A Clinical Trial of Vorinostat (MK0683, SAHA) in Combination With FDA Approved Cancer Drugs in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC)(0683-056)

This study has been terminated.

(The study was terminated based on the recommendation by the DSMB following a pre-planned protocol interim analysis because the endpoint was not achieved.)

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00473889

First received: May 14, 2007
Last updated: June 8, 2015
Last verified: June 2015
History of Changes

Purpose

This Phase III clinical trial which incorporates an initial Phase II component will determine the survival of advanced Non-small cell lung cancer patients when treated with MK0683 and paclitaxel plus carboplatin

Condition	Intervention	Phase
Stage IIIB or IV Non-Small Cell Lung Cancer	Drug: vorinostat Drug: Comparator: paclitaxel Drug: Comparator: carboplatin Drug: Comparator: placebo	Phase 2 Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)
Primary Purpose: Treatment

Official Title: A Phase II/III Randomized, Double-Blind Study of Paclitaxel Plus Carboplatin in Combination With Vorinostat or Placebo in Patients With Stage IIIB (With Pleural Effusion) or Stage IV Non-Small-Cell Lung Cancer (NSCLC)

Resource links provided by NLM:

Genetics Home Reference related topics: lung cancer

MedlinePlus related topics: Lung Cancer

Drug Information available for: Paclitaxel Carboplatin Vorinostat

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Overall Survival [Time Frame: Start of treatment to death] [Designated as safety issue: No]

  Defined as the time from date of randomization to death due to any cause. Patients without documented death at the time of the final analysis will be censored at the date of the last follow-up.

Secondary Outcome Measures:

- Progression Free Survival [Time Frame: Start of treatment to disease progression or death] [Designated as safety issue: No]

  Defined as the time from randomization to the first documented disease progression or death due to any cause, whichever occurs first. Disease progression is defined as at least a 20% increase in sum of the longest diameter of all target lesions, the appearance of a new lesion, or an increase in non-target lesions.

- Number of Participants Who Had a Disease Response to Treatment [Time Frame: Every 42 days from start of treatment until disease response] [Designated as safety issue: No]

  Response to treatment is defined as a complete response (CR) or partial response (PR) to treatment. Confirmation of response required a second assessment performed at least 4 weeks after the initial assessment. (PR is defined as at least a 30% reduction in sum of the longest diameter of all target lesions and no increase in non-target lesions).

Enrollment:	253
Study Start Date:	May 2007
Study Completion Date:	December 2008
Primary Completion Date:	December 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: 1 vorinostat; IV paclitaxel; IV carboplatin	Drug: vorinostat vorinostat 400 mg capsules once daily. Up to 6 months of treatment Other Name: Zolinza Drug: Comparator: paclitaxel intravenous (IV) paclitaxel 200 mg/m2. Up to 6 months of treatment Other Name: Taxol Drug: Comparator: carboplatin intravenous (IV) carboplatin AUC 6mg/min/ml. Up to 6 months of treatment. Other Name: Paraplatin
Placebo Comparator: 2 Placebo; IV paclitaxel; IV carboplatin	Drug: Comparator: paclitaxel intravenous (IV) paclitaxel 200 mg/m2. Up to 6 months of treatment Other Name: Taxol Drug: Comparator: carboplatin intravenous (IV) carboplatin AUC 6mg/min/ml. Up to 6 months of treatment. Other Name: Paraplatin Drug: Comparator: placebo vorinostat 400 mg placebo capsules once daily. Up to 6 months of treatment

Eligibility

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

Criteria

Inclusion Criteria:

- Males and females at least 18 years of age who have confirmed diagnosis of Non-small Cell Lung Cancer
- Patients with no systemic prior systemic treatment for lung cancer except patients at least 12 months from prior adjuvant therapy
- Adequate bone marrow,kidney and liver function
- Must be recovered and at least 4 weeks from major surgery or radiation
- ECOG (Eastern Cooperative Oncology Group) performance status of 0 or 1
- Men and women must agree to use birth control during the study
- Women able to have children must have a negative pregnancy test 14 days before study enrollment

Exclusion Criteria:

- Patients with prior treatment with other investigational agents less than 4 weeks before study enrollment
- Pregnant or nursing female patients
- Patients who are HIV positive
- Patients who have Hepatitis A, B, or C
- Patients unable to take study medication by mouth
- Patients with untreated brain cancer
- Patient eligible for treatment with bevacizumab and for whom bevacizumab is available

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT00473889

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director: Medical Monitor Merck Sharp & Dohme Corp.

More Information

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Beaumont H, Souchet S, Labatte JM, Iannessi A, Tolcher AW. Changes of lung tumour volume on CT - prediction of the reliability of assessments. Cancer Imaging. 2015 Oct 31;15:17. doi: 10.1186/s40644-015-0052-2.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00473889 History of Changes
Other Study ID Numbers:	0683-056 MK0683-056 2006_539
Study First Received:	May 14, 2007
Results First Received:	September 3, 2009
Last Updated:	June 8, 2015
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Carcinoma, Non-Small-Cell Lung	Vorinostat
Lung Neoplasms	Antimitotic Agents
Bronchial Neoplasms	Antineoplastic Agents
Carcinoma, Bronchogenic	Antineoplastic Agents, Phytogenic
Lung Diseases	Enzyme Inhibitors
Neoplasms	Histone Deacetylase Inhibitors
Neoplasms by Site	Mitosis Modulators
Respiratory Tract Diseases	Molecular Mechanisms of Pharmacological Action

Respiratory Tract Neoplasms
Thoracic Neoplasms
Carboplatin
Paclitaxel

Pharmacologic Actions
Therapeutic Uses
Tubulin Modulators

ClinicalTrials.gov processed this record on April 14, 2016

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Results First Received: September 3, 2009

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Stage IIIB or IV Non-Small Cell Lung Cancer
Interventions:	Drug: vorinostat Drug: Comparator: paclitaxel Drug: Comparator: carboplatin Drug: Comparator: placebo

Participant Flow

Hide 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 was conducted at 99 investigative sites worldwide. The first patient's first visit was 16 May 07 and the last patient's last visit was 12 Dec 2008.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment

Randomized participants were stratified by Stage (IIIB versus IV), geographic region and eligibility for treatment with bevacizumab prior to treatment assignment.

Reporting Groups

	Description
Vorinostat + Paclitaxel + Carboplatin	Experimental arm: Vorinostat capsules (400 mg) once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.
Placebo + Paclitaxel + Carboplatin	Placebo Comparator arm: Placebo capsules once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.

Participant Flow: Overall Study

	Vorinostat + Paclitaxel + Carboplatin	Placebo + Paclitaxel + Carboplatin
STARTED	**126**	**127**
COMPLETED	**43**	**63**
NOT COMPLETED	**83**	**64**
Did not receive study medication	**1**	**4**
Adverse Event	**30**	**17**
Protocol Violation	**4**	**2**
Lack of Efficacy	**28**	**29**
Lost to Follow-up	**2**	**1**
Physician Decision	**10**	**5**
Trial Terminated	**3**	**6**
Withdrawal by Subject	**5**	**0**

Baseline Characteristics

Hide Baseline Characteristics

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
Vorinostat + Paclitaxel + Carboplatin	Experimental arm: Vorinostat capsules (400 mg) once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.
Placebo + Paclitaxel + Carboplatin	Placebo Comparator arm: Placebo capsules once daily on Days -4 through 10 of Cycle 1 (25 day

	treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.
Total	Total of all reporting groups

Baseline Measures

	Vorinostat + Paclitaxel + Carboplatin	Placebo + Paclitaxel + Carboplatin	Total
Number of Participants [units: participants]	**126**	**127**	**253**
Age, Customized [units: participants]			
Less Than 65 years	**70**	**89**	**159**
65 years or Older	**56**	**38**	**94**
Gender [units: participants]			
Female	**34**	**56**	**90**
Male	**92**	**71**	**163**
Race/Ethnicity, Customized [units: participants]			
White	**79**	**79**	**158**
Black	**3**	**4**	**7**
Asian	**31**	**32**	**63**
American Indian or Alaskan Native mix	**13**	**12**	**25**
Cancer Stage [units: Participants]			
IIIB	**14**	**15**	**29**
IV	**112**	**112**	**224**
Eligibility to receive treatment with Bevacizumab [units: Participants]			
Eligible	**70**	**63**	**133**
Ineligible	**55**	**60**	**115**
Unknown	**1**	**4**	**5**
Geographic region where the participant lived [units: Participants]			
North America	**25**	**27**	**52**
Europe (United Kingdom, Italy, Germany, and Spain)	**41**	**40**	**81**
Asia	**22**	**24**	**46**
Rest of the World	**38**	**36**	**74**

Outcome Measures

Hide All Outcome Measures

1. Primary: Overall Survival [Time Frame: Start of treatment to death]

Measure Type	Primary
Measure Title	Overall Survival
Measure Description	Defined as the time from date of randomization to death due to any cause. Patients without documented death at the time of the final analysis will be censored at the date of the last follow-up.
Time Frame	Start of treatment to death
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population is defined as all randomized participants. Participants are counted in the group to which they are randomized.

Reporting Groups

	Description
Vorinostat + Paclitaxel + Carboplatin	Experimental arm: Vorinostat capsules (400 mg) once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.
Placebo + Paclitaxel + Carboplatin	Placebo Comparator arm: Placebo capsules once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.

Measured Values

	Vorinostat + Paclitaxel + Carboplatin	**Placebo + Paclitaxel + Carboplatin**
Number of Participants Analyzed [units: participants]	**126**	**127**
Overall Survival [units: Months] Median (Full Range)	**11.0 (0.2 to 17.3)**	**14.0 (0.03 to 18.7)**

Statistical Analysis 1 for Overall Survival

Groups [1]	Placebo + Paclitaxel + Carboplatin
Method [2]	Stratified Log Rank
P Value [3]	0.992

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Disease stage and bevacizumab eligibility are the stratification factors in the stratified log rank test.

[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	This is a one sided p-value, which corresponds to the null hypothesis.

2. Secondary: Progression Free Survival [Time Frame: Start of treatment to disease progression or death]

Measure Type	Secondary
Measure Title	Progression Free Survival
Measure Description	Defined as the time from randomization to the first documented disease progression or death due to any cause, whichever occurs first. Disease progression is defined as at least a 20% increase in sum of the longest diameter of all target lesions, the appearance of a new lesion, or an increase in non-target lesions.
Time Frame	Start of treatment to disease progression or death
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set (FAS) population defined as all randomized participants who have received at least one dose of study medication. There are 253 participants randomized in the study 5 didn't take any study medication. Therefore, 248 participants are included in this analysis population.

Reporting Groups

	Description
Vorinostat + Paclitaxel + Carboplatin	Experimental arm: Vorinostat capsules (400 mg) once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.
Placebo + Paclitaxel + Carboplatin	Placebo Comparator arm: Placebo capsules once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.

Measured Values

	Vorinostat + Paclitaxel + Carboplatin	**Placebo + Paclitaxel + Carboplatin**
Number of Participants Analyzed [units: participants]	**125**	**123**
Progression Free Survival [units: Months] Median (Full Range)	**4.3 (0.03 to 13.4)**	**5.5 (0.03 to 13.8)**

Statistical Analysis 1 for Progression Free Survival

Groups [1]	Placebo + Paclitaxel + Carboplatin
Method [2]	Finkelstein's Interval Censored Method

P Value [3]	0.862

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Disease stage and bevacizumab eligibility are the stratification factors in the Finkelstein's Interval Censored Method Model.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	This is a one sided p-value, which corresponds to the null hypothesis.

3. Secondary: Number of Participants Who Had a Disease Response to Treatment [Time Frame: Every 42 days from start of treatment until disease response]

Measure Type	Secondary
Measure Title	Number of Participants Who Had a Disease Response to Treatment
Measure Description	Response to treatment is defined as a complete response (CR) or partial response (PR) to treatment. Confirmation of response required a second assessment performed at least 4 weeks after the initial assessment. (PR is defined as at least a 30% reduction in sum of the longest diameter of all target lesions and no increase in non-target lesions).
Time Frame	Every 42 days from start of treatment until disease response
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set (FAS) population is defined as all randomized participants who have received at least one dose of study medication. There are 253 participants randomized in the study. Five (5) didn't take any study medication. Therefore, 248 participants are included in this analysis population.

Reporting Groups

	Description
Vorinostat + Paclitaxel + Carboplatin	Experimental arm: Vorinostat capsules (400 mg) once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.
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Measured Values

	Vorinostat + Paclitaxel + Carboplatin	**Placebo + Paclitaxel + Carboplatin**
Number of Participants Analyzed [units: participants]	**125**	**123**
Number of Participants Who Had a Disease Response to		

Treatment [units: Participants]		
Responder	28	36
Non-Responder	97	87

Statistical Analysis 1 for Number of Participants Who Had a Disease Response to Treatment

Groups [1]	Placebo + Paclitaxel + Carboplatin
Method [2]	Stratified Miettinen and Nurminen
P Value [3]	0.899

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Disease stage and bevacizumab eligibility are the stratification factors in the stratified Miettinen and Nurmimen method.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	This is a one sided p-value, which corresponds to the null hypothesis.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Adverse Events were collected from the time the patient signed the informed consent form until 30 days after the last dose of study medications. Serious Adverse Events were followed until resolution.
Additional Description	The 5 untreated patients on study are not counted in the Adverse Events tables. Further, one patient was randomized to vorinostat but took placebo; and one patient, randomized to placebo, started vorinostat for 4 days before using placebo. Both patients are counted in the placebo group for Adverse Events, yielding 124 patients in each group.

Reporting Groups

	Description
Vorinostat + Paclitaxel + Carboplatin	Experimental arm: Vorinostat capsules (400 mg) once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.
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Serious Adverse Events

	Vorinostat + Paclitaxel + Carboplatin	Placebo + Paclitaxel + Carboplatin
Total, serious adverse events		
# participants affected / at risk	**63/124 (50.81%)**	**45/124 (36.29%)**

Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**2/124 (1.61%)**	**3/124 (2.42%)**
Febrile neutropenia † 1		
# participants affected / at risk	**10/124 (8.06%)**	**5/124 (4.03%)**
Neutropenia † 1		
# participants affected / at risk	**9/124 (7.26%)**	**2/124 (1.61%)**
Thrombocytopenia † 1		
# participants affected / at risk	**2/124 (1.61%)**	**1/124 (0.81%)**
Cardiac disorders		
Atrial fibrillation † 1		
# participants affected / at risk	**2/124 (1.61%)**	**3/124 (2.42%)**
Cardiac arrest † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Myocardial infarction † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Gastrointestinal disorders		
Abdominal pain † 1		
# participants affected / at risk	**2/124 (1.61%)**	**0/124 (0.00%)**
Abdominal pain upper † 1		
# participants affected / at risk	**2/124 (1.61%)**	**0/124 (0.00%)**
Diarrhoea † 1		
# participants affected / at risk	**4/124 (3.23%)**	**1/124 (0.81%)**
Rectal perforation † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Retching † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
General disorders		
Asthenia † 1		
# participants affected / at risk	**6/124 (4.84%)**	**1/124 (0.81%)**
Death † 1		
# participants affected / at risk	**2/124 (1.61%)**	**1/124 (0.81%)**
Fatigue † 1		
# participants affected / at risk	**3/124 (2.42%)**	**1/124 (0.81%)**
Multi-organ failure † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Pyrexia † 1		
# participants affected / at risk	**5/124 (4.03%)**	**2/124 (1.61%)**
Hepatobiliary disorders		
Cholecystitis † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**

Immune system disorders		
Hypersensitivity † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Infections and infestations		
Bacteraemia † 1		
# participants affected / at risk	**2/124 (1.61%)**	**1/124 (0.81%)**
Cellulitis † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Gastroenteritis † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Neutropenic sepsis † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Pneumonia † 1		
# participants affected / at risk	**11/124 (8.87%)**	**9/124 (7.26%)**
Pulmonary sepsis † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Sepsis † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Septic shock † 1		
# participants affected / at risk	**2/124 (1.61%)**	**1/124 (0.81%)**
Staphylococcal infection † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Upper respiratory tract infection † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Injury, poisoning and procedural complications		
Accidental overdose † 1		
# participants affected / at risk	**1/124 (0.81%)**	**2/124 (1.61%)**
Femoral neck fracture † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Femur fracture † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Lumbar vertebral fracture † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Overdose † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Procedural pain † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Investigations		
Troponin increased † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Metabolism and nutrition disorders		

Anorexia † 1		
# participants affected / at risk	**1/124 (0.81%)**	**1/124 (0.81%)**
Dehydration † 1		
# participants affected / at risk	**4/124 (3.23%)**	**0/124 (0.00%)**
Hypercalcaemia † 1		
# participants affected / at risk	**1/124 (0.81%)**	**1/124 (0.81%)**
Hypokalaemia † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Hypomagnesaemia † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Hyponatraemia † 1		
# participants affected / at risk	**2/124 (1.61%)**	**2/124 (1.61%)**
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Back pain † 1		
# participants affected / at risk	**1/124 (0.81%)**	**3/124 (2.42%)**
Musculoskeletal chest pain † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Myalgia † 1		
# participants affected / at risk	**1/124 (0.81%)**	**1/124 (0.81%)**
Neck pain † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Chronic lymphocytic leukaemia † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Nasopharyngeal cancer † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Non-small cell lung cancer † 1		
# participants affected / at risk	**8/124 (6.45%)**	**11/124 (8.87%)**
Tumour pain † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Nervous system disorders		
Cerebrovascular accident † 1		
# participants affected / at risk	**1/124 (0.81%)**	**2/124 (1.61%)**
Convulsion † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Dizziness † 1		
# participants affected / at risk	**1/124 (0.81%)**	**0/124 (0.00%)**
Headache † 1		

# participants affected / at risk	0/124 (0.00%)	1/124 (0.81%)
Hemiparesis † 1		
# participants affected / at risk	1/124 (0.81%)	0/124 (0.00%)
Peripheral sensory neuropathy † 1		
# participants affected / at risk	0/124 (0.00%)	1/124 (0.81%)
Syncope † 1		
# participants affected / at risk	0/124 (0.00%)	1/124 (0.81%)
Renal and urinary disorders		
Azotaemia † 1		
# participants affected / at risk	0/124 (0.00%)	1/124 (0.81%)
Haematuria † 1		
# participants affected / at risk	2/124 (1.61%)	0/124 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Acute respiratory distress syndrome † 1		
# participants affected / at risk	2/124 (1.61%)	0/124 (0.00%)
Chronic obstructive pulmonary disease † 1		
# participants affected / at risk	1/124 (0.81%)	1/124 (0.81%)
Cough † 1		
# participants affected / at risk	1/124 (0.81%)	0/124 (0.00%)
Dyspnoea † 1		
# participants affected / at risk	5/124 (4.03%)	2/124 (1.61%)
Pleural effusion † 1		
# participants affected / at risk	3/124 (2.42%)	2/124 (1.61%)
Pneumonitis † 1		
# participants affected / at risk	0/124 (0.00%)	1/124 (0.81%)
Pneumothorax † 1		
# participants affected / at risk	1/124 (0.81%)	0/124 (0.00%)
Pulmonary embolism † 1		
# participants affected / at risk	3/124 (2.42%)	1/124 (0.81%)
Respiratory failure † 1		
# participants affected / at risk	1/124 (0.81%)	0/124 (0.00%)
Skin and subcutaneous tissue disorders		
Dermatitis † 1		
# participants affected / at risk	1/124 (0.81%)	0/124 (0.00%)
Vascular disorders		
Aortic thrombosis † 1		
# participants affected / at risk	0/124 (0.00%)	1/124 (0.81%)
Embolism † 1		
# participants affected / at risk	1/124 (0.81%)	0/124 (0.00%)
Hypotension † 1		
# participants affected / at risk	2/124 (1.61%)	0/124 (0.00%)

Peripheral ischaemia † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Superior vena caval occlusion † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**
Thrombosis † 1		
# participants affected / at risk	**0/124 (0.00%)**	**1/124 (0.81%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 11.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Adverse Events were collected from the time the patient signed the informed consent form until 30 days after the last dose of study medications. Serious Adverse Events were followed until resolution.
Additional Description	The 5 untreated patients on study are not counted in the Adverse Events tables. Further, one patient was randomized to vorinostat but took placebo; and one patient, randomized to placebo, started vorinostat for 4 days before using placebo. Both patients are counted in the placebo group for Adverse Events, yielding 124 patients in each group.

Frequency Threshold

Threshold above which other adverse events are reported	3%

Reporting Groups

	Description
Vorinostat + Paclitaxel + Carboplatin	Experimental arm: Vorinostat capsules (400 mg) once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.
Placebo + Paclitaxel + Carboplatin	Placebo Comparator arm: Placebo capsules once daily on Days -4 through 10 of Cycle 1 (25 day treatment cycle) and Days 1 through 14 of each subsequent 21 day treatment cycle; paclitaxel (200 mg/m2) and carboplatin (area under concentration/time curve of 6 mg/min/mL) administered by intravenous (IV) infusion on Day 1 of each treatment cycle.

Other Adverse Events

	Vorinostat + Paclitaxel + Carboplatin	**Placebo + Paclitaxel + Carboplatin**
Total, other (not including serious) adverse events		
# participants affected / at risk	**114/124 (91.94%)**	**117/124 (94.35%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**51/124 (41.13%)**	**42/124 (33.87%)**
Leukopenia † 1		
# participants affected / at risk	**13/124 (10.48%)**	**18/124 (14.52%)**
Lymphopenia † 1		
# participants affected / at risk	**9/124 (7.26%)**	**10/124 (8.06%)**

Neutropenia † 1		
# participants affected / at risk	**53/124 (42.74%)**	**55/124 (44.35%)**
Thrombocytopenia † 1		
# participants affected / at risk	**45/124 (36.29%)**	**23/124 (18.55%)**
Ear and labyrinth disorders		
Tinnitus † 1		
# participants affected / at risk	**0/124 (0.00%)**	**5/124 (4.03%)**
Eye disorders		
Vision blurred † 1		
# participants affected / at risk	**3/124 (2.42%)**	**5/124 (4.03%)**
Gastrointestinal disorders		
Abdominal distension † 1		
# participants affected / at risk	**2/124 (1.61%)**	**4/124 (3.23%)**
Abdominal pain † 1		
# participants affected / at risk	**9/124 (7.26%)**	**6/124 (4.84%)**
Abdominal pain upper † 1		
# participants affected / at risk	**6/124 (4.84%)**	**6/124 (4.84%)**
Constipation † 1		
# participants affected / at risk	**34/124 (27.42%)**	**26/124 (20.97%)**
Diarrhoea † 1		
# participants affected / at risk	**43/124 (34.68%)**	**36/124 (29.03%)**
Dry mouth † 1		
# participants affected / at risk	**7/124 (5.65%)**	**1/124 (0.81%)**
Dyspepsia † 1		
# participants affected / at risk	**8/124 (6.45%)**	**7/124 (5.65%)**
Dysphagia † 1		
# participants affected / at risk	**1/124 (0.81%)**	**4/124 (3.23%)**
Gastritis † 1		
# participants affected / at risk	**4/124 (3.23%)**	**1/124 (0.81%)**
Nausea † 1		
# participants affected / at risk	**46/124 (37.10%)**	**39/124 (31.45%)**
Stomatitis † 1		
# participants affected / at risk	**12/124 (9.68%)**	**11/124 (8.87%)**
Vomiting † 1		
# participants affected / at risk	**34/124 (27.42%)**	**24/124 (19.35%)**
General disorders		
Asthenia † 1		
# participants affected / at risk	**27/124 (21.77%)**	**18/124 (14.52%)**
Chills † 1		
# participants affected / at risk	**5/124 (4.03%)**	**4/124 (3.23%)**
Fatigue † 1		

# participants affected / at risk	28/124 (22.58%)	32/124 (25.81%)
Oedema peripheral † 1		
# participants affected / at risk	11/124 (8.87%)	13/124 (10.48%)
Pyrexia † 1		
# participants affected / at risk	21/124 (16.94%)	11/124 (8.87%)
Hepatobiliary disorders		
Hyperbilirubinaemia † 1		
# participants affected / at risk	4/124 (3.23%)	0/124 (0.00%)
Infections and infestations		
Influenza † 1		
# participants affected / at risk	0/124 (0.00%)	5/124 (4.03%)
Pneumonia † 1		
# participants affected / at risk	5/124 (4.03%)	2/124 (1.61%)
Upper respiratory tract infection † 1		
# participants affected / at risk	8/124 (6.45%)	12/124 (9.68%)
Urinary tract infection † 1		
# participants affected / at risk	7/124 (5.65%)	5/124 (4.03%)
Investigations		
Alanine aminotransferase increased † 1		
# participants affected / at risk	10/124 (8.06%)	13/124 (10.48%)
Aspartate aminotransferase increased † 1		
# participants affected / at risk	9/124 (7.26%)	9/124 (7.26%)
Blood alkaline phosphatase increased † 1		
# participants affected / at risk	9/124 (7.26%)	7/124 (5.65%)
Weight decreased † 1		
# participants affected / at risk	6/124 (4.84%)	10/124 (8.06%)
Metabolism and nutrition disorders		
Anorexia † 1		
# participants affected / at risk	34/124 (27.42%)	31/124 (25.00%)
Decreased appetite † 1		
# participants affected / at risk	4/124 (3.23%)	3/124 (2.42%)
Dehydration † 1		
# participants affected / at risk	6/124 (4.84%)	2/124 (1.61%)
Hyperglycaemia † 1		
# participants affected / at risk	10/124 (8.06%)	8/124 (6.45%)
Hyperkalaemia † 1		
# participants affected / at risk	4/124 (3.23%)	3/124 (2.42%)
Hypoalbuminaemia † 1		
# participants affected / at risk	12/124 (9.68%)	10/124 (8.06%)
Hypocalcaemia † 1		
# participants affected / at risk	4/124 (3.23%)	3/124 (2.42%)

Hypoglycaemia † 1		
# participants affected / at risk	2/124 (1.61%)	4/124 (3.23%)
Hypokalaemia † 1		
# participants affected / at risk	14/124 (11.29%)	10/124 (8.06%)
Hypomagnesaemia † 1		
# participants affected / at risk	5/124 (4.03%)	8/124 (6.45%)
Hyponatraemia † 1		
# participants affected / at risk	17/124 (13.71%)	12/124 (9.68%)
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	16/124 (12.90%)	27/124 (21.77%)
Back pain † 1		
# participants affected / at risk	5/124 (4.03%)	13/124 (10.48%)
Bone pain † 1		
# participants affected / at risk	12/124 (9.68%)	9/124 (7.26%)
Muscle spasms † 1		
# participants affected / at risk	2/124 (1.61%)	5/124 (4.03%)
Musculoskeletal chest pain † 1		
# participants affected / at risk	4/124 (3.23%)	2/124 (1.61%)
Musculoskeletal pain † 1		
# participants affected / at risk	8/124 (6.45%)	2/124 (1.61%)
Myalgia † 1		
# participants affected / at risk	21/124 (16.94%)	36/124 (29.03%)
Pain in extremity † 1		
# participants affected / at risk	9/124 (7.26%)	9/124 (7.26%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Tumour pain † 1		
# participants affected / at risk	4/124 (3.23%)	13/124 (10.48%)
Nervous system disorders		
Dizziness † 1		
# participants affected / at risk	9/124 (7.26%)	12/124 (9.68%)
Dysgeusia † 1		
# participants affected / at risk	11/124 (8.87%)	9/124 (7.26%)
Headache † 1		
# participants affected / at risk	13/124 (10.48%)	12/124 (9.68%)
Lethargy † 1		
# participants affected / at risk	4/124 (3.23%)	1/124 (0.81%)
Peripheral motor neuropathy † 1		
# participants affected / at risk	4/124 (3.23%)	3/124 (2.42%)
Peripheral sensory neuropathy † 1		
# participants affected / at risk	51/124 (41.13%)	61/124 (49.19%)

Tremor † 1		
# participants affected / at risk	**5/124 (4.03%)**	**0/124 (0.00%)**
Psychiatric disorders		
Anxiety † 1		
# participants affected / at risk	**6/124 (4.84%)**	**7/124 (5.65%)**
Insomnia † 1		
# participants affected / at risk	**19/124 (15.32%)**	**15/124 (12.10%)**
Renal and urinary disorders		
Dysuria † 1		
# participants affected / at risk	**3/124 (2.42%)**	**5/124 (4.03%)**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**21/124 (16.94%)**	**20/124 (16.13%)**
Dysphonia † 1		
# participants affected / at risk	**6/124 (4.84%)**	**2/124 (1.61%)**
Dyspnoea † 1		
# participants affected / at risk	**21/124 (16.94%)**	**21/124 (16.94%)**
Epistaxis † 1		
# participants affected / at risk	**8/124 (6.45%)**	**5/124 (4.03%)**
Haemoptysis † 1		
# participants affected / at risk	**2/124 (1.61%)**	**6/124 (4.84%)**
Hiccups † 1		
# participants affected / at risk	**4/124 (3.23%)**	**2/124 (1.61%)**
Productive cough † 1		
# participants affected / at risk	**6/124 (4.84%)**	**10/124 (8.06%)**
Rhinorrhoea † 1		
# participants affected / at risk	**3/124 (2.42%)**	**7/124 (5.65%)**
Skin and subcutaneous tissue disorders		
Alopecia † 1		
# participants affected / at risk	**41/124 (33.06%)**	**47/124 (37.90%)**
Dry skin † 1		
# participants affected / at risk	**4/124 (3.23%)**	**1/124 (0.81%)**
Erythema † 1		
# participants affected / at risk	**1/124 (0.81%)**	**4/124 (3.23%)**
Hyperhidrosis † 1		
# participants affected / at risk	**2/124 (1.61%)**	**5/124 (4.03%)**
Pruritus † 1		
# participants affected / at risk	**9/124 (7.26%)**	**10/124 (8.06%)**
Rash † 1		
# participants affected / at risk	**18/124 (14.52%)**	**13/124 (10.48%)**
Vascular disorders		

Deep vein thrombosis † 1		
# participants affected / at risk	**4/124 (3.23%)**	**0/124 (0.00%)**
Hypertension † 1		
# participants affected / at risk	**4/124 (3.23%)**	**5/124 (4.03%)**
Hypotension † 1		
# participants affected / at risk	**1/124 (0.81%)**	**4/124 (3.23%)**
Thrombophlebitis superficial † 1		
# participants affected / at risk	**4/124 (3.23%)**	**2/124 (1.61%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 11.0

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

The study was stopped following a pre-planned interim analysis because the goal for this study to continue was not met, based on 100 events, a reduction in the hazard ratio for progression-free survival by > 23% with a one-sided p-value < 0.1

More Information

Hide More Information

Certain Agreements:

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

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

The agreement is:

☐ 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**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ 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 **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☑ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: Merck agreements may vary with individual investigators, but will not prohibit any investigator from publishing. Merck supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp
phone: 1-800-672-6372

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Beaumont H, Souchet S, Labatte JM, Iannessi A, Tolcher AW. Changes of lung tumour volume on CT - prediction of the reliability of assessments. Cancer Imaging. 2015 Oct 31;15:17. doi: 10.1186/s40644-015-0052-2.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00473889 History of Changes
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Study First Received:	May 14, 2007
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