Protocol Registration Preview

Continue Select

Evaluation of Succinate Metoprolol on Heart Rate in the Stable Angina Patients

This study has been completed.

Sponsor:	AstraZeneca
Collaborators:	
Information provided by (Responsible Party):	AstraZeneca
ClinicalTrials.gov Identifier:	NCT01213173

Purpose

The purpose of this study is to evaluate the effects of Succinate Metoprolol(Betaloc ZOK®) (95 - 190 mg) on heart rate in the Stable angina patients.

Condition	Intervention	Phase
Angina Pectoris	Drug: Succinate Metoprolol (Betaloc ZOK®)	Phase 4

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study

Official Title: A Randomised, Open Label, Parallel Group, Multicentre, Phase IV Study on the Effect of 8 Weeks Succinate Metoprolol (Betaloc ZOK®) (95 - 190 mg) on Heart Rate in the Stable Angina Patients

Further study details as provided by AstraZeneca:
Primary Outcome Measure:

- The Impact on 24-hr Average Heart Rate Between Two Groups (Betaloc ZOK® 95mg vs. 190mg) [Time Frame: After 8 weeks treatment in the study] [Designated as safety issue: No]

Secondary Outcome Measures:

- The Impact on 24-hr Average Heart Rate From Baseline Within Groups [Time Frame: After 8 weeks treatment in the study] [Designated as safety issue: No]
- The Different Impact on 24-hr Average Heart Rate Between Two Groups [Time Frame: After 2 weeks treatment in the study] [Designated as safety issue: No]
- The Different Impact on 24-hr Average Heart Rate From Baseline Within Groups [Time Frame: After 2 weeks treatment in the study] [Designated as safety issue: No]
- The Proportion of Patients With Resting Heart Rate Controlled to ≤60bpm Between Groups [Time Frame: After 2 weeks treatment] [Designated as safety issue: No]
- The Proportion of Patients With Resting Heart Rate Controlled to ≤60bpm Between Groups [Time Frame: After 8 weeks treatment] [Designated as safety issue: No]
- The Difference of Change From Baseline in Total Ischemic Burden Between Groups [Time Frame: After 2 weeks treatment] [Designated as safety issue: No]
- The Difference of Change From Baseline in Total Ischemic Burden Between Groups [Time Frame: After 8 weeks treatment] [Designated as safety issue: No]
- The Difference of Change From Baseline in Angina Frequency Between Groups [Time Frame: After 2 weeks treatment] [Designated as safety issue: No]
- The Difference of Change From Baseline in Angina Frequency Between Groups [Time Frame: After 8 weeks treatment] [Designated as safety issue: No]
- The Change From Baseline in Total Cholesterol [Time Frame: After 8 weeks treatment] [Designated as safety issue: Yes]
- The Change From Baseline in Fasting Plasma Glucose [Time Frame: After 8 weeks treatment] [Designated as safety issue: Yes]
- The Change From Baseline in Triglycerides [Time Frame: After 8 weeks treatment] [Designated as safety issue: Yes]

Enrollment: 251
Study Start Date: October 2010
Study Completion Date: September 2011
Primary Completion Date: September 2011

Arms	Assigned Interventions
Active Comparator: 1	Drug: Succinate Metoprolol (Betaloc ZOK®) treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Experimental: 2	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Eligibility

Ages Eligible for Study: 18 Years to 75 Years
Genders Eligible for Study: Both

Inclusion Criteria:

- Provision of informed consent prior to any study specific procedures
- Chinese patients
- Heart rate ≥ 65bpm
- Has been diagnosed as Stable angina for at least 1 month and with stable angina pectoris symptoms within 2 weeks previous to enrolment(Please find the diagnose criteria of Stable angina on Appendix C)
- With Left ventricular ejection fraction ≥ 50% according to ultrasound cardiogram;
- Has been on beta-blockers for at least 4 weeks*, on the dose equivalent to Betaloc ZOK® 23.75-47.5mg/day.

Exclusion Criteria:

- Acute myocardial infarction within 6 months
- Unstable angina or Prinzmetal's angina
- II degree of AV block or greater

- Significant clinical, laboratory or electrocardiographic abnormalities that would place the subject at undue risk (in the Investigator's opinion) including:
- Significant renal impairment (serum creatinine > 2.0 mg/dL)
- Serum Alanine Aminotransferase or Aspartate Aminotransferase > 3 x upper limit of reference range
- Serum potassium < 3.0 mEq/L
- Serum sodium ≤ 130 mEq/L
- Acute or chronic hepatitis or cirrhosis (clinical diagnosis)
- Uncontrolled hyperthyroidism (clinical diagnosis)
- Systolic blood pressure ≥ 180 mmHg, or < 100mmHg at enrolment
- Patients with unstable, not compensated heart failure (pulmonary oedema, hypoperfusion or hypotension)

Contacts and Locations

Locations

China

Research Site

Tianjing, China

China, Beijing

Research Site

Beijing, Beijing, China

China, Guangdong

Research Site

Guangzhou, Guangdong, China

China, Hebei

Research Site

Tangshan, Hebei, China

China, Henan

Research Site

Zhengzhou, Henan, China

China, Jiangsu

Research Site

Nanjing, Jiangsu, China

China, Liaoning

Research Site

Jingzhou, Liaoning, China

Research Site

Shenyang, Liaoning, China

China, Shanghai

Research Site

Shanghai, Shanghai, China

China, Shanxi

Research Site

Taiyuan, Shanxi, China

Investigators

Principal Investigator:	Huo Yong	Department of Cardiology, Peking University First Hospital
Study Director:	Helen Lin	Astrazeneca China

More Information

Responsible Party: AstraZeneca
Study ID Numbers: D4022L00008
Health Authority: China: State Food and Drug Administration

Study Results

Participant Flow

Recruitment Details -- *Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations:*

Patients were enrolled in 15 centers in the People's Republic of China. The first patient was screened on 29 Oct 2010, the last patient completed the last visit on 8 Nov 2011 and the date of database lock was 21 Dec 2011. There were 231 patients in ITT population and 274 in Safety population.

From FDA guideline, it is found that for the overall safety and tolerability assessment, the set of subjects to be summarised is usually defined as those subjects who received at least one dose of the investigational drug.

According to the definition of Safety Set in SAP, All subjects who received at least one dose of randomised investigational product is included in the safety set. Safety will be analyzed according to treatment actually received.

Pre-Assignment Details -- *Significant events and approaches for the overall study following participant enrollment, but prior to group assignment:*

A total of 317 patients were screened (informed consent signed and CRF started) and 251 patients were randomized. There were 66 patients who were not randomised in the study. The most common reasons that a patient was a screen failure were voluntary discontinuation and incorrect enrolment,which included 34 and 27 patients respectively.

Reporting Groups

	Description
Active	lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg

Comparator	and last for another 6 weeks
Experimental	lead Electrocardiogram at Week 3， the dosage will be force titrated to 190mg and last for another 6 weeks

Overall Study

	Active Comparator	Experimental
STARTED	125 [1]	126 [2]
Patients Included in Safety Population	162	112
Patients Included in ITT Population	116	115
Patients Included in PP Population	102	89
COMPLETED	113 [3]	110 [4]
Not Completed	**12**	**16**
Protocol Violation	2	0
Adverse Event	4	8
Withdrawal by Subject	5	5
Incorrect Enrollment	1	3

[1] Patients who were randomized and received treatment

[2] Patients who were randomized and received treatment

[3] Patients who completed the study

[4] Patients who completed the study

Baseline Characteristics

Reporting Groups

	Description
Active Comparator	lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Experimental	lead Electrocardiogram at Week 3， the dosage will be force titrated to 190mg and last for another 6 weeks

Baseline Measures

	Active Comparator	Experimental	Total
Number of Participants	116	115	**231**
Age Continuous	59.3 ± 7.81	59.2 ± 9.25	**59.2 ± 8.53**

[units: Year] *Mean ± Standard Deviation*			
Gender, Male/Female *[units: Participants]*			
Female	74	81	**155**
Male	42	34	**76**

Outcome Measures

1. Primary Outcome Measure:

Measure Title	**The Impact on 24-hr Average Heart Rate Between Two Groups (Betaloc ZOK® 95mg vs. 190mg)**
Measure Description	Difference of the 24-hr average heart rate between two groups after 8 weeks treatment.
Time Frame	After 8 weeks treatment in the study
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active	**Arm 2 -**

	Comparator	Experimental
Number of Participants Analyzed	116	115
The Impact on 24-hr Average Heart Rate Between Two Groups (Betaloc ZOK® 95mg vs. 190mg) *[units: Bpm]* Mean ± Standard Deviation		
Baseline	71.4 ± 8.02	70.9 ± 8.19
Week 9	70.9 ± 8.71	68.6 ± 8.40

2. Secondary Outcome Measure:

Measure Title	**The Impact on 24-hr Average Heart Rate From Baseline Within Groups**
Measure Description	Difference of the 24-hr average heart rate within groups from baseline after 8 weeks treatment.
Time Frame	After 8 weeks treatment in the study
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	Arm 2 - Experimental

Number of Participants Analyzed	116	115
The Impact on 24-hr Average Heart Rate From Baseline Within Groups *[units: Bpm]* Least Square Mean (95% Confidence Interval)	-0.6244 (-1.94, 0.69)	-2.9858 (-4.23, -1.75)

3. Secondary Outcome Measure:

Measure Title	**The Different Impact on 24-hr Average Heart Rate Between Two Groups**
Measure Description	Difference of the 24-hr average heart rate between two groups after 2 weeks of treatment.
Time Frame	After 2 weeks treatment in the study
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	**Arm 2 - Experimental**
Number of Participants Analyzed	116	115
The Different Impact on 24-hr Average Heart Rate Between Two Groups *[units: Bpm]*	70.6 ± 7.75	69.2 ± 7.82

Mean ± Standard Deviation

4. Secondary Outcome Measure:

Measure Title	**The Different Impact on 24-hr Average Heart Rate From Baseline Within Groups**
Measure Description	Difference of the 24-hr average heart rate within groups from baseline after 2 weeks treatment.
Time Frame	After 2 weeks treatment in the study
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	**Arm 2 - Experimental**
Number of Participants Analyzed	116	115
The Different Impact on 24-hr Average Heart Rate From Baseline Within Groups *[units: Bpm]* Least Square Mean (95% Confidence Interval)	-0.4938 (-1.40, 0.41)	-2.1383 (-3.18, -1.10)

5. Secondary Outcome Measure:

Measure Title	**The Proportion of Patients With Resting Heart Rate Controlled to ≤60bpm Between Groups**

Measure Description	Difference in proportions of patients who had resting heart rate controlled to ≤60 bpm after 2 weeks treatment between groups
Time Frame	After 2 weeks treatment
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	**Arm 2 - Experimental**
Number of Participants Analyzed	116	115
The Proportion of Patients With Resting Heart Rate Controlled to ≤60bpm Between Groups *[units: Participants]*	25	28

6. Secondary Outcome Measure:

Measure Title	**The Proportion of Patients With Resting Heart Rate Controlled to ≤60bpm Between Groups**
Measure Description	Difference in proportions of patients who had resting heart rate controlled to ≤60 bpm after 8 weeks treatment between groups
Time Frame	After 8 weeks treatment
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	**Arm 2 - Experimental**
Number of Participants Analyzed	116	115
The Proportion of Patients With Resting Heart Rate Controlled to ≤60bpm Between Groups *[units: Participants]*	28	46

7. Secondary Outcome Measure:

Measure Title	**The Difference of Change From Baseline in Total Ischemic Burden Between Groups**
Measure Description	Difference in change from baseline in TIB between two groups after 2 weeks treatment.
Time Frame	After 2 weeks treatment
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3， the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	Arm 2 - Experimental
Number of Participants Analyzed	116	115
The Difference of Change From Baseline in Total Ischemic Burden Between Groups *[units: mm*min]* Least Spuare Mean (95% Confidence Interval)	-5.3353(-15.1422, 4.4716)	-12.9874(-20.8416, -5.1332)

8. Secondary Outcome Measure:

Measure Title	**The Difference of Change From Baseline in Total Ischemic Burden Between Groups**
Measure Description	Difference in change from baseline in TIB between two groups after 8 weeks treatment. Total Ischemic Burden (TIB) was defined as the sum of product of each ischemia episode lasting time and maximal ST elevation: TIB=∑(STmax×Tisc).
Time Frame	After 8 weeks treatment
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description

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Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	**Arm 2 - Experimental**
Number of Participants Analyzed	116	115
The Difference of Change From Baseline in Total Ischemic Burden Between Groups *[units: mm*min]* Least Spuare Mean (95% Confidence Interval)	22.2905(-14.3181, 58.8992)	-7.6586(-18.6777, 3.3604)

9. Secondary Outcome Measure:

Measure Title	**The Difference of Change From Baseline in Angina Frequency Between Groups**
Measure Description	Difference in change from baseline of angina pectoris frequency between two groups after 2 weeks treatment.
Time Frame	After 2 weeks treatment
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 -	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for

Experimental	two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	**Arm 2 - Experimental**
Number of Participants Analyzed	116	115
The Difference of Change From Baseline in Angina Frequency Between Groups *[units:~~Not Applicable~~Attacks per week]* Least Spuare Mean (95% Confidence Interval)	-0.044(-0.40, 0.31)	-0.3243(-0.55, -0.10)

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10. Secondary Outcome Measure:

Measure Title	**The Difference of Change From Baseline in Angina Frequency Between Groups**
Measure Description	Difference in change from baseline of angina pectoris frequency between two groups after 8 weeks treatment.
Time Frame	After 8 weeks treatment
Safety Issue?	No

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

ITT population was defined as all randomized subjects who had taken at least one dose of trial treatment, who had measurements at baseline for one or more efficacy variables and at least one post baseline measurement for the same variables in the treatment period.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	Arm 2 - Experimental
Number of Participants Analyzed	116	115
The Difference of Change From Baseline in Angina Frequency Between Groups *[units: ~~Not Applicable~~ Attacks per week]* Least Spuare Mean (95% Confidence Interval)	-0.3930(-0.64, -0.14)	-0.4453(-0.71, -0.18)

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11. Secondary Outcome Measure:

Measure Title	**The Change From Baseline in Total Cholesterol**
Measure Description	Difference of change from baseline in TC after 8 weeks treatment between groups.
Time Frame	After 8 weeks treatment
Safety Issue?	Yes

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

All subjects who received at least one dose of randomized investigational product was included in the safety population.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	Arm 2 - Experimental
Number of Participants Analyzed	162	112
The Change From Baseline in Total Cholesterol	-0.0505(-0.7110, 0.6101)	0.5825(-0.1029, 1.2678)

[units: mmol/L] Least Spuare Mean (95% Confidence Interval)	

12. Secondary Outcome Measure:

Measure Title	**The Change From Baseline in Fasting Plasma Glucose**
Measure Description	Difference of change from baseline in FPG after 8 weeks treatment between groups.
Time Frame	After 8 weeks treatment
Safety Issue?	Yes

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

All subjects who received at least one dose of randomized investigational product was included in the safety population.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	**Arm 2 - Experimental**
Number of Participants Analyzed	162	112
The Change From Baseline in Fasting Plasma Glucose *[units: mmol/L]* Least Spuare Mean (95% Confidence Interval)	0.3844(-0.1127, 0.6560)	0.2487(-0.0344, 0.5318)

13. Secondary Outcome Measure:

Measure Title	**The Change From Baseline in Triglycerides**

Measure Description	Difference of change from baseline in TG after 8 weeks treatment between groups.
Time Frame	After 8 weeks treatment
Safety Issue?	Yes

Population Description -- *Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate:*

All subjects who received at least one dose of randomized investigational product was included in the safety population.

Reporting Groups

	Description
Arm 1 - Active Comparator	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 47.5mg for two weeks, if tolerated and without Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Arm 2 - Experimental	Drug: Succinate Metoprolol (Betaloc ZOK®) Treatment with 95mg for two weeks, and if tolerated and without bradycardia symptoms presented, Systolic blood pressure<100mmHg and heart rate <45 bpm according to 12-lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Measured Values

	Arm 1 - Active Comparator	**Arm 2 - Experimental**
Number of Participants Analyzed	162	112
The Change From Baseline in Triglycerides *[units: mmol/L]* Least Spuare Mean (95% Confidence Interval	0.1295(-0.0375, 0.2965)	0.0937(-0.0810, 0.2683)

Reported Adverse Events

Reporting Groups

	Description
Active Comparator	lead Electrocardiogram at Week 3, the dosage will be titrated to 95mg and last for another 6 weeks
Experimental	lead Electrocardiogram at Week 3, the dosage will be force titrated to 190mg and last for another 6 weeks

Time Frame	
Additional Description	

Serious Adverse Events

	Active Comparator	Experimental
Total # participants affected/at risk	**2/162 (1.23%)**	**3/112 (2.68%)**
Cardiac disorders		
Angina pectoris † A		
# participants affected/at risk	1/162 (0.62%)	0/112 (0%)
Coronary artery occlusion † A		
# participants affected/at risk	0/162 (0%)	1/112 (0.89%)
angina unstable † A		
# participants affected/at risk	0/162 (0%)	1/112 (0.89%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Genital neoplasm malignant female † A		
# participants affected/at risk	0/162 (0%)	1/112 (0.89%)
Nervous system disorders		
VIIth nerve paralysis † A		
# participants affected/at risk	1/162 (0.62%)	0/112 (0%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA 10.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Active Comparator	Experimental
Total # participants affected/at risk	**0/162 (0%)**	**0/112 (0%)**

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.
The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Limitations and Caveats -- *Limitations of the study, such as early termination leading to small numbers of subjects analyzed and technical problems with measurement leading to unreliable or uninterpretable data:*

The sample size was insufficient for the secondary endpoints. Besides, the treatment prior to study did not correlate well with 47.5 mg metoprolol succinate, but with some higher dose. last the quality control of the study needs further improvement.

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