PRS TEST SYSTEM

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Protocol Registration Preview

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Example Factorial Study Design***

This study has been completed.

Sponsor:	PRS Training
Collaborators:	
Information provided by (Responsible Party):	, PRS Training
ClinicalTrials.gov Identifier:	

Purpose

The purpose of this study is to evaluate whether combining Marvistatin and Omega-3 Supplement is more effective at treating Heart Failure than the use of Marvistatin alone. This study will also look at two doses (5 mg versus 80 mg) of Marvistatin to see which is more effective.

Condition	Intervention	Phase
Heart Failure	Dietary Supplement: Placebo Dietary Supplement: Omega-3 Drug: Marvistatin	Phase 3

Study Type: Interventional
Study Design: Treatment, Factorial Assignment, Double Blind (Subject, Investigator, Outcomes Assessor), Randomized

Official Title: A Phase III Double-Blind, Placebo-Controlled, Randomized, Controlled, Factorial Design Trial of Two Doses of Marvistatin and Omega-3 Supplement in Participants With Heart Failure

Further study details as provided by , PRS Training:

Primary Outcome Measure:

- Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Intervention [Time Frame: Up to Day 30] [Designated as

safety issue: Yes]

Criteria used to classify as rehospitalization due to heart failure included: typical clinical manifestations of worsening heart failure and the addition of (or increase in) interventions specifically for worsening heart failure with an intravenous pharmacologic agent; mechanical or surgical intervention or ultrafiltration, hemofiltration, or dialysis specifically for management of persistent or worsening heart failure. Hospitalized participants who remained in the hospital at 30 days because of heart failure were counted as being rehospitalized for heart failure.

Secondary Outcome Measures:

- Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Randomization [Time Frame: Up to Day 30] [Designated as safety issue: Yes]

  Criteria used to classify as rehospitalization due to heart failure included: typical clinical manifestations of worsening heart failure and the addition of (or increase in) interventions specifically for worsening heart failure with an intravenous pharmacologic agent; mechanical or surgical intervention or ultrafiltration, hemofiltration, or dialysis specifically for management of persistent or worsening heart failure. Hospitalized participants who remained in the hospital at 30 days because of heart failure were counted as being rehospitalized for heart failure.

- Number of Adverse Events [Time Frame: Up to Day 30] [Designated as safety issue: Yes]

  Summary data provided in this table. See Adverse Events Module for specific Adverse Event data.

Enrollment: 600
Study Start Date: July 1998
Study Completion Date: May 2008
Primary Completion Date: May 2008

Arms	**Assigned Interventions**
Active Comparator: Marvistatin 5 mg and Omega-3 Participants completed a run-in period in which they received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement for 2 months. They then received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.	Dietary Supplement: Omega-3 Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) Drug: Marvistatin Marvistatin 5 mg tablet
Active Comparator: Marvistatin 5 mg and Placebo Participants completed a run-in period in which they received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement for 2	Dietary Supplement: Placebo Placebo Omega-3 Softgel Supplement

months. They then received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.	Drug: Marvistatin Marvistatin 5 mg tablet
Active Comparator: Marvistatin 80 mg and Omega-3 Participants completed a run-in period in which they received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement for 2 months. They then received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.	Dietary Supplement: Omega-3 Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) Drug: Marvistatin Marvistatin 80 mg tablet
Active Comparator: Marvistatin 80 mg and Placebo Participants completed a run-in period in which they received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement for 2 months. They then received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.	Dietary Supplement: Placebo Placebo Omega-3 Softgel Supplement Drug: Marvistatin Marvistatin 80 mg tablet

Patients will enter a run-in period during which they will receive Marvistatin 5 mg tablet daily and placebo Omega-3 Softgel Supplement for 2 months. Eligible patients who complete the run-in will then be randomized in a 2x2 factorial blinded design between Marvistatin 80 mg tablet once daily versus Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily versus placebo Omega-3 Softgel Supplement once daily.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both

Inclusion Criteria:

- Hospitalization for the management of Class III or IV Heart Failure using the New York Heart Association (NYHA) classification or diagnosed with Class III or IV Heart Failure within 72 hours of hospitalization for another reason
- Required to have a sufficient level of education to understand study procedures and be able to communicate with site personnel

Exclusion Criteria:

- Received an antihistamine for more than 2 days prior to randomization
- Unable to be treated by Drug X
- History of acute liver injury (e.g., hepatitis) or severe cirrhosis
- Pregnancy

- Breast-feeding
- Allergy to Drug X or Omega-3 Supplement
- Participation in a study of an investigational medication within the past 30 days

Contacts and Locations

Locations

United States, Massachusetts

Brigham and Women's Hospital at Harvard Medical School

Boston, Massachusetts, United States

United States, New York

Children's Hospital Montefiore

Bronx, New York, United States

United States, North Carolina

Duke University Medical Center

Durham, North Carolina, United States

United States, Pennsylvania

Thomas Jefferson University Hospital

Philadelphia, Pennsylvania, United States

United States, Texas

University of Texas Medical Branch at Galveston

Galveston, Texas, United States

More Information

Responsible Party: , Information Research Specialist, PRS Training
Study ID Numbers: Omega-3AR with results
Health Authority: United States: Food and Drug Administration

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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:*

This study enrolled patients hospitalized with NYHA Class III and IV Heart Failure from 5 academic medical centers in the United States. The last patient completed in May 2008.

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

Of the 600 patients screened during the run-in period between July 1998 and September 2007,

during which they received Marvistatin 5 mg tablet daily and placebo Omega-3 Softgel Supplement for 2 months. 67% (N = 400) completed the run-in and were randomized to the four intervention groups.

Reporting Groups

	Description
Marvistatin 5 mg and Omega-3	Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 5 mg and Placebo	Participants received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.
Marvistatin 80 mg and Omega-3	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 80 mg and Placebo	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.

Overall Study

	Marvistatin 5 mg and Omega-3	Marvistatin 5 mg and Placebo	Marvistatin 80 mg and Omega-3	Marvistatin 80 mg and Placebo
STARTED	100	100	100	100
COMPLETED	67	69	74	74
Not Completed	**33**	**31**	**26**	**26**
Lack of Efficacy	2	3	1	1
Physician Decision	1	1	0	0
Pregnancy	1	0	0	0
Protocol Violation	2	0	0	1
Death	10	10	9	8
Adverse Event	17	16	16	16
Moved out of Country	0	1	0	0

Baseline Characteristics

Reporting Groups

	Description
Marvistatin 5 mg and Omega-3	Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 5 mg and Placebo	Participants received Marvistatin5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.
Marvistatin 80 mg and Omega-3	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 80 mg and Placebo	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.

Baseline Measures

	Marvistatin 5 mg and Omega-3	Marvistatin 5 mg and Placebo	Marvistatin 80 mg and Omega-3	Marvistatin 80 mg and Placebo	Total
Number of Participants	100	100	100	100	**400**
Age Continuous *[units: years]* *Mean ± Standard Deviation*	63.9 ± 4.7	64.0 ± 4.8	64.5 ± 5.0	64.6 ± 5.1	**64.2 ± 4.9**
Gender, Male/Female *[units: participants]*					
Female	5	6	4	5	**20**
Male	95	94	96	95	**380**
Region of Enrollment *[units: participants]*	100	100	100	100	**400**
United States					
Study Specific Characteristic [NYHA HF Class] [1] *[units: participants]*					
Class III	92	84	97	89	**362**
Class IV	8	16	3	11	**38**
Study Specific Characteristic [Time of Heart Failure Diagnosis] [2] *[units: participants]*					

Pre-hospitalization	57	52	66	63	**238**
During hospitalization	43	48	34	37	**162**

[1] New York Heart Association (NYHA) Heart Failure (HF) Classification:

- Class III = Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.
- Class IV = Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.

[2] Participants were either hospitalized for the management of NYHA Class III or IV Heart Failure (HF) or were diagnosed with NYHA Class III or IV Heart Failure within 72 hours of hospitalization for another reason.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	**Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Intervention**
Measure Description	Criteria used to classify as rehospitalization due to heart failure included: typical clinical manifestations of worsening heart failure and the addition of (or increase in) interventions specifically for worsening heart failure with an intravenous pharmacologic agent; mechanical or surgical intervention or ultrafiltration, hemofiltration, or dialysis specifically for management of persistent or worsening heart failure. Hospitalized participants who remained in the hospital at 30 days because of heart failure were counted as being rehospitalized for heart failure.
Time Frame	Up to Day 30
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:*

Intention to Treat Analysis: All Participants who were randomized after run-in.

Reporting Groups

	Description
Marvistatin 5 mg	Marvistatin 5 mg tablet once daily

Marvistatin 80 mg	Marvistatin 80 mg tablet once daily
Omega-3	Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily
Placebo	Placebo Omega-3 Softgel Supplement once daily

Measured Values

	Marvistatin 5 mg	Marvistatin 80 mg	Omega-3	Placebo
Number of Participants Analyzed	200	200	200	200
Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Intervention *[units: participants]*	53	49	52	50

Statistical Analysis 1 for Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Intervention

Groups	Marvistatin 5 mg, Marvistatin 80 mg, Omega-3, Placebo
Method	Chi-squared
P-Value	0.96

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Statistical Analysis 2 for Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Intervention

Groups	Omega-3
Method	Other [Kaplan-Meier product-limit]
Other Estimated Parameter [Cumulative Probability]	0.28
95% Confidence Interval	0.17 to 0.39

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Other relevant estimation information:

Using Kaplan-Meier product-limit method (and Greenwood's formula for confidence interval), estimate the cumulative probability of rehospitalization/death for Omega-3.

Statistical Analysis 3 for Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Intervention

Groups	Placebo
Method	Other [Kaplan-Meier product-limit]
Other Estimated Parameter [Cumulative Probability]	0.26
95% Confidence Interval	0.15 to 0.37

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

Other relevant estimation information:

Using Kaplan-Meier product-limit method (and Greenwood's formula for confidence interval), estimate the cumulative probability of rehospitalization/death for Placebo group.

2. Secondary Outcome Measure:

Measure Title	**Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Randomization**
Measure Description	Criteria used to classify as rehospitalization due to heart failure included: typical clinical manifestations of worsening heart failure and the addition of (or increase in) interventions specifically for worsening heart failure with an intravenous pharmacologic agent; mechanical or surgical intervention or ultrafiltration, hemofiltration, or dialysis specifically for management of persistent or worsening heart failure. Hospitalized participants who remained in the hospital at 30 days because of heart failure were counted as being rehospitalized for heart failure.

Time Frame	Up to Day 30
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:*

Intention to Treat Analysis: All Participants who were randomized after run-in.

Reporting Groups

	Description
Marvistatin 5 mg and Omega-3	Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 5 mg and Placebo	Participants received Marvistatin5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.
Marvistatin 80 mg and Omega-3	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 80 mg and Placebo	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.

Measured Values

	Marvistatin 5 mg and Omega-3	**Marvistatin 5 mg and Placebo**	**Marvistatin 80 mg and Omega-3**	**Marvistatin 80 mg and Placebo**
Number of Participants Analyzed	100	100	100	100
Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Randomization *[units: participants]*	27	26	25	24

Statistical Analysis 1 for Rehospitalization for Heart Failure or Death From Any Cause During the Period From Randomization to Day 30 by Randomization

Groups	Marvistatin 5 mg and Omega-3, Marvistatin 5 mg and Placebo, Marvistatin 80 mg and Omega-3, Marvistatin 80 mg and Placebo
Method	Chi-squared
P-Value	0.97

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

3. Secondary Outcome Measure:

Measure Title	**Number of Adverse Events**
Measure Description	Summary data provided in this table. See Adverse Events Module for specific Adverse Event data.
Time Frame	Up to Day 30
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:*

Intention to Treat Analysis: All Participants who were randomized after run-in.

Reporting Groups

	Description
Marvistatin 5 mg and Omega-3	Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 5 mg and Placebo	Participants received Marvistatin5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.
Marvistatin 80 mg and Omega-3	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 80 mg and Placebo	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.

Measured Values

	Marvistatin 5 mg and Omega-3	**Marvistatin 5 mg and Placebo**	**Marvistatin 80 mg and Omega-3**	**Marvistatin 80 mg and Placebo**
Number of Participants	100	100	100	100

Analyzed				
Number of Adverse Events *[units: adverse events]*	75	88	72	81

Reported Adverse Events

Reporting Groups

	Description
Marvistatin 5 mg and Omega-3	Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 5 mg and Placebo	Participants received Marvistatin5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.
Marvistatin 80 mg and Omega-3	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.
Marvistatin 80 mg and Placebo	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.

Time Frame	up to day 30 after randomization
Additional Description	

Serious Adverse Events

	Marvistatin 5 mg and Omega-3	Marvistatin 5 mg and Placebo	Marvistatin 80 mg and Omega-3	Marvistatin 80 mg and Placebo
Total # participants affected/at risk	**30/100 (30%)**	**27/100 (27%)**	**26/100 (26%)**	**27/100 (27%)**
Cardiac disorders				
Myocardial Infarction † A				
# participants affected/at risk	17/100 (17%)	16/100 (16%)	16/100 (16%)	16/100 (16%)
General disorders				
Death † A				

# participants affected/at risk	10/100 (10%)	10/100 (10%)	9/100 (9%)	8/100 (8%)
Nervous system disorders				
Hemorrhagic stroke † A				
# participants affected/at risk	2/100 (2%)	0/100 (0%)	1/100 (1%)	1/100 (1%)
Hemorrhagic transformation stroke † A				
# participants affected/at risk	1/100 (1%)	1/100 (1%)	0/100 (0%)	2/100 (2%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 11.1

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

	Marvistatin 5 mg and Omega-3	**Marvistatin 5 mg and Placebo**	**Marvistatin 80 mg and Omega-3**	**Marvistatin 80 mg and Placebo**
Total # participants affected/at risk	**20/100 (20%)**	**27/100 (27%)**	**22/100 (22%)**	**28/100 (28%)**
Cardiac disorders				
Chest pain † A				
# participants affected/at risk	6/100 (6%)	4/100 (4%)	4/100 (4%)	1/100 (1%)
Ischemia † A				
# participants affected/at risk	7/100 (7%)	5/100 (5%)	1/100 (1%)	8/100 (8%)
Ventricular tachycardia † A				
# participants affected/at risk	8/100 (8%)	6/100 (6%)	4/100 (4%)	7/100 (7%)
General disorders				
Palpitations † A				

# participants affected/at risk	5/100 (5%)	1/100 (1%)	8/100 (8%)	5/100 (5%)
Metabolism and nutrition disorders				
Hyperglycemia † A				
# participants affected/at risk	5/100 (5%)	4/100 (4%)	3/100 (3%)	2/100 (2%)
Hyperlipidemia † A				
# participants affected/at risk	2/100 (2%)	5/100 (5%)	4/100 (4%)	6/100 (6%)
Nervous system disorders				
Dizziness † A				
# participants affected/at risk	2/100 (2%)	9/100 (9%)	6/100 (6%)	3/100 (3%)
Headache † A				
# participants affected/at risk	4/100 (4%)	8/100 (8%)	4/100 (4%)	3/100 (3%)
Respiratory, thoracic and mediastinal disorders				
Dyspnea † A				
# participants affected/at risk	5/100 (5%)	10/100 (10%)	4/100 (4%)	6/100 (6%)
Vascular disorders				
Hypertension † A				
# participants affected/at risk	1/100 (1%)	9/100 (9%)	8/100 (8%)	13/100 (13%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 11.1

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:*

[Not specified.]

Results Point of Contact:

Name/Official Title: Rain Bowe
Organization: PRS Training
Phone: 555-555-5555
Email: register@clinicaltrials.gov

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