Sponsor:

Corthera, Inc. (formerly BAS Medical, Inc.), a member of the Novartis group of companies

Generic Drug Name:

Human Relaxin /Serelaxin (RLX030)

Therapeutic Area of Trial:

Acute heart failure

Approved Indication:

Investigational

Protocol Number:

CRLX.CHF.003

Title:

A Phase II/III, Multicenter, Randomized, Double-blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Relaxin in Subjects With Acute Heart Failure

Study Phase

II/III

Study Start/End Dates

Phase II: 11 Dec 2007 to 30 Oct 2008

Phase III: 11 Oct 2009 to 14 Aug 2012

Study Design/Methodology

The RLX.CHF.003 study was designed as a two phase study including a Phase II "Pre-RELAX-AHF" [Study Pre-RELAX-AHF] and a Phase III "RELAX-AHF".

Phase II - Pre-RELAX-AHF

Pre-RELAX-AHF was the Phase II portion of a multicenter, randomized, double-blind, placebo-controlled study in subjects with AHF, hypertension and mild to moderate renal impairment. Eligible subjects were to be randomized 3:2:2:2:2 to one of the following treatment groups:

- Placebo (planned n = 90)
- Relaxin, 10 μg/kg/day (planned n = 60)
- Relaxin, 30 μg/kg/day (planned n = 60)
- Relaxin, 100 μg/kg/day (planned n = 60)
- Relaxin 250 μg/kg/day (planned n = 60).

Eligible subjects were to be randomized no more than 16 hours from the time of arrival to the Emergency Department (ED) or other hospital unit . Subjects randomized to the placebo arm were to receive standard therapy (per institutional guidelines and clinical judgment) for AHF plus placebo. Subjects randomized to an active study drug arm were to receive standard therapy plus one of 4 doses of active study drug.

Study drug treatment was to be administered as an IV infusion for 48 hours unless at any time during dosing, the subject's systolic blood pressure (SBP) was < 100 mmHg or decreased by > 40 mmHg from Baseline in 2 consecutive measurements 15 minutes apart, at which point study drug treatment was to be terminated.

Subject-reported dyspnea severity was to be collected using both a 7-point Likert scale describing the change in symptom severity from baseline and a 100 mm Visual Analog Scale (VAS) describing symptom severity at each point in time. These evaluations were to be performed at baseline (VAS only), 6, 12 and 24 hours from start of study drug infusion, then daily to Day 7 and then at Day 14. Subjects were to have clinical evaluations including: AHF symptom assessments, vitals signs, physical examination emphasizing signs of heart failure (HF), as well as an assessment of need for further IV HF treatment and of the occurrence of worsening heart failure (WHF) events at least daily to the earlier of Day 7 or discharge, and then at Day 14. Blood was to be collected at 6 hours for clinical chemistry, and blood and urine specimens were to be collected at 12, 24, and 48 hours from study drug initiation for routine safety assessments and to evaluate renal function, followed by blood evaluations daily to the earlier of Day 7 or discharge and then at Day 14. These clinical and laboratory evaluations were

mandatory at Days 5 and 14; if the subject was discharged from the hospital prior to these visits, these evaluations were to be performed as outpatient visits. The last protocol-directed in-person assessment was at Day 14.

All subjects were to receive phone calls at Days 30 and 60 from start of study drug infusion to assess the occurrence of adverse events (AEs) and serious adverse events (SAEs) (Day 30 only), mortality and hospital readmission for HF or renal dysfunction. Subjects enrolled early in the study were to receive a follow-up phone call at Day 180 to ascertain vital status and cause of death. When the last subject enrolled in the study reached the Day 60 follow up, the final Day 180 telephone contact (TC) was to be performed in all subjects not contacted prior to that time.

Safety was to be assessed by recording medical history, monitoring AEs and vital signs, and performing physical examinations and routine clinical laboratory tests as per the protocol, as well as those felt to be clinically indicated by the investigator. Adverse events and SAEs were to be collected up to Day 30 from signing of the informed consent form.

An administrative interim analysis of key safety and efficacy data from Pre-RELAX-AHF was planned after approximately 225 enrolled subjects had completed their 14-day assessments. These data were used for Phase III planning purposes.

Phase III - RELAX-AHF

In RELAX-AHF, eligible patients were randomized in a 1:1 ratio to receive either IV placebo or serelaxin (30 µg/kg/day) in a double-blind manner.

Centers

In 8 countries a total of 38 centers participated in the Phase II study: 14 sites in Russia, 4 sites in the United States (US), 8 sites in Israel, 3 sites in Poland, 3 sites in Romania, 3 sites in Belgium, 2 sites in Hungary, and 1 site in Italy.

The Phase III study was conducted at 96 centers in 11 countries: 10 centers in Argentina, 4 centers in France, 7 centers in Germany, 7 centers in Hungary, 9 centers in Israel, 6 centers in Italy, 5 centers in Netherlands, 9 centers in Poland, 8 centers in Romania, 4 centers in Spain, 27 centers in United States of America.

Test Product (s), Dose(s), and Mode(s) of Administration

In addition to standard therapy for acute heart failure (per institutional guidelines and clinical judgment), each randomized participant received a single 48-hour intravenous (IV) infusion of study drug serelaxin or matching placebo in a double-blind fashion.

During Phase II (Pre-RELAX-AHF), in addition to standard therapy, randomized participants received a single 48-hour IV infusion equivalent to 10, 30, 100 or 250 µg/kg/day serelaxin or matching placebo.

During Phase III (RELAX-AHF), in addition to standard therapy, randomized participants received a single 48-hour IV infusion equivalent to 30 µg/kg/day serelaxin or matching placebo.

Statistical Methods

Phase II - Pre-RELAX-AHF

Analysis of the primary efficacy endpoint was to be conducted in the efficacy population. A secondary analysis was to be conducted in the Modified Intent-To-Treat (MITT) population, and further analyses were to be undertaken if necessary to understand any differences between the two results. Analyses of the key secondary efficacy endpoints were to be conducted in the Efficacy population.

Continuous data were to be summarized by the mean and the two-sided 95% confidence interval (CI) of the mean (normal approximation), standard deviation (SD), median, first and third quartiles, minimum and maximum. Categorical data were to be presented by absolute and relative frequencies (n and %) along with exact two-sided 95% CI (Clopper-Pearson), as appropriate. Unless stated otherwise, two-sided p-values < 0.05 were to be considered statistically significant and percentages were to be based on available observations.

A global test comparing the combined placebo and 10 μg/kg/day groups with the combined 30, 100, and 250 μg/kg/day groups was to be performed. In addition, pooled (placebo; 10 and 30 μg/kg/day; 100 and 250 μg/kg/day) and individual treatment groups were to be compared using a logistic regression model that included the treatment effect as an explanatory variable and geographic region as a covariate. Both pooled and individual active dose groups were to be compared with placebo at the two-sided 5% significance level, without adjustment for multiple comparisons. The p-value for the Wald chi-square test of the overall treatment effect and each active treatment versus placebo in the logistic regression model were to be provided and used to evaluate the effectiveness of relaxin. The estimated odds ratios for treatment effect and associated two-sided 95% confidence limits (CLs) were also to be provided.
In an exploratory analysis of treatment effect sizes for selected efficacy endpoints, two-sided p-values of $0.05 \leq p < 0.20$ were considered trends. The treatment-by-center interaction was not to be evaluated because it was expected that many centers would enroll very few subjects. Centers were to be pooled across two prospective geographic regions (Israel, North America and Western Europe, compared to Russia and Eastern Europe), and geographic region was to be included as a covariate when evaluating the treatment effect.

For all time-to-event analyses, time (measured in days) was to be calculated as the difference between the date of randomization and the date of the event plus one day. Subjects who did not experience the event were to be censored.

Demographics and Baseline characteristics were to be summarized using the efficacy population. Subject demographics (age, sex, ethnicity, race, weight and height) at Baseline were to be summarized. Weight and height were to be converted to units of the metric system, kg and cm respectively. Screening brain natriuretic peptide (BNP), NT-pro-BNP, estimated creatinine clearance, troponin and troponin T laboratory values as reported by the investigator were to be summarized with standard descriptive statistics. The proportion of subjects with positive troponin I and/or T were to be presented.

The number and percentages of subjects meeting all eligibility criteria at Screening were also to be provided. Medical history data were to be descriptively summarized.

Product-limit (Kaplan-Meier) estimates of mortality rates at relevant time points (e.g., 30, 60, 90, and 180 days) were to be presented in the safety population, along with estimates of the hazard ratio (from Cox regression) comparing active to placebo with 95% CLs.

Adverse events were to be coded using Medical Dictionary for Regulatory Activities Version 10. All reported AEs were to be summarized by system organ class and preferred term. Disease related events were to be indicated with an asterisk. In addition, AEs will be summarized by time period of onset: from study drug initiation to Day 7, or from Day 8 to Day 14 or Day 14 to Day 30. All study-drug-related AEs, AEs with an outcome of death, AEs leading to discontinuation of treatment, and study-drug-related SAEs, SAEs with an outcome of death, and SAEs leading to study drug

discontinuation were to be summarized by percentages and frequencies. Percentages were to be based on the number of subjects in the safety population with at least one AE form completed. For the analysis by time period of onset, the percentages were to be based on the number of subjects in the safety population with the corresponding AE form completed. Odds ratios and associated 95% CIs comparing active treatment with placebo were to be presented for those events with 5 or more events in the combined treatment groups.

Mean laboratory values, and changes in laboratory values from Day 1, were to be presented by treatment group, and treatment groups compared using t-tests, in the safety population. Shift tables were to be prepared for each laboratory parameter showing the number and percentage of subjects in each treatment group with laboratory values that fell outside pre-determined ranges at each follow-up day by the classification of subjects at Day 1. Laboratory values were to be presented for each subject in a data listing with an indication of whether the value is above or below the normal reference range.

Phase III – RELAX-AHF

For Phase III, the primary global null hypothesis was that both the mean area under the dyspnea VAS change from baseline curve (VAS AUC) from baseline to Day 5 and the proportion of subjects with moderately to markedly better dyspnea at 6, 12, and 24 hours were the same in both treatment groups. The Type I error rate for this global null hypothesis was controlled for the two comparisons within it at the two-sided 0.05 level using the Hochberg approach. The VAS AUC means were compared between treatment groups using a t-test as the primary analytic method. The proportions with moderately or markedly better dyspnea at 6, 12, and 24 hours were compared between treatment groups using a chi-square test.

Assuming a standard deviation of 2700 mm-hr for the dyspnea VAS AUC, 25% of placebo patients with moderately or markedly better dyspnea at 6, 12, and 24 hours, and a correlation of 0.25 between the two endpoints, the study had approximately 81% power to detect a mean difference on the dyspnea VAS AUC of 468 mm-hr and/or a relative risk of 1.3 (absolute difference of 7.5%) on the proportion moderately or markedly better at the two-sided 0.05 significance level using the Hochberg approach.

The secondary global null hypothesis was that both the mean number of days alive and out of hospital through Day 60 was the same in both treatment groups, and the hazard for CV death or rehospitalization for HF or RF through Day 60 was the same in both groups. The Type I error rate was controlled across the two global null hypotheses at the two-sided 0.05 level by sequential testing: the secondary global null hypothesis was tested given rejection of the primary global null hypothesis. The Type I error rate for the secondary global hypothesis was controlled for the two comparisons within it at the two-sided 0.05 level using the Hochberg approach. Groups were compared with respect to the number of days alive and out of hospital using a Wilcoxon rank sum test as the primary analytic method. Treatment groups were compared with respect to the hazard ratio for CV death or HF or RF rehospitalization using a log-rank test.

Tests of additional efficacy analyses and safety analyses were performed without adjustment for multiple comparisons at the two-sided 0.05 significance level.

Study Population: Inclusion/Exclusion Criteria (Phase II and III)

Inclusion Criteria for Phase II - Pre-RELAX-AHF

1. Able to provide written informed consent
2. Male or female ≥ 18 years of age, with body weight < 115 kg
3. SBP > 125 mmHg at the time of screening
4. Hospitalized for AHF. Acute heart failure was defined as including all of the following at Screening:
    a. Dyspnea at rest or with minimal exertion
    b. Pulmonary congestion as evidenced by interstitial edema on chest radiograph
    c. Brain natriuretic peptide ≥ 350 pg/mL or N-terminal prohormone brain natriuretic peptide (NT-pro-BNP) ≥ 1400 pg/mL (measured at any time between presentation [including the ED] and screening)
5. Able to be randomized within 16 hours from presentation to the hospital, including the ED
6. Received IV furosemide of at least 40 mg (or equivalent) at any time between admission to emergency services (either ambulance or hospital, including the ED) and screening for the study
7. Impaired renal function defined as a creatinine clearance on admission between 30-75 mL/minute, calculated using the simplified Modification of Diet in Renal Disease (sMDRD) formula.

Exclusion Criteria: for Phase II - Pre-RELAX-AHF

1. Pregnant or breast-feeding women (women of child bearing potential had to have the results of a negative pregnancy test recorded prior to study drug administration)
2. Administration of IV radiographic contrast agent within 72 hours prior to Screening or acute contrast-induced nephropathy at the time of Screening
3. Temperature > 38°C (oral or equivalent), sepsis, or active infection requiring IV anti-microbial treatment
4. Current (within 2 hours prior to screening) or planned (through the completion of study drug infusion) treatment with any IV therapies, including vasodilators (including nesiritide), positive inotropic agents and vasopressors, or mechanical support (intra-aortic balloon pump, endotracheal intubation, mechanical ventilation, or any ventricular assist device), with the exception of IV nitrates at a dose of ≤ 0.1 mg/kg/hour if the subject had a SBP > 150 mmHg at Screening
5. Current (at screening) or planned ultrafiltration, hemofiltration, or dialysis
6. Diabetic nephropathy with proteinuria +2 or greater by dipstick

7. Significant pulmonary disease (history of oral daily steroid dependency, history of dependency on bronchodilators or need for intubation in the past for acute exacerbation, or currently receiving IV steroids)
8. Significant stenotic valvular disease (severe aortic stenosis [aortic valve area < 1.0 or peak gradient > 50 on prior or current echocardiogram {ECG}], severe mitral regurgitation, severe aortic regurgitation, or severe mitral stenosis)
9. Any organ transplant recipient, subject listed for transplant, or subject admitted for any transplantation
10. Major surgery within 30 days prior to Screening
11. Hematocrit < 25% or blood transfusion within 14 days prior to screening, or active, life-threatening gastrointestinal bleeding
12. Major neurologic event, including cerebrovascular events, within 60 days prior to screening
13. Clinical diagnosis of acute coronary syndrome within 45 days prior to screening (including the admission at the time of screening) as determined by both clinical and enzymatic criteria
14. Troponin ≥ 3 times the upper limit of normal between presentation and Screening
15. AHF due to significant arrhythmias (ventricular tachycardia, bradyarrhythmias with ventricular rate <45 beats per minute [bpm] or any second or third degree atrioventricular block or atrial fibrillation/flutter with ventricular response of > 120 bpm)
16. Acute myocarditis or hypertrophic obstructive, restrictive, or constrictive cardiomyopathy (did not include restrictive mitral filling patterns seen on Doppler ECG assessments of diastolic function)
17. Known hepatic impairment (total bilirubin > 3 mg/dL, albumin < 2.8 mg/dL, or increased ammonia levels if performed)
18. Non-cardiac pulmonary edema, including suspected sepsis
19. Administration of an investigational drug, implantation of investigational device, participation in another trial, within 30 days prior to screening, or previous treatment with relaxin
20. Inability to follow instructions or comply with follow-up procedures.

Inclusion Criteria for Phase III- RELAX-AHF

Patients who fulfilled all of the following criteria at screening were eligible for the study:
1. Able to provide written informed consent
2. Male or female ≥ 18 years of age, with body weight ≤ 160 kg
3. Systolic blood pressure > 125 mmHg at the start and at the end of screening
4. Hospitalized for AHF. AHF was defined as including all of the following measured at any time between presentation (including the ED) and the end of screening:
    a. Dyspnea at rest or with minimal exertion
    b. Pulmonary congestion on chest radiograph
    c. BNP ≥ 350 pg/mL or NT-pro-BNP ≥ 1400 pg/mL

5. Able to be randomized within 16 hours from presentation to the hospital, including the ED
6. Received IV furosemide of at least 40 mg (or equivalent) at any time between admission to emergency services (either ambulance or hospital, including the ED) and the start of screening for the study
7. Impaired renal function defined as an eGFR on admission between 30 - 75 mL/min/1.73 m2, calculated using the sMDRD equation.

Exclusion Criteria for Phase III- RELAX-AHF

Patients who met any of the following criteria were excluded from the study:
1. Pregnant or breast-feeding women (women of child bearing potential were to have the results of a negative pregnancy test recorded prior to study drug administration)
2. Administration of intravenous radiographic contrast agent within 72 hours prior to screening or acute contrast-induced nephropathy at the time of screening
3. Temperature > 38°C (oral or equivalent) or sepsis or active infection requiring IV antimicrobial treatment
4. Current (within 2 hours prior to screening) or planned (through the completion of study drug infusion) treatment with any IV therapies, including vasodilators (including nesiritide), positive inotropic agents and vasopressors, or mechanical support (intra-aortic balloon pump, endotracheal intubation, mechanical ventilation, or any ventricular assist device), with the exception of IV furosemide (or equivalent), or of IV nitrates at a dose of ≤ 0.1 mg/kg/hr if the patient has a systolic BP > 150 mmHg at screening
5. Current or planned ultrafiltration, hemofiltration, or dialysis
6. Known significant pulmonary disease
7. Known significant valvular disease (including any of the following: severe aortic stenosis [Aortic valve area (AVA) < 1.0 or mean gradient > 50 on prior or current echocardiogram], severe aortic regurgitation, or severe mitral stenosis)
8. Any organ transplant recipient, or patient currently listed for imminent transplant (i.e., did not exclude patients on an administrative transplant waiting list), or admitted for any transplantation
9. Major surgery within 30 days
10. Hematocrit < 25% or blood transfusion in the prior 14 days or active, life-threatening GI bleeding; or active menorrhagia or metrorrhagia
11. Major neurologic event, including cerebrovascular events, in the prior 60 days
12. Clinical diagnosis of acute coronary syndrome within 45 days prior to screening (including the present admission) as determined by both clinical and enzymatic criteria
13. Troponin ≥ 3 times the upper limit of normal (including "borderline/intermediate") between presentation and the end of screening
14. AHF due to significant arrhythmias (including any of the following: ventricular tachycardia, bradyarrhythmias with ventricular rate < 45 beats per minute (bpm) or any second or third degree AV block or atrial fibrillation/flutter with ventricular response of > 120 bpm)

15. Acute myocarditis or hypertrophic obstructive, restrictive, or constrictive cardiomyopathy (did not include restrictive mitral filling patterns seen on Doppler echocardiographic assessments of diastolic function)
16. Known hepatic impairment
17. Non-cardiac pulmonary edema, including suspected sepsis
18. Administration of an investigational drug or implantation of investigational device, or participation in another trial, within 30 days before screening or previous treatment with serelaxin
19. Inability to follow instructions or comply with follow-up procedures
20. Known hypersensitivity to serelaxin or similar substances or to any of the excipients

Participant Flow

Phase II- Pre-RELAX-AHF
Population disposition– all randomized subjects

	Placebo		Relaxin								Total	
			10mcg/kg/day		30mcg/kg/day		100mcg/kg/day		250mcg/kg/day			
	N = [62]		N = [40]		N = [43]		N = [39]		N = [50]		N = [234]	
	n	%	n	%	n	%	n	%	n	%	n	%
MITT population	61	98.4%	40	100%	42	97.7%	37	94.9%	49	98.0%	229	97.9%
Efficacy population	61	98.4%	40	100%	42	97.7%	37	94.9%	49	98.0%	229	97.9%
Safety population	61	98.4%	40	100%	42	97.7%	38	97.4%	49	98.0%	230	98.3%
Met all eligibility criteria	35	56.5%	28	70.0%	31	72.1%	18	46.2%	26	52.0%	138	59.0%
Treated with study medication	61	98.4%	40	100%	42	97.7%	38	97.4%	49	98.0%	230	98.3%
Highest dose of study medication received												
Placebo	61	98.4%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	61	26.1%
10mcg/kg/day	0	0.0%	40	100%	0	0.0%	0	0.0%	0	0.0%	40	17.1%
30mcg/kg/day	0	0.0%	0	0.0%	42	97.7%	0	0.0%	0	0.0%	42	17.9%
100mcg/kg/day	0	0.0%	0	0.0%	0	0.0%	38	97.4%	0	0.0%	38	16.2%
250mcg/kg/day	0	0.0%	0	0.0%	0	0.0%	0	0.0%	49	98.0%	49	20.9%
EOS status												
Completed Day 180	52	83.9%	38	95.0%	37	86.0%	36	92.3%	43	86.0%	206	88.0%
Lost to follow-up	0	0.0%	0	0.0%	1	2.3%	0	0.0%	1	2.0%	2	0.9%
Withdrawal	2	3.2%	0	0.0%	2	4.7%	1	2.6%	0	0.0%	5	2.1%
Died	8	12.9%	2	5.0%	3	7.0%	2	5.1%	5	10.0%	20	8.5%
Other reasons	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	2.0%	1	0.4%

EOS=end of study, MITT=Modified Intent to Treat, N=number, Withdrawal=subject withdrew consent
Note: Percentages are based on randomized subjects (N)

Phase III- RELAX-AHF

Patient disposition – n (%) of patients (ITT analysis set)

	Placebo (N=580)	Serelaxin (N=581)	Total (N=1161)
Completed Day 180			
Yes	505 (87.1)	530 (91.2)	1035 (89.1)
No	75 (12.9)	51 (8.8)	126 (10.9))
Died	65 (11.2))	41 [3] (7.1)	106 (9.1)
Withdrew Consent from Follow-up [1,2]	9 (1.6)	9 (1.5)	18 (1.6)
Lost to Follow-up	1 (0.2)	1 (0.2)	2 (0.2)
Withdrawal of Consent at any Level	28	28	56
Withdrew from Study Drug	7 (1.2)	12 (2.1)	19 (1.6)
Withdrew from Laboratory Samples	25 (4.3)	25 (4.3)	50 (4.3)
Withdrew from Examinations	19 (3.3)	19 (3.3)	38 (3.3)
Withdrew from Contact	10 (1.7)	12 (2.1)	22 (1.9)
Withdrew from Hospital Records	9 (1.6)	11 (1.9)	20 (1.7)

[1] Patients who withdrew consent from follow-up are patients who both withdrew consent from contact and withdrew consent for access to hospital records.

[2] Vital status was determined for 6 of these 18 patients through public records or regular office visits as permitted by local regulations.

[3] One patient, who withdrew consent, died on Day 104 is therefore not included as withdrawn due to death in the disposition table.

Baseline Characteristics

Phase II – Pre-RELAX-AHF

Subject demographics – Modified Intent to treat (MITT) population

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[37]	Relaxin 250mcg/kg/day N=[49]	Total N=[229]
Age (years)						
N	61	40	42	37	49	229
Mean (SD)	68.4 (9.92)	72.2 (10.96)	71.6 (9.23)	69.2 (11.59)	70.7 (11.01)	70.3 (10.52)
95% CI	65.9 ; 71.0	68.7 ; 75.7	68.7 ; 74.4	65.3 ; 73.1	67.6 ; 73.9	68.9 ; 71.6
Median	70.0	72.0	74.0	71.0	72.0	71.0
Q1 ; Q3	66.0 ; 75.0	65.5 ; 81.0	67.0 ; 78.0	61.0 ; 78.0	66.0 ; 80.0	66.0 ; 78.0
Min ; Max	40 ; 83	39 ; 91	45 ; 85	43 ; 89	48 ; 89	39 ; 91
Weight (kg)						
N	61	40	42	37	49	229
Mean (SD)	80.7 (15.59)	80.2 (16.89)	79.9 (13.01)	84.5 (24.98)	80.3 (16.73)	81.0 (17.41)
95% CI	76.7 ; 84.7	74.8 ; 85.7	75.9 ; 84.0	76.2 ; 92.9	75.5 ; 85.1	78.7 ; 83.3
Median	81.0	79.4	79.9	83.5	78.0	80.0
Q1 ; Q3	70.0 ; 89.0	66.0 ; 90.5	70.8 ; 90.0	70.0 ; 95.0	70.0 ; 90.0	69.9 ; 90.0
Min ; Max	55 ; 127	55 ; 115	52 ; 103	50 ; 168	40 ; 131	40 ; 168
Height (cm)						
N	61	40	42	37	49	229
Mean (SD)	168.6 (8.61)	164.8 (8.28)	163.4 (8.37)	166.6 (9.62)	168.6 (8.43)	166.7 (8.83)
95% CI	166.4 ; 170.8	162.2 ; 167.4	160.7 ; 166.0	163.4 ; 169.8	166.2 ; 171.0	165.5 ; 167.8
Median	170.0	165.0	164.5	165.0	168.0	167.0
Q1 ; Q3	162.0 ; 175.0	160.0 ; 170.0	157.0 ; 170.0	158.0 ; 175.0	163.0 ; 174.0	160.0 ; 173.0
Min ; Max	150 ; 183	137 ; 185	145 ; 177	153 ; 189	153 ; 187	137 ; 189
Gender						
N	61	40	42	37	49	229
Male	40 65.6%	21 52.5%	18 42.9%	19 51.4%	30 61.2%	128 55.9%
Female	21 34.4%	19 47.5%	24 57.1%	18 48.6%	19 38.8%	101 44.1%
Ethnicity						
N	61	40	42	37	49	229
Hispanic or Latino	2 3.3%	1 2.5%	1 2.4%	1 2.7%	2 4.1%	7 3.1%
Not Hispanic or Latino	59 96.7%	39 97.5%	41 97.6%	36 97.3%	47 95.9%	222 96.9%
Race						
N	61	40	42	37	49	229
White	58 95.1%	38 95.0%	42 100%	36 97.3%	48 98.0%	222 96.9%
Black or African American	3 4.9%	2 5.0%	0 0.0%	1 2.7%	1 2.0%	7 3.1%

CI=confidence interval, Max=maximum, Min=minimum, MITT=Modified Intent to Treat, N=number, SD=standard deviation
Note: Percentages are based on N

Phase III- RELAX-AHF

Demographic summary by treatment group (ITT analysis set)

		Placebo (N=580)	Serelaxin (N=581)	Total (N=1161)
Age (years)	n'	580	581	1161
	Mean (SD)	72.5 (10.78)	71.6 (11.68)	72.0 (11.24)
	95% CI	71.6, 73.4	70.6, 72.5	71.4, 72.7
	Median	74	73	74
	Q1, Q3	66.0, 80.0	65.0, 80.0	65.0, 80.0
	Min, Max	24, 96	29, 97	24, 97
Gender – n (%)	Male	357 (61.6)	368 (63.3)	725 (62.4)
	Female	223 (38.4)	213 (36.7)	436 (37.6)
Race – n (%)	American Indian or Alaska Native	0 (0.0)	1 (0.2)	1 (<0.1)
	Asian	2 (0.3)	2 (0.3)	4 (0.3)
	Black or African American	23 (4.0)	29 (5.0)	52 (4.5)
	Native Hawaiian or Pacific Islander	0 (0.0)	1 (0.2)	1 (<0.1)
	White	552 (95.2)	544 (93.6)	1096 (94.4)
	Multi-Racial	1 (0.2)	1 (0.2)	2 (0.2)
	Other	2 (0.3)	3 (0.5)	5 (0.4)
Ethnicity	Hispanics or Latino	59 (10.2)	57 (9.8)	116 (10.0)
	Other	521 (89.8)	523 (90.2)	1044 (90.0)

Weight (kg)	n'	579	580	1159
	Mean (SD)	82.8 (18.70)	81.9 (18.52)	82.3 (18.61)
	95% CI	81.2, 84.3	80.4, 83.4	81.3, 83.4
	Median	80.5	80.2	80.2
	Q1, Q3	69.3, 93.0	70.0, 91.6	70.0, 92.3
	Min, Max	40.3, 158.3	40.8, 148.1	40.3, 158.3
Height (cm)	n'	570	573	1143
	Mean (SD)	167.3 (9.54)	167.4 (9.51)	167.3 (9.52)
	95% CI	166.5, 168.1	166.6, 168.2	166.8, 167.9
	Median	168	168	168
	Q1, Q3	160.0, 173.0	160.0, 174.0	160.0, 174.0
	Min, Max	140.0, 198.0	132.0, 193.0	132.0, 198.0

n'= number of patients with measurement

Outcome Measures

Primary Outcome Result(s): Phase II- Pre-RELAX-AHF

1. Proportion of subjects with marked or moderate improvement in subject-reported dyspnea score using the Likert 7-point scale at both 12 and 24 hours following the start of study drug infusion in the absence of WHF symptoms and signs between 3 and 24 hours following the start of study drug infusion.

Primary efficacy endpoint - MITT population

		Relaxin				
	Placebo N=[61]	10mcg/kg/day N=[40]	30mcg/kg/day N=[42]	100mcg/kg/day N=[37]	250mcg/kg/day N=[49]	Total N=[229]
Dyspnea at 12 and 24 hours						
N	61	40	42	37	49	229
Marked or moderate improvement in dyspnea score at 12 and 24 hours in absence of WHF	27 44.3%	16 40.0%	21 50.0%	9 24.3%	20 40.8%	93 40.6%
Logistic regression						
Odds ratio (vs. Placebo)		0.9	1.3	0.4	0.9	
95% Wald CI		0.4 ; 1.9	0.6 ; 2.8	0.2 ; 1.0	0.4 ; 1.8	
P-value		0.698	0.547	0.051	0.696	
Chi-square test (vs. Placebo)						
Risk of marked or moderate impr.		0.8	1.3	0.4	0.9	
95% CI		0.4 ; 1.9	0.6 ; 2.8	0.2 ; 1.0	0.4 ; 1.9	
P-value		0.673	0.568	0.048	0.718	
Cochran-Mantel-Haenszel test* (vs. Placebo)						
Risk of marked or moderate impr.		0.9	1.3	0.4	0.9	
95% CI		0.4 ; 1.9	0.6 ; 2.7	0.2 ; 1.0	0.4 ; 1.9	
P-value		0.709	0.551	0.041	0.746	

CI=confidence interval, impr=improvement, MITT=Modified Intent to Treat, N=number, WHF=worsening heart failure
Note: Percentages are based on N. Logistic regression includes terms for geographical region
* Stratified by geographical region

Secondary Outcome Result(s): Phase II- Pre-RELAX-AHF

1. Proportion of subjects with renal impairment defined as a ≥ 25% increase in SCr from Baseline to Day 5

Renal impairment – MITT population

	Placebo N=[61]		Relaxin 10mcg/kg/day N=[40]		Relaxin 30mcg/kg/day N=[42]		Relaxin 100mcg/kg/day N=[37]		Relaxin 250mcg/kg/day N=[49]		Total N=[229]	
Renal impairment												
N	60		40		41		37		47		225	
Number of subjects with renal impairment	8	13.3%	4	10.0%	9	22.0%	11	29.7%	12	25.5%	44	19.6%
Logistic regression												
Odds ratio (vs. Placebo)			0.7		1.9		2.9		2.2			
95% Wald CI			0.2 ; 2.6		0.6 ; 5.3		1.0 ; 8.1		0.8 ; 5.9			
P-value			0.620		0.252		0.045		0.127			

CI=confidence interval, MITT=Modified Intent to Treat, N=number
Note: Percentages are based on N
Logistic regression includes terms for treatment effect and geographic region
Renal impairment is defined as a = 25% increase in serum creatinine from baseline to Day 5

2. Time from study drug initiation to death due to any cause or to re-hospitalization due to HF or renal dysfunction through Day 60 (the occurrence of the first of these events was to be considered).

Time to death or re-hospitalization due to HF or renal failure through Day 60 -Safety population

		Relaxin				
	Placebo N=[61]	10mcg/kg/day N=[40]	30mcg/kg/day N=[42]	100mcg/kg/day N=[38]	250mcg/kg/day N=[49]	Total N=[230]
Death or rehospitalization	11 18.0%	5 12.5%	3 7.1%	4 10.5%	4 8.2%	27 11.7%
Kaplan Meier product limit estimates						
Probability of death or rehospitalization						
Day 5	0.0	5.0	0.0	0.0	2.0	1.3
(95% CI)	. ; .	1.3 ; 18.5	. ; .	. ; .	0.3 ; 13.6	0.4 ; 4.1
Day 14	3.4	7.5	0.0	2.7	4.1	3.5
(95% CI)	0.9 ; 12.9	2.5 ; 21.5	. ; .	0.4 ; 17.7	1.0 ; 15.3	1.8 ; 7.0
Day 30	11.9	7.5	5.0	2.7	4.1	6.7
(95% CI)	5.8 ; 23.3	2.5 ; 21.5	1.3 ; 18.5	0.4 ; 17.7	1.0 ; 15.3	4.1 ; 10.8
Day 60	18.6	12.5	7.6	10.9	8.3	12.0
(95% CI)	10.8 ; 31.1	5.4 ; 27.5	2.5 ; 21.7	4.2 ; 26.5	3.2 ; 20.5	8.4 ; 17.1
Cox proportional hazards model						
Hazard ratio (vs. Placebo)		0.63	0.36	0.56	0.41	
95% Wald CI		0.22 ; 1.81	0.10 ; 1.29	0.18 ; 1.76	0.13 ; 1.28	
P-value		0.390	0.117	0.322	0.123	

CI=confidence interval, HF=heart failure, MITT=Modified Intent to Treat, N=number
Note: Percentages are based on N
Cox proportion hazards model includes term for treatment effect and is stratified by geographic region

Primary Outcome Result(s): Phase III- RELAX-AHF

1. AUC representing the change from baseline in patient-reported dyspnea measured by a 100-mm VAS through Day 5

Area under the curve (AUC, mm-hours) of change from baseline of dyspnea VAS through Day 5 (ITT analysis set)

	AUC baseline/Day 0 to Day 5		
Statistic	**Placebo (N=580)**	**Serelaxin (N=581)**	**Total (N=1161)**
n'	580	581	1161
Mean (SD)	2308 (3082)	2756 (2588)	2532 (2853)
95% CI	2057, 2559	2545, 2966	2368, 2696
Median	2436	2742	2583
Q1, Q3	1097, 4086	1170, 4239	1149, 4185
Min, Max	-11040, 10698	-7137, 11115	-11040, 11115
Mean difference		447.7	
95% CI		120.0, 775.4	
P-value [1]		0.0075	
P-value [2]		0.0819	

[1] P-value is based on a two-sided two sample t-test for serelaxin versus placebo comparing area under the curve (AUC, mm-hours) of change from baseline of dyspnea VAS from baseline to Day 5.
[2] P-values are based on two-sided Wilcoxon rank sum test for serelaxin versus placebo.

2. Moderately or markedly better patient-reported dyspnea relative to the start of study drug on the 7-point Likert scale at 6, 12 and 24 hours (at all 3 time-points).

Subjects with moderately or markedly better dyspnea by Likert scale at 6, 12 and 24 hours post-treatment (ITT analysis set)

	Subjects with moderately or markedly better dyspnea by Likert scale at 6, 12 and 24 hours [1]		
Statistic	**Placebo (N=580)**	**Serelaxin (N=581)**	**Total (N=1161)**
n'	580	581	1161
n (%)	150 (25.9)	156 (26.9)	306 (26.4)
95% CI (%)	22.30, 29.43	23.25, 30.45	23.82, 28.89
Odds ratio		1.05	
95% CI		0.81, 1.37	
P-value [2]		0.7024	

[1] Moderately or Markedly Better is defined as a score of +2 or +3 on the 7-point Likert scale.
[2] P-value is based on Chi-Square test for serelaxin versus placebo.

Secondary Outcome Result(s): Phase III- RELAX-AHF

1. Days alive and out of hospital through Day 60.

Days alive and out of hospital through Day 60 (ITT analysis set)

Statistic	Placebo (N=580)	Serelaxin (N=581)	Total (N=1161)
n'	580	581	1161
Mean (SD)	47.7 (12.11)	48.3 (11.59)	48.0 (11.85)
95% CI	46.7, 48.7	47.3, 49.2	47.3, 48.7
Median	52	52	52
Q1, Q3	45.0, 55.0	46.0, 55.0	46.0, 55.0
Min, Max	0, 60.0	0, 60.0	0, 60.0
Median difference [1]		0	
95% CI		-1.000, 0.000	
P-value [2]		0.3682	

n'= number of patients with measurement
[1] Hodges-Lehmann estimator of shift.
[2] P-value is based on two-sided Wilcoxon rank sum test for serelaxin versus placebo.

2. Cardiovascular death or re-hopsitalization due to heart failure or renal failure through Day 60

Cardiovascular death or re-hospitalization due to heart failure or renal failure through Day 60 (ITT analysis set)

	Statistic	Placebo (N=580)	Serelaxin (N=581)	Total (N=1161)
Number of Events	n (%)	75 (12.9)	76 (13.1)	151 (13.0)
Kaplan-Meier Estimates for Days to the First Event	Probability (95% CI)			
	Day 5	1.0 (0.5, 2.3)	0.7 (0.3, 1.8)	0.9 (0.5, 1.6)
	Day 14	3.5 (2.2, 5.3)	3.3 (2.1, 5.1)	3.4 (2.5, 4.6)
	Day 30	6.9 (5.1, 9.3)	7.5 (5.6, 9.9)	7.2 (5.8, 8.8)
	Day 60	13.0 (10.5, 16.1)	13.2 (10.7, 16.3)	13.1 (11.3, 15.2)
	P-value		0.8945	
Estimates by Cox Model	Hazard Ratio (95% CI) for serelaxin vs. placebo		1.02 (0.74, 1.41)	
Composite Event Components				

	Statistic	Placebo (N=580)	Serelaxin (N=581)	Total (N=1161)
Cardiovascular death	n (%)	27 (4.7)	19 (3.3)	46 (4.0)
	Probability (95% CI)			
	Day 60	4.7 (3.2, 6.8)	3.3 (2.1, 5.2)	4.0 (3.0, 5.3)
	P-value		0.2278	
	Hazard Ratio (95% CI)		0.70 (0.39, 1.26)	
HF/RF re-hospitalization	n (%)	50 (8.6)	60 (10.3)	110 (9.5)
	Probability (95% CI)			
	Day 60	9.0 (6.9, 11.7)	10.6 (8.3, 13.5)	9.8 (8.2, 11.7)
	P-value		0.3166	
	Hazard Ratio (95% CI)		1.21 (0.83, 1.76)	

n= number of patients with measurement
P-value is based on log-rank test for serelaxin versus placebo.
hazard ratio < 1.0 favors serelaxin

Additional Efficacy Outcome Results: Phase III- RELAX-AHF

3. Change from baseline in dyspnea score by VAS at 6, 12, and 24 hours; Day 5, and Day 14

Change From Baseline in Self-Reported Dyspnea Visual Analog Scale (VAS, mm) by Time Point
Population: Intent-to-Treat Set

		Value			Change From Baseline		
Time Point	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Baseline/Day 0	n'	578	575	1153			
	Mean (SD)	44.2 (19.86)	44.1 (20.12)	44.2 (19.98)			
	95% CI	42.6, 45.8	42.5, 45.8	43.0, 45.3			
	Median	45.0	46.0	45.0			
	Q1, Q3	30.0, 57.0	30.0, 57.0	30.0, 57.0			
	Min, Max	0, 100.0	0, 100.0	0, 100.0			
6 hr/Day 0	n'	578	575	1153	580	581	1161
	Mean (SD)	53.1 (21.36)	54.5 (20.27)	53.8 (20.83)	8.9 (16.06)	10.2 (16.93)	9.6 (16.51)
	95% CI	51.4, 54.9	52.8, 56.1	52.6, 55.0	7.6, 10.2	8.8, 11.6	8.6, 10.5
	Median	53.0	55.0	54.0	5.0	7.0	7.0
	Q1, Q3	40.0, 70.0	40.0, 70.0	40.0, 70.0	0, 16.0	0, 15.0	0, 15.0
	Min, Max	0, 100.0	0, 100.0	0, 100.0	-75.0, 89.0	-61.0, 95.0	-75.0, 95.0
	Mean difference					1.319	
	95% CI					-0.581, 3.220	
	P-value [1]					0.173	
	P-value [2]					0.423	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Change From Baseline in Self-Reported Dyspnea Visual Analog Scale (VAS, mm) by Time Point
Population: Intent-to-Treat Set

		Value			Change From Baseline		
Time Point	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
12 hr/Day 0	n'	578	575	1153	580	581	1161
	Mean (SD)	57.5 (22.24)	59.5 (20.28)	58.5 (21.30)	13.2 (19.72)	15.2 (18.90)	14.2 (19.33)
	95% CI	55.7, 59.3	57.8, 61.1	57.2, 59.7	11.6, 14.8	13.6, 16.7	13.1, 15.3
	Median	60.0	60.0	60.0	10.0	12.0	11.0
	Q1, Q3	45.0, 73.0	48.0, 75.0	46.0, 74.0	3.5, 21.0	4.0, 21.0	4.0, 21.0
	Min, Max	0, 100.0	0, 100.0	0, 100.0	-95.0, 88.0	-63.0, 95.0	-95.0, 95.0
	Mean difference					1.929	
	95% CI					-0.295, 4.153	
	P-value [1]					0.089	
	P-value [2]					0.186	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Change From Baseline in Self-Reported Dyspnea Visual Analog Scale (VAS, mm) by Time Point
Population: Intent-to-Treat Set

		Value			Change From Baseline		
Time Point	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
24 hr/Day 1	n'	578	575	1153	580	581	1161
	Mean (SD)	61.4 (24.04)	64.7 (20.73)	63.0 (22.50)	17.1 (25.05)	20.3 (21.73)	18.7 (23.49)
	95% CI	59.5, 63.4	63.0, 66.4	61.7, 64.3	15.1, 19.2	18.6, 22.1	17.4, 20.1
	Median	67.5	68.0	68.0	17.0	19.0	18.0
	Q1, Q3	50.0, 80.0	52.0, 80.0	50.0, 80.0	7.0, 30.0	9.0, 30.0	8.0, 30.0
	Min, Max	0, 100.0	0, 100.0	0, 100.0	-98.0, 90.0	-65.0, 95.0	-98.0, 95.0
	Mean difference					3.190	
	95% CI					0.489, 5.890	
	P-value [1]					0.021	
	P-value [2]					0.081	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Change From Baseline in Self-Reported Dyspnea Visual Analog Scale (VAS, mm) by Time Point
Population: Intent-to-Treat Set

		Value			Change From Baseline		
Time Point	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	579	575	1154	580	581	1161
	Mean (SD)	68.0 (29.60)	72.7 (24.76)	70.3 (27.38)	23.6 (33.30)	28.2 (27.85)	25.9 (30.77)
	95% CI	65.6, 70.4	70.6, 74.7	68.7, 71.9	20.9, 26.4	26.0, 30.5	24.2, 27.7
	Median	77.0	80.0	80.0	28.5	30.0	29.0
	Q1, Q3	60.0, 90.0	64.0, 90.0	61.0, 90.0	12.0, 44.0	15.0, 45.0	13.0, 45.0
	Min, Max	0, 100.0	0, 100.0	0, 100.0	-98.0, 95.0	-73.0, 95.0	-98.0, 95.0
	Mean difference					4.585	
	95% CI					1.051, 8.120	
	P-value [1]					0.011	
	P-value [2]					0.149	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Change From Baseline in Self-Reported Dyspnea Visual Analog Scale (VAS, mm) by Time Point
Population: Intent-to-Treat Set

		Value			Change From Baseline		
Time Point	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	579	576	1155	580	581	1161
	Mean (SD)	65.3 (32.73)	68.8 (29.69)	67.1 (31.29)	21.0 (36.50)	24.4 (32.37)	22.7 (34.52)
	95% CI	62.7, 68.0	66.4, 71.3	65.3, 68.9	18.0, 24.0	21.8, 27.1	20.7, 24.7
	Median	77.0	79.0	78.0	27.0	28.0	28.0
	Q1, Q3	53.0, 90.0	60.0, 90.0	58.0, 90.0	8.0, 45.0	10.0, 45.2	10.0, 45.0
	Min, Max	0, 100.0	0, 100.0	0, 100.0	-98.0, 96.0	-80.0, 94.0	-98.0, 96.0
	Mean difference					3.407	
	95% CI					-0.566, 7.379	
	P-value [1]					0.093	
	P-value [2]					0.440	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

4. Area under the curve representing the change in dyspnea VAS from baseline to Day 14, from Day 1 to Day 5, and from Day 1 to Day 14;

Area Under the Curve (AUC, mm-hr) of Change From Baseline of Dyspnea Visual Analog Scale (VAS) by Time Point
Population: Intent-to-Treat Set

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Baseline/Day 0 - Day 14	n'	580	581	1161
	Mean (SD)	7131 (10112)	8442 (8443)	7787 (9333)
	95% CI	6306, 7956	7754, 9130	7249, 8324
	Median	8150	8829	8439
	Q1, Q3	3381, 13257	3843, 13644	3546, 13494
	Min, Max	-32208, 31218	-21834, 30522	-32208, 31218
	Mean difference		1310.821	
	95% CI		238.135, 2383.508	
	P-value [1]		0.017	
	P-value [2]		0.174	
Day 1 - Day 5	n'	580	581	1161
	Mean (SD)	2033 (2772)	2436 (2290)	2234 (2549)
	95% CI	1806, 2259	2249, 2622	2088, 2381
	Median	2226	2448	2316
	Q1, Q3	1020, 3702	1020, 3816	1020, 3780
	Min, Max	-9408, 8844	-6336, 9120	-9408, 9120
Day 1 - Day 5 (continued)	Mean difference		403.281	
	95% CI		110.503, 696.060	
	P-value [1]		0.007	
	P-value [2]		0.098	

Day 1 - Day 14	n'	580	581	1161
	Mean (SD)	6855 (9846)	8122 (8199)	7489 (9078)
	95% CI	6053, 7658	7454, 8790	6967, 8012
	Median	7872	8508	8208
	Q1, Q3	3252, 12882	3684, 13212	3420, 13008
	Min, Max	-30576, 29364	-21456, 28980	-30576, 29364
	Mean difference		1266.407	
	95% CI		223.096, 2309.719	
	P-value [1]		0.017	
	P-value [2]		0.176	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

5. Markedly or moderately better dyspnea compared to baseline by Likert scale assessed separately at 6, 12, and 24 hours and then at Day 5 and at Day 14;

Subjects with Moderately or Markedly Better Dyspnea by Likert Scale By Time Point
Population: Intent-to-Treat Set

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
6 hr	n'	573 (100)	572 (100)	1145 (100)
Markedly better (3)	n (%)	50 (8.7)	56 (9.8)	106 (9.3)
Moderately better (2)	n (%)	130 (22.7)	149 (26.0)	279 (24.4)
Minimally better (1)	n (%)	215 (37.5)	214 (37.4)	429 (37.5)
No change (0)	n (%)	151 (26.4)	141 (24.7)	292 (25.5)
Minimally worse (-1)	n (%)	13 (2.3)	7 (1.2)	20 (1.7)
Moderately worse (-2)	n (%)	3 (0.5)	1 (0.2)	4 (0.3)
Markedly worse (-3)	n (%)	11 (1.9)	4 (0.7)	15 (1.3)
Markedly or Moderately Improvement In Dyspnea Score	n (%)	180 (31.4)	205 (35.8)	385 (33.6)
	Odds ratio		1.22	
	95% CI		0.95, 1.56	
	P-value [1]		0.113	
	n'	573	572	1145
	Mean (SD)	1.0 (1.13)	1.2 (1.03)	1.1 (1.08)
	95% CI	0.9, 1.1	1.1, 1.2	1.0, 1.1
	Median	1.0	1.0	1.0
	Q1, Q3	0, 2.0	0, 2.0	0, 2.0
	Min, Max	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [2]		0.000	
	95% CI		0.000, 0.000	
	P-value [3]		0.044	

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
12 hr	n'	574 (100)	572 (100)	1146 (100)
Markedly better (3)	n (%)	95 (16.6)	94 (16.4)	189 (16.5)
Moderately better (2)	n (%)	161 (28.0)	194 (33.9)	355 (31.0)
Minimally better (1)	n (%)	201 (35.0)	188 (32.9)	389 (33.9)
No change (0)	n (%)	94 (16.4)	83 (14.5)	177 (15.4)
Minimally worse (-1)	n (%)	5 (0.9)	7 (1.2)	12 (1.0)
Moderately worse (-2)	n (%)	1 (0.2)	2 (0.3)	3 (0.3)
Markedly worse (-3)	n (%)	17 (3.0)	4 (0.7)	21 (1.8)
Markedly or Moderately Improvement In Dyspnea Score	n (%)	256 (44.6)	288 (50.3)	544 (47.5)
	Odds ratio		1.26	
	95% CI		1.00, 1.59	
	P-value [1]		0.051	
	n'	574	572	1146
	Mean (SD)	1.3 (1.24)	1.5 (1.06)	1.4 (1.16)
	95% CI	1.2, 1.4	1.4, 1.5	1.3, 1.5
	Median	1.0	2.0	1.0
	Q1, Q3	1.0, 2.0	1.0, 2.0	1.0, 2.0
	Min, Max	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [2]		0.000	
	95% CI		0.000, 0.000	
	P-value [3]		0.076	

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
24 hr/Day 1	n'	574 (100)	573 (100)	1147 (100)
Markedly better (3)	n (%)	153 (26.7)	148 (25.8)	301 (26.2)
Moderately better (2)	n (%)	209 (36.4)	241 (42.1)	450 (39.2)
Minimally better (1)	n (%)	131 (22.8)	121 (21.1)	252 (22.0)
No change (0)	n (%)	45 (7.8)	42 (7.3)	87 (7.6)
Minimally worse (-1)	n (%)	3 (0.5)	9 (1.6)	12 (1.0)
Moderately worse (-2)	n (%)	1 (0.2)	2 (0.3)	3 (0.3)
Markedly worse (-3)	n (%)	32 (5.6)	10 (1.7)	42 (3.7)
Markedly or Moderately Improvement In Dyspnea Score	n (%)	362 (63.1)	389 (67.9)	751 (65.5)
	Odds ratio		1.24	
	95% CI		0.97, 1.58	
	P-value [1]		0.086	
	n'	574	573	1147
	Mean (SD)	1.6 (1.45)	1.8 (1.16)	1.7 (1.31)
	95% CI	1.5, 1.7	1.7, 1.8	1.6, 1.7
	Median	2.0	2.0	2.0
	Q1, Q3	1.0, 3.0	1.0, 3.0	1.0, 3.0
	Min, Max	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [2]		0.000	
	95% CI		0.000, 0.000	
	P-value [3]		0.249	

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	577 (100)	574 (100)	1151 (100)
Markedly better (3)	n (%)	290 (50.3)	307 (53.5)	597 (51.9)
Moderately better (2)	n (%)	156 (27.0)	162 (28.2)	318 (27.6)
Minimally better (1)	n (%)	47 (8.1)	47 (8.2)	94 (8.2)
No change (0)	n (%)	12 (2.1)	18 (3.1)	30 (2.6)
Minimally worse (-1)	n (%)	2 (0.3)	2 (0.3)	4 (0.3)
Moderately worse (-2)	n (%)	0	1 (0.2)	1 (<0.1)
Markedly worse (-3)	n (%)	70 (12.1)	37 (6.4)	107 (9.3)
Markedly or Moderately Improvement In Dyspnea Score	n (%)	446 (77.3)	469 (81.7)	915 (79.5)
	Odds ratio		1.31	
	95% CI		0.98, 1.75	
	P-value [1]		0.064	
	n'	577	574	1151
	Mean (SD)	1.8 (1.92)	2.1 (1.55)	1.9 (1.75)
	95% CI	1.6, 1.9	1.9, 2.2	1.8, 2.0
	Median	3.0	3.0	3.0
	Q1, Q3	2.0, 3.0	2.0, 3.0	2.0, 3.0
	Min, Max	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [2]		0.000	
	95% CI		0.000, 0.000	
	P-value [3]		0.087	

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	577 (100)	575 (100)	1152 (100)
Markedly better (3)	n (%)	297 (51.5)	296 (51.5)	593 (51.5)
Moderately better (2)	n (%)	127 (22.0)	137 (23.8)	264 (22.9)
Minimally better (1)	n (%)	43 (7.5)	41 (7.1)	84 (7.3)
No change (0)	n (%)	12 (2.1)	25 (4.3)	37 (3.2)
Minimally worse (-1)	n (%)	3 (0.5)	2 (0.3)	5 (0.4)
Moderately worse (-2)	n (%)	1 (0.2)	6 (1.0)	7 (0.6)
Markedly worse (-3)	n (%)	94 (16.3)	68 (11.8)	162 (14.1)
Markedly or Moderately Improvement In Dyspnea Score	n (%)	424 (73.5)	433 (75.3)	857 (74.4)
	Odds ratio		1.10	
	95% CI		0.84, 1.43	
	P-value [1]		0.479	
	n'	577	575	1152
	Mean (SD)	1.6 (2.15)	1.7 (1.96)	1.6 (2.06)
	95% CI	1.4, 1.7	1.6, 1.9	1.5, 1.8
	Median	3.0	3.0	3.0
	Q1, Q3	1.0, 3.0	2.0, 3.0	1.0, 3.0
	Min, Max	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [2]		0.000	
	95% CI		0.000, 0.000	
	P-value [3]		0.623	

Note: n' = number of patients with measurement
[1] P-values are based on Chi-Square test for RLX030 versus Placebo.
[2] Hodges-Lehmann estimator of shift.
[3] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

6. Time to moderately or markedly better self-assessed dyspnea on the 7-point Likert scale through Day 5;

Time to Moderately or Markedly Better Dyspnea Through Day 5
Population: Intent-to-Treat Set

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Cumulative Proportion With Moderately or Markedly Better Dyspnea	n'	580	581	1161
6 hr	n (%)	164 (28.3)	195 (33.6)	359 (30.9)
12 hr	n (%)	256 (44.1)	301 (51.8)	557 (48.0)
24 hr/Day 1	n (%)	363 (62.6)	412 (70.9)	775 (66.8)
48 hr/Day 2	n (%)	431 (74.3)	469 (80.7)	900 (77.5)
Day 3	n (%)	458 (79.0)	498 (85.7)	956 (82.3)
Day 4	n (%)	472 (81.4)	506 (87.1)	978 (84.2)
Day 5	n (%)	479 (82.6)	514 (88.5)	993 (85.5)
Time to Moderately or Markedly Better Dyspnea Through Day 5 (days)	n'	580	581	1161
	Mean (SD)	1.91 (2.108)	1.53 (1.867)	1.72 (2.000)
	95% CI	1.74, 2.08	1.38, 1.68	1.60, 1.83
	Median	1.00	0.50	1.00
	Q1, Q3	0.25, 3.00	0.25, 2.00	0.25, 2.00
	Min, Max	0.25, 6.00	0.25, 6.00	0.25, 6.00
	Median differences [1]		0.000	
	95% CI		0.000, 0.000	

Note: Subjects who do not report moderately or markedly better dyspnea by Day 5, or who die or have WHF by Day 5, are assigned a value of 6 days.
Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-value is based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

7. Kaplan-Meier Estimates of Time to worsening heart failure (WHF) through Day 5 and Day 14;

	Statistic		Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Number of Events	n (%)		91 (15.7)	66 (11.4)	157 (13.5)
Kaplan-Meier Estimates for Time to Worsening Heart Failure	Probability (95% CI)	Day 5	12.2 (9.8, 15.2)	6.7 (5.0, 9.1)	9.5 (7.9, 11.3)
		Day 14	15.7 (13.0, 18.9)	11.4 (9.1, 14.3)	13.6 (11.7, 15.7)
	P-value			0.024	
Estimates by Cox Model	Hazard Ratio (95% CI) (RLX030 vs Placebo)			0.70 (0.51, 0.96)	

Note: Subjects who died without a prior WHF event are assumed to have had worsening heart failure on the day of death. Worsening heart failure includes both WHF events and rehospitalizations for HF.
Note: P-value is based on log-rank test for RLX030 versus Placebo
Note: HR < 1.0 favors RLX030

8. Total doses of IV loop diuretics and oral loop diuretics through Day 5 or discharge if earlier;

Total Dose of IV Loop Diuretics in Furosemide Equivalents (mg) from Day 1 through Day 5 (Intent-to-Treat Set)

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Total Dose From Day 1 through Day 5 Or Discharge if Earlier	n'	572	570	1142
	Mean (SD)	213.0 (357.93)	161.3 (265.25)	187.2 (316.02)
	95% CI	183.6, 242.4	139.5, 183.1	168.9, 205.6
	Median	100.0	80.0	80.0
	Q1, Q3	20.0, 240.0	0, 200.0	0, 220.0
	Min, Max	0, 3300.0	0, 2100.0	0, 3300.0
	Mean difference		-51.705	
	95% CI		-88.294, -15.116	
	P-value [1]		0.00565	
	P-value [2]		0.00670	

Note: Calculation of Furosemide equivalents (mg) for Torsemide, Bumetanide and Ethacrynic Acid are actual dose (mg) multiplied by constant 2, 20 or 0.8, respectively.
Note: Each time point reflects medication use within the preceding 24 hours.
Note: Daily dose following a death imputed as the lesser of twice the last recorded dose or 160 mg.
Note: n = number of patients with measurement
Note: [1] P-value is based on t-test (equal variances) for RLX030 versus Placebo
[2] P-value is based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Total Dose of Oral Loop Diuretics in Furosemide Equivalents (mg) from Day 0 through Day 5 (Intent-to-Treat Set)

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Total Dose From Day 1 through Day 5 Or Discharge if Earlier	n'	572	570	1142
	Mean (SD)	182.7 (188.95)	192.7 (194.65)	187.7 (191.79)
	95% CI	167.2, 198.3	176.7, 208.7	176.6, 198.8
	Median	140.0	160.0	160.0
	Q1, Q3	40.0, 260.0	80.0, 240.0	60.0, 250.0
	Min, Max	0, 1800.0	0, 2250.0	0, 2250.0
	Mean difference		9.927	
	95% CI		-12.346, 32.201	
	P-value [1]		0.38204	
	P-value [2]		0.14446	

Note: Calculation of Furosemide equivalents (mg) for Torsemide, Bumetanide and Ethacrynic Acid are actual dose (mg) multiplied by constant 2, 20 or 0.8, respectively.
Note: Each time point reflects medication use within the preceding 24 hours.
Note: Daily dose following a death imputed as the lesser of twice the last recorded dose or 160 mg.
Note: n = number of patients with measurement
Note: [1] P-value is based on t-test (equal variances) for RLX030 versus Placebo
[2] P-value is based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

9. Change in body weight from randomization through Day 5 and Day 14;

Change in Body Weight (kg) From Baseline to Day 5 (Intent-to-Treat Set)

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	560	554	1114	560	554	1114
	Mean (SD)	79.6 (18.1)	79.1 (18.1)	79.3 (18.1)	-3.0 (3.3)	-2.7 (3.4)	-2.9 (3.3)
	95% CI	78.1, 81.1	77.6, 80.6	78.3, 80.4	-3.3, -2.7	-3.0, -2.4	-3.1, -2.7
	Median	77.8	77.2	77.6	-2.5	-2.1	-2.2
	Q1, Q3	66.8, 89.4	67.0, 89.1	67.0, 89.1	-4.8, -1.0	-4.0, -1.0	-4.5, -1.0
	Min, Max	34.0, 150.8	39.0, 146.4	34.0, 150.8	-22.7, 10.5	-17.7, 14.6	-22.7, 14.6
	Mean difference					0.276	
	95% CI					-0.116, 0.669	
	P-value [1]					0.167	
	P-value [2]					0.100	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Change in Body Weight (kg) From Baseline to Day 14 (Intent-to-Treat Set)

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	536	548	1084	536	548	1084
	Mean (SD)	79.3 (17.5)	78.8 (17.6)	79.0 (17.6)	-3.6 (4.4)	-3.0 (4.1)	-3.3 (4.3)
	95% CI	77.8, 80.8	77.3, 80.2	78.0, 80.1	-4.0, -3.2	-3.4, -2.7	-3.6, -3.1
	Median	78.0	77.0	77.7	-2.8	-2.4	-2.6
	Q1, Q3	67.0, 89.0	67.1, 88.7	67.0, 89.0	-5.7, -1.0	-4.5, -0.8	-5.0, -0.9
	Min, Max	36.0, 147.5	40.0, 144.3	36.0, 147.5	-31.1, 9.1	-23.0, 16.8	-31.1, 16.8
	Mean difference					0.588	
	95% CI					0.080, 1.095	
	P-value [1]					0.023	
	P-value [2]					0.038	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

10. Length of hospital stay;

Length of Hospital Stay
Population: Intent-to-Treat Set

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Length of Initial Hospital Stay (days)				
	n'	580	581	1161
	Mean (SD)	10.5 (9.59)	9.6 (9.08)	10.1 (9.34)
	95% CI	9.7, 11.3	8.9, 10.4	9.5, 10.6
	Median	8.0	7.0	8.0
	Q1, Q3	6.0, 12.0	5.0, 10.0	6.0, 11.0
	Min, Max	1.0, 62.0	1.0, 62.0	1.0, 62.0
	Median differences [1]		0.000	
	95% CI		0.000, 1.000	
	P-value [2]		0.039	

Note: Patients still in the hospital at Day 60 are censored at Day 60. Patients who died in-hospital are imputed as the maximum +1 day.
Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-value is based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

11. All cause death or re-hospitalization due to HF or RF through Day 60;

All Cause Death or Rehospitalization due to Heart Failure or Renal Failure Through Day 60
Population: Intent-to-Treat Set

	Statistic		Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Number of Events	n (%)		77 (13.3)	77 (13.3)	154 (13.3)
Kaplan-Meier Estimates for Time to the First Event Day	Probability (95% CI)	Day 5	1.0 (0.5, 2.3)	0.7 (0.3, 1.8)	0.9 (0.5, 1.6)
		Day 14	3.5 (2.2, 5.3)	3.5 (2.2, 5.3)	3.5 (2.5, 4.7)
		Day 30	6.9 (5.1, 9.3)	7.6 (5.7, 10.1)	7.3 (5.9, 8.9)
		Day 60	13.4 (10.8, 16.4)	13.4 (10.8, 16.4)	13.4 (11.5, 15.5)
	P-value			0.959	
Estimates by Cox Model	Hazard Ratio (95% CI) (RLX030 vs Placebo)			1.01 (0.74, 1.38)	
Composite Event Components	n (%)		29 (5.0)	20 (3.4)	49 (4.2)
All-cause death	Probability (95% CI)	Day 60	5.0 (3.5, 7.1)	3.5 (2.3, 5.3)	4.2 (3.2, 5.6)
	P-value			0.189	
	Hazard Ratio (95% CI) (RLX030 vs Placebo)			0.68 (0.39, 1.21)	
HF/RF rehospitalization	n (%)		50 (8.6)	60 (10.3)	110 (9.5)
	Probability (95% CI)	Day 60	9.0 (6.9, 11.7)	10.6 (8.3, 13.5)	9.8 (8.2, 11.7)
	P-value			0.317	

Note: P-value is based on log-rank test for RLX030 versus Placebo
Note: HR < 1.0 favors RLX030

12. Days alive and out of hospital through Day 30;

Days Alive and Out of Hospital Through Day 30
Population: Intent-to-Treat Set

Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Days Alive and Out of Hospital Through Day 30			
n'	580	581	1161
Mean (SD)	20.4 (6.83)	20.9 (6.44)	20.6 (6.64)
95% CI	19.8, 20.9	20.3, 21.4	20.2, 21.0
Median	23.0	23.0	23.0
Q1, Q3	17.0, 25.0	18.0, 25.0	17.0, 25.0
Min, Max	0, 30.0	0, 30.0	0, 30.0
Median differences [1]		0.000	
95% CI		-1.000, 0.000	
P-value [2]		0.29319	

Note: n' = number of patients with measurement
[1] Hodges-Lehmann estimator of shift.
[2] P-value is based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

13. Cardiovascular death through Day 180;

Cardiovascular Death Through Day 180
Population: Intent-to-Treat Set

	Statistic		Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Number of Events	n (%)		55 (9.5)	35 (6.0)	90 (7.8)
Kaplan-Meier Estimates for Time to Cardiovascular Death (days)	Probability (95% CI)	Day 5	0.9 (0.4, 2.1)	0.7 (0.3, 1.8)	0.8 (0.4, 1.5)
		Day 14	2.1 (1.2, 3.6)	0.9 (0.4, 2.1)	1.5 (0.9, 2.4)
		Day 30	3.3 (2.1, 5.1)	1.9 (1.1, 3.4)	2.6 (1.8, 3.7)
		Day 60	4.7 (3.2, 6.8)	3.3 (2.1, 5.1)	4.0 (3.0, 5.3)
		Day 180	9.6 (7.5, 12.3)	6.1 (4.4, 8.4)	7.9 (6.4, 9.6)
	P-value			0.028	
Estimates by Cox Model	Hazard Ratio (95% CI) (RLX030 vs Placebo)			0.63 (0.41, 0.96)	

Note: P-value is based on log-rank test for RLX030 versus Placebo
Note: HR < 1.0 favors RLX030

14. Change from baseline in HF signs and symptoms (patient-reported dyspnea (VAS) Day 5 and 14)

Subject-Reported General Well-Being by Visual Analog Scale (VAS, mm) by Time Point
Population: Intent-to-Treat Set

		Value			Change From Baseline		
Time Point	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Baseline/Day 0	n'	578	576	1154			
	Mean (SD)	45.0 (19.28)	44.1 (19.51)	44.5 (19.39)			
	95% CI	43.4, 46.5	42.5, 45.7	43.4, 45.7			
	Median	45.0	45.5	45.0			
	Q1, Q3	30.0, 59.0	30.0, 55.6	30.0, 57.0			
	Min, Max	0, 100.0	0, 100.0	0, 100.0			
Day 5	n'	579	576	1155	580	581	1161
	Mean (SD)	67.2 (29.55)	71.8 (25.07)	69.5 (27.49)	22.1 (32.79)	27.5 (27.65)	24.8 (30.43)
	95% CI	64.8, 69.6	69.8, 73.9	67.9, 71.1	19.5, 24.8	25.2, 29.8	23.1, 26.6
	Median	77.0	80.0	79.0	28.0	30.0	29.0
	Q1, Q3	60.0, 89.0	63.0, 90.0	60.0, 90.0	10.0, 43.0	13.0, 44.0	12.0, 43.0
	Min, Max	0, 100.0	0, 100.0	0, 100.0	-98.0, 93.0	-81.0, 95.0	-98.0, 95.0
	Mean difference					5.365	
	95% CI					1.872, 8.857	
	P-value [1]					0.003	
	P-value [2]					0.030	

Day 14	n'	579	576	1155	580	581	1161
	Mean (SD)	64.4 (32.54)	67.7 (29.54)	66.0 (31.11)	19.3 (35.69)	23.4 (31.43)	21.4 (33.67)
	95% CI	61.7, 67.0	65.3, 70.1	64.2, 67.8	16.4, 22.2	20.8, 25.9	19.4, 23.3
	Median	75.0	78.0	76.0	25.5	29.0	27.0
	Q1, Q3	54.0, 90.0	59.5, 90.0	55.0, 90.0	5.0, 43.0	10.0, 42.0	8.7, 43.0
	Min, Max	0, 100.0	0, 100.0	0, 100.0	-98.0, 93.0	-81.0, 93.0	-98.0, 93.0
	Mean difference					4.023	
	95% CI					0.151, 7.895	
	P-value [1]					0.042	
	P-value [2]					0.191	

Note: n' = number of patients with measurement
Note: [1] P-values are based on t-test (equal variances) for RLX030 versus Placebo
[2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

15. Subject-Reported General well-being using Likert scale (Day 5 and 14)

Subject-Reported General Well-Being by Likert Scale by Time Point
Population: Intent-to-Treat Set

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	577 (100)	573 (100)	1150 (100)
Markedly better (3)	n (%)	269 (46.6)	288 (50.3)	557 (48.4)
Moderately better (2)	n (%)	179 (31.0)	172 (30.0)	351 (30.5)
Minimally better (1)	n (%)	38 (6.6)	51 (8.9)	89 (7.7)
No change (0)	n (%)	17 (2.9)	17 (3.0)	34 (3.0)
Minimally worse (-1)	n (%)	3 (0.5)	5 (0.9)	8 (0.7)
Moderately worse (-2)	n (%)	0	0	0
Markedly worse (-3)	n (%)	71 (12.3)	40 (7.0)	111 (9.7)
	n'	577	573	1150
	Mean (SD)	1.7 (1.92)	2.0 (1.59)	1.8 (1.77)
	95% CI	1.6, 1.9	1.8, 2.1	1.7, 1.9
	Median	2.0	3.0	2.0
	Q1, Q3	2.0, 3.0	2.0, 3.0	2.0, 3.0
	Min, Max	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]		0.000	
	95% CI		0.000, 0.000	
	P-value [2]		0.103	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Subject-Reported General Well-Being by Likert Scale by Time Point
Population: Intent-to-Treat Set

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	577 (100)	575 (100)	1152 (100)
Markedly better (3)	n (%)	272 (47.1)	274 (47.7)	546 (47.4)
Moderately better (2)	n (%)	145 (25.1)	157 (27.3)	302 (26.2)
Minimally better (1)	n (%)	39 (6.8)	43 (7.5)	82 (7.1)
No change (0)	n (%)	18 (3.1)	20 (3.5)	38 (3.3)
Minimally worse (-1)	n (%)	3 (0.5)	5 (0.9)	8 (0.7)
Moderately worse (-2)	n (%)	4 (0.7)	6 (1.0)	10 (0.9)
Markedly worse (-3)	n (%)	96 (16.6)	70 (12.2)	166 (14.4)
	n'	577	575	1152
	Mean (SD)	1.5 (2.17)	1.7 (1.97)	1.6 (2.07)
	95% CI	1.3, 1.6	1.5, 1.8	1.4, 1.7
	Median	2.0	2.0	2.0
	Q1, Q3	1.0, 3.0	1.0, 3.0	1.0, 3.0
	Min, Max	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]		0.000	
	95% CI		0.000, 0.000	
	P-value [2]		0.427	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

16. Change from Baseline in Physician Assessment of Signs and Symptoms of Heart Failure – Dyspnea on Exertion (Day 5, 14 and 60)

Physician Assessment of Signs and Symptoms of Heart Failure: Dyspnea on Exertion
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Baseline/Day 0	n'	573 (100)	567 (100)	1140 (100)			
None (0)	n (%)	2 (0.3)	2 (0.4)	4 (0.4)			
Mild (1)	n (%)	27 (4.7)	26 (4.6)	53 (4.6)			
Moderate (2)	n (%)	168 (29.3)	166 (29.3)	334 (29.3)			
Severe (3)	n (%)	376 (65.6)	373 (65.8)	749 (65.7)			
	n'	573	567	1140			
	Mean (SD)	2.6 (0.60)	2.6 (0.59)	2.6 (0.59)			
	95% CI	2.6, 2.7	2.6, 2.7	2.6, 2.6			
	Median	3.0	3.0	3.0			
	Q1, Q3	2.0, 3.0	2.0, 3.0	2.0, 3.0			
	Min, Max	0, 3.0	0, 3.0	0, 3.0			

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Dyspnea on Exertion
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	579 (100)	576 (100)	1155 (100)			
None (0)	n (%)	176 (30.4)	183 (31.8)	359 (31.1)			
Mild (1)	n (%)	225 (38.9)	241 (41.8)	466 (40.3)			
Moderate (2)	n (%)	99 (17.1)	102 (17.7)	201 (17.4)			
Severe (3)	n (%)	79 (13.6)	50 (8.7)	129 (11.2)			
	n'	579	576	1155	580	581	1161
	Mean (SD)	1.1 (1.00)	1.0 (0.92)	1.1 (0.96)	-1.5 (1.07)	-1.5 (0.97)	-1.5 (1.02)
	95% CI	1.1, 1.2	1.0, 1.1	1.0, 1.1	-1.5, -1.4	-1.6, -1.5	-1.5, -1.4
	Median	1.0	1.0	1.0	-2.0	-2.0	-2.0
	Q1, Q3	0, 2.0	0, 2.0	0, 2.0	-2.0, -1.0	-2.0, -1.0	-2.0, -1.0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 1.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.285	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Dyspnea on Exertion
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	579 (100)	576 (100)	1155 (100)			
None (0)	n (%)	165 (28.5)	190 (33.0)	355 (30.7)			
Mild (1)	n (%)	231 (39.9)	212 (36.8)	443 (38.4)			
Moderate (2)	n (%)	85 (14.7)	91 (15.8)	176 (15.2)			
Severe (3)	n (%)	98 (16.9)	83 (14.4)	181 (15.7)			
	n'	579	576	1155	580	581	1161
	Mean (SD)	1.2 (1.03)	1.1 (1.03)	1.2 (1.03)	-1.4 (1.14)	-1.5 (1.08)	-1.4 (1.11)
	95% CI	1.1, 1.3	1.0, 1.2	1.1, 1.2	-1.5, -1.3	-1.5, -1.4	-1.5, -1.4
	Median	1.0	1.0	1.0	-2.0	-2.0	-2.0
	Q1, Q3	0, 2.0	0, 2.0	0, 2.0	-2.0, -1.0	-2.0, -1.0	-2.0, -1.0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 1.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.461	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Dyspnea on Exertion
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 60	n'	513 (100)	523 (100)	1036 (100)			
None (0)	n (%)	160 (31.2)	157 (30.0)	317 (30.6)			
Mild (1)	n (%)	167 (32.6)	187 (35.8)	354 (34.2)			
Moderate (2)	n (%)	70 (13.6)	70 (13.4)	140 (13.5)			
Severe (3)	n (%)	116 (22.6)	109 (20.8)	225 (21.7)			
	n'	513	523	1036	513	523	1036
	Mean (SD)	1.3 (1.13)	1.3 (1.10)	1.3 (1.11)	-1.3 (1.25)	-1.3 (1.17)	-1.3 (1.21)
	95% CI	1.2, 1.4	1.2, 1.3	1.2, 1.3	-1.4, -1.2	-1.4, -1.2	-1.4, -1.2
	Median	1.0	1.0	1.0	-1.0	-1.0	-1.0
	Q1, Q3	0, 2.0	0, 2.0	0, 2.0	-2.0, 0	-2.0, 0	-2.0, 0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 2.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.932	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

17. Change from Baseline in Physician Assessment of Signs and Symptoms of Heart Failure: Orthopnea (Day 5, 14 and 60)

Physician Assessment of Signs and Symptoms of Heart Failure: Orthopnea
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Baseline/Day 0	n'	578 (100)	576 (100)	1154 (100)			
None (0)	n (%)	24 (4.2)	24 (4.2)	48 (4.2)			
1 pillow (10 cm) (1)	n (%)	107 (18.5)	105 (18.2)	212 (18.4)			
2 pillows (20 cm) (2)	n (%)	226 (39.1)	213 (37.0)	439 (38.0)			
> 30 degrees (3)	n (%)	221 (38.2)	234 (40.6)	455 (39.4)			
	n'	578	576	1154			
	Mean (SD)	2.1 (0.85)	2.1 (0.86)	2.1 (0.85)			
	95% CI	2.0, 2.2	2.1, 2.2	2.1, 2.2			
	Median	2.0	2.0	2.0			
	Q1, Q3	2.0, 3.0	2.0, 3.0	2.0, 3.0			
	Min, Max	0, 3.0	0, 3.0	0, 3.0			

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Orthopnea
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	579 (100)	576 (100)	1155 (100)			
None (0)	n (%)	327 (56.5)	334 (58.0)	661 (57.2)			
1 pillow (10 cm) (1)	n (%)	116 (20.0)	134 (23.3)	250 (21.6)			
2 pillows (20 cm) (2)	n (%)	58 (10.0)	63 (10.9)	121 (10.5)			
> 30 degrees (3)	n (%)	78 (13.5)	45 (7.8)	123 (10.6)			
	n'	579	576	1155	580	581	1161
	Mean (SD)	0.8 (1.08)	0.7 (0.95)	0.7 (1.02)	-1.3 (1.18)	-1.4 (1.09)	-1.4 (1.14)
	95% CI	0.7, 0.9	0.6, 0.8	0.7, 0.8	-1.4, -1.2	-1.5, -1.4	-1.4, -1.3
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 1.0	0, 1.0	-2.0, -1.0	-2.0, -1.0	-2.0, -1.0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 2.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.075	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Orthopnea
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	579 (100)	577 (100)	1156 (100)			
None (0)	n (%)	323 (55.8)	325 (56.3)	648 (56.1)			
1 pillow (10 cm) (1)	n (%)	110 (19.0)	113 (19.6)	223 (19.3)			
2 pillows (20 cm) (2)	n (%)	46 (7.9)	60 (10.4)	106 (9.2)			
> 30 degrees (3)	n (%)	100 (17.3)	79 (13.7)	179 (15.5)			
	n'	579	577	1156	580	581	1161
	Mean (SD)	0.9 (1.15)	0.8 (1.09)	0.8 (1.12)	-1.2 (1.27)	-1.3 (1.22)	-1.3 (1.24)
	95% CI	0.8, 1.0	0.7, 0.9	0.8, 0.9	-1.3, -1.1	-1.4, -1.2	-1.3, -1.2
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 2.0	0, 1.0	0, 1.0	-2.0, 0	-2.0, 0	-2.0, 0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.444	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Orthopnea
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 60	n'	513 (100)	523 (100)	1036 (100)			
None (0)	n (%)	293 (57.1)	284 (54.3)	577 (55.7)			
1 pillow (10 cm) (1)	n (%)	75 (14.6)	81 (15.5)	156 (15.1)			
2 pillows (20 cm) (2)	n (%)	30 (5.8)	54 (10.3)	84 (8.1)			
> 30 degrees (3)	n (%)	115 (22.4)	104 (19.9)	219 (21.1)			
	n'	513	523	1036	513	523	1036
	Mean (SD)	0.9 (1.23)	1.0 (1.20)	0.9 (1.22)	-1.2 (1.33)	-1.2 (1.36)	-1.2 (1.34)
	95% CI	0.8, 1.0	0.9, 1.1	0.9, 1.0	-1.3, -1.1	-1.3, -1.1	-1.3, -1.1
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 2.0	0, 2.0	0, 2.0	-2.0, 0	-2.0, 0	-2.0, 0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.848	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

18. Change from Baseline in Physician Assessment of Signs and Symptoms of Heart Failure: Edema (Day 5, 14 and 60)

Physician Assessment of Signs and Symptoms of Heart Failure: Edema
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Baseline/Day 0	n'	577 (100)	577 (100)	1154 (100)			
0 (0)	n (%)	118 (20.5)	126 (21.8)	244 (21.1)			
1+ (1)	n (%)	168 (29.1)	171 (29.6)	339 (29.4)			
2+ (2)	n (%)	176 (30.5)	173 (30.0)	349 (30.2)			
3+ (3)	n (%)	115 (19.9)	107 (18.5)	222 (19.2)			
	n'	577	577	1154			
	Mean (SD)	1.5 (1.03)	1.5 (1.03)	1.5 (1.03)			
	95% CI	1.4, 1.6	1.4, 1.5	1.4, 1.5			
	Median	2.0	1.0	1.0			
	Q1, Q3	1.0, 2.0	1.0, 2.0	1.0, 2.0			
	Min, Max	0, 3.0	0, 3.0	0, 3.0			

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Edema
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	578 (100)	577 (100)	1155 (100)			
0 (0)	n (%)	381 (65.9)	428 (74.2)	809 (70.0)			
1+ (1)	n (%)	82 (14.2)	79 (13.7)	161 (13.9)			
2+ (2)	n (%)	39 (6.7)	26 (4.5)	65 (5.6)			
3+ (3)	n (%)	76 (13.1)	44 (7.6)	120 (10.4)			
	n'	578	577	1155	580	581	1161
	Mean (SD)	0.7 (1.07)	0.5 (0.89)	0.6 (0.99)	-0.8 (1.21)	-1.0 (1.13)	-0.9 (1.17)
	95% CI	0.6, 0.8	0.4, 0.5	0.5, 0.6	-0.9, -0.7	-1.1, -0.9	-1.0, -0.8
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 1.0	0, 1.0	-2.0, 0	-2.0, 0	-2.0, 0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.031	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Edema
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	579 (100)	577 (100)	1156 (100)			
0 (0)	n (%)	370 (63.9)	418 (72.4)	788 (68.2)			
1+ (1)	n (%)	86 (14.9)	67 (11.6)	153 (13.2)			
2+ (2)	n (%)	23 (4.0)	22 (3.8)	45 (3.9)			
3+ (3)	n (%)	100 (17.3)	70 (12.1)	170 (14.7)			
	n'	579	577	1156	580	581	1161
	Mean (SD)	0.7 (1.14)	0.6 (1.03)	0.7 (1.09)	-0.7 (1.32)	-0.9 (1.30)	-0.8 (1.31)
	95% CI	0.7, 0.8	0.5, 0.6	0.6, 0.7	-0.9, -0.6	-1.0, -0.8	-0.9, -0.7
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 1.0	0, 1.0	-2.0, 0	-2.0, 0	-2.0, 0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.070	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Edema
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 60	n'	513 (100)	523 (100)	1036 (100)			
0 (0)	n (%)	310 (60.4)	339 (64.8)	649 (62.6)			
1+ (1)	n (%)	76 (14.8)	62 (11.9)	138 (13.3)			
2+ (2)	n (%)	17 (3.3)	17 (3.3)	34 (3.3)			
3+ (3)	n (%)	110 (21.4)	105 (20.1)	215 (20.8)			
	n'	513	523	1036	513	523	1036
	Mean (SD)	0.9 (1.22)	0.8 (1.20)	0.8 (1.21)	-0.6 (1.40)	-0.7 (1.42)	-0.7 (1.41)
	95% CI	0.8, 1.0	0.7, 0.9	0.7, 0.9	-0.7, -0.5	-0.8, -0.6	-0.7, -0.6
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 1.0	0, 1.0	-2.0, 0	-2.0, 0	-2.0, 0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.409	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

19. Change from Baseline in Physician Assessment of Signs and Symptoms of Heart Failure: Rales (Day 5, 14 and 60)

Physician Assessment of Signs and Symptoms of Heart Failure: Rales
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Baseline/Day 0	n'	578 (100)	577 (100)	1155 (100)			
No rales (0)	n (%)	33 (5.7)	27 (4.7)	60 (5.2)			
Rales < 1/3 (1)	n (%)	238 (41.2)	229 (39.7)	467 (40.4)			
Rales 1/3-2/3 (2)	n (%)	264 (45.7)	264 (45.8)	528 (45.7)			
Rales > 2/3 (3)	n (%)	43 (7.4)	57 (9.9)	100 (8.7)			
	n'	578	577	1155			
	Mean (SD)	1.5 (0.72)	1.6 (0.73)	1.6 (0.72)			
	95% CI	1.5, 1.6	1.5, 1.7	1.5, 1.6			
	Median	2.0	2.0	2.0			
	Q1, Q3	1.0, 2.0	1.0, 2.0	1.0, 2.0			
	Min, Max	0, 3.0	0, 3.0	0, 3.0			

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Rales
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	579 (100)	577 (100)	1156 (100)			
No rales (0)	n (%)	431 (74.4)	453 (78.5)	884 (76.5)			
Rales < 1/3 (1)	n (%)	79 (13.6)	82 (14.2)	161 (13.9)			
Rales 1/3-2/3 (2)	n (%)	0	5 (0.9)	5 (0.4)			
Rales > 2/3 (3)	n (%)	69 (11.9)	37 (6.4)	106 (9.2)			
	n'	579	577	1156	580	581	1161
	Mean (SD)	0.5 (0.98)	0.4 (0.79)	0.4 (0.90)	-1.1 (1.15)	-1.2 (0.99)	-1.1 (1.07)
	95% CI	0.4, 0.6	0.3, 0.4	0.4, 0.5	-1.1, -1.0	-1.3, -1.2	-1.2, -1.1
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 0	0, 0	-2.0, -1.0	-2.0, -1.0	-2.0, -1.0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.020	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Rales
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	579 (100)	577 (100)	1156 (100)			
No rales (0)	n (%)	437 (75.5)	454 (78.7)	891 (77.1)			
Rales < 1/3 (1)	n (%)	46 (7.9)	53 (9.2)	99 (8.6)			
Rales 1/3-2/3 (2)	n (%)	2 (0.3)	2 (0.3)	4 (0.3)			
Rales > 2/3 (3)	n (%)	94 (16.2)	68 (11.8)	162 (14.0)			
	n'	579	577	1156	580	581	1161
	Mean (SD)	0.6 (1.11)	0.5 (0.98)	0.5 (1.05)	-1.0 (1.28)	-1.1 (1.15)	-1.1 (1.22)
	95% CI	0.5, 0.7	0.4, 0.5	0.5, 0.6	-1.1, -0.9	-1.2, -1.1	-1.1, -1.0
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 0	0, 0	0, 0	-2.0, -0.5	-2.0, -1.0	-2.0, -1.0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.052	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Rales
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 60	n'	513 (100)	523 (100)	1036 (100)			
No rales (0)	n (%)	370 (72.1)	390 (74.6)	760 (73.4)			
Rales < 1/3 (1)	n (%)	33 (6.4)	30 (5.7)	63 (6.1)			
Rales 1/3-2/3 (2)	n (%)	3 (0.6)	3 (0.6)	6 (0.6)			
Rales > 2/3 (3)	n (%)	107 (20.9)	100 (19.1)	207 (20.0)			
	n'	513	523	1036	513	523	1036
	Mean (SD)	0.7 (1.21)	0.6 (1.18)	0.7 (1.20)	-0.8 (1.41)	-1.0 (1.36)	-0.9 (1.38)
	95% CI	0.6, 0.8	0.5, 0.7	0.6, 0.7	-1.0, -0.7	-1.1, -0.9	-1.0, -0.8
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 1.0	0, 1.0	-2.0, 0	-2.0, 0	-2.0, 0
	Min, Max	0, 3.0	0, 3.0	0, 3.0	-3.0, 3.0	-3.0, 3.0	-3.0, 3.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.141	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

20. Physician Assessment of Signs and Symptoms of Heart Failure: Jugular venous pulse (Day 5, 14 and 60)

Physician Assessment of Signs and Symptoms of Heart Failure: Jugular venous pulse
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Baseline/Day 0	n'	566 (100)	560 (100)	1126 (100)			
< 6 cm (0)	n (%)	144 (25.4)	132 (23.6)	276 (24.5)			
6-10 cm (1)	n (%)	250 (44.2)	265 (47.3)	515 (45.7)			
> 10 cm (2)	n (%)	172 (30.4)	163 (29.1)	335 (29.8)			
	n'	566	560	1126			
	Mean (SD)	1.0 (0.75)	1.1 (0.72)	1.1 (0.74)			
	95% CI	1.0, 1.1	1.0, 1.1	1.0, 1.1			
	Median	1.0	1.0	1.0			
	Q1, Q3	0, 2.0	1.0, 2.0	1.0, 2.0			
	Min, Max	0, 2.0	0, 2.0	0, 2.0			

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Jugular venous pulse
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 5	n'	573 (100)	569 (100)	1142 (100)			
< 6 cm (0)	n (%)	421 (73.5)	440 (77.3)	861 (75.4)			
6-10 cm (1)	n (%)	74 (12.9)	79 (13.9)	153 (13.4)			
> 10 cm (2)	n (%)	78 (13.6)	50 (8.8)	128 (11.2)			
	n'	573	569	1142	580	581	1161
	Mean (SD)	0.4 (0.72)	0.3 (0.63)	0.4 (0.67)	-0.6 (0.94)	-0.7 (0.82)	-0.7 (0.89)
	95% CI	0.3, 0.5	0.3, 0.4	0.3, 0.4	-0.7, -0.6	-0.8, -0.7	-0.7, -0.6
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 0	0, 0	-1.0, 0	-1.0, 0	-1.0, 0
	Min, Max	0, 2.0	0, 2.0	0, 2.0	-2.0, 2.0	-2.0, 2.0	-2.0, 2.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.202	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Physician Assessment of Signs and Symptoms of Heart Failure: Jugular venous pulse
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 14	n'	574 (100)	570 (100)	1144 (100)			
< 6 cm (0)	n (%)	415 (72.3)	424 (74.4)	839 (73.3)			
6-10 cm (1)	n (%)	58 (10.1)	65 (11.4)	123 (10.8)			
> 10 cm (2)	n (%)	101 (17.6)	81 (14.2)	182 (15.9)			
	n'	574	570	1144	580	581	1161
	Mean (SD)	0.5 (0.78)	0.4 (0.72)	0.4 (0.75)	-0.6 (1.01)	-0.6 (0.92)	-0.6 (0.96)
	95% CI	0.4, 0.5	0.3, 0.5	0.4, 0.5	-0.7, -0.5	-0.7, -0.6	-0.7, -0.6
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 1.0	0, 1.0	-1.0, 0	-1.0, 0	-1.0, 0
	Min, Max	0, 2.0	0, 2.0	0, 2.0	-2.0, 2.0	-2.0, 2.0	-2.0, 2.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.499	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

Table 14.2.2.3

Physician Assessment of Signs and Symptoms of Heart Failure: Jugular venous pulse
Population: Intent-to-Treat Set

		Value			Change From Baseline		
	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Day 60	n'	508 (100)	519 (100)	1027 (100)			
< 6 cm (0)	n (%)	346 (68.1)	355 (68.4)	701 (68.3)			
6-10 cm (1)	n (%)	48 (9.4)	61 (11.8)	109 (10.6)			
> 10 cm (2)	n (%)	114 (22.4)	103 (19.8)	217 (21.1)			
	n'	508	519	1027	513	523	1036
	Mean (SD)	0.5 (0.84)	0.5 (0.80)	0.5 (0.82)	-0.5 (1.07)	-0.5 (1.02)	-0.5 (1.04)
	95% CI	0.5, 0.6	0.4, 0.6	0.5, 0.6	-0.6, -0.4	-0.6, -0.5	-0.6, -0.5
	Median	0	0	0	-1.0	-1.0	-1.0
	Q1, Q3	0, 1.0	0, 1.0	0, 1.0	-1.0, 0	-1.0, 0	-1.0, 0
	Min, Max	0, 2.0	0, 2.0	0, 2.0	-2.0, 2.0	-2.0, 2.0	-2.0, 2.0
	Median differences [1]					0.000	
	95% CI					0.000, 0.000	
	P-value [2]					0.577	

Note: n' = number of patients with measurement
Note: [1] Hodges-Lehmann estimator of shift.
Note: [2] P-values are based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

21. Days of the initial hospitalization from randomization spent in the intensive care unit/coronary care unit (ICU/CCU);

Days in the ICU/CCU
Population: Intent-to-Treat Set

	Statistic	Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Days in ICU/CCU				
	n'	578	574	1152
	Mean (SD)	3.9 (6.98)	3.5 (7.11)	3.7 (7.04)
	95% CI	3.3, 4.4	3.0, 4.1	3.3, 4.1
	Median	2.0	2.0	2.0
	Q1, Q3	1.0, 4.0	0, 4.0	0, 4.0
	Min, Max	0, 49.0	0, 49.0	0, 49.0
	Median differences [1]		0.000	
	95% CI		0.000, 0.000	
	P-value [2]		0.029	

Note: n' = number of patients with measurement
[1] Hodges-Lehmann estimator of shift.
[2] P-value is based on two-sided Wilcoxon rank sum test for RLX030 versus Placebo

22. All cause death through Day 30;

All Cause Death through Day 30
Population: Intent-to-Treat Set

	Statistic		Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Number of Events	n (%)		19 (3.3)	12 (2.1)	31 (2.7)
Kaplan-Meier Estimates for Time to Death (days)	Probability (95% CI)	Day 1	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
		Day 2	0.2 (0.0, 1.2)	0.0 (0.0, 0.0)	0.1 (0.0, 0.6)
		Day 3	0.5 (0.2, 1.6)	0.5 (0.2, 1.6)	0.5 (0.2, 1.1)
		Day 4	0.7 (0.3, 1.8)	0.5 (0.2, 1.6)	0.6 (0.3, 1.3)
		Day 5	0.9 (0.4, 2.1)	0.7 (0.3, 1.8)	0.8 (0.4, 1.5)
		Day 14	2.1 (1.2, 3.6)	1.0 (0.5, 2.3)	1.6 (1.0, 2.5)
		Day 30	3.3 (2.1, 5.1)	2.1 (1.2, 3.6)	2.7 (1.9, 3.8)
	P-value			0.202	
Estimates by Cox Model	Hazard Ratio (95% CI) (RLX030 vs Placebo)			0.63 (0.30, 1.29)	

Note: P-value is based on log-rank test for RLX030 versus Placebo
Note: HR < 1.0 favors RLX030

23. All cause death or worsening HF or re-hospitalization due to HF through Day 30;

All-Cause Death or Worsening Heart Failure or Rehospitalization for Heart Failure through Day 30
Population: Intent-to-Treat Set

	Statistic		Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Number of Events	n (%)		110 (19.0)	90 (15.5)	200 (17.2)
Kaplan-Meier Estimates for Time to the First Event Day	Probability (95% CI)	Day 1	6.2 (4.5, 8.5)	2.6 (1.6, 4.3)	4.4 (3.4, 5.7)
		Day 2	9.1 (7.1, 11.8)	3.3 (2.1, 5.1)	6.2 (5.0, 7.8)
		Day 3	10.5 (8.3, 13.3)	5.7 (4.1, 7.9)	8.1 (6.7, 9.8)
		Day 4	11.6 (9.2, 14.4)	6.2 (4.5, 8.5)	8.9 (7.4, 10.7)
		Day 5	12.2 (9.8, 15.2)	6.7 (5.0, 9.1)	9.5 (7.9, 11.3)
		Day 14	15.7 (13.0, 18.9)	11.4 (9.1, 14.3)	13.6 (11.7, 15.7)
		Day 30	19.0 (16.0, 22.4)	15.6 (12.9, 18.8)	17.3 (15.2, 19.6)
	P-value			0.089	
Estimates by Cox Model	Hazard Ratio (95% CI) (RLX030 vs Placebo)			0.79 (0.60, 1.04)	
Composite Event Components	n (%)		19 (3.3)	12 (2.1)	31 (2.7)
All-cause death	Probability (95% CI)	Day 30	3.3 (2.1, 5.1)	2.1 (1.2, 3.6)	2.7 (1.9, 3.8)
	P-value			0.202	
	Hazard Ratio (95% CI) (RLX030 vs Placebo)			0.63 (0.30, 1.29)	

Note: P-value is based on log-rank test for RLX030 versus Placebo
Note: HR < 1.0 favors RLX030

24. Cardiovascular death or re-hospitalization due to HF or RF through Day 30;

Cardiovascular Death or Rehospitalization due to Heart Failure or Renal Failure Through Day 30
Population: Intent-to-Treat Set

	Statistic		Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Number of Events	n (%)		40 (6.9)	43 (7.4)	83 (7.1)
Kaplan-Meier Estimates for Time to the First Event Day	Probability (95% CI)	Day 5	1.0 (0.5, 2.3)	0.7 (0.3, 1.8)	0.9 (0.5, 1.6)
		Day 14	3.5 (2.2, 5.3)	3.3 (2.1, 5.1)	3.4 (2.5, 4.6)
		Day 30	6.9 (5.1, 9.3)	7.5 (5.6, 9.9)	7.2 (5.8, 8.8)
	P-value			0.726	
Estimates by Cox Model	Hazard Ratio (95% CI) (RLX030 vs Placebo)			1.08 (0.70, 1.66)	
Composite Event Components	n (%)		19 (3.3)	11 (1.9)	30 (2.6)
CV death	Probability (95% CI)	Day 30	3.3 (2.1, 5.1)	1.9 (1.1, 3.4)	2.6 (1.8, 3.7)
	P-value			0.140	
	Hazard Ratio (95% CI) (RLX030 vs Placebo)			0.58 (0.27, 1.21)	
HF/RF rehospitalization	n (%)		21 (3.6)	33 (5.7)	54 (4.7)
	Probability (95% CI)	Day 30	3.7 (2.4, 5.7)	5.8 (4.2, 8.1)	4.8 (3.7, 6.2)
	P-value			0.098	
	Hazard Ratio (95% CI) (RLX030 vs Placebo)			1.58 (0.91, 2.73)	

Note: P-value is based on log-rank test for RLX030 versus Placebo
Note: HR < 1.0 favors RLX030

25. Cardiovascular death or re-hospitalization due to HF or RF through 30 days following discharge from the index hospitalization.

Cardiovascular Death or Rehospitalization due to Heart Failure or Renal Failure Through 30 Days after Discharge from the Index Hospitalization
Population: Intent-to-Treat Set

	Statistic		Placebo (N=580)	RLX030 (N=581)	Total (N=1161)
Number of Events	n (%)		42 (7.2)	50 (8.6)	92 (7.9)
Kaplan-Meier Estimates for Time to the First Event Day	Probability (95% CI)	Day 5	0.9 (0.4, 2.1)	2.0 (1.1, 3.5)	1.4 (0.9, 2.3)
		Day 14	3.7 (2.4, 5.6)	4.4 (3.0, 6.5)	4.1 (3.1, 5.4)
		Day 30	7.4 (5.6, 9.9)	8.9 (6.8, 11.6)	8.2 (6.7, 9.9)
	P-value			0.360	
Estimates by Cox Model	Hazard Ratio (95% CI) (RLX030 vs Placebo)			1.21 (0.80, 1.82)	
Composite Event Components	n (%)		11 (1.9)	7 (1.2)	18 (1.6)
CV death	Probability (95% CI)	Day 30	1.9 (1.1, 3.5)	1.2 (0.6, 2.6)	1.6 (1.0, 2.5)
	P-value			0.343	
	Hazard Ratio (95% CI) (RLX030 vs Placebo)			0.63 (0.25, 1.64)	
HF/RF rehospitalization	n (%)		31 (5.3)	44 (7.6)	75 (6.5)
	Probability (95% CI)	Day 30	5.6 (3.9, 7.8)	7.9 (5.9, 10.4)	6.7 (5.4, 8.3)
	P-value			0.115	

Note: P-value is based on log-rank test for RLX030 versus Placebo
Note: HR < 1.0 favors RLX030

26. Death from any cause through Day 180 (Safety population)

			Placebo (N=570)	Serelaxin (N=568)	Total (N=1138)
Number of Events	n (%)		64 (11.2)	41 (7.2)	105 (9.2)
Kaplan-Meier Estimates for Time to Death (days)	Probability (95% CI)	Day 5	0.9 (0.4, 2.1)	0.7 (0.3, 1.9)	0.8 (0.4, 1.5)
		Day 14	2.1 (1.2, 3.7)	1.1 (0.5, 2.3)	1.6 (1.0, 2.5)
		Day 30	3.3 (2.1, 5.2)	2.1 (1.2, 3.7)	2.7 (1.9, 3.9)
		Day 60	5.1 (3.6, 7.3)	3.5 (2.3, 5.4)	4.3 (3.3, 5.7)
		Day 180	11.3 (9.0, 14.2)	7.3 (5.4, 9.8)	9.3 (7.7, 11.1)
	P-value			0.019	
Estimates by Cox Model	Hazard Ratio (95% CI) (serelaxin vs. placebo)			0.63 (0.42, 0.93)	

Note: P-value is based on log-rank test for serelaxin versus placebo.
Note: hazard ratio < 1.0 favors serelaxin

Safety Results : PHASE II- Pre-RELAX-AHF

Pre-RELAX-AHF: Adverse Events by System Organ Class (Safety Population)

Adverse event SOC name MedDRA preferred term	Placebo N = [61]		Relaxin 10mcg/kg/day N = [40]		Relaxin 30mcg/kg/day N = [42]		Relaxin 100mcg/kg/day N = [38]		Relaxin 250mcg/kg/day N = [49]		Relaxin Total N = [230]	
	n	%	n	%	n	%	n	%	n	%	n	%
Subjects with at least one AE	47	77.0%	33	82.5%	25	59.5%	24	63.2%	25	51.0%	154	67.0%
Total number of AEs	124		91		58		71		67		411	
BLOOD AND LYMPHATIC SYSTEM DISORDERS	4	6.6%	1	2.5%	1	2.4%	1	2.6%	1	2.0%	8	3.5%
CARDIAC DISORDERS	21	34.4%	11	27.5%	9	21.4%	7	18.4%	6	12.2%	54	23.5%
CARDIAC FAILURE CONGESTIVE*	10	16.4%	5	12.5%	4	9.5%	7	18.4%	0	0.0%	26	11.3%
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1	1.6%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	2	0.9%
EAR AND LABYRINTH DISORDERS	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
ENDOCRINE DISORDERS	0	0.0%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
EYE DISORDERS	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
GASTROINTESTINAL DISORDERS	2	3.3%	7	17.5%	4	9.5%	4	10.5%	3	6.1%	20	8.7%
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS**	3	4.9%	6	15.0%	2	4.8%	4	10.5%	3	6.1%	18	7.8%
HEPATOBILIARY DISORDERS	0	0.0%	1	2.5%	0	0.0%	1	2.6%	1	2.0%	3	1.3%
IMMUNE SYSTEM DISORDERS	0	0.0%	0	0.0%	0	0.0%	1	2.6%	0	0.0%	1	0.4%
INFECTIONS AND INFESTATIONS	6	9.8%	2	5.0%	8	19.0%	6	15.8%	4	8.2%	26	11.3%
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2	3.3%	2	5.0%	1	2.4%	1	2.6%	0	0.0%	6	2.6%

AE=adverse event, MedDRA=Medical Dictionary for Regulatory Activities, N=number, SOC=system organ class
* Disease-Related Event
Note: Percentages are based on safety population (N)
A subject is counted only once within the specified SOC and preferred term
Dictionary - MedDRA version 10.0
Adverse Events are defined as AEs with onset after study drug initiation

Pre-RELAX-AHF: Adverse events by system organ class (Safety population) (cont.)

Adverse event SOC name MedDRA preferred term	Placebo N = [61] n	%	Relaxin 10mcg/kg/day N = [40] n	%	Relaxin 30mcg/kg/day N = [42] n	%	Relaxin 100mcg/kg/day N = [38] n	%	Relaxin 250mcg/kg/day N = [49] n	%	Total N = [230] n	%
INVESTIGATIONS	5	8.2%	2	5.0%	3	7.1%	5	13.2%	2	4.1%	17	7.4%
METABOLISM AND NUTRITION DISORDERS	8	13.1%	6	15.0%	2	4.8%	3	7.9%	6	12.2%	25	10.9%
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1	1.6%	5	12.5%	3	7.1%	1	2.6%	7	14.3%	17	7.4%
NERVOUS SYSTEM DISORDERS	7	11.5%	4	10.0%	5	11.9%	4	10.5%	3	6.1%	23	10.0%
PSYCHIATRIC DISORDERS	4	6.6%	0	0.0%	1	2.4%	2	5.3%	2	4.1%	9	3.9%
RENAL AND URINARY DISORDERS	5	8.2%	1	2.5%	2	4.8%	6	15.8%	1	2.0%	15	6.5%
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	0	0.0%	1	2.5%	0	0.0%	0	0.0%	1	2.0%	2	0.9%
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	6	9.8%	4	10.0%	2	4.8%	2	5.3%	4	8.2%	18	7.8%
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1	1.6%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	2	0.9%
VASCULAR DISORDERS	14	23.0%	15	37.5%	8	19.0%	7	18.4%	11	22.4%	55	23.9%
HYPOTENSION*	6	9.8%	9	22.5%	5	11.9%	4	10.5%	10	20.4%	34	14.8%

AE=adverse event, MedDRA=Medical Dictionary for Regulatory Activities, N=number, SOC=system organ class
* Disease-Related Event
Note: Percentages are based on safety population (N)
A subject is counted only once within the specified SOC and preferred term
Dictionary - MedDRA version 10.0
Adverse Events are defined as AEs with onset after study drug initiation

Pre-RELAX-AHF: Serious adverse events with outcome death (Safety population)

Adverse event SOC name MedDRA preferred term	Placebo N = [61] n	%	Relaxin 10mcg/kg/day N = [40] n	%	Relaxin 30mcg/kg/day N = [42] n	%	Relaxin 100mcg/kg/day N = [38] n	%	Relaxin 250mcg/kg/day N = [49] n	%	Total N = [230] n	%
Subjects with at least one SAE	4	6.6%	2	5.0%	1	2.4%	1	2.6%	2	4.1%	10	4.3%
Total number of SAEs	5		2		2		1		2		12	
CARDIAC DISORDERS	3	4.9%	1	2.5%	0	0.0%	0	0.0%	2	4.1%	6	2.6%
CARDIAC FAILURE ACUTE*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	1	2.0%	2	0.9%
CARDIAC FAILURE CHRONIC*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
CARDIAC FAILURE*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	1	2.0%	2	0.9%
VENTRICULAR FIBRILLATION*	0	0.0%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
INFECTIONS AND INFESTATIONS	0	0.0%	1	2.5%	1	2.4%	0	0.0%	0	0.0%	2	0.9%
PNEUMONIA	0	0.0%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	1	0.4%
PYELONEPHRITIS	0	0.0%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
NERVOUS SYSTEM DISORDERS	0	0.0%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	1	0.4%
CEREBROVASCULAR ACCIDENT	0	0.0%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	1	0.4%
RENAL AND URINARY DISORDERS	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
RENAL FAILURE*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1	1.6%	0	0.0%	0	0.0%	1	2.6%	0	0.0%	2	0.9%
ACUTE RESPIRATORY FAILURE*	0	0.0%	0	0.0%	0	0.0%	1	2.6%	0	0.0%	1	0.4%
RESPIRATORY DISTRESS*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%

MedDRA=Medical Dictionary for Regulatory Activities, N=number, SAE=serious adverse event, SOC=system organ class
* Disease-related event
Note: Percentages are based on safety population (N)
A subject is counted only once within the specified SOC and preferred term
Dictionary - MedDRA version 10.0
Adverse Events are defined as AEs with onset after study drug initiation

Pre-RELAX-AHF: Serious adverse events (Safety population)

Adverse event SOC name MedDRA preferred term	Placebo N = [61] n	%	Relaxin 10mcg/kg/day N = [40] n	%	Relaxin 30mcg/kg/day N = [42] n	%	Relaxin 100mcg/kg/day N = [38] n	%	Relaxin 250mcg/kg/day N = [49] n	%	Relaxin Total N = [230] n	%
Subjects with at least one SAE	10	16.4%	7	17.5%	7	16.7%	3	7.9%	8	16.3%	35	15.2%
Total number of SAEs	13		8		12		3		11		47	
CARDIAC DISORDERS	5	8.2%	3	7.5%	1	2.4%	0	0.0%	2	4.1%	11	4.8%
CARDIAC FAILURE ACUTE*	2	3.3%	1	2.5%	0	0.0%	0	0.0%	1	2.0%	4	1.7%
CARDIAC FAILURE CHRONIC*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
CARDIAC FAILURE CONGESTIVE*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
CARDIAC FAILURE*	1	1.6%	1	2.5%	1	2.4%	0	0.0%	1	2.0%	4	1.7%
VENTRICULAR FIBRILLATION*	0	0.0%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
GASTROINTESTINAL DISORDERS	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	2.0%	1	0.4%
COLITIS	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	2.0%	1	0.4%
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	0	0.0%	2	5.0%	0	0.0%	0	0.0%	1	2.0%	3	1.3%
NON-CARDIA CHEST PAIN*	0	0.0%	2	5.0%	0	0.0%	0	0.0%	1	2.0%	3	1.3%
INFECTIONS AND INFESTATIONS	1	1.6%	1	2.5%	5	11.9%	0	0.0%	3	6.1%	10	4.3%
BRONCHITIS	0	0.0%	0	0.0%	1	2.4%	0	0.0%	1	2.0%	2	0.9%
CELLULITIS	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	2.0%	1	0.4%
PNEUMONIA	1	1.6%	0	0.0%	3	7.1%	0	0.0%	0	0.0%	4	1.7%
PYELONEPHRITIS	0	0.0%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
URINARY TRACT INFECTION	0	0.0%	0	0.0%	1	2.4%	0	0.0%	1	2.0%	2	0.9%
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1	1.6%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	2	0.9%
FALL	0	0.0%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
HEAD INJURY	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%

MedDRA=Medical Dictionary for Regulatory Activities, N=number, SAE=serious adverse event, SOC=system organ class
* Disease-Related Event
Note: Percentages are based on safety population (N)
A subject is counted only once within the specified SOC and preferred term
Dictionary - MedDRA version 10.0
Adverse Events are defined as AEs with onset after study drug initiation

Pre-RELAX-AHF: Serious adverse events (Safety population) (cont.)

Adverse event SOC name MedDRA preferred term	Placebo N = [61] n	%	Relaxin 10mcg/kg/day N = [40] n	%	Relaxin 30mcg/kg/day N = [42] n	%	Relaxin 100mcg/kg/day N = [38] n	%	Relaxin 250mcg/kg/day N = [49] n	%	Total N = [230] n	%
METABOLISM AND NUTRITION DISORDERS	1	1.6%	1	2.5%	0	0.0%	0	0.0%	1	2.0%	3	1.3%
HYPERGLYCAEMIA	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
HYPERKALAEMIA*	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	2.0%	1	0.4%
HYPOGLYCAEMIA	0	0.0%	1	2.5%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	0.0%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	1	0.4%
PAIN IN EXTREMITY	0	0.0%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	1	0.4%
NERVOUS SYSTEM DISORDERS	1	1.6%	0	0.0%	3	7.1%	0	0.0%	0	0.0%	4	1.7%
CEREBROVASCULAR ACCIDENT	1	1.6%	0	0.0%	2	4.8%	0	0.0%	0	0.0%	3	1.3%
SYNCOPE	0	0.0%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	1	0.4%
RENAL AND URINARY DISORDERS	1	1.6%	0	0.0%	1	2.4%	2	5.3%	0	0.0%	4	1.7%
RENAL FAILURE*	1	1.6%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	2	0.9%
URINARY RETENTION	0	0.0%	0	0.0%	0	0.0%	2	5.3%	0	0.0%	2	0.9%
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	2	3.3%	0	0.0%	0	0.0%	1	2.6%	1	2.0%	4	1.7%
ACUTE PULMONARY OEDEMA*	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	2.0%	1	0.4%
ACUTE RESPIRATORY FAILURE*	0	0.0%	0	0.0%	0	0.0%	1	2.6%	0	0.0%	1	0.4%
DYSPNOEA*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
RESPIRATORY DISTRESS*	1	1.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	0.4%
VASCULAR DISORDERS	0	0.0%	0	0.0%	1	2.4%	0	0.0%	2	4.1%	3	1.3%
EMBOLISM	0	0.0%	0	0.0%	1	2.4%	0	0.0%	0	0.0%	1	0.4%
HYPOTENSION*	0	0.0%	0	0.0%	0	0.0%	0	0.0%	2	4.1%	2	0.9%

MedDRA=Medical Dictionary for Regulatory Activities, N=number, SAE=serious adverse event, SOC=system organ class
* Disease-Related Event
Note: Percentages are based on safety population (N)
A subject is counted only once within the specified SOC and preferred term
Dictionary - MedDRA version 10.0
Adverse Events are defined as AEs with onset after study drug initiation

Safety Results: Phase III- RELAX-AHF

RELAX-AHF: Incidence of adverse events by primary SOC from study drug initiation through Day 5 (Safety population)

System Organ Class	Placebo (N=570) n (%)	Serelaxin (N=568) n (%)	Total (N=1138) n (%)
Total number of AEs	**703**	**539**	**1242**
Patients with at least one AE	**305 (53.5)**	**280 (49.3)**	**585 (51.4)**
Blood and lymphatic system disorders	6 (1.1)	10 (1.8)	16 (1.4)
Cardiac disorders	90 (15.8)	70 (12.3)	160 (14.1)
Ear and labyrinth disorders	3 (0.5)	2 (0.4)	5 (0.4)
Endocrine disorders	3 (0.5)	1 (0.2)	4 (0.4)
Eye disorders	1 (0.2)	3 (0.5)	4 (0.4)
Gastrointestinal disorders	59 (10.4)	45 (7.9)	104 (9.1)
General disorders and administration site conditions	39 (6.8)	32 (5.6)	71 (6.2)
Hepatobiliary disorders	10 (1.8)	1 (0.2)	11 (1.0)
Infections and infestations	27 (4.7)	24 (4.2)	51 (4.5)
Injury, poisoning and procedural complications	0	3 (0.5)	3 (0.3)
Investigations	40 (7.0)	31 (5.5)	71 (6.2)
Metabolism and nutrition disorders	68 (11.9)	71 (12.5)	139 (12.2)
Musculoskeletal and connective tissue disorders	21 (3.7)	27 (4.8)	48 (4.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (0.4)	4 (0.7)	6 (0.5)
Nervous system disorders	45 (7.9)	30 (5.3)	75 (6.6)
Psychiatric disorders	31 (5.4)	22 (3.9)	53 (4.7)
Renal and urinary disorders	32 (5.6)	26 (4.6)	58 (5.1)
Reproductive system and breast disorders	0	2 (0.4)	2 (0.2)
Respiratory, thoracic and mediastinal disorders	59 (10.4)	31 (5.5)	90 (7.9)
Skin and subcutaneous tissue disorders	2 (0.4)	7 (1.2)	9 (0.8)
Vascular disorders	41 (7.2)	29 (5.1)	70 (6.2)

Both non-serious AEs and SAEs through Day 5 are included. Subjects are counted once per SOC.

RELAX-AHF: Incidence of adverse events (at least 1% in any treatment group) by preferred term from study drug initiation through Day 5 (Safety population)

Preferred Term	Placebo (N=570) n (%)	Serelaxin (N=568) n (%)	Total (N=1138) n (%)
Total number of AEs	**703**	**539**	**1242**
Patients with at least one AE	**305 (53.5)**	**280 (49.3)**	**585 (51.4)**
Hypokalaemia*	35 (6.1)	42 (7.4)	77 (6.8)
Cardiac failure congestive*	32 (5.6)	19 (3.3)	51 (4.5)
Headache	28 (4.9)	15 (2.6)	43 (3.8)
Blood creatinine increased*	22 (3.9)	14 (2.5)	36 (3.2)
Constipation	16 (2.8)	13 (2.3)	29 (2.5)
Dyspnoea*	23 (4.0)	11 (1.9)	34 (3.0)
Diarrhoea	20 (3.5)	11 (1.9)	31 (2.7)
Chest pain*	6 (1.1)	11 (1.9)	17 (1.5)
Urinary tract infection	5 (0.9)	11 (1.9)	16 (1.4)
Hypoglycaemia	16 (2.8)	10 (1.8)	26 (2.3)
Hypotension (symptomatic)	0	10 (1.8)	10 (0.9)
Renal failure*	23 (4.0)	9 (1.6)	32 (2.8)
Hyperuricaemia	10 (1.8)	8 (1.4)	18 (1.6)
Insomnia	9 (1.6)	8 (1.4)	17 (1.5)
Vomiting	7 (1.2)	8 (1.4)	15 (1.3)
Dizziness	11 (1.9)	7 (1.2)	18 (1.6)

Back pain	3 (0.5)	7 (1.2)	10 (0.9)
Anaemia	2 (0.4)	6 (1.1)	8 (0.7)
Non-cardiac chest pain*	6 (1.1)	6 (1.1)	12 (1.1)
Pain in extremity	6 (1.1)	6 (1.1)	12 (1.1)
Hyperglycaemia	3 (0.5)	6 (1.1)	9 (0.8)
Hypertension*	18 (3.2)	5 (0.9)	23 (2.0)
Nausea	11 (1.9)	5 (0.9)	16 (1.4)
Asthenia	10 (1.8)	5 (0.9)	15 (1.3)
Hypotension* (asymptomatic)	9 (1.6)	5 (0.9)	14 (1.2)
Ventricular tachycardia*	10 (1.8)	4 (0.7)	14 (1.2)
Cardiac failure*	9 (1.6)	4 (0.7)	13 (1.1)
Confusional state	8 (1.4)	4 (0.7)	12 (1.1)
Pneumonia	6 (1.1)	3 (0.5)	9 (0.8)
Cough	10 (1.8)	2 (0.4)	12 (1.1)

* Disease-related event (DRE).
Both non-serious AEs and SAEs through Day 5 are included. Subjects are counted once per preferred term.

RELAX-AHF: Serious Adverse Events and Deaths

SAEs with an outcome of death, other SAEs and AEs leading to permanent discontinuation of study drug (Safety population)

	Placebo (N=570) n (%)	Serelaxin (N=568) n (%)	Total (N=1138) n (%)
Patients with any AEs	320 (56.1)	305 (53.7)	625 (54.9)
SAE(s) with an outcome of death	15 (2.6)	10 (1.8)	25 (2.2)
SAE(s)	78 (13.7)	86 (15.1)	164 (14.4)
Discontinued study drug due to AE(s)	22 (3.9)	26 (4.6)	48 (4.2)
Discontinued study drug due to SAE(s)	3 (0.5)	5 (0.9)	8 (0.7)
Discontinued study drug due to drug-related SAE(s)	0	1 (0.2)	1 (<0.1)

Note: Incident AEs are considered those AEs with an onset date and time after the initiation of study drug.
The number of subjects with any AE includes all AEs and SAEs reported through Day 14.

Other Relevant Findings

Pre-RELAX-AHF: Summary of hematology: Hemoglobin (g/dL) Safety population

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Baseline						
N	56	37	34	34	41	202
Mean (SD)	13.10 (1.826)	13.13 (1.872)	13.04 (1.634)	13.01 (1.982)	12.91 (1.908)	13.04 (1.831)
95% CI	12.61 ; 13.59	12.51 ; 13.75	12.47 ; 13.61	12.32 ; 13.71	12.30 ; 13.51	12.79 ; 13.30
Median	13.35	13.20	13.40	13.05	13.10	13.20
Q1 ; Q3	11.65 ; 14.20	12.00 ; 14.50	12.00 ; 14.40	11.80 ; 14.30	12.00 ; 14.20	12.00 ; 14.30
Min ; Max	9.8 ; 17.9	7.5 ; 16.8	8.9 ; 15.2	8.3 ; 16.7	8.8 ; 16.7	7.5 ; 17.9
P-value (vs. Placebo)		0.943	0.874	0.832	0.612	
12 hours						
N	51	35	36	30	39	191
Mean (SD)	12.58 (1.861)	12.67 (1.776)	12.32 (1.776)	12.55 (2.175)	12.85 (1.681)	12.60 (1.837)
95% CI	12.05 ; 13.10	12.06 ; 13.28	11.72 ; 12.92	11.73 ; 13.36	12.31 ; 13.40	12.33 ; 12.86
Median	12.30	12.70	12.80	12.70	13.10	12.80
Q1 ; Q3	11.20 ; 13.90	11.50 ; 14.20	10.85 ; 13.60	11.20 ; 13.60	11.40 ; 14.20	11.30 ; 13.90
Min ; Max	8.6 ; 17.2	7.2 ; 15.9	8.4 ; 15.5	7.7 ; 16.5	9.6 ; 15.9	7.2 ; 17.2
P-value (vs. Placebo)		0.808	0.515	0.948	0.471	
12 hours (change from baseline)						
N	48	32	29	28	35	172
Mean (SD)	-0.48 (0.799)	-0.44 (0.770)	-0.39 (0.737)	-0.36 (0.760)	-0.28 (0.797)	-0.40 (0.771)
95% CI	-0.71 ; -0.25	-0.72 ; -0.16	-0.67 ; -0.11	-0.66 ; -0.07	-0.55 ; -0.00	-0.51 ; -0.28
Median	-0.50	-0.40	-0.60	-0.30	-0.30	-0.40
Q1 ; Q3	-0.90 ; 0.00	-0.90 ; -0.05	-0.70 ; 0.00	-0.70 ; 0.00	-1.00 ; 0.40	-0.90 ; 0.00
Min ; Max	-2.5 ; 1.2	-2.1 ; 1.3	-1.8 ; 1.0	-2.4 ; 1.2	-1.6 ; 1.7	-2.5 ; 1.7
P-value (vs. Placebo)		0.822	0.604	0.520	0.253	
24 hours						
N	51	36	38	31	37	193
Mean (SD)	12.84 (1.823)	12.90 (1.506)	12.47 (1.667)	12.70 (2.334)	12.88 (1.613)	12.76 (1.783)
95% CI	12.32 ; 13.35	12.39 ; 13.41	11.92 ; 13.02	11.85 ; 13.56	12.34 ; 13.41	12.51 ; 13.01
Median	12.70	12.80	12.85	12.30	13.00	12.90
Q1 ; Q3	11.30 ; 14.10	11.95 ; 14.10	11.40 ; 13.70	11.60 ; 14.40	12.00 ; 13.90	11.50 ; 14.10
Min ; Max	9.7 ; 16.9	9.6 ; 15.4	9.0 ; 15.3	7.9 ; 18.0	9.6 ; 16.1	7.9 ; 18.0
P-value (vs. Placebo)		0.862	0.333	0.776	0.915	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hemoglobin (g/dL) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
24 hours (change from baseline)						
N	47	34	31	31	31	174
Mean (SD)	-0.20 (0.792)	-0.42 (0.988)	-0.36 (0.738)	-0.25 (1.039)	-0.31 (0.838)	-0.30 (0.874)
95% CI	-0.43 ; 0.03	-0.77 ; -0.08	-0.63 ; -0.09	-0.63 ; 0.13	-0.61 ; 0.00	-0.43 ; -0.17
Median	0.10	-0.35	-0.30	-0.30	-0.40	-0.30
Q1 ; Q3	-1.00 ; 0.30	-1.30 ; 0.30	-0.80 ; 0.10	-0.80 ; 0.30	-0.90 ; 0.60	-0.90 ; 0.30
Min ; Max	-2.0 ; 1.8	-2.8 ; 1.8	-2.2 ; 1.2	-2.4 ; 3.1	-1.8 ; 1.0	-2.8 ; 3.1
P-value (vs. Placebo)		0.262	0.379	0.816	0.572	
48 hours						
N	50	37	33	35	39	194
Mean (SD)	12.90 (1.981)	12.74 (1.845)	12.32 (1.810)	12.75 (2.147)	12.93 (1.721)	12.75 (1.901)
95% CI	12.34 ; 13.47	12.12 ; 13.35	11.68 ; 12.97	12.02 ; 13.49	12.37 ; 13.48	12.48 ; 13.02
Median	13.15	13.00	12.60	13.10	12.80	13.00
Q1 ; Q3	11.30 ; 14.50	11.40 ; 13.60	10.60 ; 13.70	11.20 ; 14.00	11.70 ; 14.20	11.30 ; 14.00
Min ; Max	9.5 ; 16.7	7.5 ; 18.0	8.5 ; 15.1	7.9 ; 16.5	8.5 ; 15.9	7.5 ; 18.0
P-value (vs. Placebo)		0.690	0.182	0.745	0.953	
48 hours (change from baseline)						
N	46	34	28	31	33	172
Mean (SD)	0.03 (1.045)	-0.31 (1.161)	-0.42 (0.858)	-0.10 (0.898)	-0.13 (0.900)	-0.17 (0.991)
95% CI	-0.28 ; 0.34	-0.71 ; 0.10	-0.75 ; -0.09	-0.43 ; 0.23	-0.45 ; 0.19	-0.31 ; -0.02
Median	0.10	-0.40	-0.45	-0.20	-0.40	-0.30
Q1 ; Q3	-0.90 ; 0.90	-1.30 ; 0.40	-0.85 ; 0.20	-0.70 ; 0.50	-0.80 ; 0.50	-0.90 ; 0.50
Min ; Max	-2.3 ; 1.9	-2.0 ; 3.3	-2.3 ; 1.2	-2.0 ; 2.1	-1.5 ; 1.7	-2.3 ; 3.3
P-value (vs. Placebo)		0.178	0.061	0.569	0.475	
Day 3						
N	47	32	34	28	36	177
Mean (SD)	13.04 (1.842)	13.10 (2.102)	12.39 (1.685)	12.98 (2.086)	13.08 (1.939)	12.93 (1.919)
95% CI	12.50 ; 13.59	12.35 ; 13.86	11.80 ; 12.98	12.17 ; 13.79	12.42 ; 13.74	12.64 ; 13.21
Median	13.00	13.50	12.25	12.80	13.35	13.20
Q1 ; Q3	11.70 ; 14.10	11.70 ; 14.05	11.10 ; 13.50	12.00 ; 14.05	11.75 ; 14.30	11.70 ; 14.10
Min ; Max	9.1 ; 17.0	7.4 ; 19.0	8.6 ; 15.5	8.2 ; 16.3	8.2 ; 16.5	7.4 ; 19.0
P-value (vs. Placebo)		0.896	0.105	0.887	0.932	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hemoglobin (g/dL) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 3 (change from baseline)						
N	43	30	26	25	29	153
Mean (SD)	-0.00 (0.986)	-0.23 (1.202)	-0.18 (1.000)	0.03 (0.802)	-0.18 (1.152)	-0.11 (1.033)
95% CI	-0.31 ; 0.30	-0.68 ; 0.22	-0.59 ; 0.22	-0.30 ; 0.36	-0.61 ; 0.26	-0.27 ; 0.06
Median	-0.30	-0.25	-0.30	0.10	-0.40	-0.20
Q1 ; Q3	-0.70 ; 0.80	-1.20 ; 0.30	-0.90 ; 0.30	-0.30 ; 0.50	-0.90 ; 0.70	-0.80 ; 0.50
Min ; Max	-1.9 ; 2.5	-2.3 ; 4.3	-1.9 ; 2.3	-1.3 ; 2.1	-2.1 ; 1.7	-2.3 ; 4.3
P-value (vs. Placebo)		0.371	0.462	0.883	0.496	
Day 4						
N	44	26	31	26	34	161
Mean (SD)	13.18 (1.886)	13.23 (1.727)	12.76 (1.739)	12.35 (2.108)	12.79 (2.027)	12.89 (1.904)
95% CI	12.60 ; 13.75	12.54 ; 13.93	12.12 ; 13.40	11.50 ; 13.21	12.08 ; 13.49	12.59 ; 13.19
Median	13.00	13.40	13.00	12.30	13.50	13.00
Q1 ; Q3	12.30 ; 14.00	11.90 ; 14.50	11.20 ; 14.00	11.20 ; 13.70	10.80 ; 14.30	11.60 ; 14.10
Min ; Max	9.7 ; 18.4	10.0 ; 16.5	9.0 ; 15.5	8.3 ; 16.3	8.4 ; 15.9	8.3 ; 18.4
P-value (vs. Placebo)		0.896	0.337	0.097	0.384	
Day 4 (change from baseline)						
N	40	24	25	24	27	140
Mean (SD)	0.14 (0.956)	0.17 (1.191)	0.21 (0.988)	-0.23 (0.926)	-0.11 (1.128)	0.05 (1.033)
95% CI	-0.17 ; 0.44	-0.33 ; 0.68	-0.20 ; 0.62	-0.62 ; 0.16	-0.56 ; 0.33	-0.13 ; 0.22
Median	0.25	0.15	0.10	-0.20	-0.10	0.10
Q1 ; Q3	-0.55 ; 0.80	-0.55 ; 1.00	-0.40 ; 0.60	-0.90 ; 0.30	-1.20 ; 0.80	-0.70 ; 0.70
Min ; Max	-2.1 ; 1.9	-2.1 ; 2.6	-1.4 ; 2.5	-2.0 ; 2.0	-1.9 ; 1.7	-2.1 ; 2.6
P-value (vs. Placebo)		0.890	0.764	0.138	0.328	
Day 5						
N	50	33	38	33	43	197
Mean (SD)	12.92 (2.041)	13.21 (1.912)	12.83 (1.687)	12.97 (2.002)	12.74 (1.890)	12.92 (1.902)
95% CI	12.34 ; 13.50	12.53 ; 13.89	12.28 ; 13.39	12.26 ; 13.68	12.16 ; 13.32	12.65 ; 13.19
Median	13.05	13.50	13.00	13.00	12.90	13.00
Q1 ; Q3	11.50 ; 14.00	11.90 ; 14.20	11.80 ; 14.00	11.70 ; 14.50	11.50 ; 14.10	11.70 ; 14.20
Min ; Max	9.4 ; 18.7	9.6 ; 16.6	9.1 ; 15.9	9.1 ; 16.7	9.0 ; 15.7	9.0 ; 18.7
P-value (vs. Placebo)		0.512	0.833	0.915	0.669	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hemoglobin (g/dL) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 5 (change from baseline)						
N	46	32	30	29	36	173
Mean (SD)	-0.19 (1.050)	0.01 (1.146)	0.17 (1.066)	-0.05 (0.980)	-0.32 (1.098)	-0.10 (1.071)
95% CI	-0.51 ; 0.12	-0.40 ; 0.43	-0.23 ; 0.56	-0.42 ; 0.32	-0.69 ; 0.05	-0.26 ; 0.06
Median	-0.10	0.00	0.20	-0.10	-0.60	-0.10
Q1 ; Q3	-1.00 ; 0.40	-0.70 ; 0.60	-0.40 ; 0.60	-0.60 ; 0.50	-1.00 ; 0.45	-0.80 ; 0.50
Min ; Max	-3.0 ; 2.3	-2.0 ; 3.4	-2.1 ; 2.5	-2.2 ; 2.4	-2.4 ; 2.6	-3.0 ; 3.4
P-value (vs. Placebo)		0.414	0.151	0.561	0.591	
Day 6						
N	35	19	24	25	25	128
Mean (SD)	13.08 (1.693)	13.35 (1.618)	12.63 (1.742)	12.74 (2.150)	12.69 (1.783)	12.89 (1.797)
95% CI	12.50 ; 13.66	12.57 ; 14.13	11.89 ; 13.36	11.85 ; 13.63	11.96 ; 13.43	12.58 ; 13.21
Median	13.20	13.30	12.80	12.50	13.30	13.05
Q1 ; Q3	11.70 ; 13.80	12.50 ; 14.70	11.35 ; 14.20	11.50 ; 14.30	11.20 ; 14.30	11.55 ; 14.30
Min ; Max	9.9 ; 17.3	10.0 ; 15.7	9.0 ; 15.3	8.8 ; 16.7	9.6 ; 15.2	8.8 ; 17.3
P-value (vs. Placebo)		0.572	0.328	0.500	0.399	
Day 6 (change from baseline)						
N	33	17	20	23	20	113
Mean (SD)	0.01 (1.034)	0.26 (0.931)	0.07 (1.013)	-0.06 (1.054)	-0.17 (0.949)	0.01 (0.996)
95% CI	-0.35 ; 0.38	-0.22 ; 0.74	-0.40 ; 0.54	-0.52 ; 0.40	-0.61 ; 0.27	-0.17 ; 0.20
Median	-0.20	0.20	0.00	-0.10	-0.15	0.00
Q1 ; Q3	-0.60 ; 0.70	0.00 ; 1.00	-0.65 ; 0.80	-0.50 ; 0.60	-0.85 ; 0.55	-0.60 ; 0.70
Min ; Max	-2.2 ; 1.9	-1.5 ; 1.7	-2.1 ; 2.3	-2.6 ; 2.2	-2.0 ; 1.9	-2.6 ; 2.3
P-value (vs. Placebo)		0.413	0.843	0.798	0.525	
Day 7						
N	36	13	20	22	19	110
Mean (SD)	12.77 (1.621)	13.73 (2.100)	12.64 (1.698)	12.79 (2.175)	12.96 (2.217)	12.90 (1.913)
95% CI	12.22 ; 13.31	12.46 ; 15.00	11.85 ; 13.43	11.83 ; 13.76	11.89 ; 14.03	12.53 ; 13.26
Median	12.75	14.00	13.00	12.90	13.20	13.00
Q1 ; Q3	11.70 ; 13.80	12.70 ; 14.60	11.65 ; 13.85	11.40 ; 14.50	10.60 ; 14.50	11.60 ; 14.30
Min ; Max	9.7 ; 16.6	9.7 ; 17.5	9.5 ; 15.0	9.2 ; 16.0	10.0 ; 16.9	9.2 ; 17.5
P-value (vs. Placebo)		0.096	0.784	0.962	0.716	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hemoglobin (g/dL) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 7 (change from baseline)						
N	34	12	18	22	13	99
Mean (SD)	-0.05 (1.081)	0.52 (1.123)	0.06 (1.106)	-0.01 (1.176)	-0.24 (1.542)	0.02 (1.173)
95% CI	-0.42 ; 0.33	-0.19 ; 1.24	-0.49 ; 0.61	-0.53 ; 0.51	-1.17 ; 0.69	-0.21 ; 0.26
Median	0.20	0.35	0.00	-0.10	-0.40	0.00
Q1 ; Q3	-0.80 ; 0.70	-0.15 ; 1.25	-0.50 ; 0.70	-0.50 ; 0.90	-1.30 ; 0.60	-0.60 ; 0.80
Min ; Max	-2.1 ; 2.0	-1.3 ; 2.6	-3.1 ; 2.0	-2.9 ; 2.0	-2.3 ; 2.7	-3.1 ; 2.7
P-value (vs. Placebo)		0.126	0.748	0.902	0.633	
Day 14						
N	52	33	37	33	42	197
Mean (SD)	12.88 (1.770)	13.30 (1.444)	12.48 (1.584)	13.10 (2.136)	13.17 (1.922)	12.97 (1.792)
95% CI	12.39 ; 13.37	12.79 ; 13.81	11.95 ; 13.00	12.34 ; 13.86	12.57 ; 13.77	12.72 ; 13.22
Median	12.80	13.50	12.40	12.60	13.45	13.00
Q1 ; Q3	11.70 ; 13.95	12.20 ; 14.50	11.40 ; 13.70	11.40 ; 14.50	12.10 ; 14.40	11.80 ; 14.20
Min ; Max	9.7 ; 17.6	10.5 ; 15.6	8.9 ; 15.3	8.8 ; 17.6	8.8 ; 16.9	8.8 ; 17.6
P-value (vs. Placebo)		0.255	0.272	0.606	0.453	
Day 14 (change from baseline)						
N	48	30	29	29	34	170
Mean (SD)	-0.16 (0.977)	0.01 (1.057)	-0.28 (1.345)	0.23 (1.049)	-0.16 (1.281)	-0.08 (1.135)
95% CI	-0.44 ; 0.13	-0.38 ; 0.41	-0.79 ; 0.23	-0.17 ; 0.63	-0.60 ; 0.29	-0.25 ; 0.09
Median	0.20	0.15	0.00	0.20	-0.15	0.10
Q1 ; Q3	-0.85 ; 0.45	-0.60 ; 0.80	-0.80 ; 0.50	-0.30 ; 0.90	-1.10 ; 0.80	-0.80 ; 0.70
Min ; Max	-2.5 ; 2.0	-2.4 ; 1.7	-4.0 ; 2.1	-1.9 ; 2.3	-3.7 ; 2.4	-4.0 ; 2.4
P-value (vs. Placebo)		0.472	0.644	0.105	0.999	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hematocrit (%) Safety population

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Baseline						
N	56	37	34	34	41	202
Mean (SD)	41.34 (5.204)	42.50 (5.337)	41.49 (5.124)	41.83 (5.471)	41.24 (5.744)	41.64 (5.339)
95% CI	39.95 ; 42.73	40.72 ; 44.28	39.70 ; 43.27	39.92 ; 43.74	39.43 ; 43.05	40.90 ; 42.38
Median	41.65	42.30	42.95	41.90	42.40	42.30
Q1 ; Q3	37.80 ; 44.65	39.80 ; 45.80	38.90 ; 44.80	37.60 ; 45.60	37.30 ; 45.30	38.30 ; 45.30
Min ; Max	30.9 ; 54.5	30.4 ; 60.0	29.5 ; 49.3	30.5 ; 52.2	28.2 ; 52.2	28.2 ; 60.0
P-value (vs. Placebo)		0.301	0.898	0.675	0.929	
12 hours						
N	51	35	36	30	39	191
Mean (SD)	39.75 (5.282)	40.90 (4.952)	39.32 (5.412)	39.93 (6.238)	40.85 (4.538)	40.13 (5.251)
95% CI	38.26 ; 41.23	39.20 ; 42.60	37.49 ; 41.15	37.60 ; 42.26	39.38 ; 42.32	39.38 ; 40.88
Median	40.00	41.00	39.35	39.75	41.20	40.20
Q1 ; Q3	35.50 ; 43.40	37.60 ; 44.30	36.25 ; 43.70	36.20 ; 44.30	36.50 ; 44.70	36.60 ; 44.10
Min ; Max	29.4 ; 51.9	30.7 ; 53.9	26.6 ; 48.7	26.7 ; 51.9	32.4 ; 48.6	26.6 ; 53.9
P-value (vs. Placebo)		0.312	0.712	0.888	0.300	
12 hours (change from baseline)						
N	48	32	29	28	35	172
Mean (SD)	-1.62 (2.417)	-1.81 (2.547)	-1.47 (3.092)	-1.54 (2.465)	-0.89 (2.711)	-1.47 (2.620)
95% CI	-2.32 ; -0.91	-2.73 ; -0.89	-2.65 ; -0.29	-2.50 ; -0.59	-1.82 ; 0.04	-1.86 ; -1.07
Median	-1.55	-1.85	-0.50	-1.40	-1.30	-1.50
Q1 ; Q3	-2.85 ; -0.20	-3.70 ; 0.20	-3.00 ; 0.70	-3.50 ; 0.35	-3.50 ; 1.40	-3.50 ; 0.35
Min ; Max	-7.6 ; 3.6	-6.1 ; 4.8	-9.1 ; 3.5	-5.8 ; 4.1	-5.8 ; 4.2	-9.1 ; 4.8
P-value (vs. Placebo)		0.733	0.816	0.899	0.202	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hematocrit (%) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
24 hours						
N	51	36	38	31	37	193
Mean (SD)	40.61 (5.191)	41.26 (4.943)	39.73 (5.233)	40.85 (7.027)	41.07 (5.032)	40.68 (5.430)
95% CI	39.15 ; 42.07	39.59 ; 42.93	38.01 ; 41.45	38.27 ; 43.42	39.40 ; 42.75	39.91 ; 41.45
Median	41.70	41.70	41.00	40.90	41.70	41.50
Q1 ; Q3	36.70 ; 43.90	37.55 ; 44.80	37.10 ; 43.40	37.00 ; 47.30	37.60 ; 45.00	37.10 ; 43.90
Min ; Max	30.0 ; 53.2	30.7 ; 51.4	30.0 ; 50.0	27.8 ; 56.8	29.5 ; 53.0	27.8 ; 56.8
P-value (vs. Placebo)		0.559	0.433	0.861	0.675	
24 hours (change from baseline)						
N	47	34	31	31	31	174
Mean (SD)	-0.50 (2.649)	-1.66 (3.249)	-1.25 (2.448)	-0.85 (3.127)	-0.87 (3.336)	-0.99 (2.952)
95% CI	-1.28 ; 0.27	-2.79 ; -0.53	-2.15 ; -0.35	-2.00 ; 0.30	-2.10 ; 0.35	-1.43 ; -0.55
Median	-0.40	-2.10	-0.90	-0.60	-1.30	-0.90
Q1 ; Q3	-1.90 ; 1.10	-3.90 ; 0.30	-2.60 ; 0.70	-3.90 ; 0.80	-3.20 ; 1.20	-2.90 ; 0.90
Min ; Max	-7.5 ; 5.6	-10.6 ; 6.7	-6.5 ; 3.0	-6.0 ; 5.8	-6.0 ; 8.5	-10.6 ; 8.5
P-value (vs. Placebo)		0.082	0.215	0.603	0.588	
48 hours						
N	50	37	33	35	39	194
Mean (SD)	41.27 (6.020)	41.59 (5.501)	39.07 (5.682)	40.98 (6.634)	41.03 (5.002)	40.86 (5.795)
95% CI	39.56 ; 42.98	39.76 ; 43.43	37.05 ; 41.08	38.70 ; 43.26	39.41 ; 42.65	40.04 ; 41.68
Median	42.50	41.10	38.80	41.30	41.40	41.30
Q1 ; Q3	36.20 ; 46.20	38.90 ; 44.60	35.10 ; 43.10	36.50 ; 45.00	37.00 ; 45.20	36.80 ; 44.80
Min ; Max	31.5 ; 52.9	30.9 ; 61.1	27.2 ; 50.2	28.9 ; 53.7	30.6 ; 49.5	27.2 ; 61.1
P-value (vs. Placebo)		0.797	0.100	0.833	0.840	
48 hours (change from baseline)						
N	46	34	28	31	33	172
Mean (SD)	0.42 (3.074)	-0.57 (4.127)	-1.45 (3.546)	-0.25 (3.600)	-0.64 (3.454)	-0.40 (3.556)
95% CI	-0.50 ; 1.33	-2.01 ; 0.87	-2.83 ; -0.08	-1.57 ; 1.08	-1.86 ; 0.59	-0.94 ; 0.13
Median	0.90	-1.05	-1.25	-0.30	-1.10	-0.70
Q1 ; Q3	-1.60 ; 2.50	-3.10 ; 1.10	-3.30 ; 0.95	-2.80 ; 2.30	-2.20 ; 0.90	-2.85 ; 2.00
Min ; Max	-7.2 ; 6.3	-6.9 ; 11.8	-9.1 ; 5.3	-7.6 ; 8.3	-7.8 ; 7.2	-9.1 ; 11.8
P-value (vs. Placebo)		0.225	0.019	0.390	0.156	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hematocrit (%) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 3						
N	47	32	34	28	36	177
Mean (SD)	41.77 (5.156)	42.68 (6.090)	39.32 (4.597)	41.56 (6.263)	41.26 (5.640)	41.33 (5.564)
95% CI	40.26 ; 43.29	40.48 ; 44.87	37.72 ; 40.92	39.13 ; 43.99	39.35 ; 43.16	40.50 ; 42.15
Median	42.70	42.35	39.85	41.05	42.25	42.00
Q1 ; Q3	37.60 ; 45.30	37.55 ; 45.90	35.40 ; 43.00	38.25 ; 45.60	38.10 ; 45.15	37.60 ; 44.90
Min ; Max	32.1 ; 52.3	32.0 ; 62.5	29.4 ; 47.6	29.7 ; 52.4	25.5 ; 50.0	25.5 ; 62.5
P-value (vs. Placebo)		0.480	0.030	0.872	0.665	
Day 3 (change from baseline)						
N	43	30	26	25	29	153
Mean (SD)	0.41 (3.423)	-0.25 (4.183)	-1.03 (3.371)	0.36 (2.628)	-0.34 (3.976)	-0.12 (3.567)
95% CI	-0.65 ; 1.46	-1.81 ; 1.32	-2.40 ; 0.33	-0.73 ; 1.44	-1.86 ; 1.17	-0.69 ; 0.45
Median	0.00	-0.25	-1.20	-0.30	-1.40	-0.60
Q1 ; Q3	-2.70 ; 2.80	-2.70 ; 2.00	-2.70 ; 1.20	-1.70 ; 1.80	-2.50 ; 2.00	-2.50 ; 2.00
Min ; Max	-5.5 ; 8.9	-7.7 ; 13.2	-8.9 ; 5.1	-3.5 ; 6.5	-8.9 ; 7.6	-8.9 ; 13.2
P-value (vs. Placebo)		0.466	0.093	0.949	0.395	
Day 4						
N	44	26	31	26	34	161
Mean (SD)	42.35 (5.280)	42.03 (5.137)	40.69 (5.154)	39.80 (6.579)	40.33 (5.906)	41.14 (5.617)
95% CI	40.74 ; 43.95	39.96 ; 44.11	38.80 ; 42.58	37.14 ; 42.45	38.27 ; 42.39	40.27 ; 42.01
Median	42.90	42.25	41.60	39.50	41.80	41.70
Q1 ; Q3	38.20 ; 45.15	38.70 ; 46.00	35.00 ; 43.40	34.10 ; 43.60	34.70 ; 45.20	36.50 ; 44.80
Min ; Max	32.2 ; 56.8	31.8 ; 53.3	31.7 ; 49.7	29.1 ; 54.5	28.8 ; 50.6	28.8 ; 56.8
P-value (vs. Placebo)		0.809	0.180	0.079	0.117	
Day 4 (change from baseline)						
N	40	24	25	24	27	140
Mean (SD)	1.03 (3.603)	0.19 (3.496)	0.61 (3.185)	-0.74 (3.399)	-0.20 (3.756)	0.27 (3.518)
95% CI	-0.12 ; 2.18	-1.29 ; 1.66	-0.70 ; 1.93	-2.18 ; 0.69	-1.69 ; 1.28	-0.32 ; 0.86
Median	1.00	0.60	0.30	-0.90	0.40	0.40
Q1 ; Q3	-1.65 ; 3.35	-2.55 ; 2.80	-1.20 ; 2.70	-2.45 ; 0.55	-3.40 ; 3.40	-2.25 ; 2.75
Min ; Max	-5.4 ; 10.2	-6.5 ; 6.1	-5.6 ; 7.8	-6.1 ; 7.5	-7.6 ; 5.4	-7.6 ; 10.2
P-value (vs. Placebo)		0.363	0.636	0.056	0.181	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hematocrit (%) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 5						
N	50	33	38	33	43	197
Mean (SD)	41.28 (6.104)	42.46 (6.083)	40.86 (5.294)	41.77 (6.616)	40.37 (5.326)	41.28 (5.862)
95% CI	39.55 ; 43.02	40.31 ; 44.62	39.12 ; 42.60	39.42 ; 44.11	38.73 ; 42.01	40.46 ; 42.11
Median	40.90	42.00	41.05	41.60	41.90	41.50
Q1 ; Q3	36.40 ; 44.90	38.80 ; 46.50	37.20 ; 44.70	36.90 ; 47.30	36.20 ; 44.70	36.70 ; 44.90
Min ; Max	30.7 ; 61.0	33.5 ; 56.1	31.0 ; 52.3	30.4 ; 56.0	29.7 ; 48.2	29.7 ; 61.0
P-value (vs. Placebo)		0.391	0.735	0.734	0.448	
Day 5 (change from baseline)						
N	46	32	30	29	36	173
Mean (SD)	-0.32 (3.722)	0.07 (3.528)	0.74 (3.238)	0.14 (4.378)	-1.22 (3.886)	-0.18 (3.773)
95% CI	-1.43 ; 0.78	-1.21 ; 1.34	-0.47 ; 1.95	-1.53 ; 1.80	-2.53 ; 0.10	-0.74 ; 0.39
Median	-0.35	-0.15	0.75	-0.90	-0.95	-0.40
Q1 ; Q3	-3.40 ; 2.50	-2.30 ; 2.75	-1.20 ; 2.50	-2.90 ; 3.20	-3.75 ; 1.10	-2.70 ; 2.20
Min ; Max	-7.5 ; 7.7	-7.8 ; 7.4	-6.6 ; 8.6	-6.6 ; 9.0	-9.6 ; 8.9	-9.6 ; 9.0
P-value (vs. Placebo)		0.646	0.205	0.628	0.291	
Day 6						
N	35	19	24	25	25	128
Mean (SD)	41.45 (4.743)	43.05 (4.707)	39.81 (5.278)	41.03 (6.970)	40.70 (5.257)	41.15 (5.437)
95% CI	39.82 ; 43.08	40.78 ; 45.32	37.58 ; 42.04	38.15 ; 43.91	38.53 ; 42.87	40.20 ; 42.10
Median	40.80	42.30	41.45	39.40	41.90	41.45
Q1 ; Q3	37.60 ; 45.10	39.90 ; 47.00	35.80 ; 43.70	35.50 ; 47.30	37.90 ; 44.00	37.10 ; 45.00
Min ; Max	33.4 ; 52.0	34.4 ; 50.6	28.8 ; 49.9	30.3 ; 55.3	28.8 ; 49.4	28.8 ; 55.3
P-value (vs. Placebo)		0.241	0.217	0.781	0.564	
Day 6 (change from baseline)						
N	33	17	20	23	20	113
Mean (SD)	0.15 (3.302)	0.66 (2.742)	0.17 (3.304)	0.17 (4.077)	-0.10 (3.129)	0.19 (3.319)
95% CI	-1.02 ; 1.32	-0.75 ; 2.07	-1.37 ; 1.72	-1.59 ; 1.93	-1.56 ; 1.37	-0.43 ; 0.81
Median	0.40	0.30	0.45	-0.50	-0.30	0.10
Q1 ; Q3	-2.30 ; 2.60	-0.60 ; 2.20	-2.35 ; 2.75	-1.60 ; 1.80	-2.20 ; 1.70	-2.10 ; 2.40
Min ; Max	-7.0 ; 5.0	-5.0 ; 5.9	-6.2 ; 5.9	-6.2 ; 9.9	-4.7 ; 7.3	-7.0 ; 9.9
P-value (vs. Placebo)		0.587	0.978	0.983	0.792	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: Hematocrit (%) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 7						
N	36	13	20	22	19	110
Mean (SD)	40.79 (5.065)	44.98 (5.379)	39.94 (4.893)	41.20 (6.489)	41.83 (7.101)	41.39 (5.841)
95% CI	39.07 ; 42.50	41.73 ; 48.23	37.64 ; 42.23	38.32 ; 44.07	38.40 ; 45.25	40.28 ; 42.49
Median	41.45	46.20	40.20	39.75	43.00	41.40
Q1 ; Q3	36.35 ; 44.70	41.10 ; 48.90	37.85 ; 43.20	36.10 ; 47.60	34.60 ; 46.60	36.50 ; 46.20
Min ; Max	29.6 ; 50.2	36.0 ; 52.4	28.4 ; 48.0	31.0 ; 52.6	31.0 ; 55.3	28.4 ; 55.3
P-value (vs. Placebo)		0.015	0.545	0.790	0.532	
Day 7 (change from baseline)						
N	34	12	18	22	13	99
Mean (SD)	0.17 (3.796)	2.40 (3.691)	0.19 (3.463)	0.08 (3.891)	-0.29 (5.058)	0.36 (3.929)
95% CI	-1.15 ; 1.50	0.05 ; 4.75	-1.53 ; 1.92	-1.64 ; 1.81	-3.35 ; 2.76	-0.42 ; 1.15
Median	0.15	1.80	0.95	0.20	0.00	0.40
Q1 ; Q3	-2.50 ; 2.70	-0.50 ; 5.75	-2.00 ; 2.00	-2.50 ; 1.90	-4.70 ; 3.30	-2.10 ; 2.70
Min ; Max	-7.3 ; 9.4	-2.2 ; 9.1	-9.1 ; 6.5	-8.6 ; 7.2	-7.9 ; 8.5	-9.1 ; 9.4
P-value (vs. Placebo)		0.085	0.982	0.933	0.735	
Day 14						
N	52	33	37	33	42	197
Mean (SD)	40.67 (4.966)	42.79 (4.849)	39.81 (5.156)	41.97 (6.507)	41.67 (5.873)	41.29 (5.502)
95% CI	39.28 ; 42.05	41.07 ; 44.51	38.09 ; 41.53	39.66 ; 44.27	39.84 ; 43.50	40.52 ; 42.07
Median	40.45	42.40	40.10	40.90	42.50	40.90
Q1 ; Q3	37.25 ; 43.55	39.40 ; 45.40	36.00 ; 42.60	38.30 ; 46.50	38.80 ; 45.80	37.70 ; 45.00
Min ; Max	32.8 ; 53.6	33.5 ; 57.2	30.8 ; 48.9	30.2 ; 53.2	28.0 ; 52.1	28.0 ; 57.2
P-value (vs. Placebo)		0.056	0.433	0.300	0.369	
Day 14 (change from baseline)						
N	48	30	29	29	34	170
Mean (SD)	-0.54 (3.000)	0.02 (3.375)	-0.86 (4.851)	0.79 (3.690)	-0.49 (3.924)	-0.26 (3.730)
95% CI	-1.41 ; 0.33	-1.24 ; 1.28	-2.70 ; 0.99	-0.61 ; 2.20	-1.85 ; 0.88	-0.82 ; 0.31
Median	0.15	-0.10	-0.40	0.70	-0.55	-0.15
Q1 ; Q3	-2.40 ; 1.60	-1.90 ; 2.40	-4.10 ; 2.80	-1.50 ; 3.30	-3.20 ; 2.80	-2.50 ; 2.30
Min ; Max	-7.0 ; 6.3	-6.9 ; 6.2	-10.4 ; 7.1	-6.8 ; 8.2	-10.2 ; 7.3	-10.4 ; 8.2
P-value (vs. Placebo)		0.447	0.725	0.087	0.939	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: RBC (x10^12/L) Safety population

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Baseline						
N	56	37	34	34	41	202
Mean (SD)	4.339 (0.4757)	4.493 (0.6048)	4.381 (0.6016)	4.375 (0.5648)	4.329 (0.6103)	4.378 (0.5628)
95% CI	4.212 ; 4.466	4.291 ; 4.694	4.171 ; 4.591	4.178 ; 4.572	4.136 ; 4.522	4.300 ; 4.456
Median	4.330	4.470	4.445	4.345	4.350	4.390
Q1 ; Q3	3.965 ; 4.675	4.090 ; 4.840	4.000 ; 4.700	3.900 ; 4.730	3.910 ; 4.800	4.000 ; 4.710
Min ; Max	3.23 ; 5.74	3.27 ; 6.56	3.00 ; 5.72	3.23 ; 5.42	2.74 ; 5.62	2.74 ; 6.56
P-value (vs. Placebo)		0.175	0.715	0.744	0.929	
12 hours						
N	51	35	36	30	39	191
Mean (SD)	4.195 (0.5137)	4.325 (0.5370)	4.148 (0.6622)	4.159 (0.6138)	4.282 (0.5276)	4.222 (0.5653)
95% CI	4.051 ; 4.340	4.140 ; 4.509	3.923 ; 4.372	3.929 ; 4.388	4.111 ; 4.453	4.141 ; 4.303
Median	4.240	4.270	4.220	4.020	4.330	4.240
Q1 ; Q3	3.790 ; 4.540	3.890 ; 4.670	3.740 ; 4.660	3.790 ; 4.610	3.970 ; 4.660	3.820 ; 4.640
Min ; Max	3.03 ; 5.47	3.53 ; 6.02	2.82 ; 5.66	3.12 ; 5.68	3.17 ; 5.40	2.82 ; 6.02
P-value (vs. Placebo)		0.263	0.705	0.773	0.438	
12 hours (change from baseline)						
N	48	32	29	28	35	172
Mean (SD)	-0.152 (0.2539)	-0.156 (0.2537)	-0.126 (0.2570)	-0.136 (0.2115)	-0.061 (0.2493)	-0.127 (0.2467)
95% CI	-0.226 ; -0.079	-0.247 ; -0.064	-0.223 ; -0.028	-0.218 ; -0.054	-0.147 ; 0.025	-0.164 ; -0.090
Median	-0.135	-0.170	-0.180	-0.140	-0.080	-0.135
Q1 ; Q3	-0.320 ; 0.010	-0.280 ; -0.035	-0.330 ; 0.050	-0.300 ; -0.010	-0.270 ; 0.150	-0.295 ; 0.020
Min ; Max	-0.80 ; 0.38	-0.71 ; 0.39	-0.58 ; 0.31	-0.63 ; 0.30	-0.44 ; 0.43	-0.80 ; 0.43
P-value (vs. Placebo)		0.950	0.657	0.776	0.106	
24 hours						
N	51	36	38	31	37	193
Mean (SD)	4.279 (0.5108)	4.346 (0.4782)	4.199 (0.6235)	4.266 (0.6857)	4.260 (0.5226)	4.270 (0.5580)
95% CI	4.136 ; 4.423	4.184 ; 4.508	3.995 ; 4.404	4.015 ; 4.518	4.086 ; 4.435	4.191 ; 4.350
Median	4.220	4.325	4.265	4.180	4.230	4.250
Q1 ; Q3	3.930 ; 4.710	3.990 ; 4.670	3.690 ; 4.650	3.830 ; 4.640	3.980 ; 4.550	3.940 ; 4.640
Min ; Max	3.19 ; 5.36	3.31 ; 5.43	3.06 ; 5.77	3.24 ; 6.37	2.94 ; 5.45	2.94 ; 6.37
P-value (vs. Placebo)		0.541	0.508	0.922	0.864	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: RBC (x10^12/L) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
24 hours (change from baseline)						
N	47	34	31	31	31	174
Mean (SD)	-0.065 (0.2605)	-0.145 (0.3230)	-0.114 (0.2443)	-0.076 (0.3174)	-0.092 (0.2980)	-0.096 (0.2864)
95% CI	-0.141 ; 0.012	-0.258 ; -0.033	-0.203 ; -0.024	-0.192 ; 0.041	-0.202 ; 0.017	-0.139 ; -0.053
Median	-0.050	-0.130	-0.090	-0.040	-0.110	-0.090
Q1 ; Q3	-0.300 ; 0.140	-0.360 ; 0.090	-0.300 ; 0.050	-0.300 ; 0.130	-0.330 ; 0.200	-0.300 ; 0.110
Min ; Max	-0.73 ; 0.60	-1.13 ; 0.56	-0.58 ; 0.43	-0.64 ; 0.95	-0.59 ; 0.42	-1.13 ; 0.95
P-value (vs. Placebo)		0.218	0.409	0.866	0.667	
48 hours						
N	50	37	33	35	39	194
Mean (SD)	4.329 (0.6009)	4.354 (0.5400)	4.143 (0.6457)	4.280 (0.6037)	4.301 (0.5090)	4.288 (0.5791)
95% CI	4.158 ; 4.500	4.174 ; 4.534	3.914 ; 4.372	4.072 ; 4.487	4.136 ; 4.466	4.206 ; 4.370
Median	4.305	4.330	4.220	4.260	4.290	4.290
Q1 ; Q3	3.950 ; 4.750	3.990 ; 4.740	3.630 ; 4.540	3.760 ; 4.750	3.940 ; 4.630	3.900 ; 4.710
Min ; Max	3.13 ; 5.36	3.49 ; 6.00	2.85 ; 5.69	3.26 ; 5.65	3.13 ; 5.34	2.85 ; 6.00
P-value (vs. Placebo)		0.844	0.183	0.710	0.815	
48 hours (change from baseline)						
N	46	34	28	31	33	172
Mean (SD)	0.028 (0.3493)	-0.088 (0.3748)	-0.135 (0.2835)	-0.031 (0.2936)	-0.060 (0.2981)	-0.049 (0.3269)
95% CI	-0.075 ; 0.132	-0.218 ; 0.043	-0.245 ; -0.025	-0.139 ; 0.077	-0.166 ; 0.045	-0.098 ; 0.000
Median	0.100	-0.120	-0.125	-0.080	-0.100	-0.085
Q1 ; Q3	-0.240 ; 0.310	-0.360 ; 0.140	-0.305 ; 0.025	-0.250 ; 0.230	-0.270 ; 0.030	-0.300 ; 0.190
Min ; Max	-0.67 ; 0.62	-0.64 ; 1.06	-0.76 ; 0.46	-0.54 ; 0.64	-0.58 ; 0.56	-0.76 ; 1.06
P-value (vs. Placebo)		0.158	0.040	0.438	0.240	
Day 3						
N	47	32	34	28	36	177
Mean (SD)	4.351 (0.5072)	4.480 (0.6300)	4.144 (0.5471)	4.345 (0.5780)	4.278 (0.5815)	4.319 (0.5684)
95% CI	4.202 ; 4.500	4.253 ; 4.707	3.953 ; 4.335	4.121 ; 4.569	4.082 ; 4.475	4.235 ; 4.403
Median	4.360	4.415	4.180	4.310	4.325	4.320
Q1 ; Q3	3.940 ; 4.670	4.185 ; 4.625	3.740 ; 4.450	3.970 ; 4.810	3.955 ; 4.600	3.930 ; 4.650
Min ; Max	3.16 ; 5.32	3.51 ; 6.32	3.02 ; 5.45	3.25 ; 5.60	2.70 ; 5.52	2.70 ; 6.32
P-value (vs. Placebo)		0.319	0.083	0.961	0.544	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: RBC (x10^12/L) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 3 (change from baseline)						
N	43	30	26	25	29	153
Mean (SD)	0.024 (0.3420)	-0.060 (0.3979)	-0.074 (0.3353)	0.031 (0.2653)	-0.059 (0.3814)	-0.024 (0.3478)
95% CI	-0.082 ; 0.129	-0.208 ; 0.089	-0.210 ; 0.061	-0.078 ; 0.141	-0.204 ; 0.086	-0.079 ; 0.032
Median	-0.080	-0.055	-0.100	0.050	-0.070	-0.050
Q1 ; Q3	-0.180 ; 0.320	-0.260 ; 0.160	-0.240 ; 0.020	-0.130 ; 0.140	-0.360 ; 0.210	-0.230 ; 0.200
Min ; Max	-0.70 ; 0.76	-0.78 ; 1.38	-0.66 ; 0.79	-0.39 ; 0.62	-0.72 ; 0.66	-0.78 ; 1.38
P-value (vs. Placebo)		0.341	0.250	0.925	0.342	
Day 4						
N	44	26	31	26	34	161
Mean (SD)	4.458 (0.5705)	4.373 (0.4878)	4.305 (0.5428)	4.200 (0.6404)	4.212 (0.5991)	4.321 (0.5732)
95% CI	4.285 ; 4.632	4.176 ; 4.570	4.105 ; 4.504	3.941 ; 4.459	4.003 ; 4.421	4.232 ; 4.410
Median	4.490	4.495	4.370	4.045	4.315	4.350
Q1 ; Q3	4.020 ; 4.775	3.990 ; 4.680	3.930 ; 4.770	3.700 ; 4.720	3.900 ; 4.580	3.940 ; 4.680
Min ; Max	3.35 ; 5.98	3.46 ; 5.45	3.08 ; 5.39	3.18 ; 5.52	2.92 ; 5.52	2.92 ; 5.98
P-value (vs. Placebo)		0.525	0.245	0.085	0.068	
Day 4 (change from baseline)						
N	40	24	25	24	27	140
Mean (SD)	0.121 (0.4601)	0.004 (0.3508)	0.067 (0.3132)	-0.060 (0.3118)	-0.037 (0.3730)	0.030 (0.3792)
95% CI	-0.026 ; 0.268	-0.144 ; 0.152	-0.062 ; 0.196	-0.191 ; 0.072	-0.184 ; 0.111	-0.034 ; 0.093
Median	0.085	-0.035	0.040	-0.050	-0.030	0.030
Q1 ; Q3	-0.140 ; 0.370	-0.225 ; 0.275	-0.120 ; 0.130	-0.265 ; 0.090	-0.370 ; 0.300	-0.215 ; 0.235
Min ; Max	-0.69 ; 2.09	-0.68 ; 0.65	-0.47 ; 0.78	-0.68 ; 0.78	-0.63 ; 0.57	-0.69 ; 2.09
P-value (vs. Placebo)		0.290	0.608	0.095	0.144	
Day 5						
N	50	33	38	33	43	197
Mean (SD)	4.306 (0.5648)	4.457 (0.5738)	4.316 (0.5692)	4.338 (0.6425)	4.241 (0.5463)	4.324 (0.5750)
95% CI	4.146 ; 4.467	4.254 ; 4.660	4.129 ; 4.503	4.110 ; 4.565	4.073 ; 4.409	4.244 ; 4.405
Median	4.320	4.540	4.355	4.340	4.210	4.340
Q1 ; Q3	3.910 ; 4.630	4.110 ; 4.770	3.830 ; 4.680	3.820 ; 4.870	3.900 ; 4.690	3.910 ; 4.710
Min ; Max	3.00 ; 6.04	3.40 ; 6.08	3.12 ; 5.65	3.25 ; 5.46	2.95 ; 5.27	2.95 ; 6.08
P-value (vs. Placebo)		0.240	0.938	0.815	0.575	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: RBC (x10^12/L) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 5 (change from baseline)						
N	46	32	30	29	36	173
Mean (SD)	-0.051 (0.3605)	-0.009 (0.3585)	0.051 (0.3204)	0.002 (0.3453)	-0.116 (0.3812)	-0.030 (0.3557)
95% CI	-0.158 ; 0.056	-0.138 ; 0.121	-0.069 ; 0.171	-0.129 ; 0.133	-0.245 ; 0.013	-0.083 ; 0.023
Median	-0.040	0.020	0.095	-0.050	-0.125	-0.020
Q1 ; Q3	-0.210 ; 0.170	-0.195 ; 0.195	-0.170 ; 0.210	-0.230 ; 0.130	-0.325 ; 0.115	-0.240 ; 0.190
Min ; Max	-1.03 ; 0.84	-0.72 ; 0.88	-0.54 ; 0.78	-0.63 ; 0.79	-1.12 ; 0.88	-1.12 ; 0.88
P-value (vs. Placebo)		0.611	0.212	0.529	0.436	
Day 6						
N	35	19	24	25	25	128
Mean (SD)	4.373 (0.4559)	4.601 (0.5221)	4.225 (0.4847)	4.338 (0.6561)	4.280 (0.5529)	4.354 (0.5380)
95% CI	4.216 ; 4.529	4.349 ; 4.852	4.020 ; 4.429	4.068 ; 4.609	4.052 ; 4.509	4.260 ; 4.448
Median	4.310	4.630	4.370	4.130	4.440	4.360
Q1 ; Q3	4.120 ; 4.700	4.150 ; 5.030	3.960 ; 4.560	3.950 ; 5.050	3.970 ; 4.650	3.965 ; 4.770
Min ; Max	3.48 ; 5.33	3.80 ; 5.61	3.23 ; 4.89	3.22 ; 5.42	2.90 ; 5.10	2.90 ; 5.61
P-value (vs. Placebo)		0.101	0.237	0.813	0.483	
Day 6 (change from baseline)						
N	33	17	20	23	20	113
Mean (SD)	0.019 (0.3481)	0.101 (0.3237)	0.035 (0.3134)	0.009 (0.3534)	-0.029 (0.3409)	0.024 (0.3346)
95% CI	-0.104 ; 0.143	-0.066 ; 0.267	-0.112 ; 0.182	-0.144 ; 0.162	-0.189 ; 0.131	-0.039 ; 0.086
Median	0.060	0.120	-0.005	-0.010	-0.035	0.020
Q1 ; Q3	-0.220 ; 0.270	0.010 ; 0.310	-0.205 ; 0.220	-0.210 ; 0.220	-0.260 ; 0.200	-0.210 ; 0.230
Min ; Max	-0.73 ; 0.62	-0.54 ; 0.53	-0.55 ; 0.70	-0.71 ; 0.74	-0.76 ; 0.75	-0.76 ; 0.75
P-value (vs. Placebo)		0.428	0.870	0.911	0.623	
Day 7						
N	36	13	20	22	19	110
Mean (SD)	4.318 (0.5197)	4.805 (0.5907)	4.275 (0.5251)	4.397 (0.6396)	4.360 (0.7624)	4.391 (0.6106)
95% CI	4.143 ; 4.494	4.448 ; 5.162	4.029 ; 4.521	4.113 ; 4.680	3.993 ; 4.727	4.276 ; 4.506
Median	4.375	4.780	4.385	4.300	4.160	4.380
Q1 ; Q3	3.850 ; 4.650	4.580 ; 5.050	3.995 ; 4.670	3.840 ; 5.100	3.740 ; 4.970	3.920 ; 4.810
Min ; Max	3.10 ; 5.19	3.83 ; 5.87	3.14 ; 5.12	3.32 ; 5.38	3.19 ; 5.84	3.10 ; 5.87
P-value (vs. Placebo)		0.008	0.767	0.611	0.811	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

Pre-RELAX-AHF: Summary of hematology: RBC (x10^12/L) Safety population (Contd.)

	Placebo N=[61]	Relaxin 10mcg/kg/day N=[40]	Relaxin 30mcg/kg/day N=[42]	Relaxin 100mcg/kg/day N=[38]	Relaxin 250mcg/kg/day N=[49]	Total N=[230]
Day 7 (change from baseline)						
N	34	12	18	22	13	99
Mean (SD)	0.019 (0.3967)	0.200 (0.4019)	0.032 (0.3832)	0.030 (0.3749)	-0.044 (0.5174)	0.037 (0.4046)
95% CI	-0.120 ; 0.157	-0.055 ; 0.455	-0.158 ; 0.223	-0.137 ; 0.196	-0.357 ; 0.269	-0.043 ; 0.118
Median	0.055	0.210	-0.030	0.000	-0.040	0.000
Q1 ; Q3	-0.220 ; 0.340	-0.110 ; 0.500	-0.110 ; 0.270	-0.100 ; 0.280	-0.340 ; 0.260	-0.210 ; 0.310
Min ; Max	-0.83 ; 0.78	-0.37 ; 0.81	-1.05 ; 0.62	-0.88 ; 0.64	-0.78 ; 0.86	-1.05 ; 0.86
P-value (vs. Placebo)		0.182	0.907	0.920	0.659	
Day 14						
N	52	33	37	33	42	197
Mean (SD)	4.315 (0.4647)	4.533 (0.5979)	4.269 (0.6027)	4.389 (0.6125)	4.375 (0.6258)	4.368 (0.5760)
95% CI	4.185 ; 4.444	4.321 ; 4.745	4.068 ; 4.470	4.172 ; 4.607	4.180 ; 4.570	4.287 ; 4.449
Median	4.275	4.500	4.200	4.200	4.500	4.340
Q1 ; Q3	4.020 ; 4.570	4.060 ; 4.860	3.820 ; 4.720	4.000 ; 4.900	4.010 ; 4.650	4.000 ; 4.720
Min ; Max	3.23 ; 5.66	3.58 ; 6.05	3.23 ; 5.50	3.28 ; 5.54	2.93 ; 5.66	2.93 ; 6.05
P-value (vs. Placebo)		0.063	0.684	0.526	0.597	
Day 14 (change from baseline)						
N	48	30	29	29	34	170
Mean (SD)	-0.038 (0.3260)	0.015 (0.3797)	-0.037 (0.4544)	0.090 (0.3494)	-0.009 (0.4440)	-0.001 (0.3864)
95% CI	-0.132 ; 0.057	-0.127 ; 0.157	-0.209 ; 0.136	-0.043 ; 0.223	-0.164 ; 0.146	-0.059 ; 0.058
Median	-0.005	0.020	0.070	0.080	-0.010	0.035
Q1 ; Q3	-0.230 ; 0.155	-0.240 ; 0.330	-0.240 ; 0.270	-0.090 ; 0.320	-0.320 ; 0.300	-0.240 ; 0.290
Min ; Max	-0.77 ; 0.69	-0.72 ; 0.85	-1.42 ; 0.75	-0.59 ; 0.85	-1.13 ; 1.03	-1.42 ; 1.03
P-value (vs. Placebo)		0.518	0.992	0.111	0.742	

Note: P-values for comparisons versus Placebo are from two-sided two-sample t-test.

RELAX-AHF: Hematology Test Results: Hemoglobin (g/dL) - Actual and Change From Baseline Population: Safety

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 0	n'	543	541	1084			
	Mean (SD)	12.8 (1.81)	12.8 (1.91)	12.8 (1.86)			
	95% CI	12.6, 12.9	12.7, 13.0	12.7, 12.9			
	Median	12.7	12.8	12.8			
	Q1, Q3	11.5, 13.9	11.4, 14.3	11.4, 14.1			
	Min, Max	7.7, 18.8	5.6, 18.3	5.6, 18.8			
Day 1	n'	531	524	1055	510	507	1017
	Mean (SD)	12.7 (1.91)	12.6 (1.96)	12.7 (1.94)	0 (0.82)	-0.2 (0.87)	-0.1 (0.85)
	95% CI	12.6, 12.9	12.4, 12.8	12.6, 12.8	-0.1, 0.1	-0.3, -0.2	-0.2, -0.1
	Median	12.8	12.6	12.7	0	-0.3	-0.1
	Q1, Q3	11.4, 14.0	11.1, 14.0	11.3, 14.0	-0.5, 0.5	-0.8, 0.2	-0.6, 0.4
	Min, Max	8.1, 18.8	7.2, 18.8	7.2, 18.8	-4.7, 6.0	-4.6, 6.0	-4.7, 6.0
	Mean difference					-0.2456	
	95% CI					-0.3497, -0.1414	
	P-value[1]					<.001	
	P-value[2]					<.001	
Day 2	n'	523	514	1037	504	494	998
	Mean (SD)	13.0 (1.93)	12.7 (1.97)	12.8 (1.95)	0.2 (0.94)	-0.1 (0.96)	0 (0.96)
	95% CI	12.8, 13.1	12.5, 12.9	12.7, 13.0	0.1, 0.2	-0.2, -0.1	-0.1, 0.1
	Median	13.0	12.8	12.9	0.1	-0.2	0
	Q1, Q3	11.6, 14.3	11.2, 14.0	11.4, 14.2	-0.4, 0.7	-0.8, 0.4	-0.6, 0.6
	Min, Max	7.6, 18.0	7.6, 19.4	7.6, 19.4	-5.1, 4.1	-3.0, 4.3	-5.1, 4.3
	Mean difference					-0.2977	
	95% CI					-0.4153, -0.1801	
	P-value[1]					<.001	
	P-value[2]					<.001	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: Hemoglobin (g/dL) - Actual and Change From Baseline Population: Safety (Contd.)

Study Day	Statistic	Actual			Change From Baseline		
		Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 3	n'	477	463	940	460	449	909
	Mean (SD)	13.0 (1.86)	12.7 (2.06)	12.8 (1.96)	0.2 (1.00)	-0.1 (1.15)	0 (1.08)
	95% CI	12.8, 13.1	12.5, 12.9	12.7, 13.0	0.1, 0.3	-0.2, 0	0, 0.1
	Median	13.0	12.7	12.9	0.2	-0.1	0
	Q1, Q3	11.6, 14.2	11.2, 14.1	11.4, 14.2	-0.4, 0.8	-0.8, 0.5	-0.6, 0.7
	Min, Max	7.5, 18.2	4.2, 19.5	4.2, 19.5	-5.3, 3.9	-8.6, 6.3	-8.6, 6.3
	Mean difference					-0.2799	
	95% CI					-0.4198, -0.1400	
	P-value[1]					<.001	
	P-value[2]					<.001	
Day 4	n'	422	403	825	406	391	797
	Mean (SD)	12.9 (1.83)	12.8 (2.03)	12.9 (1.93)	0.1 (1.05)	0 (1.18)	0.1 (1.12)
	95% CI	12.7, 13.1	12.6, 13.0	12.8, 13.0	0, 0.2	-0.1, 0.1	0, 0.2
	Median	12.9	13.0	12.9	0.1	0	0
	Q1, Q3	11.6, 14.3	11.4, 14.3	11.5, 14.3	-0.5, 0.8	-0.7, 0.7	-0.6, 0.7
	Min, Max	7.6, 18.2	7.7, 18.6	7.6, 18.6	-5.8, 4.2	-3.3, 7.7	-5.8, 7.7
	Mean difference					-0.1011	
	95% CI					-0.2561, 0.0539	
	P-value[1]					0.201	
	P-value[2]					0.017	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: Hemoglobin (g/dL) - Actual and Change From Baseline Population: Safety (Contd.)

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 5	n'	511	514	1025	492	493	985
	Mean (SD)	13.0 (1.90)	12.9 (1.98)	12.9 (1.94)	0.1 (1.05)	0.1 (1.15)	0.1 (1.10)
	95% CI	12.8, 13.1	12.7, 13.0	12.8, 13.0	0.1, 0.2	0, 0.2	0, 0.2
	Median	13.0	12.9	13.0	0.1	-0.1	0
	Q1, Q3	11.6, 14.2	11.5, 14.3	11.5, 14.3	-0.5, 0.8	-0.7, 0.8	-0.6, 0.8
	Min, Max	8.3, 18.7	8.0, 19.6	8.0, 19.6	-5.8, 3.9	-3.1, 6.7	-5.8, 6.7
	Mean difference					-0.0733	
	95% CI					-0.2106, 0.0640	
	P-value[1]					0.295	
	P-value[2]					0.037	
Day 14	n'	493	514	1007	473	494	967
	Mean (SD)	13.0 (1.83)	12.9 (1.96)	12.9 (1.90)	0.2 (1.23)	0.1 (1.29)	0.1 (1.26)
	95% CI	12.8, 13.1	12.7, 13.1	12.8, 13.0	0.1, 0.3	0, 0.2	0.1, 0.2
	Median	12.9	12.9	12.9	0.2	0.1	0.2
	Q1, Q3	11.7, 14.2	11.5, 14.3	11.5, 14.3	-0.6, 0.9	-0.6, 0.8	-0.6, 0.9
	Min, Max	8.8, 18.9	6.0, 17.4	6.0, 18.9	-4.9, 4.9	-8.0, 6.6	-8.0, 6.6
	Mean difference					-0.1025	
	95% CI					-0.2616, 0.0565	
	P-value[1]					0.206	
	P-value[2]					0.309	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: Hemoglobin (g/dL) - Actual and Change From Baseline Population: Safety (Contd.)

Study Day	Statistic	Actual			Change From Baseline		
		Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 60	n'	467	464	931	444	441	885
	Mean (SD)	12.7 (1.62)	12.7 (1.77)	12.7 (1.70)	-0.1 (1.39)	-0.2 (1.35)	-0.1 (1.37)
	95% CI	12.6, 12.9	12.6, 12.9	12.6, 12.8	-0.2, 0	-0.3, 0	-0.2, 0
	Median	12.6	12.8	12.7	0	-0.1	-0.1
	Q1, Q3	11.6, 13.8	11.4, 13.9	11.5, 13.9	-0.9, 0.8	-0.9, 0.6	-0.9, 0.7
	Min, Max	7.9, 17.1	7.9, 17.3	7.9, 17.3	-5.7, 4.7	-7.7, 5.0	-7.7, 5.0
	Mean difference					-0.0721	
	95% CI					-0.2531, 0.1089	
	P-value[1]					0.435	
	P-value[2]					0.364	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: HCT (RATIO) - Actual and Change From Baseline Population: Safety

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 0	n'	543	541	1084			
	Mean (SD)	0.413 (0.0557)	0.414 (0.0583)	0.414 (0.0570)			
	95% CI	0.408, 0.418	0.409, 0.419	0.410, 0.417			
	Median	0.412	0.415	0.413			
	Q1, Q3	0.372, 0.450	0.377, 0.452	0.374, 0.451			
	Min, Max	0.244, 0.604	0.183, 0.581	0.183, 0.604			
Day 1	n'	531	524	1055	510	507	1017
	Mean (SD)	0.412 (0.0609)	0.407 (0.0607)	0.409 (0.0608)	-0.001 (0.0323)	-0.009 (0.0313)	-0.005 (0.0320)
	95% CI	0.407, 0.417	0.402, 0.412	0.406, 0.413	-0.004, 0.001	-0.011, -0.006	-0.007, -0.003
	Median	0.411	0.406	0.409	-0.003	-0.008	-0.005
	Q1, Q3	0.372, 0.450	0.365, 0.442	0.368, 0.446	-0.019, 0.016	-0.028, 0.009	-0.023, 0.014
	Min, Max	0.248, 0.689	0.233, 0.621	0.233, 0.689	-0.171, 0.255	-0.147, 0.196	-0.171, 0.255
	Mean difference					-0.00740	
	95% CI					-0.0113, -0.00348	
	P-value[1]					<.001	
	P-value[2]					<.001	
Day 2	n'	523	514	1037	504	494	998
	Mean (SD)	0.420 (0.0608)	0.410 (0.0609)	0.415 (0.0610)	0.006 (0.0366)	-0.006 (0.0358)	0 (0.0366)
	95% CI	0.415, 0.425	0.405, 0.415	0.412, 0.419	0.002, 0.009	-0.009, -0.002	-0.002, 0.002
	Median	0.420	0.411	0.416	0.005	-0.006	0
	Q1, Q3	0.380, 0.460	0.366, 0.449	0.370, 0.455	-0.016, 0.027	-0.030, 0.018	-0.023, 0.023
	Min, Max	0.256, 0.643	0.251, 0.611	0.251, 0.643	-0.180, 0.136	-0.113, 0.151	-0.180, 0.151
	Mean difference					-0.0111	
	95% CI					-0.0156, -0.00660	
	P-value[1]					<.001	
	P-value[2]					<.001	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: HCT (RATIO) - Actual and Change From Baseline Population: Safety (Contd.)

Study Day	Statistic	Actual			Change From Baseline		
		Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 3	n'	477	463	940	460	449	909
	Mean (SD)	0.420 (0.0584)	0.410 (0.0648)	0.415 (0.0618)	0.007 (0.0381)	-0.004 (0.0418)	0.002 (0.0403)
	95% CI	0.415, 0.426	0.404, 0.416	0.411, 0.419	0.004, 0.011	-0.008, 0	-0.001, 0.004
	Median	0.422	0.406	0.414	0.007	-0.006	0.001
	Q1, Q3	0.381, 0.457	0.368, 0.451	0.375, 0.454	-0.017, 0.030	-0.029, 0.018	-0.023, 0.026
	Min, Max	0.254, 0.596	0.140, 0.634	0.140, 0.634	-0.181, 0.143	-0.262, 0.213	-0.262, 0.213
	Mean difference					-0.0116	
	95% CI					-0.0168, -0.00639	
	P-value[1]					<.001	
	P-value[2]					<.001	
Day 4	n'	422	403	825	406	391	797
	Mean (SD)	0.418 (0.0576)	0.414 (0.0633)	0.416 (0.0604)	0.004 (0.0378)	0 (0.0426)	0.002 (0.0402)
	95% CI	0.412, 0.423	0.407, 0.420	0.412, 0.420	0.001, 0.008	-0.004, 0.004	0, 0.005
	Median	0.415	0.410	0.413	0.003	-0.003	0
	Q1, Q3	0.376, 0.458	0.369, 0.455	0.372, 0.456	-0.018, 0.030	-0.026, 0.024	-0.021, 0.028
	Min, Max	0.256, 0.599	0.230, 0.593	0.230, 0.599	-0.201, 0.150	-0.128, 0.273	-0.201, 0.273
	Mean difference					-0.00427	
	95% CI					-0.00986, 0.00132	
	P-value[1]					0.134	
	P-value[2]					0.035	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: HCT (RATIO) - Actual and Change From Baseline Population: Safety (Contd.)

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 5	n'	511	514	1025	492	493	985
	Mean (SD)	0.417 (0.0603)	0.413 (0.0599)	0.415 (0.0601)	0.003 (0.0375)	-0.001 (0.0392)	0.001 (0.0384)
	95% CI	0.412, 0.423	0.408, 0.418	0.412, 0.419	0, 0.007	-0.004, 0.003	-0.001, 0.004
	Median	0.416	0.414	0.414	0.003	-0.004	0
	Q1, Q3	0.374, 0.456	0.373, 0.453	0.373, 0.455	-0.020, 0.026	-0.027, 0.023	-0.023, 0.024
	Min, Max	0.262, 0.637	0.249, 0.618	0.249, 0.637	-0.206, 0.142	-0.102, 0.206	-0.206, 0.206
	Mean difference					-0.00412	
	95% CI					-0.00891, 0.000677	
	P-value[1]					0.092	
	P-value[2]					0.011	
Day 14	n'	493	514	1007	473	494	967
	Mean (SD)	0.417 (0.0578)	0.412 (0.0600)	0.415 (0.0589)	0.004 (0.0411)	-0.002 (0.0433)	0.001 (0.0423)
	95% CI	0.412, 0.422	0.407, 0.417	0.411, 0.418	0, 0.007	-0.005, 0.002	-0.002, 0.004
	Median	0.414	0.410	0.412	0.003	0	0.002
	Q1, Q3	0.374, 0.455	0.370, 0.453	0.372, 0.453	-0.022, 0.030	-0.026, 0.021	-0.024, 0.026
	Min, Max	0.279, 0.618	0.179, 0.587	0.179, 0.618	-0.172, 0.138	-0.273, 0.207	-0.273, 0.207
	Mean difference					-0.00530	
	95% CI					-0.0106, 0.000028	
	P-value[1]					0.051	
	P-value[2]					0.054	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: HCT (RATIO) - Actual and Change From Baseline Population: Safety (Contd.)

Study Day	Statistic	Actual: Placebo (N=570)	Actual: RLX030 (N=568)	Actual: Total (N=1138)	Change From Baseline: Placebo (N=570)	Change From Baseline: RLX030 (N=568)	Change From Baseline: Total (N=1138)
Day 60	n'	467	464	931	444	441	885
	Mean (SD)	0.408 (0.0505)	0.407 (0.0540)	0.407 (0.0522)	-0.007 (0.0459)	-0.011 (0.0452)	-0.009 (0.0456)
	95% CI	0.403, 0.413	0.402, 0.412	0.404, 0.411	-0.011, -0.003	-0.015, -0.007	-0.012, -0.006
	Median	0.408	0.404	0.406	-0.006	-0.011	-0.008
	Q1, Q3	0.373, 0.442	0.370, 0.444	0.371, 0.443	-0.036, 0.025	-0.037, 0.016	-0.036, 0.020
	Min, Max	0.264, 0.564	0.257, 0.574	0.257, 0.574	-0.188, 0.145	-0.208, 0.159	-0.208, 0.159
	Mean difference					-0.00379	
	95% CI					-0.00980, 0.00223	
	P-value[1]					0.217	
	P-value[2]					0.087	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: RBC (x10^12/L) - Actual and Change From Baseline Population: Safety

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 0	n'	543	541	1084			
	Mean (SD)	4.38 (0.646)	4.40 (0.625)	4.39 (0.635)			
	95% CI	4.33, 4.44	4.35, 4.45	4.35, 4.43			
	Median	4.37	4.40	4.40			
	Q1, Q3	3.94, 4.75	3.99, 4.80	3.97, 4.77			
	Min, Max	2.57, 7.18	1.78, 6.11	1.78, 7.18			
Day 1	n'	531	524	1055	510	507	1017
	Mean (SD)	4.37 (0.671)	4.33 (0.641)	4.35 (0.656)	-0.01 (0.295)	-0.08 (0.300)	-0.04 (0.300)
	95% CI	4.32, 4.43	4.27, 4.38	4.31, 4.39	-0.03, 0.02	-0.11, -0.06	-0.06, -0.03
	Median	4.35	4.30	4.32	-0.01	-0.08	-0.04
	Q1, Q3	3.95, 4.77	3.93, 4.75	3.93, 4.76	-0.17, 0.17	-0.26, 0.07	-0.22, 0.12
	Min, Max	2.45, 6.93	2.11, 6.44	2.11, 6.93	-1.59, 2.34	-1.23, 2.20	-1.59, 2.34
	Mean difference					-0.0797	
	95% CI					-0.1163, -0.0431	
	P-value[1]					<.001	
	P-value[2]					<.001	
Day 2	n'	523	514	1037	504	494	998
	Mean (SD)	4.45 (0.669)	4.36 (0.641)	4.40 (0.657)	0.05 (0.334)	-0.05 (0.342)	0 (0.342)
	95% CI	4.39, 4.51	4.30, 4.41	4.36, 4.44	0.02, 0.08	-0.08, -0.02	-0.02, 0.02
	Median	4.41	4.32	4.37	0.06	-0.07	0
	Q1, Q3	4.02, 4.86	3.92, 4.78	3.99, 4.82	-0.14, 0.24	-0.28, 0.15	-0.21, 0.21
	Min, Max	2.55, 6.74	2.43, 7.25	2.43, 7.25	-1.72, 1.33	-1.00, 1.98	-1.72, 1.98
	Mean difference					-0.1055	
	95% CI					-0.1475, -0.0635	
	P-value[1]					<.001	
	P-value[2]					<.001	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: RBC (x10^12/L) - Actual and Change From Baseline Population: Safety (Contd.)

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 3	n'	477	463	940	460	449	909
	Mean (SD)	4.44 (0.651)	4.37 (0.686)	4.40 (0.669)	0.06 (0.349)	-0.03 (0.399)	0.02 (0.377)
	95% CI	4.38, 4.49	4.31, 4.43	4.36, 4.45	0.03, 0.10	-0.07, 0.01	-0.01, 0.04
	Median	4.43	4.34	4.38	0.05	-0.05	0.02
	Q1, Q3	4.02, 4.82	3.96, 4.83	4.00, 4.82	-0.15, 0.28	-0.27, 0.19	-0.21, 0.24
	Min, Max	2.42, 6.65	1.28, 7.82	1.28, 7.82	-1.77, 1.32	-2.54, 2.31	-2.54, 2.31
	Mean difference					-0.0959	
	95% CI					-0.1446, -0.0472	
	P-value[1]					<.001	
	P-value[2]					<.001	
Day 4	n'	422	403	825	406	391	797
	Mean (SD)	4.41 (0.642)	4.40 (0.686)	4.41 (0.663)	0.05 (0.361)	0.01 (0.416)	0.03 (0.389)
	95% CI	4.35, 4.47	4.34, 4.47	4.36, 4.45	0.01, 0.08	-0.04, 0.05	0, 0.05
	Median	4.35	4.37	4.36	0.04	-0.02	0
	Q1, Q3	4.03, 4.81	3.96, 4.85	3.98, 4.83	-0.16, 0.29	-0.27, 0.24	-0.22, 0.26
	Min, Max	2.89, 6.55	2.09, 7.33	2.09, 7.33	-1.99, 1.37	-1.01, 2.88	-1.99, 2.88
	Mean difference					-0.0406	
	95% CI					-0.0948, 0.0135	
	P-value[1]					0.141	
	P-value[2]					0.019	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: RBC (x10^12/L) - Actual and Change From Baseline Population: Safety (Contd.)

		Actual			Change From Baseline		
Study Day	Statistic	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)	Placebo (N=570)	RLX030 (N=568)	Total (N=1138)
Day 5	n'	511	514	1025	492	493	985
	Mean (SD)	4.44 (0.660)	4.42 (0.669)	4.43 (0.664)	0.05 (0.368)	0.02 (0.402)	0.03 (0.385)
	95% CI	4.38, 4.50	4.36, 4.48	4.39, 4.47	0.02, 0.08	-0.02, 0.05	0.01, 0.06
	Median	4.44	4.44	4.44	0.03	-0.01	0.01
	Q1, Q3	3.99, 4.84	3.99, 4.83	3.99, 4.84	-0.18, 0.27	-0.25, 0.25	-0.21, 0.26
	Min, Max	2.48, 6.76	2.15, 7.53	2.15, 7.53	-2.03, 1.43	-0.97, 2.49	-2.03, 2.49
	Mean difference					-0.0296	
	95% CI					-0.0778, 0.0185	
	P-value[1]					0.228	
	P-value[2]					0.033	
Day 14	n'	493	514	1007	473	494	967
	Mean (SD)	4.47 (0.645)	4.44 (0.654)	4.45 (0.650)	0.09 (0.423)	0.04 (0.449)	0.06 (0.437)
	95% CI	4.42, 4.53	4.38, 4.49	4.41, 4.49	0.05, 0.13	0, 0.08	0.04, 0.09
	Median	4.45	4.42	4.44	0.09	0.06	0.07
	Q1, Q3	4.01, 4.89	3.99, 4.85	4.00, 4.87	-0.19, 0.34	-0.22, 0.29	-0.21, 0.33
	Min, Max	3.07, 6.72	2.04, 7.00	2.04, 7.00	-1.71, 1.45	-2.85, 2.44	-2.85, 2.44
	Mean difference					-0.0457	
	95% CI					-0.1008, 0.00941	
	P-value[1]					0.104	
	P-value[2]					0.121	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

RELAX-AHF: Hematology Test Results: RBC (x10^12/L) - Actual and Change From Baseline Population: Safety (Contd.)

Study Day	Statistic	Actual: Placebo (N=570)	Actual: RLX030 (N=568)	Actual: Total (N=1138)	Change From Baseline: Placebo (N=570)	Change From Baseline: RLX030 (N=568)	Change From Baseline: Total (N=1138)
Day 60	n'	467	464	931	444	441	885
	Mean (SD)	4.40 (0.604)	4.40 (0.614)	4.40 (0.609)	0 (0.471)	-0.03 (0.474)	-0.01 (0.473)
	95% CI	4.35, 4.46	4.34, 4.45	4.36, 4.44	-0.04, 0.05	-0.07, 0.02	-0.04, 0.02
	Median	4.36	4.39	4.36	0.02	-0.01	0.01
	Q1, Q3	4.02, 4.80	3.99, 4.76	4.00, 4.78	-0.27, 0.31	-0.30, 0.24	-0.29, 0.28
	Min, Max	2.75, 6.37	2.60, 6.53	2.60, 6.53	-1.94, 1.34	-2.29, 1.81	-2.29, 1.81
	Mean difference					-0.0314	
	95% CI					-0.0938, 0.0310	
	P-value[1]					0.324	
	P-value[2]					0.207	

[1] P-value is based on two-sided two sample t-test for RLX030 versus Placebo.
[2] P-value is based on Wilcoxon rank sum test for RLX030 versus Placebo.
Note: n' = number of patients with measurement

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Reason for Update

One more outcome measure added and spelling mistakes got corrected.