.2 mm Hg and 149.9 mm Hg to 151.9 mm Hg, respectively. The average baseline sitting HR was also comparable across treatment groups, ranging from 72.2 bpm to 72.9 bpm.

Efficacy

By study end, all doses of nebivolol were found to have lowered BP (Table 2). Least squares (LS) mean reductions in trough SiDBP from baseline to Week 12 (primary efficacy endpoint) were significantly greater with all nebivolol doses compared with placebo ($P = .002$ for nebivolol 5 mg and $P < .001$ for nebivolol 10 mg and 20 mg; Figure 1A). Similarly, all doses of nebivolol resulted in LS mean reductions in trough SiSBP from baseline to end of study, although only the LS mean reduction with the 20 mg dose reached statistical significance ($P < .001$ vs placebo; Figure 1B). The LS mean decreases in BP were apparent by Week 2, and were sustained throughout the remainder of the study (Figure 1A,B).

All nebivolol doses significantly reduced peak SiDBP and SiSBP in a dose-dependent manner. The LS mean reductions

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Table 1. Patient Baseline Demographics and Clinical Characteristics (Intent-to-Treat Population)

Baseline Characteristic	Placebo n (%)	Nebivolol 5 mg n (%)	Nebivolol 10 mg n (%)	Nebivolol 20 mg n (%)	Total n (%)	*P* Value[a]
n	75	244	244	244	807	
Age (years)						
Mean (SD)	51.2 (10.0)	53.9 (11.1)	53.8 (11.2)	53.4 (11.1)	53.4 (11.0)	0.287
Median	50.0	54.0	53.0	53.0	53.0	
Range	27.0–73.0	23.0–79.0	22.0–82.0	28.0–80.0	22.0–82.0	
Age group						
<65 years	67 (89.3)	199 (81.6)	197 (80.7)	197 (80.7)	660 (81.8)	0.357
≥65 years	8 (110.7)	45 (18.4)	47 (19.3)	47 (19.3)	147 (18.2)	
Gender						
Male	39 (52.0)	131 (53.7)	131 (53.7)	131 (53.7)	432 (53.5)	0.994
Female	36 (48.0)	113 (46.3)	113 (46.3)	113 (46.3)	375 (46.5)	
Race[b]						
Black	11 (14.7)	31 (12.7)	33 (13.5)	30 (12.3)	105 (13.0)	0.947
Nonblack	64 (85.3)	213 (87.3)	211 (86.5)	214 (87.7)	702 (87.0)	
White	60 (80.0)	190 (77.9)	191 (78.3)	192 (78.7)	633 (78.4)	
Asian	0 (0.0)	4 (1.6)	2 (0.8)	3 (1.2)	9 (1.1)	
Hispanic	4 (5.3)	19 (7.8)	17 (7.0)	19 (7.8)	59 (7.3)	
Other	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.1)	
Diabetes status						
Yes	4 (5.3)	9 (3.7)	12 (4.9)	12 (4.9)	37 (4.6)	0.881
No	71 (94.7)	235 (96.3)	232 (95.1)	232 (95.1)	770 (95.4)	
BMI (kg/m^2)[c]						
<30	48 (64.0)	152 (62.6)	145 (59.4)	137 (56.4)	482 (59.9)	0.473
≥30	27 (36.0)	91 (37.4)	99 (40.6)	106 (43.6)	323 (40.1)	
Missing[c]	0	1	0	1	2	
SiDBP (mm Hg)						
Mean (SD)	98.7 (3.3)	99.1 (3.8)	98.9 (4.4)	99.2 (3.7)	99.0 (3.9)	0.775
SiSBP (mm Hg)						
Mean (SD)	149.9 (12.5)	151.8 (13.2)	150.5 (13.1)	151.9 (14.8)	151.3 (13.6)	0.505
Sitting heart rate (bpm)						
Mean (SD)	72.7 (8.3)	72.9 (8.3)	72.2 (8.7)	72.8 (8.7)	72.7 (8.5)	0.814

Abbreviations: BMI, body mass index; bpm, beats per minute; SD, standard deviation; SiDBP, sitting diastolic blood pressure; SiSBP, sitting systolic blood pressure. [a]From analysis of variance with main effect treatment for continuous variables, from a χ^2 test for discrete variables. [b]Test of race was black versus nonblack. [c]Not used in percentage calculation or testing.

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Table 2. Effect of Nebivolol on Blood Pressure and Heart Rate in Stage I-II Hypertensive Patients (Intent-to-Treat Population)[a]

Variable	Placebo	Nebivolol 5 mg	Nebivolol 10 mg	Nebivolol 20 mg
Trough SiDBP (mm Hg)				
n	75	244	244	244
Mean Δ from baseline (SD)	−7.2 (8.2)	−10.6 (7.7)	−11.2 (8.1)	−12.0 (8.4)
Step-down trend test *P* value[b,c]		0.002	<.001	<.001
Trough SiSBP (mm Hg)				
n	75	244	244	244
Mean Δ from baseline (SD)	−7.9 (12.8)	−12.1 (14.1)	−10.7 (14.8)	−14.6 (15.4)
Step-down trend test *P* value[b,c]		0.035[d]	0.086	<.001
Trough sitting HR (bpm)				
n	62	218	208	219
Mean Δ from baseline (SD)	−0.9 (7.4)	−5.9 (8.0)	−6.9 (8.5)	−7.9 (8.1)
Step-down trend test *P* value[b,c]		<.001	<.001	<.001

Abbreviations: bpm, beats per minute; SD, standard deviation; SiDBP, sitting diastolic blood pressure; SiSBP, sitting systolic blood pressure. [a]Intent-to-treat (last observation carried forward) approach used, except for trough sitting heart rate, where intent-to-treat observed cases was performed. [b]From analysis of covariance with factor treatment and covariates (baseline blood pressure, metabolism rate, diabetes status, gender, race, and age group). [c]Step-down testing scheme began with treatments placebo through nebivolol 20 mg and proceeded to step-down until the trend test contained only nebivolol 5 mg and placebo. [d] *P* value associated with lower dose not applicable in the context of step-down trend testing due to the nonsignificant result at the higher dose.

in peak SiDBP following treatment with nebivolol 5 mg, 10 mg, and 20 mg were −10.5 mm Hg, −11.6 mm Hg, and −12.2 mm Hg, respectively, compared with a −7.0 mm Hg reduction with placebo ($P<.001$ vs placebo for all doses). The reductions with nebivolol in LS mean peak SiSBP ranged from −7.7 mm Hg to −10.7 mm Hg compared with a −4.7 mm Hg reduction with placebo ($P = .004$ for nebivolol 10 mg; $P<.001$ for nebivolol 20 mg).

The placebo-subtracted trough-to-peak ratios for change in SiDBP from baseline to Week 12 were 0.9, 0.8, and 0.9 for nebivolol 5 mg, 10 mg, and 20 mg, respectively, demonstrating a sustained effect throughout the dosing interval with once-daily dosing.

Effects on Heart Rate: From baseline to end of study, nebivolol significantly lowered trough sitting HR at all doses compared with placebo (Table 2). The LS mean placebo-subtracted reductions in HR ranged from −5.1 bpm to −7.2 bpm ($P<.001$ for all doses).

Response Rates: Significantly more nebivolol-treated patients were responders compared with placebo-treated patients (Figure 2). Response rates with once-daily nebivolol 5 mg, 10 mg, and 20 mg were 66.0% ($P = .009$), 66.8% ($P = .005$), and 68.9% ($P = .002$), respectively, compared with 49.3% with placebo.

Safety and Tolerability

Extent of Exposure and Patient Compliance: A total of 732 nebivolol-treated patients and 75 placebo-treated patients were treated in this study. Patient compliance ranged from 90.5% to 94.5% in the ITT population. The rate of compliance was similar across the nebivolol 5 mg, 10 mg, and 20 mg groups (94.0%, 92.2%, and 94.5%, respectively) and was comparable with that of the placebo group (90.5%).

Adverse Events: A total of 27 patients (36.0%) in the placebo group and 311 nebivolol-treated patients (42.5%, in all 3 nebivolol groups combined) experienced an AE. The percentages of patients experiencing AEs with nebivolol 5 mg (39.3%) and 10 mg (39.8%) were comparable with the percentage of those taking placebo; patients treated with nebivolol 20 mg had a significantly higher rate of AEs (48.4%) compared with placebo ($P = .028$). The most commonly reported AEs for the combined nebivolol group versus placebo were headache (7.5% vs 5.3%), fatigue (3.8% vs 1.3%), and nasopharyngitis (3.7% vs 4.0%; Table 3). Most treatment-emergent AEs were mild or moderate in intensity. The incidence of AEs commonly associated with β-blocker use was low in the combined nebivolol group, with rates mostly similar to placebo: bradycardia (0.8% vs 0%), orthostatic hypotension (0.4% vs 0%), dizziness (2.9% vs 1.3%), unspecified sexual dysfunction (0.1% vs 0%),

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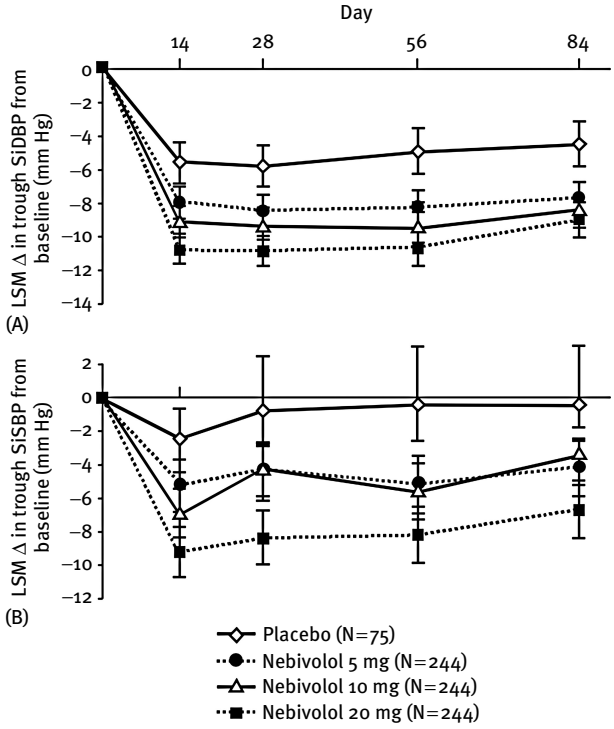

Figure 1. (A) Least squares mean change from baseline to study end in trough sitting diastolic blood pressure[a]; (B) Least squares mean change from baseline to study end in trough sitting systolic blood pressure[a]. [a]Least squares mean (±standard error) change for intent-to-treat population.

and depression (0.5% vs 0%), for nebivolol versus placebo, respectively.

A total of 22 patients (18 treated with nebivolol [2.5%] and 4 in the placebo group [5.3%]) withdrew due to treatment-emergent AEs (TEAEs). The most common reasons for withdrawal due to TEAEs (≥2 patients) were headache, atrial fibrillation, nausea, and diarrhea.

Seven serious AEs (SAEs) occurred in 6 patients treated with nebivolol (0.82%), 2 each in the nebivolol 5 mg, 10 mg, and 20 mg groups; no SAEs occurred in the placebo group. Of the 7 SAEs, 3 were deemed possibly related to nebivolol treatment: shortness of breath, myocardial infarction, and ruptured aortic aneurysm. All other SAEs were considered unrelated to nebivolol treatment. The SAEs resulted in withdrawal from the trial in all cases.

At study end, there were no statistically significant changes from baseline in mean total cholesterol, low-density lipoprotein cholesterol, triglycerides, and glucose levels with nebivolol treatment (Table 4). However, small decreases in mean high-density lipoprotein cholesterol (HDL-C) occurred in all nebivolol dose groups, which reached statistical significance in the nebivolol 10 mg and 20 mg groups ($P = .03$ vs placebo).

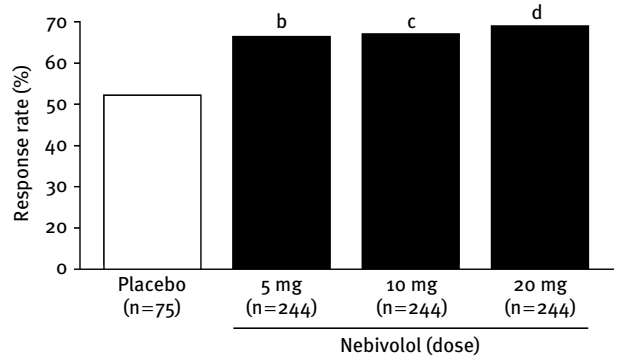

Figure 2. Response rates[a] at study end for all treatment groups. [a]Patient with a trough sitting diastolic blood pressure of <90 mm Hg at study end or a reduction of ≥10 mm Hg from baseline. [b]$P = .009$; [c]$P = .005$; [d] $P = .002$ vs placebo.

Discussion

This study demonstrates that once-daily nebivolol effectively lowered BP in patients with stage I-II hypertension. Nebivolol significantly reduced trough SiDBP compared with placebo. Significant reductions in SiSBP were also observed with nebivolol 20 mg. A significant proportion of nebivolol-treated patients responded to treatment compared with placebo; response rates in the nebivolol groups ranged from 66.0% to 68.9% versus 49.3% in the placebo group.

Nebivolol treatment was safe and well tolerated, with an overall AE incidence comparable to that of placebo. In total, 87.6% of patients on nebivolol and 81.3% of those on placebo completed the study; treatment compliance was high (>90%) and was comparable across treatment groups. There was a dose-related trend with regard to AE frequency, suggesting that further investigation of the risk:benefit of nebivolol doses ≥20 mg may be warranted. The incidence of AEs traditionally associated with β-blockers (eg, sexual dysfunction, dyspnea, and fatigue) was low with nebivolol and was not significantly different than with placebo. These data support results from a recent analysis of pooled data from the US placebo-controlled trials of nebivolol monotherapy (1.25–40 mg) which demonstrated that nebivolol was well tolerated, with an incidence of typical β-blocker AEs that was comparable to or less frequent than that observed with placebo.[9] Published data show that typical β-blocker AEs are reported less frequently with nebivolol than with atenolol.[10] Very few patients withdrew due to TEAEs in this study, and none of the discontinuations was associated with typical β-blocker-related AEs. The high cardioselectivity and endothelial-dependent vasodilatory properties of nebivolol may contribute to its BP-lowering effects as well as its safety and tolerability profile.

Nebivolol produces vasodilation via increased NO bioavailability, a characteristic that may be of particular clinical importance, since NO affects many aspects of endothelial

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Table 3. Summary of the Most Frequently Reported Treatment-Emergent Adverse Events for all Treatment Groups (Intent-To-Treat Population)

Adverse Event (MedDRA term)	Placebo n = 75 n (%)	Nebivolol 5 mg n = 244 n (%)	Nebivolol 10 mg n = 244 n (%)	Nebivolol 20 mg n = 244 n (%)	Total Nebivolol n = 732 n (%)
Headache NOS	4 (5.3)	24 (9.8)	15 (6.1)	16 (6.6)	55 (7.5)
Fatigue	1 (1.3)	5 (2.0)	7 (2.9)	16 (6.6)	28 (3.8)
Nasopharyngitis	3 (4.0)	11 (4.5)	6 (2.5)	10 (4.1)	27 (3.7)
URT infection NOS	1 (1.3)	9 (3.7)	5 (2.0)	8 (3.3)	22 (3.0)
Dizziness	1 (1.3)	4 (1.6)	7 (2.9)	10 (4.1)	21 (2.9)
Diarrhea NOS	1 (1.3)	5 (2.0)	3 (1.2)	7 (2.9)	15 (2.0)
Nausea	0	1 (0.4)	8 (3.3)	6 (2.5)	15 (2.0)
Insomnia	1 (1.3)	3 (1.2)	2 (0.8)	8 (3.3)	13 (1.8)
UT infection NOS	0	5 (2.0)	0	5 (2.0)	10 (1.4)
Sinusitis NOS	2 (2.7)	3 (1.2)	4 (1.6)	1 (0.4)	8 (1.1)
Back pain	0	0	5 (2.0)	3 (1.2)	8 (1.1)
Bradycardia NOS	0	1 (0.4)	0	5 (2.0)	6 (0.8)
Constipation	2 (2.7)	1 (0.4)	2 (0.8)	1 (0.4)	4 (0.5)
Elevated blood triglycerides	2 (2.7)	1 (0.4)	3 (1.2)	0	4 (0.5)

Abbreviations: MedDRA, Medical Dictionary for Regulatory Activities; NOS, not otherwise specified; URT, upper respiratory tract; UT, urinary tract.

Table 4. Mean Change from Baseline to End of Study in Metabolic Parameters[a]

Laboratory Parameter (mg/dL)	Placebo	Nebivolol 5 mg	Nebivolol 10 mg	Nebivolol 20 mg
Total cholesterol				
n	72	231	231	234
Baseline mean	206.2	214.3	211.3	212.4
Mean Δ from baseline (SD)	−2.2 (28.8)	−0.4 (27.0)	−1.3 (28.5)	−3.5 (25.8)
P value[b]		.27	.54	.95
LDL-C				
n	54	168	175	181
Baseline mean	119.6	124.9	122.4	123.5
Mean Δ from baseline (SD)	−1.6 (28.1)	−0.6 (20.5)	−1.9 (24.4)	−1.8 (22.8)
P value[b]		.48	.93	.80
HDL-C				
n	57	178	188	194
Baseline mean	52.3	55.7	55.5	57.1

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Table 4. (*Continued*)

Laboratory Parameter (mg/dL)	Placebo	Nebivolol 5 mg	Nebivolol 10 mg	Nebivolol 20 mg
Mean Δ from baseline (SD)	0.67 (1.5)	−2.0 (8.7)	−2.5 (9.7)	−2.9 (9.1)
P value[b]		.08	.03	.03
Triglycerides				
n	72	231	231	234
Baseline mean	163.1	170.9	156.6	162.3
Mean Δ from baseline (SD)	6.7 (77.9)	24.8 (95.6)	30.0 (111.0)	17.4 (87.5)
P value[b]		.11	.07	.37
Glucose				
n	72	231	230	234
Baseline mean	101.3	103.1	103.0	104.5
Mean Δ from baseline (SD)	1.8 (18.4)	0.9 (19.7)	1.0 (22.0)	1.2 (15.3)
P value[b]		.97	.88	.86

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation. [a]Intent-to-treat, observed cases. [b]From an analysis of covariance model with treatment as factor and screening measurement as covariate.

function and cardiovascular physiology.[11,12] Nebivolol has also been shown to increase NO bioactivity, both in healthy volunteers and in patients with hypertension.[13–15] Agents that increase NO bioactivity may provide cardiovascular benefits beyond BP-lowering effects.

β-Blockers have been reported to have deleterious effects on metabolic parameters (eg, serum glucose and lipids) making them potentially unsuitable for certain patients. In this study, nebivolol treatment had neutral effects on the majority of the metabolic parameters evaluated. However, the clinical significance of the observed decreases in HDL-C is unclear and may warrant further investigation. These findings are consistent with previously reported data on nebivolol.[7,8]

In this study, the response rates for the nebivolol dose groups and the reductions in DBP and SBP were similar to those reported in previous trials.[7,16,17] An equivalent reduction in DBP and SBP was observed in this study. This finding is consistent with what was seen in the other registration trials of nebivolol,[7,8] and could reflect a β-blocker class effect or an effect specific to this agent. No apparent differences in efficacy or safety were evident when patient subgroups were analyzed; however, numbers in each group were too low to allow definitive conclusions to be drawn.

In conclusion, nebivolol monotherapy was effective in reducing BP in patients with stage I-II hypertension. Nebivolol provided antihypertensive benefits with a favorable safety and tolerability profile, with a low incidence of β-blocker-associated AEs and largely neutral effects on metabolic parameters. These data suggest that nebivolol may provide a valuable therapeutic option for patients with stage I-II hypertension.

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