ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 11/23/2010

ClinicalTrials.gov ID: NCT00424190

Study Identification

Unique Protocol ID:	P903-06
Brief Title:	Comparative Study of Ceftaroline vs. Vancomycin Plus Aztreonam in Adult Subjects With Complicated Skin Infections (cSSSI)
Official Title:	A Phase 3, Multicenter, Randomized, Double-blind, Comparative Study to Evaluate the Safety and Efficacy of Ceftaroline Versus Vancomycin Plus Aztreonam in Adult Subjects With Complicated Skin and Skin Structure Infection
Secondary IDs:	

Study Status

Record Verification:	November 2010
Overall Status:	Completed
Study Start:	February 2007
Primary Completion:	November 2007 [Actual]
Study Completion:	November 2007 [Actual]

Sponsor/Collaborators

Sponsor:	Forest Laboratories
Responsible Party:	
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes

	Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: IND 71,371 Serial Number: 054 Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 10/30/2006 Board Name: Comite Independiente De Etica Para Ensayos En Farmcologia Clinica Board Affiliation: Latin Trials Argentina S.A. Phone: 4952-3892 Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration United States: Institutional Review Board Italy: National Bioethics Committee Italy: Ministry of Health Germany: Ethics Commission Germany: Federal Institute for Drugs and Medical Devices Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Poland: Ministry of Health Switzerland: Ethikkommission Switzerland: Swissmedic Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Argentina: Human Research Bioethics Committee Brazil: National Committee of Ethics in Research Brazil: Ministry of Health Brazil: National Health Surveillance Agency Chile: Comisión Nacional de Investigación Científica y Tecnológica Chile: Instituto de Salud Pública de Chile Mexico: Ethics Committee Mexico: Ministry of Health Mexico: Federal Commission for Protection Against Health Risks Peru: Ethics Committee Peru: General Directorate of Pharmaceuticals, Devices, and Drugs Peru: Ministry of Health Romania: National Medicines Agency Romania: State Institute for Drug Control Russia: Ethics Committee Russia: Ministry of Health of the Russian Federation Ukraine: Ministry of Health

Ukraine: State Pharmacological Center - Ministry of Health

Study Description

Brief Summary: The purpose of this study is to determine whether ceftaroline is effective and safe in the treatment of complicated skin infections in adults.

Detailed Description: Additional purpose of the study is to compare ceftaroline effectivity versus Vancomycin plus Aztreonam in the treatment of complicated skin infections in adults.

Conditions

Conditions: Bacterial Infections

Keywords: Abscess
Antibacterial
Antibiotic
Antimicrobial
Bacterial infection, skin
Ceftaroline
Ceftaroline acetate
Cellulitis
Cephalosporin
Complicated skin and skin structure infection
cSSSI
Intravenous
MRSA
PPI-0903
Prodrug
Skin disease, bacterial
Skin infection
Staphylococcal skin infection
Staphylococcus aureus
Streptococcal skin infection
Surgical site infection
TAK-599

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 3

Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	698 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Ceftaroline for Injection	Drug: Ceftaroline 600 mg parenteral infused over 60 minutes, every 12 hours for 5 to 14 days Other Names: • Experimental
Active Comparator: IV Vancomycin and IV Aztreonam	Drug: IV Vancomycin plus IV Aztreonam vancomycin at 1 g parenteral infused over 60 minutes followed by aztreonam 1 g infused over 60 minutes, every 12 hours, for 5 to 14 days. Other Names: • Active Comparator

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Skin and skin structure infection (SSSI) that involves deeper soft tissue or requires significant surgical intervention, or cellulitis or abscess on lower extremity which occurs in subjects with diabetes mellitus or well-documented peripheral vascular disease.

Exclusion Criteria:

- Prior treatment of current cSSSI with an antimicrobial.
- Failure of vancomycin or aztreonam as therapy for the current cSSSI, or prior isolation of an organism with in vitro resistance to vancomycin or aztreonam.

Contacts/Locations

Study Officials: Ralph Corey, MD
Study Principal Investigator
Duke University

Locations: United States, Washington
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Sao Paulo, Brazil, 04039-020

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	Patients were recruited worldwide from February 2007 to November 2007
Pre-Assignment Details	Patients were screened for up to 24 hours

Reporting Groups

	Description
Ceftaroline Fosamil for Injection	Ceftaroline fosamil 600 mg administered IV over 60 minutes every 12 hours followed by placebo administered over 60 minutes every 12 hours
IV Vancomycin Plus IV Aztreonam	Vancomycin 1 g administered over 60 minutes every 12 hours followed by aztreonam 1 g administered over 60 minutes every 12 hours

Overall Study

	Ceftaroline Fosamil for Injection	IV Vancomycin Plus IV Aztreonam
Started	351	347
Completed	329	317
Not Completed	22	30
Withdrew consent	3	4
Death	3	0
Noncompliance	1	2
Request of sponsor or investigator	0	2
Diagnosis of osteomyelitis	0	1
Other	15	21

Baseline Characteristics

Reporting Groups

	Description
Ceftaroline Fosamil for Injection	Ceftaroline fosamil 600 mg administered IV over 60 minutes every 12 hours followed by placebo administered over 60 minutes every 12 hours
IV Vancomycin Plus IV Aztreonam	Vancomycin 1 g administered over 60 minutes every 12 hours followed by aztreonam 1 g administered over 60 minutes every 12 hours

Baseline Measures

	Ceftaroline Fosamil for Injection	IV Vancomycin Plus IV Aztreonam	Total
Number of Participants	351	347	698
Age, Continuous [units: years] Mean (Standard Deviation)	49.2 (17.17)	47.2 (17.01)	48.2 (17.10)

	Ceftaroline Fosamil for Injection	IV Vancomycin Plus IV Aztreonam	Total
Age, Customized [units: participants]			
>=65 years	57	72	129
<18 years	0	0	0
>=18 years and < 65 years	294	275	569
Gender, Male/Female [units: participants]			
Female	131	129	260
Male	220	218	438
Race/Ethnicity, Customized [units: participants]			
Non-Hispanic	268	270	538
Hispanic	83	77	160

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Clinical Cure Rate at Test of Cure (MITT Population)
Measure Description	Cure: Total resolution of all signs and symptoms of the baseline infection, or improvement of the infection such that no further antimicrobial therapy was necessary. Failure: Requirement of alternative antimicrobial therapy for primary infection of cSSSI due to inadequate response, recurrence, new infection at the same site; treatment-limiting AE; requirement for surgery due to failure of study drug; diagnosis of osteomyelitis after Study Day 8; or death caused by cSSSI. Indeterminate: Inability to determine an outcome
Time Frame	8-15 days after the end of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

MITT (Modified Intent to Treat) - Any randomized subjects that received any amount of study drug

Reporting Groups

	Description
Ceftaroline Fosamil for Injection	Ceftaroline fosamil 600 mg administered IV over 60 minutes every 12 hours followed by placebo administered over 60 minutes every 12 hours
IV Vancomycin Plus IV Aztreonam	Vancomycin 1 g administered over 60 minutes every 12 hours followed by aztreonam 1 g administered over 60 minutes every 12 hours

Measured Values

	Ceftaroline Fosamil for Injection	IV Vancomycin Plus IV Aztreonam
Number of Participants Analyzed	351	347
Clinical Cure Rate at Test of Cure (MITT Population) [units: participants]		
Clinical Cure	304	297
Clinical Failure	29	21
Indeterminate	18	29

Statistical Analysis 1 for Clinical Cure Rate at Test of Cure (MITT Population)

Statistical Analysis Overview	Comparison Groups	Ceftaroline Fosamil for Injection, IV Vancomycin Plus IV Aztreonam
	Comments	The primary objective of this study was to determine the noninferiority in clinical cure rate of ceftaroline in comparison with vancomycin plus aztreonam in adult subjects with cSSSI.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	A two-sided 95% confidence interval (CI) for the observed difference in the primary outcome measure between ceftaroline and vancomycin plus aztreonam was calculated. Noninferiority was concluded if the lower limit of the 95% CI was higher than –10%.

Method of Estimation	Estimation Parameter	Risk Difference (RD)
	Estimated Value	1.0
	Confidence Interval	(2-Sided) 95% -4.2 to 6.2
	Estimation Comments	Risk difference corresponds to Ceftaroline clinical cure rate minus Vancomycin plus Aztreonam clinical cure rate. The confidence interval was calculated using the Miettinen and Nurminen method without adjustment.

2. Primary Outcome Measure:

Measure Title	Clinical Cure Rate of Ceftaroline Compared With That of Vancomycin Plus Aztreonam Treatment at TOC in the Clinically Evaluable (CE) Population
Measure Description	
Time Frame	8-15 days after last dose of study drug
Safety Issue?	No

Outcome Measure Data Not Reported

3. Secondary Outcome Measure:

Measure Title	Microbiological Success Rate at the TOC Visit
Measure Description	
Time Frame	8-15 days after last dose of study drug
Safety Issue?	No

Outcome Measure Data Not Reported

4. Secondary Outcome Measure:

Measure Title	Clinical Response at the End of Therapy (EOT) Visit
Measure Description	
Time Frame	Last day of study drug administration
Safety Issue?	No

Outcome Measure Data Not Reported

5. Secondary Outcome Measure:

Measure Title	Clinical and Microbiological Response by Pathogen at the TOC Visit
Measure Description	
Time Frame	8-15 days after last dose of study drug
Safety Issue?	No

Outcome Measure Data Not Reported

6. Secondary Outcome Measure:

Measure Title	Clinical Relapse at the Late Follow Up (LFU) Visit

Measure Description	
Time Frame	21 to 35 days after the last dose of study drug
Safety Issue?	No

Outcome Measure Data Not Reported

7. Secondary Outcome Measure:

Measure Title	Microbiological Reinfection or Recurrence at the LFU Visit
Measure Description	
Time Frame	21 to 35 days after the last dose of study drug
Safety Issue?	No

Outcome Measure Data Not Reported

8. Secondary Outcome Measure:

Measure Title	Assess Safety
Measure Description	Comparisons of the number of participants with Adverse Events
Time Frame	First dose of study drug through TOC visit
Safety Issue?	No

Outcome Measure Data Not Reported

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	All safety analysis was performed on the Safety Population, those subjects that had received any amount of the actual study drug.

Reporting Groups

	Description
Ceftaroline Fosamil for Injection	Ceftaroline fosamil 600 mg administered IV over 60 minutes every 12 hours followed by placebo administered over 60 minutes every 12 hours
IV Vancomycin Plus IV Aztreonam	Vancomycin 1 g administered over 60 minutes every 12 hours followed by aztreonam 1 g administered over 60 minutes every 12 hours

Serious Adverse Events

	Ceftaroline Fosamil for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	16/351 (4.56%)		12/347 (3.46%)	
Cardiac disorders				
Cardiac failure congestive [A] *	1/351 (0.28%)	1	1/347 (0.29%)	1
Cardiopulmonary failure [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Coronary artery disease [A] †	0/351 (0%)	0	1/347 (0.29%)	1
Gastrointestinal disorders				
Constipation [A] †	0/351 (0%)	0	1/347 (0.29%)	1
Hematochezia [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Intestinal ischemia [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Peptic ulcer hemorrhage [A] †	1/351 (0.28%)	1	0/347 (0%)	0
General disorders				
Generalized edema [A] †	0/351 (0%)	0	1/347 (0.29%)	1
Immune system disorders				
Hypersensitivity [A] †	1/351 (0.28%)	1	1/347 (0.29%)	1
Infections and infestations				
Cellulitis [A] †	2/351 (0.57%)	2	1/347 (0.29%)	1
Clostridial infection [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Osteomyelitis [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Renal abscess [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Viral infection [A] †	0/351 (0%)	0	1/347 (0.29%)	1
Wound infection [A] †	0/351 (0%)	0	1/347 (0.29%)	1
Investigations				

	Ceftaroline Fosamil for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Electrocardiogram ST segment elevation [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Metabolism and nutrition disorders				
Hyperglycemia [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Musculoskeletal and connective tissue disorders				
Back pain [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Bronchial carcinoma [A] †	0/351 (0%)	0	1/347 (0.29%)	1
Neoplasm malignant [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Nervous system disorders				
Cerebrovascular accident [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Syncope [A] †	0/351 (0%)	0	1/347 (0.29%)	1
Transient ischemic attack [A] †	0/351 (0%)	0	1/347 (0.29%)	1
Respiratory, thoracic and mediastinal disorders				
Pleurisy [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Respiratory failure [A] †	1/351 (0.28%)	1	0/347 (0%)	0
Vascular disorders				
Arterial thrombosis limb [A] †	0/351 (0%)	0	1/347 (0.29%)	1

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (9.1)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 2%

	Ceftaroline Fosamil for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	128/351 (36.47%)		162/347 (46.69%)	
Gastrointestinal disorders				
Constipation [A] †	8/351 (2.28%)	8	6/347 (1.73%)	6
Diarrhea [A] †	12/351 (3.42%)	12	11/347 (3.17%)	11
Nausea [A] †	20/351 (5.7%)	20	16/347 (4.61%)	16
Vomiting [A] †	9/351 (2.56%)	9	9/347 (2.59%)	9
General disorders				
Fatigue [A] †	1/351 (0.28%)	1	7/347 (2.02%)	7
Pyrexia [A] †	4/351 (1.14%)	4	9/347 (2.59%)	9
Investigations				
Aspartate aminotransferase increased [A] †	3/351 (0.85%)	3	7/347 (2.02%)	7
Nervous system disorders				
Dizziness [A] †	8/351 (2.28%)	8	6/347 (1.73%)	6
Headache [A] †	18/351 (5.13%)	18	13/347 (3.75%)	13
Psychiatric disorders				
Insomnia [A] †	5/351 (1.42%)	5	9/347 (2.59%)	9
Skin and subcutaneous tissue disorders				
Erythema [A] †	3/351 (0.85%)	3	9/347 (2.59%)	9
Pruritus [A] †	11/351 (3.13%)	11	29/347 (8.36%)	29
Pruritus generalized [A] †	13/351 (3.7%)	13	16/347 (4.61%)	16
Rash [A] †	12/351 (3.42%)	12	8/347 (2.31%)	8
Vascular disorders				

	Ceftaroline Fosamil for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Hypertension [A] †	1/351 (0.28%)	1	7/347 (2.02%)	7

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (9.1)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

There is NOT 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.

Results Point of Contact:

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