ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: October 3, 2019

ClinicalTrials.gov ID: NCT00676663

Study Identification

Unique Protocol ID:	SNDX-275-0301
Brief Title:	Study to Evaluate Exemestane With and Without Entinostat (SNDX-275) in Treatment of Postmenopausal Women With Advanced Breast Cancer (ENCORE301)
Official Title:	A Phase 2, Randomized, Double-Blind, Multicenter Study of Exemestane With and Without SNDX-275 in Postmenopausal Women With Locally Recurrent or Metastatic Estrogen Receptor-Positive Breast Cancer, Progressing on Treatment With a Non-Steroidal Aromatase Inhibitor
Secondary IDs:	2009-012623-28 [EudraCT Number]

Study Status

Record Verification:	October 2019
Overall Status:	Completed
Study Start:	June 13, 2008 [Actual]
Primary Completion:	January 29, 2011 [Actual]
Study Completion:	November 26, 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Syndax Pharmaceuticals
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	Yes
U.S. FDA-regulated Device:	No
Unapproved/Uncleared Device:	No
U.S. FDA IND/IDE:	Yes
IND/IDE Information:	FDA Center: CDER IND/IDE Number: 64722 Serial Number: Has Expanded Access: No
Human Subjects Review:	Board Status: Approved Approval Number: SCC004949 Board Name: Scripps Health Cancer Center IRB Board Affiliation: OHRP Phone: 858-652-5563 Email: SCCIRB@scrippshealth.org Address: 11025 North Torrey Pines Road La Jolla, CA 92037
Data Monitoring:	Yes
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary:	The purpose of this study is to evaluate the safety and efficacy of entinostat in combination with exemestane in the treatment of advanced breast cancer.
Detailed Description:	

Conditions

Conditions:	Breast Cancer Estrogen Receptor-Positive Breast Cancer Breast Cancer, Estrogen Receptor-Positive ER+ Breast Cancer

Keywords: Breast Neoplasms
Breast Tumor
Mammary Neoplasms

Study Design

Study Type: Interventional
Primary Purpose: Treatment
Study Phase: Phase 2
Interventional Study Model: Parallel Assignment
Number of Arms: 2
Masking: Triple (Participant, Care Provider, Investigator)
Allocation: Randomized
Enrollment: 130 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Exemestane 25 mg + Entinostat 5 mg Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.	Drug: entinostat Entinostat 5 mg tablet orally once per week Other Names: • SNDX-275 Drug: exemestane Exemestane 25 mg tablet orally once daily Other Names: • Aromasin®
Placebo Comparator: Exemestane 25 mg + Placebo Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.	Drug: exemestane Exemestane 25 mg tablet orally once daily Other Names: • Aromasin® Drug: Placebo Placebo-matching entinostat tablet orally once per week

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Sex: Female

Gender Based:

Accepts Healthy Volunteers: No

Criteria: Inclusion Criteria:

- Postmenopausal female patients
- Histologically or cytologically confirmed estrogen receptor positive (ER+) breast cancer
- Relapsed or progressed on prior treatment with aromatase inhibitor (AI)
- Metastatic disease must be measurable
- Patients receiving palliative radiation at the non-target lesions must have a 2 week wash out period following completion of the treatment prior to enrollment
- Patient may have had one prior chemotherapy as part of first line therapy as long as it was received before initiation of prior AI
- Eastern Cooperative Oncology Group (ECOG) performance status: 0 to 1
- Laboratory parameters: a)Hemoglobin ≥ 9.0 g/dL; platelets ≥ 100.0 x 10^9/L; Absolute Neutrophil Count (ANC ≥) 1.5 x 10^9/L without the use of hematopoietic growth factors b)Creatinine less than 2.5 times the upper limit of normal for the institution c)Aspartate transaminase (AST) and alanine transaminase (ALT) less than 2.5 times the upper limit of normal for the institution
- Able to understand and give written informed consent and comply with study procedures

Exclusion Criteria:

- Relapse on treatment with non-steroidal AI after less than 12 months for patients in the adjuvant setting
- Progressive disease after less than 3 months treatment with most recent AI for patients with metastatic disease
- Rapidly progressive, life-threatening metastases
- Any palliative radiotherapy to the measurable lesion
- Previous treatment with SNDX-275 or any other histone deacetylase (HDAC) inhibitor including valproic acid
- Allergy to benzamides or inactive components of the study drug
- A history of allergies to any active or inactive ingredients of exemestane
- Any concomitant medical condition that precludes adequate study treatment compliance
- Patient is currently enrolled in (or completed within 30 days before study drug administration) another investigational drug study
- Patient is currently receiving treatment with valproic acid, Zolinza (vorinostat) or any other HDAC inhibitor or deoxyribonucleic acid (DNA) methyltransferase inhibitor or any systemic anticancer treatment (with the exception of Lupron)

Contacts/Locations

Central Contact Person: Judy Billingsley, RN, BSN, OCN

Telephone: 781-419-1408
Email: jbillingsley@syndax.com

Central Contact Backup:

Study Officials: Denise Yardley, MD
Study Principal Investigator
Sarah Cannon Cancer Center

Locations: **United States, Colorado**
University of Colorado
Aurora, Colorado, United States

United States, California
Moores UCSD Cancer Center
La Jolla, California, United States

United States, Florida
University of Southern Florida -Moffitt Cancer Center
Tampa, Florida, United States

United States, North Carolina
Carolinas Healthcare System Clinical Trials
Charlotte, North Carolina, United States

United States, Indiana
Indiana University Indiana Cancer Pavilion
Indianapolis, Indiana, United States

United States, Maryland
University of Maryland Greenebaum Cancer Center
Baltimore, Maryland, United States

United States, Tennessee
Chattanooga Oncology Hematology Associates
Chattanooga, Tennessee, United States

United States, California
California Cancer Care
Greenbrae, California, United States

United States, Florida
Florida Cancer Specialists
Fort Myers, Florida, United States

United States, Virginia

Virginia Cancer Institute
Richmond, Virginia, United States

United States, North Carolina
Wake Forest University Baptist Medical Center
Winston-Salem, North Carolina, United States

United States, Georgia
Medical College of Georgia
Augusta, Georgia, United States

United States, Ohio
Oncology Hematology Care
Cincinnati, Ohio, United States

United States, Tennessee
Sarah Cannon Cancer Center
Nashville, Tennessee, United States

Canada, Ontario
RSM Durham Regional Cancer Center - Lakeridge Health
Oshawa, Ontario, Canada

St. Joseph's Health Centre
Toronto, Ontario, Canada

United States, Missouri
Kansas City Cancer Center
Kansas City, Missouri, United States

United States, Florida
Hematology Oncology Associates
Lake Worth, Florida, United States

Palm Beach Cancer Institute
West Palm Beach, Florida, United States

United States, Colorado
Rocky Mountain Cancer Center
Denver, Colorado, United States

United States, South Carolina
Cancer Centers of the Carolinas
Greenville, South Carolina, United States

United States, Illinois

Cancer Care & Hematology Specialists of Chicagoland
Niles, Illinois, United States

United States, Texas
Longview Cancer Center
Longview, Texas, United States

South Texas Cancer Center
McAllen, Texas, United States

United States, New Jersey
Hematology-Oncology Associates of Northern New Jersey
Morristown, New Jersey, United States

United States, Washington
Columbia Basin Hematology & Oncology
Kennewick, Washington, United States

United States, Arizona
Hematology Oncology Associates
Phoenix, Arizona, United States

United States, Washington
Puget Sound Cancer Center
Seattle, Washington, United States

United States, Texas
Allison Cancer Center
Midland, Texas, United States

United States, Connecticut
Hartford Hospital Cancer Clinical Research Office
Hartford, Connecticut, United States

United States, Florida
Memorial Cancer Institute
Hollywood, Florida, United States

Czechia
Fakultani Nemocnice Kralavske Vinohadry
Praque, Czechia

Fakultni nemocnice Olomouc
Olomouc, Czechia

Radiologicke centrum Multiscan, s.r.o.

Pardubice, Czechia

Hungary
Semmelweis Egyetem
Budapest, Hungary

Borsod-Abaus Zemplen Megyei Korhaz es Egyetemi
Miskolc, Hungary

National Health Centre of Hungary
Budapest, Hungary

Radiologicke centrum Multiscan
Debrecen, Hungary

Clinfan Ltd SMO, County Hospital Szekszard
Szekszárd, Hungary

Russia
Arkhangelsk Regional Clinical Oncology Dispensary
Arkhangelsk, Russia

Blokhin Russian Oncology Research Center of Russian Academy of Medical Sciences
Moscow, Russia

Leningrad Regional Oncology Dispensary
Saint-Petersburg, Russia

Stavropol Territory Clinical Oncology Dispensary
Stavropol, Russia

Murmansk Regional Clinical Oncology Dispensary
Murmansk, Russia

United States, California
Scripps Health
La Jolla, California, United States

Hungary
Allami Egeszseguegi Koezpont
Budapest, Hungary

Russia
Russian Research Centre of Radiology and Surgery
Saint Petersburg, Russia

IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Study Results

Participant Flow

Recruitment Details	Participants took part in the study at 38 investigative sites in the United States, Canada, Czech Republic, Hungary and Russia from 13 June 2008 to 26 November 2012.
Pre-assignment Details	Participants with a diagnosis of metastatic breast cancer were enrolled equally in one of two treatment arms: exemestane 25 mg plus entinostat 5 mg or exemestane 25 mg plus placebo.

Reporting Groups

	Description
Exemestane 25 mg + Placebo	Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.
Exemestane 25 mg + Entinostat 5 mg	Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

Overall Study

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
Started	66	64
Completed	21	26
Not Completed	45	38
Death	43	27

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
Withdrew Consent	1	8
Lost to Follow-up	1	3

Baseline Characteristics

Baseline Analysis Population Description

Full Analysis Set included all randomized participants.

Reporting Groups

	Description
Exemestane 25 mg + Placebo	Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.
Exemestane 25 mg + Entinostat 5 mg	Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

Baseline Measures

		Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg	Total
Overall Number of Participants		66	64	130
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	66 participants	64 participants	130 participants
		62.7 (10.06)	62.2 (11.72)	62.4 (10.87)
Age, Customized Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	66 participants	64 participants	130 participants
[Not specified]	18 to 44 years	2 3.03%	3 4.69%	5 3.85%
	45 to 64 years	38 57.58%	32 50%	70 53.85%

		Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg	Total
	65 to 74 years	19 28.79%	19 29.69%	38 29.23%
	≥75 years	7 10.61%	10 15.62%	17 13.08%
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	66 participants	64 participants	130 participants
	Female	66 100%	64 100%	130 100%
	Male	0 0%	0 0%	0 0%
Race/Ethnicity, Customized Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	66 participants	64 participants	130 participants
[Not specified]	Hispanic or Latino	1 1.52%	3 4.69%	4 3.08%
	Not Hispanic or Latino	65 98.48%	61 95.31%	126 96.92%
Race/Ethnicity, Customized Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	66 participants	64 participants	130 participants
[Not specified]	Black/ African American	5 7.58%	4 6.25%	9 6.92%
	White	61 92.42%	60 93.75%	121 93.08%
Height [1] Mean (Standard Deviation) Unit of measure: centimeters (cm)	Number Analyzed	65 participants	63 participants	128 participants
		164.9 (6.38)	162.7 (6.44)	163.8 (6.48)
		[1] Measure Analysis Population Description: Height data is only available for n= 65, 63 participants.		

		Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg	Total
Weight Mean (Standard Deviation) Unit of measure: kilograms (kg)	Number Analyzed	66 participants	64 participants	130 participants
		73.2 (17.47)	75.6 (16.66)	74.3 (17.05)
Eastern Cooperative Oncology Group (ECOG) Performance Status [1] Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	66 participants	64 participants	130 participants
	Score=0	50 75.76%	40 62.5%	90 69.23%
	Score=1	16 24.24%	24 37.5%	40 30.77%
		[1] Measure Description: ECOG Performance status is an assessment of a participant's general well-being and activities of daily of life. Scores range from 0=perfect health (asymptomatic; able to carry out activities without restriction) to 5=death.		

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Progression-free Survival (PFS)
Measure Description	PFS is defined as the number of months from the date of randomization to the earlier of progressive disease (PD) or death due to any cause.
Time Frame	From date of randomization to discontinuation due to disease progression or death up to primary completion date (Median follow-up 6 months)

Analysis Population Description

Full Analysis Set included all randomized participants.

Reporting Groups

	Description
Exemestane 25 mg + Placebo	Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

	Description
Exemestane 25 mg + Entinostat 5 mg	Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

Measured Values

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
Overall Number of Participants Analyzed	66	64
Progression-free Survival (PFS) Median (95% Confidence Interval) Unit of measure: months	2.27 (1.81 to 3.68)	4.28 (3.26 to 5.36)

Statistical Analysis 1 for Progression-free Survival (PFS)

Statistical Analysis Overview	Comparison Group Selection	Exemestane 25 mg + Placebo, Exemestane 25 mg + Entinostat 5 mg
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.06
	Comments	[Not specified]
	Method	Log Rank
	Comments	P-value is stratified by the randomization stratification factors and is 1-sided, with a 0.10 threshold for significance.

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.73
	Confidence Interval	(2-Sided) 95% 0.49 to 1.09
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Objective Response Rate (ORR)

Measure Description	ORR is defined as the percentage of participants with response during treatment classified as complete response (CR) or partial response (PR), as assessed by the investigator based on Response Evaluation Criteria in Solid Tumors (RECIST), version 1.0. CR is defined as the disappearance of all target lesions. PR is defined as at least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD.
Time Frame	From date of randomization to discontinuation due to disease progression or intolerable Adverse Event (AE) up to primary completion date (Median follow-up 6 months)

Analysis Population Description

Full Analysis Set included all randomized participants.

Reporting Groups

	Description
Exemestane 25 mg + Placebo	Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.
Exemestane 25 mg + Entinostat 5 mg	Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

Measured Values

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
Overall Number of Participants Analyzed	66	64
Objective Response Rate (ORR) Number (95% Confidence Interval) Unit of measure: percentage of participants	4.6 (1.0 to 12.7)	4.7 (1.0 to 13.1)

3. Secondary Outcome Measure:

Measure Title	Clinical Benefit Rate (CBR)
Measure Description	CBR is defined as the percentage of participants with overall response (CR + PR) plus stable disease (SD) for 6 months as assessed by the investigator based on RECIST, version 1.0. CR is defined as the disappearance of all target lesions. PR is defined as at least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD. SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started.
Time Frame	From date of randomization to discontinuation due to disease progression or intolerable AE up to primary completion date (Median follow-up 6 months)

Analysis Population Description

Full Analysis Set included all randomized participants.

Reporting Groups

	Description
Exemestane 25 mg + Placebo	Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.
Exemestane 25 mg + Entinostat 5 mg	Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

Measured Values

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
Overall Number of Participants Analyzed	66	64
Clinical Benefit Rate (CBR) Number (95% Confidence Interval) Unit of measure: percentage of participants	25.8 (15.8 to 38.0)	26.6 (16.3 to 39.1)

4. Secondary Outcome Measure:

Measure Title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)
Measure Description	An AE is defined as any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. Worsening of a pre-existing medical condition was considered an AE if there was either an increase in severity, frequency, or duration of the condition or an association with significantly worse outcomes. Abnormal clinical laboratory findings determined by the investigator to be clinically significant were recorded as AEs. A TEAE is an AE that starts after the administration of study drug. A SAE is any AE that is fatal, life threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth effect or other significant medical hazard.
Time Frame	First dose to within 30 days of last dose of study drug (Up to Approximately 2 Years)

Analysis Population Description

Safety Population included all randomized participants who received at least one dose of study drug.

Reporting Groups

	Description
Exemestane 25 mg + Placebo	Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.
Exemestane 25 mg + Entinostat 5 mg	Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

Measured Values

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
Overall Number of Participants Analyzed	66	63
Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) Measure Type: Count of Participants Unit of measure: participants		
TEAE	56 84.85%	60 95.24%
Serious TEAE	8 12.12%	10 15.87%

5. Other Pre-specified Outcome Measure:

Measure Title	Overall Survival (OS)
Measure Description	OS was defined as the number of months elapsed between the date of randomization and the date of death (whatever the cause).
Time Frame	First dose of study drug to end of study (Median follow-up 24 months in the EE arm and 26.4 months in the EP arm)

Analysis Population Description

Full Analysis Set included all randomized participants.

Reporting Groups

	Description
Exemestane 25 mg + Placebo (EP)	Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

	Description
Exemestane 25 mg + Entinostat 5 mg (EE)	Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

Measured Values

	Exemestane 25 mg + Placebo (EP)	Exemestane 25 mg + Entinostat 5 mg (EE)
Overall Number of Participants Analyzed	66	64
Overall Survival (OS) Median (95% Confidence Interval) Unit of measure: months	19.84 (17.04 to 26.71)	28.13 (21.15 to NA) [1]

[1] Upper Confidence Interval was not estimable due to the low number of participants with events.

Statistical Analysis 1 for Overall Survival (OS)

Statistical Analysis Overview	Comparison Group Selection	Exemestane 25 mg + Placebo (EP), Exemestane 25 mg + Entinostat 5 mg (EE)
	Comments	[Not specified]
	Type of Statistical Test	Superiority
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.018
	Comments	P-value is stratified by the randomization stratification factors and is 1-sided.
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.59
	Confidence Interval	(2-Sided) 95% 0.36 to 0.97
	Estimation Comments	Hazard ratio was estimated from a Cox proportional hazards model. Placebo serves as the reference treatment group for the interpretation of the hazard ratio.

Reported Adverse Events

Time Frame	First dose to within 30 days of last dose of study drug (Up to approximately 2 Years)
Adverse Event Reporting Description	Safety population included all randomized participants who received at least 1 dose of study drug.

Reporting Groups

	Description
Exemestane 25 mg + Placebo	Exemestane (Aromasin®) 25 mg tablets orally once daily plus a placebo-matching entinostat tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.
Exemestane 25 mg + Entinostat 5 mg	Exemestane (Aromasin®) 25 mg tablets orally once daily plus an entinostat 5 mg tablet orally once per week on Days 1, 8, 15 and 22 of each 28-day treatment cycle until development of progressive disease (PD) or unacceptable toxicity or closure of the study by the Sponsor, whichever occurred first.

All-Cause Mortality

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Total All-Cause Mortality	/	/

Serious Adverse Events

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Total	8/66 (12.12%)	10/63 (15.87%)
Blood and lymphatic system disorders		
Anemia group [A] †	1/66 (1.52%)	1/63 (1.59%)
Leukopenia group [A] †	1/66 (1.52%)	0/63 (0%)
Thrombocytopenia group [A] †	1/66 (1.52%)	0/63 (0%)
Cardiac disorders		
Atrial tachycardia [A] †	0/66 (0%)	1/63 (1.59%)
Gastrointestinal disorders		
Constipation [A] †	1/66 (1.52%)	0/63 (0%)

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Enterocutaneous fistula [A] †	1/66 (1.52%)	0/63 (0%)
Ileus [A] †	0/66 (0%)	1/63 (1.59%)
Oesophagitis [A] †	0/66 (0%)	1/63 (1.59%)
Pancreatic mass [A] †	1/66 (1.52%)	0/63 (0%)
Pancreatitis acute [A] †	0/66 (0%)	1/63 (1.59%)
General disorders		
Asthenia [A] †	1/66 (1.52%)	0/63 (0%)
Pyrexia [A] †	1/66 (1.52%)	0/63 (0%)
Infections and infestations		
Sepsis [A] †	1/66 (1.52%)	0/63 (0%)
Injury, poisoning and procedural complications		
Overdose [A] †	0/66 (0%)	1/63 (1.59%)
Procedural nausea [A] †	1/66 (1.52%)	0/63 (0%)
Radiation pneumonitis [A] †	0/66 (0%)	1/63 (1.59%)
Metabolism and nutrition disorders		
Hypercalcaemia [A] †	1/66 (1.52%)	0/63 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Malignant pleural effusion [A] †	0/66 (0%)	1/63 (1.59%)
Renal and urinary disorders		
Urinary tract infection [A] †	1/66 (1.52%)	0/63 (0%)
Respiratory, thoracic and mediastinal disorders		
Chronic obstructive pulmonary disease [A] †	1/66 (1.52%)	0/63 (0%)
Dyspnoea [A] †	0/66 (0%)	1/63 (1.59%)

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Lobar pneumonia [A] †	1/66 (1.52%)	1/63 (1.59%)
Lung infiltration [A] †	0/66 (0%)	1/63 (1.59%)
Pleural effusion [A] †	0/66 (0%)	1/63 (1.59%)
Pneumonia [A] †	0/66 (0%)	2/63 (3.17%)
Pneumonitis [A] †	0/66 (0%)	1/63 (1.59%)
Vascular disorders		
Deep vein thrombosis [A] †	0/66 (0%)	1/63 (1.59%)
Vena cava thrombosis [A] †	0/66 (0%)	1/63 (1.59%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (10.1)

Other Adverse Events

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

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Total	51/66 (77.27%)	58/63 (92.06%)
Blood and lymphatic system disorders		
Anemia group [A] †	7/66 (10.61%)	12/63 (19.05%)
Leukopenia group [A] †	1/66 (1.52%)	9/63 (14.29%)
Neutropenia group [A] †	1/66 (1.52%)	19/63 (30.16%)
Thrombocytopenia group [A] †	3/66 (4.55%)	12/63 (19.05%)
Cardiac disorders		
Tachycardia [A] †	4/66 (6.06%)	3/63 (4.76%)
Gastrointestinal disorders		
Abdominal pain upper [A] †	6/66 (9.09%)	5/63 (7.94%)

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Constipation [A] †	10/66 (15.15%)	6/63 (9.52%)
Diarrhoea [A] †	8/66 (12.12%)	11/63 (17.46%)
Dyspepsia [A] †	2/66 (3.03%)	9/63 (14.29%)
Nausea [A] †	10/66 (15.15%)	25/63 (39.68%)
Pyrexia [A] †	3/66 (4.55%)	4/63 (6.35%)
Vomiting [A] †	3/66 (4.55%)	13/63 (20.63%)
General disorders		
Asthenia [A] †	4/66 (6.06%)	3/63 (4.76%)
Chills [A] †	0/66 (0%)	4/63 (6.35%)
Fatigue [A] †	17/66 (25.76%)	30/63 (47.62%)
Hot flush [A] †	6/66 (9.09%)	5/63 (7.94%)
Oedema peripheral [A] †	3/66 (4.55%)	13/63 (20.63%)
Pain [A] †	4/66 (6.06%)	10/63 (15.87%)
Investigations		
Alanine aminotransferase increased [A] †	6/66 (9.09%)	3/63 (4.76%)
Aspartate aminotransferase increased [A] †	7/66 (10.61%)	3/63 (4.76%)
Blood alkaline phosphatase increased [A] †	5/66 (7.58%)	5/63 (7.94%)
Blood lactate dehydrogenase increased [A] †	1/66 (1.52%)	4/63 (6.35%)
Electrocardiogram QT prolonged [A] †	6/66 (9.09%)	1/63 (1.59%)
Weight decreased [A] †	12/66 (18.18%)	13/63 (20.63%)
Metabolism and nutrition disorders		
Anorexia [A] †	5/66 (7.58%)	8/63 (12.7%)
Hypokalaemia [A] †	2/66 (3.03%)	6/63 (9.52%)

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Hypophosphataemia [A] †	3/66 (4.55%)	4/63 (6.35%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	11/66 (16.67%)	7/63 (11.11%)
Back pain [A] †	11/66 (16.67%)	10/63 (15.87%)
Bone pain [A] †	2/66 (3.03%)	5/63 (7.94%)
Muscle spasms [A] †	2/66 (3.03%)	7/63 (11.11%)
Muscular weakness [A] †	1/66 (1.52%)	4/63 (6.35%)
Musculoskeletal chest pain [A] †	3/66 (4.55%)	6/63 (9.52%)
Myalgia [A] †	5/66 (7.58%)	2/63 (3.17%)
Pain in extremity [A] †	4/66 (6.06%)	10/63 (15.87%)
Nervous system disorders		
Headache [A] †	7/66 (10.61%)	9/63 (14.29%)
Insomnia [A] †	7/66 (10.61%)	7/63 (11.11%)
Neuropathy [A] †	0/66 (0%)	4/63 (6.35%)
Psychiatric disorders		
Anxiety [A] †	3/66 (4.55%)	6/63 (9.52%)
Renal and urinary disorders		
Urinary tract infection [A] †	0/66 (0%)	5/63 (7.94%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	3/66 (4.55%)	8/63 (12.7%)
Dyspnoea [A] †	7/66 (10.61%)	12/63 (19.05%)
Upper respiratory tract infection [A] †	4/66 (6.06%)	2/63 (3.17%)
Skin and subcutaneous tissue disorders		

	Exemestane 25 mg + Placebo	Exemestane 25 mg + Entinostat 5 mg
	Affected/At Risk (%)	Affected/At Risk (%)
Rash [A] †	2/66 (3.03%)	4/63 (6.35%)
Vascular disorders		
Vascular disorders [A] †	3/66 (4.55%)	8/63 (12.7%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (10.1)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Publication of the results of the multi-center Study shall not be made before the first multi-site publication by Sponsor or Publications Committee. No Public Presentation by Institution or Investigator will be made until Study Documentation/Results from all sites are received and analyzed by Sponsor. Separate publication by Investigator will be delayed for a period of 18 months until the initial publication by Committee or Sponsor, or a determination is made not to make such publication.

Results Point of Contact:

Name/Official Title: Michael Meyers, MD, PhD, Chief Medical Officer
Organization: Syndax Pharmaceuticals, Inc.
Phone: +1-646-690-7620
Email: mmeyers@syndax.com