ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: February 8, 2021

ClinicalTrials.gov ID: NCT00606502

Study Identification

Unique Protocol ID:	PDX-012
Brief Title:	Study of Pralatrexate vs. Erlotinib for Non-Small Cell Lung Cancer After at Least 1 Prior Platinum-based Treatment
Official Title:	A Randomized, Phase 2b, Multi-center Study of Pralatrexate Versus Erlotinib in Patients With Stage IIIB/IV Non-small Cell Lung Cancer After Failure of at Least 1 Prior Platinum-based Treatment
Secondary IDs:	2007-004673-26 [EudraCT Number]

Study Status

Record Verification:	February 2021
Overall Status:	Completed
Study Start:	January 2008 []
Primary Completion:	June 24, 2010 [Actual]
Study Completion:	June 24, 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Spectrum Pharmaceuticals, Inc
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	
U.S. FDA-regulated Device:	

Unapproved/Uncleared Device:	No
U.S. FDA IND/IDE:	Yes
IND/IDE Information:	FDA Center: CDER IND/IDE Number: 52,604 Serial Number: 159 Has Expanded Access: No
Human Subjects Review:	Board Status: Approved Approval Number: 12/06/2007 Board Name: Kansas University Human Subjects Committee Board Affiliation: The University of Kansas Medical Center Phone: 913-588-1240 Email: humansubjects@kumc.edu Address: Kansas University Human Subjects Committee Kansas University Medical Center Mail-Stop 1032 3901 Rainbow Blvd Kansas City, KS 66160
Data Monitoring:	
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary:	The purpose of this clinical study is to determine the effectiveness (ability to provide beneficial treatment of the disease) and safety of pralatrexate compared to erlotinib when given to non-small cell lung cancer (NSCLC) patients who are current or former cigarette smokers and who have received at least 1 prior treatment with a platinum drug (cisplatin or carboplatin)
Detailed Description:	

Conditions

Conditions:	Non-small Cell Lung Cancer
Keywords:	Stage IIIB/IV non-small cell lung cancer Non-small cell lung cancer NSCLC Lung Cancer Pralatrexate

Erlotinib
Tarceva
PDX
Smoking
Smoker

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Interventional Study Model:	Parallel Assignment
Number of Arms:	2
Masking:	None (Open Label)
Allocation:	Randomized
Enrollment:	201 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Pralatrexate Intravenous (IV) push administration over 3-5 minutes into a patent IV line containing normal saline (0.9% sodium chloride).	Drug: Pralatrexate Intravenous (IV) push administration over 3-5 minutes into a patent IV line containing normal saline (0.9% sodium chloride). Initial dose: 230 mg/m2, increased to 270 mg/m2 if patient does not have specific adverse events (AEs) as per the protocol after receipt of 2 consecutive doses 2 weeks apart. Reductions allowed in 40 mg/m2 decrements to 190 mg/m2 per the protocol defined dose modifications. Protocol amended dose: 190 mg/m2, then 230 mg/m2 if patient does not have specific AEs per the protocol after receipt of 2 consecutive doses 2 weeks apart. Reductions allowed in 40 mg/2 decrements to 150 mg/m2 per the protocol defined dose modifications. Administered on days 1 and 15 of a 4-week cycle (every 2 weeks) until criteria for discontinuation per the protocol are met. Other Names: • FOLOTYN • PDX • Pralatrexate • (RS)-10-propargyl-10-deazaaminopterin

Arms	Assigned Interventions
	Dietary Supplement: Vitamin B12 1 mg intramuscular injection Administered within 10 weeks of randomization, every 8-10 weeks throughout the study and for at least 30 days after last dose of study treatment. Other Names: • Cyanocobalamin Dietary Supplement: Folic Acid 1-1.25 mg orally Administered daily for at least 7 days prior to randomization, throughout the study and for at least 30 days after last dose of study treatment. Other Names: • Vitamin B9 • Folate • Folacin
Active Comparator: Erlotinib 150 mg orally in tablet form Administered daily 1 hour before or 2 hours after ingestion of food until criteria for discontinuation per the protocol are met.	Drug: Erlotinib 150 mg orally in tablet form Administered daily 1 hour before or 2 hours after ingestion of food until criteria for discontinuation per the protocol are met. Other Names: • Tarceva® • Erlotinib hydrochloride Dietary Supplement: Vitamin B12 1 mg intramuscular injection Administered within 10 weeks of randomization, every 8-10 weeks throughout the study and for at least 30 days after last dose of study treatment. Other Names: • Cyanocobalamin Dietary Supplement: Folic Acid 1-1.25 mg orally Administered daily for at least 7 days prior to randomization, throughout the study and for at least 30 days after last dose of study treatment. Other Names: • Vitamin B9 • Folate • Folacin

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Sex: All

Gender Based:

Accepts Healthy Volunteers: No

Criteria: Inclusion Criteria:

- Confirmed Stage IIIB/ IV non-small cell lung cancer (NSCLC).
- Relapsed after treatment with 1 or 2 prior chemotherapy regimens, including at least 1 platinum-based treatment. Patients may have received pemetrexed as 1 of the prior therapies. Patients may not have received investigational therapy as their only prior therapy.
- Recovered from the toxic effects of prior therapy.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
- Smoked ≥ 100 cigarettes in their lifetime, whether a former or current cigarette smoker.
- Adequate blood, liver and kidney function as defined by laboratory values.
- Received 1-1.25 mg daily oral folic acid for at least 7 days prior to randomization and 1 mg intramuscular injection of vitamin B12 within 10 weeks prior to randomization.
- Women of childbearing potential must use medically acceptable birth control and have a negative serum pregnancy test within 14 days prior to randomization. Patients who are postmenopausal for at least 1 year (> 12 months since last menses) or are surgically sterilized do not require this test.
- Men who are not surgically sterile must use medically safe and effective birth control from the time of study randomization, and agree to continue practicing until at least 90 days after the last administration of study treatment.
- Accessible for repeat dosing and follow-up.
- Give written informed consent.

Exclusion Criteria:

- Active concurrent primary malignancy (except non-melanoma skin cancer or in situ carcinoma of the cervix). If there is a history of prior malignancy, the patient must be disease-free for ≥ 5 years. Patients with other prior malignancies less than 5 years before study entry may still be enrolled if they have received treatment resulting in complete resolution of the cancer and currently have no evidence of active or recurrent disease.
- Use of investigational drugs, biologics, or devices within 4 weeks prior to randomization.
- Previous exposure to pralatrexate or erlotinib.
- Women who are pregnant or breastfeeding.
- Congestive Heart Failure Class III/IV according to New York Heart Association (NYHA) Functional Classification.
- Uncontrolled hypertension.

- Human immunodeficiency virus (HIV)-positive diagnosis with a CD4 count of <100 mm3 or detectable viral load within the past 3 months, and is receiving combination anti-retroviral therapy.
- Symptomatic central nervous system metastases or lesions for which treatment is required.
- Major surgery within 2 weeks of study randomization.
- Receipt of any conventional systemic chemotherapy within 4 weeks (6 weeks for nitrosoureas, mitomycin C), or radiation therapy (RT) within 2 weeks, prior to randomization.
- Active infection or any serious underlying medical condition, which would impair the ability of the patient to receive protocol treatment.
- Dementia or significantly altered mental status that would prohibit the understanding and giving of informed consent or limit study compliance.

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IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Study Results

Participant Flow

Recruitment Details	Patients were enrolled between January 2008 and June 2009 across 43 study sites in 6 countries.

Reporting Groups

	Description
Pralatrexate	190 or 230 mg/m2 starting dose with increases or decreases to 150 to 270 mg/m2 per protocol, administered as an IV push over 3-5 minutes on days 1 and 15 of a 4-week cycle (ie, every 2 weeks)
Erlotinib	150 mg tablet taken orally daily

Randomization

	Pralatrexate	Erlotinib
Started	100	101
Completed	97	101
Not Completed	3	0
Randomized but not treated	3	0

Treatment

	Pralatrexate	Erlotinib
Started	97	101
Completed	97	98
Not Completed	0	3

	Pralatrexate	Erlotinib
Treatment ongoing at time of data cutoff	0	3

Baseline Characteristics

Reporting Groups

	Description
Pralatrexate	
Erlotinib	

Baseline Measures

		Pralatrexate	Erlotinib	Total
Overall Number of Participants		100	101	201
Age, Customized Measure Type: Number Unit of measure: participants	Number Analyzed	100 participants	101 participants	201 participants
Between 18 and 65 years		58	60	118
>=65 years		42	41	83
Age, Continuous Median (Standard Deviation) Unit of measure: years	Number Analyzed	100 participants	101 participants	201 participants
		63.0 (9.0)	62.0 (9.1)	63.0 (9.0)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	100 participants	101 participants	201 participants
	Female	31 31%	33 32.67%	64 31.84%
	Male	69 69%	68 67.33%	137 68.16%

		Pralatrexate	Erlotinib	Total
Region of Enrollment Measure Type: Number Unit of measure: participants	Number Analyzed	100 participants	101 participants	201 participants
United States		31	37	68
Czech Republic		17	20	37
Hungary		17	15	32
India		11	12	23
Brazil		13	9	22
Argentina		11	8	19

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Overall Survival (OS) of Patients Receiving Pralatrexate vs. Erlotinib
Measure Description	OS was defined as the length of time from randomization until death due to any cause. Patients who were alive at the time of the data cut-off date were censored at the last contact date.
Time Frame	Assessed from date of randomization no less frequently than every 16 weeks for up to 2 years after randomization.
Anticipated Reporting Date	December 2012

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Pralatrexate	
Erlotinib	

Measured Values

	Pralatrexate	Erlotinib
Overall Number of Participants Analyzed	100	101

	Pralatrexate	Erlotinib
Overall Survival (OS) of Patients Receiving Pralatrexate vs. Erlotinib Median (95% Confidence Interval) Unit of measure: Months Survival	6.7 (5.3 to 9.0)	7.0 (3.9 to 7.9)

Statistical Analysis 1 for Overall Survival (OS) of Patients Receiving Pralatrexate vs. Erlotinib

Statistical Analysis Overview	Comparison Group Selection	Pralatrexate, Erlotinib
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Cox Proportional Hazard
	Estimated Value	0.84
	Confidence Interval	(2-Sided) 95% 0.61 to 1.14
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Response Rate (RR) to Treatment of Patients Receiving Pralatrexate vs. Erlotinib
Measure Description	Number of patients whose tumors responded to Pralatrexate or Erlotinib, using the Response Criteria in Solid Tumors (RECIST).
Time Frame	Assessed every 8 weeks for the first 24 weeks, then every 16 weeks for up to 2 years or until PD or start of subsequent treatment.

Analysis Population Description

Based on all treated patients with measurable disease at baseline. Patients who were declared unevaluable for response were considered nonresponders and were included in the calculation of response rate. Patients were unevaluable if they were off-treatment prior to first response assessment, never received treatment or had unconfirmed responses.

Reporting Groups

	Description
Pralatrexate	

	Description
Erlotinib	

Measured Values

	Pralatrexate	Erlotinib
Overall Number of Participants Analyzed	97	98
Response Rate (RR) to Treatment of Patients Receiving Pralatrexate vs. Erlotinib Measure Type: Number Unit of measure: Participants		
Complete + Partial Response	2	7
Complete Response (CR)	0	1
Partial Response (PR)	2	6
Stable Disease (SD)	33	35
Progressive Disease (PD)	29	36
Disease Control (CR+PR+SD)	35	42
Unable to Evaluate	2	0
Missing (off or no treatment, not confirmed)	31	20

3. Secondary Outcome Measure:

Measure Title	Progression-free Survival (PFS) of Patients Receiving Pralatrexate vs. Erlotinib
Measure Description	PFS was calculated as the number of days from randomization to the date of radiological evidence of PD or death due to any cause.
Time Frame	Assessed every 8 weeks for the first 24 weeks, then every 16 weeks for up to 2 years or until PD or start of subsequent treatment.

Analysis Population Description

Patients who were alive without a disease response assessment of PD as of the data cut-off date were censored at the last disease assessment date or the date of randomization, whichever was later. Patients with no response assessments after baseline were censored at date of randomization resulting in a duration of PFS of 1 day.

Reporting Groups

	Description
Pralatrexate	
Erlotinib	

Measured Values

	Pralatrexate	Erlotinib
Overall Number of Participants Analyzed	100	101
Progression-free Survival (PFS) of Patients Receiving Pralatrexate vs. Erlotinib Median (95% Confidence Interval) Unit of measure: months	3.4 (2.1 to 4.7)	2.8 (2.1 to 3.7)

4. Secondary Outcome Measure:

Measure Title	Adverse Events of Patients Receiving Pralatrexate vs. Erlotinib
Measure Description	
Time Frame	Assessed every 2 weeks while on treatment through safety follow-up visit (35 +/-5 days post-last dose) or early termination visit (at time of withdrawal).

Analysis Population Description

Adverse Events (AEs) and Serious AEs (SAEs) are presented regardless of causality for patients who received at least one dose of Pralatrexate or Erlotinib. Events were graded by the investigator using the NCI CTCAE Scale (version 3.0) which provides a grading scale for each AE term.

Grade 3 = Severe

Grade 4 = Life-threatening or disabling

Reporting Groups

	Description
Pralatrexate	
Erlotinib	

Measured Values

	Pralatrexate	Erlotinib
Overall Number of Participants Analyzed	97	101

	Pralatrexate	Erlotinib
Adverse Events of Patients Receiving Pralatrexate vs. Erlotinib Measure Type: Number Unit of measure: Treated Participants		
At least one AE	75	77
Grade 3 AEs	25	18
Grade 4 AEs	5	0
At least one SAE	14	2

Reported Adverse Events

Time Frame	Assessed every 2 weeks while on treatment through safety follow-up visit (35 +/-5 days post-last dose) or early termination visit (at time of withdrawal).
Adverse Event Reporting Description	Events reported for all patients who received at least one dose of Pralatrexate or Erlotinib.

Reporting Groups

	Description
Pralatrexate	
Erlotinib	

All-Cause Mortality

	Pralatrexate	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total All-Cause Mortality	/	/

Serious Adverse Events

	Pralatrexate	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	31/97 (31.96%)	32/101 (31.68%)
Blood and lymphatic system disorders		
anaemia [A] †	2/97 (2.06%)	0/101 (0%)
leukopenia [A] †	3/97 (3.09%)	0/101 (0%)
neutropenia [A] †	1/97 (1.03%)	0/101 (0%)
pancytopenia [A] †	1/97 (1.03%)	0/101 (0%)
thrombocytopenia [A] †	4/97 (4.12%)	0/101 (0%)
Cardiac disorders		
atrial fibrillation [A] †	1/97 (1.03%)	1/101 (0.99%)
cardio-respiratory arrest [A] †	1/97 (1.03%)	1/101 (0.99%)
pericardial effusion [A] †	1/97 (1.03%)	2/101 (1.98%)
Gastrointestinal disorders		
abdominal pain [A] †	0/97 (0%)	3/101 (2.97%)
anal inflammation [A] †	1/97 (1.03%)	0/101 (0%)
diarrhoea [A] †	1/97 (1.03%)	1/101 (0.99%)
dysphagia [A] †	0/97 (0%)	1/101 (0.99%)
gastrointestinal haemorrhage [A] †	1/97 (1.03%)	1/101 (0.99%)
nausea [A] †	0/97 (0%)	1/101 (0.99%)
stomatitis [A] †	9/97 (9.28%)	0/101 (0%)
vomiting [A] †	0/97 (0%)	2/101 (1.98%)
General disorders		
asthenia [A] †	0/97 (0%)	1/101 (0.99%)

	Pralatrexate	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
fatigue [A] †	1/97 (1.03%)	0/101 (0%)
multimorbidity [A] †	1/97 (1.03%)	0/101 (0%)
non-cardiac chest pain [A] †	0/97 (0%)	1/101 (0.99%)
pyrexia [A] †	2/97 (2.06%)	4/101 (3.96%)
sudden death [A] †	1/97 (1.03%)	0/101 (0%)
Hepatobiliary disorders		
bile duct obstruction [A] †	1/97 (1.03%)	0/101 (0%)
hyperbilirubinaemia [A] †	1/97 (1.03%)	0/101 (0%)
Infections and infestations		
chest wall abscess [A] †	0/97 (0%)	1/101 (0.99%)
infection [A] †	1/97 (1.03%)	0/101 (0%)
influenza [A] †	1/97 (1.03%)	0/101 (0%)
pneumonia [A] †	2/97 (2.06%)	3/101 (2.97%)
pulmonary sepsis [A] †	0/97 (0%)	1/101 (0.99%)
respiratory tract infection [A] †	1/97 (1.03%)	1/101 (0.99%)
sepsis [A] †	3/97 (3.09%)	3/101 (2.97%)
septic shock [A] †	1/97 (1.03%)	0/101 (0%)
urosepsis [A] †	0/97 (0%)	1/101 (0.99%)
Injury, poisoning and procedural complications		
femur fracture [A] †	1/97 (1.03%)	1/101 (0.99%)
Metabolism and nutrition disorders		
anorexia [A] †	0/97 (0%)	1/101 (0.99%)
dehydration [A] †	1/97 (1.03%)	4/101 (3.96%)

	Pralatrexate	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
hypoglycaemia [A] †	0/97 (0%)	1/101 (0.99%)
hyponatraemia [A] †	1/97 (1.03%)	0/101 (0%)
Musculoskeletal and connective tissue disorders		
arthralgia [A] †	1/97 (1.03%)	0/101 (0%)
back pain [A] †	0/97 (0%)	1/101 (0.99%)
flank pain [A] †	0/97 (0%)	1/101 (0.99%)
musculoskeletal chest pain [A] †	1/97 (1.03%)	2/101 (1.98%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
cancer pain [A] †	0/97 (0%)	1/101 (0.99%)
renal cell carcinoma [A] †	0/97 (0%)	1/101 (0.99%)
Nervous system disorders		
cerebral infarction [A] †	0/97 (0%)	1/101 (0.99%)
convulsion [A] †	1/97 (1.03%)	3/101 (2.97%)
headache [A] †	1/97 (1.03%)	0/101 (0%)
Psychiatric disorders		
confusional state [A] †	1/97 (1.03%)	0/101 (0%)
Respiratory, thoracic and mediastinal disorders		
acute respiratory distress syndrome [A] †	1/97 (1.03%)	0/101 (0%)
aspiration [A] †	0/97 (0%)	1/101 (0.99%)
dyspnoea [A] †	5/97 (5.15%)	4/101 (3.96%)
haemoptysis [A] †	1/97 (1.03%)	1/101 (0.99%)
hypoxia [A] †	1/97 (1.03%)	1/101 (0.99%)
pleural effusion [A] †	0/97 (0%)	1/101 (0.99%)

	Pralatrexate	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
pneumonitis [A] †	1/97 (1.03%)	0/101 (0%)
pneumothorax [A] †	0/97 (0%)	1/101 (0.99%)
respiratory distress [A] †	1/97 (1.03%)	0/101 (0%)
respiratory failure [A] †	5/97 (5.15%)	1/101 (0.99%)
Vascular disorders		
arterial thrombosis [A] †	0/97 (0%)	1/101 (0.99%)
deep vein thrombosis [A] †	1/97 (1.03%)	0/101 (0%)
hypotension [A] †	1/97 (1.03%)	0/101 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (11.0)

Other Adverse Events

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

	Pralatrexate	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	91/97 (93.81%)	94/101 (93.07%)
Blood and lymphatic system disorders		
anaemia [A] †	20/97 (20.62%)	12/101 (11.88%)
thrombocytopenia [A] †	12/97 (12.37%)	1/101 (0.99%)
Eye disorders		
conjunctivitis [A] †	6/97 (6.19%)	5/101 (4.95%)
Gastrointestinal disorders		
constipation [A] †	3/97 (3.09%)	8/101 (7.92%)
diarrhoea [A] †	15/97 (15.46%)	32/101 (31.68%)
nausea [A] †	12/97 (12.37%)	17/101 (16.83%)

	Pralatrexate	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
stomatitis [A] †	62/97 (63.92%)	4/101 (3.96%)
vomiting [A] †	10/97 (10.31%)	10/101 (9.9%)
General disorders		
asthenia [A] †	15/97 (15.46%)	8/101 (7.92%)
fatigue [A] †	25/97 (25.77%)	16/101 (15.84%)
oedema peripheral [A] †	5/97 (5.15%)	7/101 (6.93%)
Infections and infestations		
bronchitis [A] †	5/97 (5.15%)	8/101 (7.92%)
Investigations		
weight decreased [A] †	8/97 (8.25%)	10/101 (9.9%)
Metabolism and nutrition disorders		
anorexia [A] †	16/97 (16.49%)	19/101 (18.81%)
hypokalaemia [A] †	5/97 (5.15%)	8/101 (7.92%)
Musculoskeletal and connective tissue disorders		
back pain [A] †	3/97 (3.09%)	10/101 (9.9%)
musculoskeletal pain [A] †	4/97 (4.12%)	9/101 (8.91%)
Respiratory, thoracic and mediastinal disorders		
cough [A] †	11/97 (11.34%)	17/101 (16.83%)
dyspnoea [A] †	12/97 (12.37%)	22/101 (21.78%)
Skin and subcutaneous tissue disorders		
dermatitis acneiform [A] †	4/97 (4.12%)	28/101 (27.72%)
dry skin [A] †	2/97 (2.06%)	9/101 (8.91%)
rash maculo-papular [A] †	4/97 (4.12%)	21/101 (20.79%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA (11.0)

Limitations and Caveats

The date of the CRF database cut-off for patients (no further case report form or query data entry) was 24 Jun 2010. As of the CRF data cut-off date, 3 patients, remained on therapy.

More Information

Certain Agreements:

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

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

Allos agreements with investigators (PIs) may vary. The PI may publish/make public data from the study after the earlier of publication by Allos or 24 months after database lock. Allos is allowed 60 days to review and comment on the communication prior to public release. Allos can request removal of confidential information (other than study results).

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