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

ClinicalTrials.gov ID: NCT00423657

Study Identification

Unique Protocol ID:	P903-07
Brief Title:	Comparative Study of Ceftaroline vs. Vancomycin Plus Aztreonam in Adult Subjects With Complicated Skin Infections
Official Title:	A Phase 3, Multicenter, Randomized, Double-blind, Comparative Study to Evaluate the Safety and Efficacy of Ceftaroloine Versus Vancomycin Plus Aztreonam in Adult Subjects With Complicated Skin and Skin Structure Infection (cSSSI)
Secondary IDs:	

Study Status

Record Verification:	November 2010
Overall Status:	Completed
Study Start:	March 2007
Primary Completion:	December 2007 [Actual]
Study Completion:	December 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: 06/25/2007 Board Name: South East Research Ethics Committee Board Affiliation: National Research Ethics Service Phone: 01227 931 662 Email: jane-martin@stmrec.fsnet.co.uk
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration United States: Institutional Review Board United Kingdom: Medicines and Healthcare Products Regulatory Agency United Kingdom: Research Ethics Committee Austria: Ethikkommission Austria: Federal Ministry for Health and Women 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 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 Latvia: State Agency of Medicines 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: Additonal purpose of this 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:	680 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Ceftaroline fosamil for Injection Ceftaroline fosamil 600 mg administered intravenously over 60 minutes every 12 hours, followed by placebo administered over 60 minutes every 12 hours.	Drug: ceftaroline 600 mg parenteral infused over 60 minutes, every 12 hours for 5 to 14 days Other Names: • Experimental Drug: Placebo Ceftaroline fosamil 600 mg administered intravenously over 60 minutes every 12 hours, followed by placebo administered over 60 minutes every 12 hours. Other Names: • Placebo
Active Comparator: 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.	Drug: vancomycin plus 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: Mark Wilcox, MD
Study Principal Investigator
Old Medical School

Locations: United States, Florida
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References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

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

Reporting Groups

	Description
Ceftaroline for Injection	Ceftaroline fosamil 600 mg administered intravenously 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 for Injection	IV Vancomycin Plus IV Aztreonam
Started	342	338
Completed	316	313

	Ceftaroline for Injection	IV Vancomycin Plus IV Aztreonam
Not Completed	26	25
Withdrew consent	10	8
Non-compliance	0	1
Other	15	16
Request of sponsor/investigator	1	0

Baseline Characteristics

Reporting Groups

	Description
Ceftaroline for Injection	Ceftaroline fosamil 600 mg administered intravenously 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 for Injection	IV Vancomycin Plus IV Aztreonam	Total
Number of Participants	342	338	680
Age, Categorical [units: participants]			
<18 years	0	0	0
>=18 and < 65 years	281	291	572
>=65 years	61	47	108
Age, Continuous [units: years] Mean (Standard Deviation)	47.8 (16.98)	47.5 (16.07)	47.7 (16.52)
Gender, Male/Female [units: participants]			
Female	118	137	255
Male	224	201	425

	Ceftaroline for Injection	IV Vancomycin Plus IV Aztreonam	Total
Ethnicity (NIH/OMB) [units: participants]			
Hispanic or Latino	63	59	122
Not Hispanic or Latino	279	279	558
Unknown or Not Reported	0	0	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Clinical Cure Rate at Test of Cure (TOC) (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 last dose of study drug administration
Safety Issue?	No

Analysis Population Description

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

Reporting Groups

	Description
Ceftaroline for Injection	Ceftaroline fosamil 600 mg administered intravenously 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 for Injection	IV Vancomycin Plus IV Aztreonam
Number of Participants Analyzed	342	338
Clinical Cure Rate at Test of Cure (TOC) (MITT Population)		

	Ceftaroline for Injection	IV Vancomycin Plus IV Aztreonam
[units: participants]		
Clinical Cure	291	289
Clinical Failure	25	28
Indeterminate	26	21

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

Statistical Analysis Overview	Comparison Groups	Ceftaroline 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	-0.4
	Confidence Interval	(2-Sided) 95% -5.8 to 5.0
	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	The Primary Efficacy Outcome Measure Was the Per-subject Clinical Cure Rate at the TOC Visit in the CE Populations.
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	To Evaluate the Microbiological Success Rate at the TOC Visit
Measure Description	
Time Frame	8-15 days after the last dose of study drug
Safety Issue?	No

Outcome Measure Data Not Reported

4. Secondary Outcome Measure:

Measure Title	To Evaluate the 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	To Evaluate the 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	To Evaluate Clnical 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	To Evaluate Microbiological Reinfection or Recurrence at the LFU Visit
Measure Description	

Time Frame	21-35 days after last dose of study drug
Safety Issue?	Yes

Outcome Measure Data Not Reported

8. Secondary Outcome Measure:

Measure Title	To Evaluate Safety
Measure Description	
Time Frame	first study drug dose through TOC
Safety Issue?	Yes

Outcome Measure Data Not Reported

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	All safety analyses were performed on the Safety Population which consists of all subjects who received any amount of actual study drug.

Reporting Groups

	Description
Ceftaroline for Injection	Ceftaroline fosamil 600 mg administered intravenously 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 for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	14/341 (4.11%)		16/339 (4.72%)	
Blood and lymphatic system disorders				
Anemia [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Coagulopathy [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Cardiac disorders				

	Ceftaroline for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Bradycardia [A] †	1/341 (0.29%)	1	1/339 (0.29%)	1
Myocardial infarction [A] †	1/341 (0.29%)	1	1/339 (0.29%)	1
Sinoatrial block [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Gastrointestinal disorders				
Abdominal pain [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Ileus [A] †	0/341 (0%)	0	1/339 (0.29%)	1
General disorders				
Condition aggravated [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Multi-organ failure [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Hepatobiliary disorders				
Hepatitis [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Immune system disorders				
Anaphylactic shock [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Anaphylactoid reaction [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Infections and infestations				
Bacteremia [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Central line infection [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Osteomyelitis [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Pneumonia [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Sepsis [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Wound infection [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Injury, poisoning and procedural complications				
Accidental overdose [A] †	1/341 (0.29%)	1	0/339 (0%)	0

	Ceftaroline for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Dislocation of joint prosthesis [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Postprocedural hemorrhage [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Metabolism and nutrition disorders				
Diabetes mellitus inadequate control [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Musculoskeletal and connective tissue disorders				
Osteoarthritis [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Chronic lymphocytic leukemia recurrent [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Nervous system disorders				
Convulsion [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Loss of consciousness [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Renal and urinary disorders				
Acute prerenal failure [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Renal failure [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Renal failure acute [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Respiratory, thoracic and mediastinal disorders				
Acute pulmonary edema [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Acute respiratory failure [A] †	0/341 (0%)	0	1/339 (0.29%)	1
Pulmonary embolism [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Vascular disorders				
Hypotension [A] †	1/341 (0.29%)	1	0/339 (0%)	0
Thrombophlebitis [A] †	0/341 (0%)	0	1/339 (0.29%)	1

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

Other Adverse Events

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

	Ceftaroline for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	144/341 (42.23%)		159/339 (46.9%)	
Blood and lymphatic system disorders				
Anemia [A] †	4/341 (1.17%)	4	8/339 (2.36%)	8
Gastrointestinal disorders				
Constipation [A] †	10/341 (2.93%)	10	11/339 (3.24%)	11
Diarrhea [A] †	22/341 (6.45%)	22	15/339 (4.42%)	15
Nausea [A] †	21/341 (6.16%)	21	19/339 (5.6%)	19
Vomiting [A] †	11/341 (3.23%)	11	9/339 (2.65%)	9
General disorders				
Pyrexia [A] †	5/341 (1.47%)	5	7/339 (2.06%)	7
Investigations				
Alanine aminotransferase increase [A] †	5/341 (1.47%)	5	7/339 (2.06%)	7
Blood pressure increased [A] †	7/341 (2.05%)	7	4/339 (1.18%)	4
Metabolism and nutrition disorders				
Hypokalemia [A] †	5/341 (1.47%)	5	9/339 (2.65%)	9
Nervous system disorders				
Headache [A] †	18/341 (5.28%)	18	18/339 (5.31%)	18
Psychiatric disorders				
Insomnia [A] †	12/341 (3.52%)	12	8/339 (2.36%)	8
Skin and subcutaneous tissue disorders				
Erythema [A] †	2/341 (0.59%)	2	8/339 (2.36%)	8

	Ceftaroline for Injection		IV Vancomycin Plus IV Aztreonam	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Pruritus [A] †	13/341 (3.81%)	13	28/339 (8.26%)	28
Rash [A] †	11/341 (3.23%)	11	10/339 (2.95%)	10
Vascular disorders				
Hypertension [A] †	8/341 (2.35%)	8	3/339 (0.88%)	3

† 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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