Trial record **1 of 1** for: H3E-MC-JMHR
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A Study for Patients With Head and Neck Cancer

This study has been completed.

Sponsor:
Eli Lilly and Company

Information provided by:
Eli Lilly and Company

ClinicalTrials.gov Identifier:
NCT00415194

First received: December 20, 2006
Last updated: June 23, 2011
Last verified: June 2011
History of Changes

Full Text View | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Results First Received: March 10, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Head and Neck Neoplasms
Interventions:	

	Drug: pemetrexed Drug: cisplatin Drug: 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
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m^2) administered intravenously (IV) plus cisplatin 75 mg/m^2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m^2 on Day 1 every 21 days.

	Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Participant Flow: Overall Study

	Pemetrexed/Cisplatin	Placebo/Cisplatin
STARTED	**398**	**397**
Received at Least 1 Dose of Study Drug	**392**	**385**
COMPLETED	**70**	**55**
NOT COMPLETED	**328**	**342**
Adverse Event	**37**	**32**
Entry Criteria Not Met	**4**	**8**
Lost to Follow-up	**1**	**0**
Physician Decision	**10**	**16**
Progressive Disease	**180**	**217**
Protocol Violation	**4**	**2**
Withdrawal by Subject	**28**	**21**
Death Due to Study Disease	**26**	**29**
Death Due to Study Drug Related AE	**11**	**1**
Death Due to Procedural Related AE	**0**	**1**
Death Due to AE (Other Causes)	**27**	**15**

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
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m^2) administered intravenously (IV) plus cisplatin 75 mg/m^2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m^2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Total	Total of all reporting groups

Baseline Measures

	Pemetrexed/Cisplatin	**Placebo/Cisplatin**	**Total**

Overall Participants Analyzed [Units: Participants]	**398**	**397**	**795**
Age [Units: Years] Mean (Standard Deviation)	**57.45 (9.54)**	**57.78 (9.36)**	**57.62 (9.44)**
Gender [Units: Participants]			
Female	**56**	**53**	**109**
Male	**342**	**344**	**686**
Race/Ethnicity, Customized [Units: Participants]			
African	**17**	**12**	**29**
Caucasian	**243**	**233**	**476**
East Asian	**55**	**65**	**120**
Hispanic	**11**	**16**	**27**
West Asian (Indian sub-continent)	**72**	**70**	**142**
Unknown	**0**	**1**	**1**
Region of Enrollment [Units: Participants]			
Argentina	**5**	**10**	**15**
Belgium	**7**	**10**	**17**
Brazil	**16**	**12**	**28**
China	**5**	**7**	**12**
Denmark	**7**	**3**	**10**
France	**3**	**3**	**6**
Germany	**50**	**48**	**98**
Hungary	**23**	**22**	**45**

India	**72**	**75**	**147**
Italy	**19**	**21**	**40**
Korea, Republic of	**29**	**24**	**53**
Mexico	**9**	**8**	**17**
Netherlands	**8**	**11**	**19**
Poland	**10**	**10**	**20**
Romania	**20**	**22**	**42**
Russian Federation	**23**	**20**	**43**
South Africa	**11**	**9**	**20**
Spain	**31**	**29**	**60**
Taiwan	**21**	**25**	**46**
United States	**29**	**28**	**57**
Previously Treated for Head and Neck Cancer (HNC) [Units: Participants]			
No	**35**	**39**	**74**
Yes	**363**	**358**	**721**
Prior Treatment with Platinum-Based Therapy [Units: Participants]			
No	**213**	**228**	**441**
Yes	**185**	**169**	**354**
Distant Metastasis [Units: Participants]			
No	**165**	**155**	**320**
Yes	**233**	**242**	**475**
Eastern Cooperative Oncology Group (ECOG) Performance Status [1] [Units: Participants]			

0	**90**	**90**	**180**
1	**257**	**253**	**510**
2	**51**	**53**	**104**
Missing Data	**0**	**1**	**1**

[1] These scales and criteria are used by doctors and researchers to assess how a patient's disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis:

1. Fully active, able to carry on all pre-disease performance without restriction
2. Restricted in strenuous activity,able to carry out work of a light or sedentary nature
3. Ambulatory, but unable to carry out any work activities. Capable of only limited selfcare
4. Completely disabled. Cannot carry on any selfcare.
5. Dead

Primary Site of Disease [Units: Participants]			
Hypopharynx	**63**	**59**	**122**
Larynx	**103**	**102**	**205**
Oral Cavity	**138**	**123**	**261**
Oropharynx	**86**	**106**	**192**
Other	**8**	**7**	**15**

Outcome Measures

Hide All Outcome Measures

1. Primary: Overall Survival (OS) [Time Frame: Baseline to date of death from any cause up to 36 months]

Measure Type	Primary
Measure Title	Overall Survival (OS)

Measure Description	OS duration is defined as the time from the date of randomization to the date of death from any cause. For each participant who is not known to have died as of the data-inclusion cut-off date, OS duration will be censored at the date of the participant's last contact prior to that cut-off date.
Time Frame	Baseline to date of death from any cause up to 36 months
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 - defines the treatment group as those to which participants were assigned by random allocation, even if a participant did not take the assigned treatment, did not receive the correct treatment, or otherwise did not follow the protocol.

Reporting Groups

	Description
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m^2) administered intravenously (IV) plus cisplatin 75 mg/m^2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m^2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose.

	Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Measured Values

	Pemetrexed/Cisplatin	Placebo/Cisplatin
Participants Analyzed [Units: Participants]	**398**	**397**
Overall Survival (OS) [Units: Months] Median (95% Confidence Interval)	**7.33** **(6.34 to 8.38)**	**6.28** **(5.52 to 7.06)**

Statistical Analysis 1 for Overall Survival (OS)

Groups [1]	All groups
Method [2]	Stratified Log Rank
P Value [3]	0.082
Hazard Ratio (HR) [4]	0.87
95% Confidence Interval	0.75 to 1.02

[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:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

	No text entered.
[4]	Other relevant estimation information:
	No text entered.

2. Secondary: Progression-free Survival (PFS) [Time Frame: baseline to measured progressive disease up to 33 months]

Measure Type	Secondary
Measure Title	Progression-free Survival (PFS)
Measure Description	Objective PFS is defined as the time from date of randomization to date of objectively determined progressive disease (PD) or death from any cause, whichever comes first. PD was defined by Response Evaluation Criteria in Solid Tumors (RECIST). PD=at least a 20% increase in sum of longest diameter of target lesions. For participants who are not known to have died as of the data-inclusion cut-off date, and who do not have progressive disease, PFS will be censored at the date of the last objective progression-free disease assessment prior to the date of any subsequent systemic anticancer therapy.
Time Frame	baseline to measured progressive disease up to 33 months
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 - defines the treatment group as those to which participants were assigned by random allocation, even if a participant did not take the assigned treatment, did not receive the correct treatment, or otherwise did not follow the protocol.

Reporting Groups

	Description
Pemetrexed/Cisplatin	

	Pemetrexed 500 milligrams per meter square (mg/m^2) administered intravenously (IV) plus cisplatin 75 mg/m^2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m^2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Measured Values

	Pemetrexed/Cisplatin	**Placebo/Cisplatin**
Participants Analyzed [Units: Participants]	**398**	**397**
Progression-free Survival (PFS) [Units: Months] Median (95% Confidence Interval)	**3.61** **(3.15 to 4.07)**	**2.79** **(2.69 to 3.22)**

Statistical Analysis 1 for Progression-free Survival (PFS)

Groups [1]	All groups
Method [2]	Stratified Log Rank

P Value [3]	0.166
Hazard Ratio (HR) [4]	0.88
95% Confidence Interval	0.76 to 1.03

[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:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

3. Secondary: Percent of Participants With a Tumor Response (Response Rate) [Time Frame: Baseline to progressive disease or discontinuation of study treatment up to 11 months]

Measure Type	Secondary
Measure Title	Percent of Participants With a Tumor Response (Response Rate)
Measure Description	Tumor Response is evaluated as CR (Complete Response) or PR (Partial Response) per Response Evaluation Criteria in Solid Tumors (RECIST criteria). Possible evaluations include: CR: Disappearance of all target lesions. PR: At least a 30% decrease in the size of target lesions. Response rate (%) = (number of participants with CR+PR/number of participants)*100
Time Frame	Baseline to progressive disease or discontinuation of study treatment up to 11 months

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 - defines the treatment group as those to which participants were assigned by random allocation, even if a participant did not take the assigned treatment, did not receive the correct treatment, or otherwise did not follow the protocol.

Reporting Groups

	Description
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m^2) administered intravenously (IV) plus cisplatin 75 mg/m^2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m^2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Measured Values

	Pemetrexed/Cisplatin	**Placebo/Cisplatin**

Participants Analyzed [Units: Participants]	**398**	**397**
Percent of Participants With a Tumor Response (Response Rate) [Units: Percentage of participants]	**12.1**	**8.1**

Statistical Analysis 1 for Percent of Participants With a Tumor Response (Response Rate)

Groups [1]	All groups
Method [2]	Unadjusted normal distribution
P Value [3]	0.061

[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:
	p-value is based on an unadjusted, normal distribution approximation for differences in rates.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

4. Secondary: Duration of Response (DoR) [Time Frame: time of response to progressive disease up to 24 months]

Measure Type	Secondary
Measure Title	Duration of Response (DoR)
Measure Description	

	DoR is time from first observation of complete response (CR) or partial response (PR) to first observation of PD or death. Response is objective status of CR or PR using RECIST criteria. CR is disappearance of lesions. PR is >30% decrease in size of lesions. Responder is any participant with CR or PR. PD is at least 20% increase in sum of longest diameter of target lesions. For participants alive as of data-inclusion cut-off date and who do not have PD, DoR will be censored at date of last objective progression-free disease assessment before date of any subsequent systemic anticancer therapy.
Time Frame	time of response to progressive disease up to 24 months
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.
ITT population with a confirmed best response of complete response (CR) or partial response (PR).

Reporting Groups

	Description
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m^2) administered intravenously (IV) plus cisplatin 75 mg/m^2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m^2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose.

	Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Measured Values

	Pemetrexed/Cisplatin	Placebo/Cisplatin
Participants Analyzed [Units: Participants]	**48**	**32**
Duration of Response (DoR) [Units: Months] Median (95% Confidence Interval)	**5.29** **(4.21 to 5.98)**	**4.37** **(3.58 to 6.44)**

Statistical Analysis 1 for Duration of Response (DoR)

Groups [1]	All groups
Method [2]	Stratified Log Rank
P Value [3]	0.811
Hazard Ratio (HR) [4]	0.92
95% Confidence Interval	0.56 to 1.53

[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:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

	No text entered.
[4]	Other relevant estimation information:
	No text entered.

5. Secondary: Time to Treatment Worsening in Functional Assessment of Cancer Therapy - Head and Neck Cancer (FACT-H&N) Total Score [Time Frame: Baseline (</=Day 1 of first dose) and Day 1 of every subsequent cycle to 30-day post-study completion up to 33 months]

Measure Type	Secondary
Measure Title	Time to Treatment Worsening in Functional Assessment of Cancer Therapy - Head and Neck Cancer (FACT-H&N) Total Score
Measure Description	FACT-H&N consists of 39 items with 5-point rating scale from 0 (not at all) to 4 (very much). FACT-H&N Total score ranges from 0 to 148. Higher score represents a better quality of life. Time to worsening was defined as the first date of worsening in the FACT H&N Total score that was considered at least the prospectively defined minimally important difference (MID) as compared with participant's baseline score, or date of death from any cause. The MID for FACT H&N Total score was a decrease of 12 points.
Time Frame	Baseline (</=Day 1 of first dose) and Day 1 of every subsequent cycle to 30-day post-study completion up to 33 months
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 with at least Baseline data.

Reporting Groups

	Description
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m^2) administered intravenously (IV) plus cisplatin 75 mg/m^2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m^2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Measured Values

	Pemetrexed/Cisplatin	Placebo/Cisplatin
Participants Analyzed [Units: Participants]	**271**	**270**
Time to Treatment Worsening in Functional Assessment of Cancer Therapy - Head and Neck Cancer (FACT-H&N) Total Score [Units: Months] Median (95% Confidence Interval)	**3.29** **(2.76 to 4.11)**	**2.89** **(2.40 to 3.19)**

Statistical Analysis 1 for Time to Treatment Worsening in Functional Assessment of Cancer Therapy - Head and Neck Cancer (FACT-H&N) Total Score

Groups [1]	All groups
Method [2]	Stratified Log Rank
P Value [3]	0.20
Hazard Ratio (HR) [4]	0.86
95% Confidence Interval	0.69 to 1.07

[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:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

6. Secondary: Correlation Between Biomarkers and Treatment Effect [Time Frame: Baseline]

Measure Type	Secondary
Measure Title	Correlation Between Biomarkers and Treatment Effect

Measure Description	Correlation between highly up/downregulated genes and clinical response (Overall Survival (OS) and Progression-Free Survival (PFS)). OS is is defined as the time from the date of randomization to the date of death from any cause. PFS is defined as the time from the date of randomization to the date of objectively determined progressive disease or death from any cause, whichever comes first. 0 participants were analyzed; Reason: The relatively low number of samples collected would not have yielded a meaningful genomic analysis and the decision was made to not analyze the data.
Time Frame	Baseline
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.
Zero participants were analyzed because the relatively low number of samples collected would not have yielded a meaningful genomic analysis.

Reporting Groups

	Description
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m^2) administered intravenously (IV) plus cisplatin 75 mg/m^2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m^2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment.

	Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Measured Values

	Pemetrexed/Cisplatin	Placebo/Cisplatin
Participants Analyzed [Units: Participants]	**0**	**0**
Correlation Between Biomarkers and Treatment Effect [Units: Correlation coefficient]		

No statistical analysis provided for Correlation Between Biomarkers and Treatment Effect

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	Participants who received at least one dose of study drug were included in the safety population included here.

Reporting Groups

	Description
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m2) administered intravenously (IV) plus cisplatin 75 mg/m2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after

	last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Serious Adverse Events

	Pemetrexed/Cisplatin	Placebo/Cisplatin
Total, serious adverse events		
# participants affected / at risk	**185/392 (47.19%)**	**132/385 (34.29%)**
Blood and lymphatic system disorders		
Agranulocytosis † 1		
# participants affected / at risk	**3/392 (0.77%)**	**0/385 (0.00%)**
# events	**6**	**0**
Anaemia † 1		
# participants affected / at risk	**22/392 (5.61%)**	**17/385 (4.42%)**
# events	**27**	**20**
Anaemia of malignant disease † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Bone marrow toxicity † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Febrile neutropenia † 1		
# participants affected / at risk	**12/392 (3.06%)**	**0/385 (0.00%)**
# events	**13**	**0**

Leukopenia † 1		
# participants affected / at risk	**14/392 (3.57%)**	**1/385 (0.26%)**
# events	**16**	**1**
Lymphadenitis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Neutropenia † 1		
# participants affected / at risk	**12/392 (3.06%)**	**3/385 (0.78%)**
# events	**13**	**3**
Thrombocytopenia † 1		
# participants affected / at risk	**11/392 (2.81%)**	**3/385 (0.78%)**
# events	**12**	**3**
Cardiac disorders		
Acute myocardial infarction † 1		
# participants affected / at risk	**3/392 (0.77%)**	**0/385 (0.00%)**
# events	**3**	**0**
Atrial fibrillation † 1		
# participants affected / at risk	**2/392 (0.51%)**	**0/385 (0.00%)**
# events	**2**	**0**
Atrial flutter † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Cardiac arrest † 1		
# participants affected / at risk	**2/392 (0.51%)**	**0/385 (0.00%)**
# events	**2**	**0**
Cardiac failure † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**

Cardio-respiratory arrest † 1		
# participants affected / at risk	2/392 (0.51%)	1/385 (0.26%)
# events	2	1
Cardiopulmonary failure † 1		
# participants affected / at risk	3/392 (0.77%)	2/385 (0.52%)
# events	3	2
Myocardial infarction † 1		
# participants affected / at risk	1/392 (0.26%)	2/385 (0.52%)
# events	1	2
Myocardial ischaemia † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Congenital, familial and genetic disorders		
Tracheo-oesophageal fistula † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Ear and labyrinth disorders		
Deafness † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Tinnitus † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Vertigo † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Gastrointestinal disorders		
Abdominal pain † 1		

# participants affected / at risk	2/392 (0.51%)	1/385 (0.26%)
# events	4	1
Aphagia † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Constipation † 1		
# participants affected / at risk	4/392 (1.02%)	2/385 (0.52%)
# events	4	2
Diarrhoea † 1		
# participants affected / at risk	14/392 (3.57%)	1/385 (0.26%)
# events	14	1
Disbacteriosis † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Duodenal ulcer † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Duodenal ulcer haemorrhage † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Duodenal ulcer perforation † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Dysphagia † 1		
# participants affected / at risk	6/392 (1.53%)	3/385 (0.78%)
# events	6	3
Gastric ulcer haemorrhage † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1

Gastric ulcer perforation † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Gastritis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**2**	**0**
Gastrointestinal haemorrhage † 1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Gastrointestinal necrosis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Gastrooesophageal reflux disease † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Glossodynia † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Haematemesis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Ileus † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Intestinal infarction † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Mesenteric artery thrombosis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**

# events	1	0
Mouth haemorrhage † 1		
# participants affected / at risk	2/392 (0.51%)	2/385 (0.52%)
# events	2	3
Nausea † 1		
# participants affected / at risk	13/392 (3.32%)	7/385 (1.82%)
# events	14	7
Oesophageal stenosis † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Oesophagitis † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Peritonitis † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Stomatitis † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Tongue oedema † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Vomiting † 1		
# participants affected / at risk	22/392 (5.61%)	9/385 (2.34%)
# events	24	9
General disorders		
Adhesion † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0

Asthenia † 1		
# participants affected / at risk	**6/392 (1.53%)**	**9/385 (2.34%)**
# events	**8**	**9**
Chest pain † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Chills † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Death † 1		
# participants affected / at risk	**4/392 (1.02%)**	**4/385 (1.04%)**
# events	**4**	**4**
Face oedema † 1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Fatigue † 1		
# participants affected / at risk	**7/392 (1.79%)**	**5/385 (1.30%)**
# events	**7**	**5**
General physical health deterioration † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Influenza like illness † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Local swelling † 1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Localised oedema † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**

# events	1	0
Malaise † 1		
# participants affected / at risk	1/392 (0.26%)	1/385 (0.26%)
# events	1	1
Mucosal inflammation † 1		
# participants affected / at risk	1/392 (0.26%)	1/385 (0.26%)
# events	1	1
Multi-organ failure † 1		
# participants affected / at risk	1/392 (0.26%)	1/385 (0.26%)
# events	1	1
Oedema peripheral † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Pain † 1		
# participants affected / at risk	0/392 (0.00%)	2/385 (0.52%)
# events	0	2
Performance status decreased † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Pyrexia † 1		
# participants affected / at risk	9/392 (2.30%)	6/385 (1.56%)
# events	9	7
Sudden cardiac death † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Hepatobiliary disorders		
Cholecystitis acute † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)

# events	1	0
Hepatic failure † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Immune system disorders		
Hypersensitivity † 1		
# participants affected / at risk	0/392 (0.00%)	2/385 (0.52%)
# events	0	2
Infections and infestations		
Abdominal infection † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Abdominal wall abscess † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Abscess † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Acinetobacter infection † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Bronchitis † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Bronchopneumonia † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Candida sepsis † 1		

# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Catheter site infection † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Cellulitis † 1		
# participants affected / at risk	1/392 (0.26%)	1/385 (0.26%)
# events	1	1
Central line infection † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Empyema † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Gastroenteritis † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Gastrointestinal infection † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Herpes zoster † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Infection † 1		
# participants affected / at risk	1/392 (0.26%)	3/385 (0.78%)
# events	1	3
Lower respiratory tract infection † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0

Lung infection † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Oral candidiasis † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Oral infection † 1		
# participants affected / at risk	**2/392 (0.51%)**	**0/385 (0.00%)**
# events	**2**	**0**
Pneumonia † 1		
# participants affected / at risk	**26/392 (6.63%)**	**7/385 (1.82%)**
# events	**29**	**9**
Pseudomonal sepsis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Pseudomonas infection † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**2**
Pulmonary tuberculosis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Respiratory tract infection † 1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Sepsis † 1		
# participants affected / at risk	**4/392 (1.02%)**	**4/385 (1.04%)**
# events	**4**	**4**
Septic shock † 1		
# participants affected / at risk	**3/392 (0.77%)**	**2/385 (0.52%)**

# events	3	2
Skin infection † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Staphylococcal infection † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Staphylococcal sepsis † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Superinfection bacterial † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Tracheitis † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Urinary tract infection † 1		
# participants affected / at risk	1/392 (0.26%)	1/385 (0.26%)
# events	1	1
Wound infection † 1		
# participants affected / at risk	0/392 (0.00%)	2/385 (0.52%)
# events	0	2
Injury, poisoning and procedural complications		
Femoral neck fracture † 1		
# participants affected / at risk	2/392 (0.51%)	1/385 (0.26%)
# events	2	1
Femur fracture † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0

Gastrointestinal stoma complication † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Gastrostomy failure † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Humerus fracture † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Post procedural haemorrhage † 1		
# participants affected / at risk	1/392 (0.26%)	3/385 (0.78%)
# events	2	3
Thoracic vertebral fracture † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Tracheal obstruction † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Investigations		
Aspiration bronchial † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Blood alkaline phosphatase increased † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Blood creatinine increased † 1		
# participants affected / at risk	4/392 (1.02%)	1/385 (0.26%)
# events	4	1

Blood electrolytes abnormal † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Blood pressure increased † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Creatinine renal clearance decreased † 1		
# participants affected / at risk	**1/392 (0.26%)**	**2/385 (0.52%)**
# events	**1**	**2**
ECG signs of myocardial ischaemia † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Glomerular filtration rate decreased † 1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Haemoglobin decreased † 1		
# participants affected / at risk	**7/392 (1.79%)**	**4/385 (1.04%)**
# events	**9**	**4**
Lymphocyte count decreased † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Neutrophil count decreased † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Platelet count decreased † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Weight decreased † 1		
# participants affected / at risk	**3/392 (0.77%)**	**0/385 (0.00%)**

# events	3	0
White blood cell count decreased † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
White blood cell count increased † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Metabolism and nutrition disorders		
Anorexia † 1		
# participants affected / at risk	5/392 (1.28%)	5/385 (1.30%)
# events	5	6
Cachexia † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Decreased appetite † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Dehydration † 1		
# participants affected / at risk	9/392 (2.30%)	7/385 (1.82%)
# events	9	7
Diabetic foot † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Hypercalcaemia † 1		
# participants affected / at risk	1/392 (0.26%)	2/385 (0.52%)
# events	1	2
Hyperglycaemia † 1		
# participants affected / at risk	1/392 (0.26%)	1/385 (0.26%)
# events	1	1

Hyperkalaemia † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Hypocalcaemia † 1		
# participants affected / at risk	**1/392 (0.26%)**	**2/385 (0.52%)**
# events	**2**	**2**
Hypokalaemia † 1		
# participants affected / at risk	**6/392 (1.53%)**	**7/385 (1.82%)**
# events	**7**	**7**
Hypomagnesaemia † 1		
# participants affected / at risk	**1/392 (0.26%)**	**2/385 (0.52%)**
# events	**1**	**3**
Hyponatraemia † 1		
# participants affected / at risk	**9/392 (2.30%)**	**5/385 (1.30%)**
# events	**9**	**5**
Hypophagia † 1		
# participants affected / at risk	**2/392 (0.51%)**	**0/385 (0.00%)**
# events	**2**	**0**
Hypovolaemia † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Shock hypoglycaemic † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**

Back pain † 1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Musculoskeletal chest pain † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Myalgia † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Neck pain † 1		
# participants affected / at risk	**0/392 (0.00%)**	**2/385 (0.52%)**
# events	**0**	**2**
Osteoarthritis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Trismus † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Cancer pain † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Infected neoplasm † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Intracranial tumour haemorrhage † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**

Metastases to bone [†1]		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Metastatic pain [†1]		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Oncologic complication [†1]		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Skin neoplasm bleeding [†1]		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Tumour haemorrhage [†1]		
# participants affected / at risk	**1/392 (0.26%)**	**4/385 (1.04%)**
# events	**1**	**6**
Tumour pain [†1]		
# participants affected / at risk	**4/392 (1.02%)**	**1/385 (0.26%)**
# events	**4**	**1**
Nervous system disorders		
Anoxic encephalopathy [†1]		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Cerebral infarction [†1]		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Cerebral ischaemia [†1]		
# participants affected / at risk	**2/392 (0.51%)**	**1/385 (0.26%)**
# events	**2**	**1**

Cerebrovascular accident † 1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Coma † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Convulsion † 1		
# participants affected / at risk	**0/392 (0.00%)**	**3/385 (0.78%)**
# events	**0**	**3**
Dizziness † 1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Encephalitis † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Hydrocephalus † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Lethargy † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Loss of consciousness † 1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Polyneuropathy † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Spinal cord compression † 1		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**

# events	0	1
Syncope † 1		
# participants affected / at risk	3/392 (0.77%)	4/385 (1.04%)
# events	4	4
Psychiatric disorders		
Depression † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Disorientation † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Psychotic disorder † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Suicidal ideation † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Suicide attempt † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Renal and urinary disorders		
Renal failure † 1		
# participants affected / at risk	7/392 (1.79%)	4/385 (1.04%)
# events	9	5
Renal failure acute † 1		
# participants affected / at risk	3/392 (0.77%)	2/385 (0.52%)
# events	4	2
Renal impairment † 1		

# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Reproductive system and breast disorders		
Benign prostatic hyperplasia † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Respiratory, thoracic and mediastinal disorders		
Acute respiratory failure † 1		
# participants affected / at risk	1/392 (0.26%)	1/385 (0.26%)
# events	1	1
Bronchial secretion retention † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Cough † 1		
# participants affected / at risk	2/392 (0.51%)	1/385 (0.26%)
# events	2	1
Dyspnoea † 1		
# participants affected / at risk	10/392 (2.55%)	15/385 (3.90%)
# events	10	15
Haemoptysis † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Hypoxia † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Laryngeal dyspnoea † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0

Laryngeal oedema [†1]		
# participants affected / at risk	**4/392 (1.02%)**	**0/385 (0.00%)**
# events	**4**	**0**
Lung infiltration [†1]		
# participants affected / at risk	**2/392 (0.51%)**	**0/385 (0.00%)**
# events	**2**	**0**
Pharyngeal stenosis [†1]		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Pneumonia aspiration [†1]		
# participants affected / at risk	**2/392 (0.51%)**	**1/385 (0.26%)**
# events	**2**	**1**
Pneumonitis [†1]		
# participants affected / at risk	**2/392 (0.51%)**	**1/385 (0.26%)**
# events	**2**	**1**
Pneumothorax [†1]		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Pulmonary embolism [†1]		
# participants affected / at risk	**2/392 (0.51%)**	**1/385 (0.26%)**
# events	**2**	**1**
Pulmonary oedema [†1]		
# participants affected / at risk	**0/392 (0.00%)**	**1/385 (0.26%)**
# events	**0**	**1**
Respiratory distress [†1]		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Respiratory failure [†1]		
# participants affected / at risk	**2/392 (0.51%)**	**2/385 (0.52%)**

# events	2	2
Respiratory tract haemorrhage † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Rhinorrhoea † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Stridor † 1		
# participants affected / at risk	0/392 (0.00%)	2/385 (0.52%)
# events	0	2
Upper airway obstruction † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Skin and subcutaneous tissue disorders		
Angioedema † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Skin ulcer † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Subcutaneous emphysema † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Swelling face † 1		
# participants affected / at risk	1/392 (0.26%)	1/385 (0.26%)
# events	1	1
Vascular disorders		
Circulatory collapse † 1		

# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Deep vein thrombosis † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Embolism † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Femoral artery occlusion † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Haemodynamic instability † 1		
# participants affected / at risk	0/392 (0.00%)	1/385 (0.26%)
# events	0	1
Haemorrhage † 1		
# participants affected / at risk	1/392 (0.26%)	3/385 (0.78%)
# events	1	3
Hypotension † 1		
# participants affected / at risk	4/392 (1.02%)	1/385 (0.26%)
# events	4	2
Orthostatic hypotension † 1		
# participants affected / at risk	2/392 (0.51%)	0/385 (0.00%)
# events	2	0
Peripheral ischaemia † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0
Phlebitis † 1		
# participants affected / at risk	1/392 (0.26%)	0/385 (0.00%)
# events	1	0

Shock †1		
# participants affected / at risk	**1/392 (0.26%)**	**1/385 (0.26%)**
# events	**1**	**1**
Shock haemorrhagic †1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Subclavian vein thrombosis †1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Superior vena caval occlusion †1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**
Venous thrombosis †1		
# participants affected / at risk	**1/392 (0.26%)**	**0/385 (0.00%)**
# events	**1**	**0**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 12.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	Participants who received at least one dose of study drug were included in the safety population included here.

Frequency Threshold

Threshold above which other adverse events are reported	5

Reporting Groups

	Description
Pemetrexed/Cisplatin	Pemetrexed 500 milligrams per meter square (mg/m2) administered intravenously (IV) plus cisplatin 75 mg/m2 IV on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.
Placebo/Cisplatin	Placebo (approximately 100 mL normal saline) administered IV plus cisplatin 75 mg/m2 on Day 1 every 21 days. Pretreatment - Both Treatment Arms: Dexamethasone administered orally (po): 4 milligrams (mg) twice daily (BID) taken on the day before, the day of, and day after study treatment. Vitamin B12 administered intramuscularly (im): 1000 micrograms (µg) taken 1 to 2 weeks before treatment and every 9 weeks until 3 weeks after last treatment dose. Folic Acid administered orally (po): 350 µg to 1000 µg taken 1 to 2 weeks before treatment and continue daily until 3 weeks after last treatment dose.

Other Adverse Events

	Pemetrexed/Cisplatin	Placebo/Cisplatin
Total, other (not including serious) adverse events		
# participants affected / at risk	**343/392 (87.50%)**	**316/385 (82.08%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**118/392 (30.10%)**	**79/385 (20.52%)**
# events	**133**	**88**
Leukopenia † 1		
# participants affected / at risk	**38/392 (9.69%)**	**24/385 (6.23%)**
# events	**57**	**35**
Neutropenia † 1		
# participants affected / at risk	**67/392 (17.09%)**	**35/385 (9.09%)**

# events	105	48
Thrombocytopenia † 1		
# participants affected / at risk	28/392 (7.14%)	17/385 (4.42%)
# events	33	22
Gastrointestinal disorders		
Constipation † 1		
# participants affected / at risk	56/392 (14.29%)	53/385 (13.77%)
# events	63	65
Diarrhoea † 1		
# participants affected / at risk	42/392 (10.71%)	33/385 (8.57%)
# events	50	35
Dysphagia † 1		
# participants affected / at risk	19/392 (4.85%)	22/385 (5.71%)
# events	19	23
Nausea † 1		
# participants affected / at risk	118/392 (30.10%)	106/385 (27.53%)
# events	199	153
Vomiting † 1		
# participants affected / at risk	62/392 (15.82%)	79/385 (20.52%)
# events	81	104
General disorders		
Asthenia † 1		
# participants affected / at risk	36/392 (9.18%)	31/385 (8.05%)
# events	41	35
Fatigue † 1		
# participants affected / at risk	67/392 (17.09%)	53/385 (13.77%)
# events	88	57
Mucosal inflammation † 1		

# participants affected / at risk	25/392 (6.38%)	8/385 (2.08%)
# events	30	8
Pain † 1		
# participants affected / at risk	16/392 (4.08%)	20/385 (5.19%)
# events	19	23
Pyrexia † 1		
# participants affected / at risk	40/392 (10.20%)	19/385 (4.94%)
# events	44	21
Investigations		
Creatinine renal clearance decreased † 1		
# participants affected / at risk	32/392 (8.16%)	31/385 (8.05%)
# events	34	36
Weight decreased † 1		
# participants affected / at risk	45/392 (11.48%)	50/385 (12.99%)
# events	47	51
Metabolism and nutrition disorders		
Anorexia † 1		
# participants affected / at risk	52/392 (13.27%)	44/385 (11.43%)
# events	63	50
Hypokalaemia † 1		
# participants affected / at risk	25/392 (6.38%)	14/385 (3.64%)
# events	28	15
Hypomagnesaemia † 1		
# participants affected / at risk	40/392 (10.20%)	29/385 (7.53%)
# events	47	30
Hyponatraemia † 1		
# participants affected / at risk	21/392 (5.36%)	24/385 (6.23%)
# events	27	25

Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Tumour pain † 1		
# participants affected / at risk	**23/392 (5.87%)**	**23/385 (5.97%)**
# events	**25**	**26**
Psychiatric disorders		
Insomnia † 1		
# participants affected / at risk	**23/392 (5.87%)**	**23/385 (5.97%)**
# events	**24**	**23**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**23/392 (5.87%)**	**20/385 (5.19%)**
# events	**25**	**21**
Dyspnoea † 1		
# participants affected / at risk	**18/392 (4.59%)**	**21/385 (5.45%)**
# events	**19**	**21**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 12.0

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
No text entered.

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.

Results Point of Contact:

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Responsible Party:	Chief Medical Officer, Eli Lilly
ClinicalTrials.gov Identifier:	NCT00415194 History of Changes
Other Study ID Numbers:	8431 **H3E-MC-JMHR** (Other Identifier: Eli Lilly and Company)
Study First Received:	December 20, 2006
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Last Updated:	June 23, 2011
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