Factorial Study Design Example (With Results)

This study has been completed.

Sponsor: PRS Results Training

Information provided by (Responsible Party): PRS Results Training

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).

Full Text View

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: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Factorial Assignment
Masking: Double Blind (Subject, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

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

Further study details as provided by PRS Results 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 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

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.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

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

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:	PRS Results Training
Study ID Numbers:	TTTFactorialR
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, for 30 days.
Marvistatin 5 mg and Placebo	Participants received Marvistatin 5 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily, for 30 days.
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, for 30 days.
Marvistatin 80 mg and Placebo	Participants received Marvistatin 80 mg tablet once daily and placebo Omega-3 Softgel Supplement once daily, for 30 days.

Overall Study

	Number of Participants			
	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

Analysis 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.)

[No text entered.]

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.

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]					
United States	100	100	100	100	400
NYHA HF Class [A] [units: participants]					
Class III	92	97	84	89	362
Class IV	8	3	16	11	38
Time of Heart Failure Diagnosis [B] [units: participants]					
Pre-hospitalization	57	66	52	63	238
During hospitalization	43	34	48	37	162

[A] 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.

[B] 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

Analysis 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. Participants who were randomized to "Marvistatin 5 mg and Omega-3" or "Marvistatin 5 mg and Placebo".
Marvistatin 80 mg	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	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	Placebo Omega-3 Softgel Supplement once daily. Participants who were randomized to "Marvistatin 5 mg and Placebo" or "Marvistatin 80 mg and Placebo".

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

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

[A] Other relevant estimation information:

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

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

[A] Other relevant estimation information:

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 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

Analysis 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 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.

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

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

Analysis 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 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.

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

Adverse Events

Time Frame	Up to day 30 after randomization
Additional Description	[No text entered.]

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.

Serious Adverse Events

	# Participants Affected/At Risk			
	Marvistatin 5 mg and Omega-3	**Marvistatin 5 mg and Placebo**	**Marvistatin 80 mg and Omega-3**	**Marvistatin 80 mg and Placebo**
Total, serious adverse events	**30/100 (30%)**	**27/100 (27%)**	**26/100 (26%)**	**27/100 (27%)**
Cardiac disorders				
Myocardial Infarction † 1	17/100 (17%)	16/100 (16%)	16/100 (16%)	16/100 (16%)
General disorders				
Death † 1	10/100 (10%)	10/100 (10%)	9/100 (9%)	8/100 (8%)
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%)

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

Other Adverse Events

Frequency Threshold

Threshold above which other adverse events are reported: 5%

	# Participants Affected/At Risk			
	Marvistatin 5 mg and Omega-3	**Marvistatin 5 mg and Placebo**	**Marvistatin 80 mg and Omega-3**	**Marvistatin 80 mg and Placebo**
Total, other (not including serious) adverse events	**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%)
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%)

† Indicates events were collected by systematic assessment.
1 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.)

[No text entered.]

Results Point of Contact

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