Factorial Study Design Example (With Results)

Disclaimer: The following information is fictional and is only intended for the purpose of illustrating key concepts for results data entry in the Protocol Registration and Results System (PRS).

ClinicalTrials.gov Identifier: NCT00055594

Recruitment Status: Completed
First Posted: July 5, 2017
Results First Posted: May 24, 2019
Last Update Posted: May 24, 2019

Sponsor:

PRS Results Training

Information provided by (Responsible Party):

PRS Results Training

Study Description

Brief Summary:

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 or disease	Intervention/treatment	Phase
Heart Failure	Dietary Supplement: Placebo Dietary Supplement: Omega-3 Drug: Marvistatin	Phase 3

Detailed Description:

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.

Study Design

Study Type:	Interventional
Actual Enrollment:	600 participants
Allocation:	Randomized
Intervention Model:	Factorial Assignment
Masking:	Double (Participant, Investigator)
Primary Purpose:	Treatment
Official Title:	A Phase III Double-Blind, Placebo-Controlled, Randomized, Factorial Design Trial of Two Doses of Marvistatin and Omega-3 Supplement in Patients With Heart Failure
Actual Study Start Date:	July 5, 2017
Actual Primary Completion Date:	May 24, 2018
Actual Study Completion Date:	May 24, 2018

Arms and Interventions

Arm	Intervention/treatment
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 months. They then received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.	Dietary Supplement: Placebo Placebo Omega-3 Softgel Supplement 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

Outcome Measures

Primary Outcome Measure:

1. 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]

   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:

1. 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]

   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.

2. Number of Adverse Events (Including Death) [Time Frame: Up to Day 30]

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

Eligibility Criteria

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)
Sexes Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

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 Marvistatin
- History of acute liver injury (e.g., hepatitis) or severe cirrhosis
- Pregnancy
- Breast-feeding
- Allergy to Marvistatin 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, 02115

United States, New York

Children's Hospital Montefiore

Bronx, New York, United States, 10467

United States, North Carolina

Duke University Medical Center

Durham, North Carolina, United States, 27710

United States, Pennsylvania

Thomas Jefferson University Hospital

Philadelphia, Pennsylvania, United States, 19107

United States, Texas

University of Texas Medical Branch at Galveston

Galveston, Texas, United States, 77555

Study Documents (Full-Text)

Documents provided by PRS Results Training

Study Protocol and Statistical Analysis Plan [PDF] April 30, 2017

More Information

Responsible Party:	PRS Results Training
ClinicalTrials.gov Identifier:	NCT00055594
Other Study ID Numbers:	TTTFactorialR
First Posted:	July 5, 2017
Results First Posted:	May 24, 2019
Last Update Posted:	May 24, 2019
Last Verified:	April 2019

Human Subjects Protection Review Board Status:	Approved
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Study Results

Study Type	Interventional
Study Design	Allocation: Randomized; Intervention Model: Factorial Assignment; Masking: Double (Participant, Investigator); Primary Purpose: Treatment
Condition	Heart Failure
Interventions	Dietary Supplement: Placebo Dietary Supplement: Omega-3 Drug: Marvistatin
Enrollment	600

Participant Flow

Recruitment Details	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 on May 24, 2018.
Pre-assignment Details	Of the 600 patients screened during the run-in period between July 5, 2017 and April 2018, 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.

Arm/Group Title	Marvistatin 5 mg and Omega-3	Marvistatin 5 mg and Placebo	Marvistatin 80 mg and Omega-3	Marvistatin 80 mg and Placebo
Arm/Group Description	Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily, for 30 days.	Participants received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily, for 30 days.	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily, for 30 days.	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily, for 30 days.
Period Title: **Overall Study**				
Started	100	100	100	100
Completed	67	69	74	74
Not Completed	33	31	26	26
Reason Not Completed				
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

Arm/Group Title		Marvistatin 5 mg and Omega-3	Marvistatin 5 mg and Placebo	Marvistatin 80 mg and Omega-3	Marvistatin 80 mg and Placebo	Total
Arm/Group Description		Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.	Participants received Marvistatin5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.	Total of all reporting groups
Overall Number of Baseline Participants		100	100	100	100	400
Baseline Analysis Population Description		[Not Specified]				
Age, Continuous Mean (Standard Deviation) Unit of Measure: years						
	Number Analyzed	100 participants	100 participants	100 participants	100 participants	400 participants
		63.9 (4.7)	64.0 (4.8)	64.5 (5.0)	64.6 (5.1)	64.3 (4.9)

Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants						
	Number Analyzed	100 participants	100 participants	100 participants	100 participants	400 participants
	Female	5 5%	6 6%	4 4%	5 5%	20 5%
	Male	95 95%	94 94%	96 96%	95 95%	380 95%
Ethnicity (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants						
	Number Analyzed	100 participants	100 participants	100 participants	100 participants	400 participants
	Hispanic or Latino	8 8%	7 7%	5 5%	6 6%	26 6.5%
	Not Hispanic or Latino	92 92%	93 93%	95 95%	94 94%	374 93.5%
	Unknown or Not Reported	0 0%	0 0%	0 0%	0 0%	0 0%

Race (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants						
	Number Analyzed	100 participants	100 participants	100 participants	100 participants	400 participants
	American Indian or Alaska Native	0 0%	0 0%	0 0%	0 0%	0 0%
	Asian	0 0%	0 0%	0 0%	0 0%	0 0%
	Native Hawaiian or Other Pacific Islander	0 0%	0 0%	0 0%	0 0%	0 0%
	Black or African American	14 14%	15 15%	13 13%	17 17%	59 14.75%
	White	86 86%	85 85%	87 87%	83 83%	341 85.25%
	More than one race	0 0%	0 0%	0 0%	0 0%	0 0%
	Unknown or Not Reported	0 0%	0 0%	0 0%	0 0%	0 0%

Region of Enrollment Measure Type: Count of Participants Unit of measure: participants						
United States	Number Analyzed	100 participants	100 participants	100 participants	100 participants	400 participants
		100 100%	100 100%	100 100%	100 100%	400 100%
NYHA HF Class [1] Measure Type: Count of Participants Unit of measure: participants						
	Number Analyzed	100 participants	100 participants	100 participants	100 participants	400 participants
	Class III	92 92%	97 97%	84 84%	89 89%	362 90.5%
	Class IV	8 8%	3 3%	16 16%	11 11%	38 9.5%

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

- Class III = Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea.
- Class IV = Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

Time of Heart Failure Diagnosis [1] Measure Type: Count of Participants Unit of measure: participants						
	Number Analyzed	100 participants	100 participants	100 participants	100 participants	400 participants
	Pre-hospitalization	57 57%	66 66%	52 52%	63 63%	238 59.5%
	During hospitalization	43 43%	34 34%	48 48%	37 37%	162 40.5%
		[1] Measure Description: 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

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

Outcome Measure Data

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

Arm/Group Title	Marvistatin 5 mg	Marvistatin 80 mg	Omega-3	Placebo
Arm/Group Description:	Marvistatin 5 mg tablet once daily. Participants who were randomized to "Marvistatin 5 mg and Omega-3" or "Marvistatin 5 mg and Placebo."	Marvistatin 80 mg tablet once daily. Participants who were randomized to "Marvistatin 80 mg and Omega-3" or "Marvistatin 80 mg and Placebo."	Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily. Participants who were randomized to "Marvistatin 5 mg and Omega-3" or "Marvistatin 80 mg and Omega-3."	Placebo Omega-3 Softgel Supplement once daily. Participants who were randomized to "Marvistatin 5 mg and Placebo" or "Marvistatin 80 mg and Placebo."
Overall Number of Participants Analyzed	200	200	200	200
Measure Type: Count of Participants Unit of Measure: participants	53 26.5%	49 24.5%	52 26%	50 25%

Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Marvistatin 5 mg, Marvistatin 80 mg, Omega-3, Placebo
	Comments	[Not specified]
	Type of Statistical Test	Other
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.96
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Statistical Analysis 2

Statistical Analysis Overview	Comparison Group Selection	Omega-3
	Comments	[Not specified]
	Type of Statistical Test	Other
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[Cumulative Probability]
	Estimated Value	0.28
	Confidence Interval	(2-Sided) 95% 0.17 to 0.39
	Estimation Comments	Using Kaplan-Meier product-limit method (and Greenwood's formula for confidence interval), estimated the cumulative probability of rehospitalization/death for Omega-3.

Statistical Analysis 3

Statistical Analysis Overview	Comparison Group Selection	Placebo
	Comments	[Not specified]
	Type of Statistical Test	Other
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[Cumulative Probability]
	Estimated Value	0.26
	Confidence Interval	(2-Sided) 95% 0.15 to 0.37
	Estimation Comments	Using Kaplan-Meier product-limit method (and Greenwood's formula for confidence interval), estimated the cumulative probability of rehospitalization/death for Placebo group.

2. Secondary Outcome

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

Outcome Measure Data

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

Arm/Group Title	Marvistatin 5 mg and Omega-3	Marvistatin 5 mg and Placebo	Marvistatin 80 mg and Omega-3	Marvistatin 80 mg and Placebo
Arm/Group Description:	Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.	Participants received Marvistatin5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.
Overall Number of Participants Analyzed	100	100	100	100
Measure Type: Count of Participants Unit of Measure: participants	27 27%	26 26%	25 25%	24 24%

Statistical Analysis 1

Statistical Analysis Overview	Comparison Group Selection	Marvistatin 5 mg and Omega-3, Marvistatin 5 mg and Placebo, Marvistatin 80 mg and Omega-3, Marvistatin 80 mg and Placebo
	Comments	[Not specified]
	Type of Statistical Test	Other
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.97
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

3. Secondary Outcome

Title	Number of Adverse Events (Including Death)
Description	Summary data provided in this outcome measure. See Adverse Events Module for specific Adverse Event data.
Time Frame	Up to Day 30

Outcome Measure Data

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

Arm/Group Title	Marvistatin 5 mg and Omega-3	Marvistatin 5 mg and Placebo	Marvistatin 80 mg and Omega-3	Marvistatin 80 mg and Placebo
Arm/Group Description:	Participants received Marvistatin 5 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.	Participants received Marvistatin5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.	Participants received Marvistatin 80 mg tablet once daily and Omega-3 Softgel Supplement (900 mg EPA, 5 g DHA) once daily.	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily.
Overall Number of Participants Analyzed	100	100	100	100
Measure Type: Number Unit of Measure: adverse events	75	88	72	81

Adverse Events

Time Frame	Up to day 30 after randomization
Adverse Event Reporting Description	
Source Vocabulary Name for Table Default	MedDRA (11.1)
Collection Approach for Table Default	Systematic Assessment

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

All-Cause Mortality

	Marvistatin 5 mg and Omega-3	**Marvistatin 5 mg and Placebo**	**Marvistatin 80 mg and Omega-3**	**Marvistatin 80 mg and Placebo**
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	10/100 (10%)	10/100 (10%)	9/100 (9%)	8/100 (8%)

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
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	20/100 (20%)	17/100 (17%)	17/100 (17%)	19/100 (19%)
Cardiac disorders				
Myocardial infarction † 1	17/100 (17%)	16/100 (16%)	16/100 (16%)	16/100 (16%)
Nervous system disorders				
Hemorrhagic stroke † 1	2/100 (2%)	0/100 (0%)	1/100 (1%)	1/100 (1%)
Hemorrhagic transformation stroke † 1	1/100 (1%)	1/100 (1%)	0/100 (0%)	2/100 (2%)

1 Term from vocabulary, MedDRA (11.1)

† Indicates events were collected by systematic assessment

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%

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

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

1 Term from vocabulary, MedDRA (11.1)

† Indicates events were collected by systematic assessment

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

All 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.

Results Point of Contact

Name/Title:	PRS Training Lead
Organization:	PRS Results Training
Phone:	555-555-5555
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Responsible Party:	PRS Results Training
ClinicalTrials.gov Identifier:	NCT00055594
Other Study ID Numbers:	TTTFactorialR
First Submitted:	June 30, 2017
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