Non-Interventional Study Protocol
C2661041

Multinational Retrospective Chart Review Study to Assess the Characteristics, Treatment Outcomes and Resource Use among Adult Patients Hospitalised for Community-Acquired Pneumonia (CAP) and Complicated Skin or Soft Tissue Infections (cSSTI) Treated with Zinforo® (ceftaroline fosamil) in a Usual Care Setting

Statistical Analysis Plan
(SAP)

Version: FINAL v2.0

Author: PPD

Date: 3- Dec-2020

TABLE OF CONTENTS

LIST OF TABLES

1 AMENDMENTS FROM PREVIOUS VERSION(S)

Not applicable.

2 INTRODUCTION

Community-acquired pneumonia (CAP) is a common respiratory illness, involving an acute infection of the lungs.[1-6] CAP is associated with considerable morbidity, mortality,[5,7,8] resource use and healthcare costs.[2,4,8,9] Complicated skin and soft-tissue infections (cSSTI) include infected ulcers, infected burns and major abscesses that require hospitalization and represents a major clinical problem[10-12] as they are also associated with considerable morbidity, mortality, resource use and healthcare costs.[13-17] Current treatment options for cSSTI are compromised by resistance in particular countries and tolerability issues. In patients with CAP or cSSTI (particularly those at risk of treatment failure), there is a need for an alternative treatment option that will improve empiric treatment success rates by providing activity against a range of suspected causative pathogens (including methicillin-resistant *S. aureus* (MRSA) and S. *pneumoniae*) combined with a good tolerability profile.

Ceftaroline fosamil (Telflaro in the United States [US]; Zinforo® ex-US) is a novel 5th generation cephalosporin with rapid bactericidal action against a broad range of common Gram positive and Gram negative pathogens. Zinforo® is approved in the European Union (EU) in adults and children from time of birth for the treatment of cSSTI and CAP. The recommended treatment duration for cSSTI is 5 to 14 days and the recommended duration of treatment for CAP is 5 to 7 days.

Zinforo® is an effective treatment for patients hospitalised with CAP or cSSTI, including those at risk of treatment failure and/or with intolerance/contraindications to commonly-used antibiotics.[18-26] At present, the real-world use and effectiveness of Zinforo® in treating patients hospitalized with CAP and cSTTI has not been evaluated in a usual care setting in Europe and Latin America.

2.1.1 STUDY DESIGN

This is a multinational, multicentre, observational, retrospective cohort study. The hospital medical records of patients with cSSTI or CAP treated with Zinforo® in a usual care setting and who meet the eligibility criteria will be reviewed. For eligible patients, relevant data will be extracted from the hospital medical records from 3-months before the date of the index hospital admission until 30-days after the hospital discharge date or death, whichever occurs first.

2.1.2 STUDY POPULATION

Patients must meet all of the following inclusion criteria to be eligible for this study:

1. Age 18 years or older at admission date to the hospital.

2. Received four (4) or more consecutive IV doses of Zinforo® in usual care on or before 31-May-2019.
3. Admitting diagnosis to the hospital was either CAP or cSSTI (see diagnostic criteria as specified in the study protocol).

Patients meeting any of the following exclusion criteria are not eligible for this study:

1. Patients who were participating in an interventional clinical trial during the same hospital admission in which Zinforo® was administered
2. Patients whose hospital medical records are missing documentation of the diagnostic criteria for either cSSTI or CAP
3. Patients whose hospital medical records are missing details of dosing with Zinforo®
4. Patients whose hospital medical records are missing information on the success/failure of Zinforo® treatment and the reason why treatment was discontinued
5. Patients whose hospital medical records are missing discharge date and status information.

CAP-specific Exclusion Criteria:

- Patients admitted hospital for another medical condition who developed signs and symptoms of hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP) 48-hours or more after the admission date are not eligible for this study.

cSSTI-specific Exclusion Criteria:

- Patients with uncomplicated SSTI are not eligible for this study.
- Patients with skin and soft tissue infection complicated by the presence of orthopedic or joint replacement prostheses are not eligible for this study.
- Patients with known or suspected endocarditis, osteomyelitis, or septic arthritis are not eligible for this study

Hospital sites participating in this study will identify all patients who were dispensed four or more intravenous (IV) doses of Zinforo® in usual care on or before 31-May-2019 by querying their hospital pharmacy dispensing records. Potentially eligible patients treated with Zinforo® for either CAP or cSSTI will be identified by querying hospital discharge records for diagnosis codes indicative of either CAP or cSSTI using the World Health Organization International Classification of Diseases 10th revision (ICD-10; see Annex 3 for the list of ICD-10 codes). The hospital medical records of potentially eligible patients treated with Zinforo® will be screened manually by site staff to identify the subset of eligible CAP and cSTTI patients who meet all inclusion criteria without meeting any of the exclusion criteria.

2.1.3 DATA SOURCE

Data for this study are collected by a retrospective medical chart extraction from participating hospitals in Europe and Latin America that have treated patients with CAP or cSSTI in usual care during the study period. All data are entered by sites into electronic case report forms (eCRFs). De-identified data are collected following the Health Insurance Portability and Accountability Act (HIPAA)-compliant safe harbor approach.

2.1.4 STUDY OBJECTIVES

The overall study aim of this study is to provide real world evidence (RWE) on the characteristics, clinical management, treatment outcomes and healthcare resource use of adult patients aged 18 years and older admitted to the hospital for CAP or cSSTI who received Zinforo® in a usual care setting in Europe and Latin America on or before 31-May-2019.

Specific objectives of this study are to analyze for the CAP and cSSTI cohorts:

- Objective 1 "Patient characteristics": To describe the characteristics of patients hospitalized for CAP or cSSTI who received Zinforo® in a usual care setting in Europe and Latin America on or before 31-May-2019
- Objective 2 "Use of Zinforo": To describe physicians' use of Zinforo® in the clinical management of patients hospitalized for CAP or cSSTI in relation to their use of other antibiotics (first-line vs. second-line/salvage, monotherapy vs. combination therapy, empiric vs. definitive therapy)
- Objective 3 "Clinical response": To estimate the proportion of patients hospitalized for CAP or cSSTI who responded to Zinforo® (clinical response defined as no further intravenous (IV) antibiotic, switch to an oral antibiotic, or IV antibiotic treatment streamlining/de-escalation prior to discharge from the hospital);
- Objectives 4 "Additional clinical outcomes": To describe the clinical outcomes (eg, hospital readmission, mortality) of patients hospitalized for CAP or cSSTI after starting Zinforo® stratified by clinical response;
- Objective 5 "Treatment modification": To estimate the proportion of patients hospitalized for CAP or cSSTI who had treatment modification of Zinforo® (defined as switch to another IV antibiotic due to an adverse reaction, drug-drug interaction, insufficient response or a microbiological diagnosis indicating that the pathogen is not susceptible to Zinforo®)
- Objective 6 "Healthcare resource use": To describe the healthcare resource use of patients hospitalized for CAP or cSSTI after starting Zinforo® stratified by clinical response.

3 HYPOTHESES AND DECISION RULES

This study is purely descriptive in nature and there are no a priori hypotheses specified. Hence, no statistical tests or formal statistical inference will be performed.

3.1.1 STATISTICAL HYPOTHESES

Not applicable.

3.1.2 STATISTICAL DECISION RULES

Not applicable.

4 ANALYSIS SETS/POPULATIONS

4.1.1 FULL ANALYSIS SET

The data set will be split by the type of infection (CAP, cSSTI) into two separate analyses sets. The analyses will be performed separately for each of these data sets which will include all subjects with the respective type of infection who are eligible for the study and whose data was entered into the study database (see Section 2.1.1 for eligibility criteria).

4.1.2 SAFETY ANALYSIS SET

Not applicable.

4.1.3 OTHER ANALYSIS SET

No other analysis data sets will be defined.

4.1.4 SUBGROUPS

For selected outcomes, subgroup analyses will be conducted by geography (Europe including Russia, Latin America).

Certain outcomes will be stratified by covariates of interest provided each of the strata exceeds the minimum sample size of 30 patients (5% of total) as specified in the protocol. Covariates for stratified analyses will include:

- For cSSTI patients: Early response within 3 days
- For CAP patients: Early response within 4 days
- Line of treatment
- Age: >65 or ≤65

5 ENDPOINTS AND COVARIATES

5.1.1 EFFECTIVENESS OUTCOMES

5.1.2 TREATMENT RESPONSE TO ZINFORO®

As described in the protocol the clinical response is measured according to the following widely accepted criteria:

- CAP patients: demonstrating clinical stability (defined according to the IDSA guidelines as temperature of ≤37.8 C°, heart rate of ≤100 beats/min, respiratory rate of ≤24 breaths/min, systolic blood pressure of ≥90mmHg, oxygen saturation of ≥90%, and confusion/disorientation recorded as absent) and clinical improvement (defined as improvement of at least 1 of 4 symptoms present at baseline (i.e., cough, dyspnea, pleuritic chest pain, sputum production) with worsening of none.)

- cSSTI patients: ≥20% reduction from baseline infection area and cessation of spread measured by total infection area

Making referencing to the definitions above the following variables will be extracted from charts to assess the clinical response to Zinforo® treatment received during index hospitalization:

- Clinical response, Yes / No, dichotomous from CRF
  - If "Yes", time to clinical response
- Clinical Cure, Yes / No, dichotomous from CRF
  - If "Yes", time to clinical cure
- Clinical failure defined as any one of the following:
  - Treatment modification due to adverse event (AE)
  - Time to modification (days from treatment initiation)
  - Drug-drug interaction
  - Insufficient response (followed by switch)
  - Death due to index infection
  - Death due to other cause
  - Relapse or recurrence

For CAP patients specifically, the following effectiveness outcomes will be assessed:

- Time to clinical stability (according to the guidelines from the Infectious Disease Society of America, (IDSA))
- Time to clinical improvement (defined as improvement of at least 1 of 4 symptoms present at baseline)

For cSSTI patients specifically, the following effectiveness outcomes will be assessed:

- Time to ≥20% reduction from baseline infection area

- Time to cessation of spread measured by total infection area
- Time to cessation of spread measured by infection length and width
    - oral switch,
    - time to symptom resolution,
    - time to clinical stability (Halm criteria),
    - time to oral switch.

The following effectiveness endpoint on early response will be calculated based on the abstracted information:

For cSSTI patients:

- Time to clinical response: Calculated as maximum of:
    - Time to ≥20% reduction from baseline infection area
    - Time to cessation of spread measured by total infection area
    - Time to cessation of spread measured by infection length and width

- Early response within 3 days (3 levels):
    - 1: Response according to dichotomous CRF item = "Yes" AND time to response ≤ 3 days
    - 2: Response = "Yes" AND time to response >3 days
    - 3: No response according to dichotomous CRF item

For CAP patients:

- Time to clinical response: Calculated as maximum of:
    - Time to clinical stability
    - Time to clinical improvement

- Early response within 4 days (3 levels):
    - 1: Response according to dichotomous CRF item = "Yes" AND time to response ≤ 4 days
    - 2: Response = "Yes" AND "Time to response" > 4 days
    - 3: No response according to dichotomous CRF item

5.1.3 ADDITIONAL CLINICAL OUTCOMES

- Discharge status
- Rehospitalization within 30 days after discharge
- Vital status 30 days after discharge

Etiology of clinical failure is also assessed:

- Minimum inhibitory concentrations (MIC) of antibacterial drugs
    - Day of assessment since index hospitalization
    - MIC of ceftaroline for all isolated pathogens

- MIC of oxacillin, vancomycin, linezolid, and daptomycin for S. aureus
- MIC of ceftriaxone for MSSA
- MIC of penicillin and ceftriaxone for S. pneumonia

5.1.4 TREATMENT MODIFICATIONS / AE

The following variables are extracted from charts of eligible patients to assess proportion of patients who had treatment modification of Zinforo® treatment:

- Treatment switch to another IV antibiotic due to adverse event (AE)
- Drug-drug interaction
- Insufficient response
- Microbiological diagnosis

AEs resulting in treatment modification are also collected:

- Infections and infestations
- Blood and lymphatic system disorders
- Immune system disorders
- Nervous system disorders
- Vascular disorders
- Gastrointestinal disorders
- Hepatobiliary disorders
- Renal urinary disorders
- General disorders and administrative site conditions
- Investigations
- Other

- Seriousness of AE
- Type of criteria applied to assess seriousness of AE

5.1.5 OTHER ENDPOINTS

Beyond the range of effectiveness endpoints specified above (sections 5.1.1), the additional outcomes listed below will be analysed.

5.1.6 PATIENT CHARACERISTICS AT INDEX HOSPITALIZATION

The following variables on patient characteristics are collected from the patient charts:

- Patient demographics at index hospitalization
  - Year of patient hospitalization
  - Sex
  - Age category: >65 and ≤65 years
  - Country
  - Race, ethnicity

- Height (cm)
- Weight (kg)
- Patient's type of residence/cohabitation
- Smoking habits

- Medical history of patients treated with Zinforo®
  - Medical conditions that the patient presented with at index visit hospitalization
  - Hospitalization for any reason in the 3 months before the index visit
  - Invasive major surgical treatment in the 3 months before the index visit hospitalization
  - Therapies in the 3 months before the index visit hospitalization
    - Antimicrobial (e.g. antibiotics, antivirals)
    - Immunosuppressors/ immunomodulators
    - Anticoagulants
    - Non-steroid anti-inflammatory agents (NSAIs)
    - Home infusion therapy
    - Home wound care provided by a medical professional

- CAP-specific characteristics
  - Radiographic findings
  - Triggering signs and symptoms at diagnosis
  - Severity of CAP
  - Prognostic Scoring system
  - Time of CAP diagnosis
  - Recurrence of infection
  - Microbiologic diagnosis / type of investigation performed
  - PCF determination of H1N1 influence virus
  - Influenca vaccination status (12 month pre index)
  - Pneumococcal vaccination status
  - Biomarkers used for monitoring

- cSSTI-specific characteristics
  - Type of lesion involved
  - Type of body area involved
  - Extension of the skin infection in (sqcm)
  - Level of infection
  - Anatomical structures that were affected
  - Time of c SSTI diagnose
  - Recurrence of infection?
  - Triggering signs and symptoms at diagnosis
  - Systemic signs of cSSTI diagnosis
  - Diagnostic tests performed

- Microbiological diagnosis
- Methicillin susceptible S. aureus (MSSA)

5.1.7 PHYSICIANS' USE OF ZINFORO® DURING INDEX HOSPITALIZATION

- Pre Zinforo® treatment
  - Antibiotic class
  - Line of therapy
  - Route of administration
  - Duration of treatment Time from admission to 1st dose
  - Time from symptom onset to 1st dose
  - Treatment type
  - Daily dose
  - Treatment modified (Reason)
  - Treatment response/ failure
  - Time to clinical response / failure
  - Clinical failure details

- Zinforo® treatment
  - Duration of treatment
  - Time from admission to 1st dose
  - Time from symptom onset to 1st dose
  - Treatment type
  - Daily dose
  - Number of infusions per day
  - Administration location
  - Zinforo® as monotherapy/ combination (including further details of combination therapy)
  - Concomitant therapy

- Post Zinforo® antibiotic treatment
  - Generic name of treatment
  - Line of therapy
  - Route of administration
  - Time from Zinforo® discontinuation to initiation of new treatment
  - Daily dose
  - Number of doses administered
  - Administration location
  - Reason for switch to this treatment:
  - Treatment response
  - Clinical cure achieved?
  - Clinical failure details

5.1.8 HEALTHCARE RESOURCE USE AND COST FOR PATIENTS STARTING ZINFORO®

The following variables are collected in the CRF on the resource utilization for patients starting Zinforo® during index hospitalization:

- Duration of index hospitalization
- Duration in intensive care unit during index hospitalization
- Renal replacement therapy initiated after initiating Zinforo®
- Treatments (Surgery / blood pressure support) during index hospitalization
- Home-based care through a health-care agency (e.g. for wounds, intravenous infusions), nursing services, etc. after discharge (days)
- Re-hospitalization within 30 days of initial discharge:
    - Number of times and days
    - Reason: Index infection, other

- Development of sepsis during index hospitalization
    - Sepsis
        - Severe sepsis
        - Septic shock

- Patient treatment during index hospitalization
    - Quick sepsis-related organ failure assessment (qSOFA) conducted at the time of the index hospitalization admission:
    - Patient requiring isolation
    - Patient requiring mechanical ventilation
    - Patient requiring oxygen therapy
    - Patient requiring parenteral nutrition
    - Patient suffer acute renal failure necessitating renal replacement therapy during index
    - Patient receiving during index therapy surgery or blood pressure support
- Total doses of Zinforo®
- Total dose of other antibiotics in combination therapy with Zinforo®
- Total doses of other antibiotics post Zinforo® treatment

To get an indication for the economic impact related to the treatment of CAP and cSSTI approximate hospitalization cost will be calculated based on the calculated sum of hospital days and a list of country specific per diem rates. To assess a range of the cost and depending on the data available from each of the countries two per diem rates will be used for the cost calculation: The average per diem rate of hospitals providing standard services for these type of infections and average per diem rate of hospitals providing the highest level of medical services. “Standard” or secondary level hospitals are anticipated to be institutions that are primarily treating referral cases, with bed size ranging from 200

to 800 beds. Advanced or tertiary-level/teaching hospitals will be typically comprise hospitals intended for referral cases, with a teaching component and highly specialised staff and technical equipment, including ICU and bed size ranging from 300 to 1,500 beds. The cost estimates will be expressed in both national currency as well as in USD using sector specific exchange rate or power purchasing parities:

- Country specific calculation of approximate hospitalization cost:
  - Cost assuming a standard level hospital
    Total hospital cost= total number of bed days * per diem rate standard hospital (local currency / USD)
  - Cost of advanced level hospitals
    Total hospital cost= total number of bed days * per diem rate advanced hospital (local currency / USD)

6 HANDLING OF MISSING VALUES

No imputation for missing values will be performed. Missing values will be tabulated in the descriptive tables.

7 STATISTICAL METHODOLOGY AND STATISTICAL ANALYSES

7.1.1 SAMPLE SIZE

Given that this study is purely descriptive in nature and since there are no a priori hypotheses specified, a formal sample size calculation is not applicable. It is anticipated that approximately 600 eligible CAP and cSSTI patients from 35-40 participating sites will be sufficient to conduct this study.

7.1.2 STATISTICAL METHODS

All study outcomes (effectiveness, clinical outcomes, and other endpoints) will be analysed using descriptive statistics to summarize patient and disease characteristics, treatment patterns, and treatment outcomes and health care resource utilisation. Means, standard deviations, medians, minimums and maximums will be provided for continuous variables when performing descriptive analysis of continuous data. Absolute counts and percentages will be provided when performing descriptive analysis of categorical data.

The following variables will be calculated from the information collected in the CRF:

- Body mass index (BMI): Weight(kg) / (Height(cm)*0.01)^2
- Geographic region, 2 levels:
  - 1: Europe (France, Greece, Italy, Spain, Russia)
  - 2: Latin America (Brazil, Columbia, Mexico)

Data analyses will be performed separately for the two patient cohorts: CAP and cSSTI. No analyses combining these two patient cohorts will be performed.

Within these patient groups data will be presented in aggregate, as well as stratified by patient and disease characteristics of interest, such as geographic region (see section 4.1.4).

Due to the descriptive nature of the analyses no formal statistical tests will be conducted.. All statistical analyses will be executed using statistical software SAS version 9.4 or later.

7.1.3 STATISTICAL ANALYSES

7.1.4 SPECIFIC APPROACH

Using the endpoints described in section 5.1.6, patient characteristics will be described by summarizing patient demographics at index hospitalization, as well as patient's medical history. CAP-specific characteristics and cSSTI-specific characteristics will also be summarized for each patient cohort respectively. To describe physicians' use of Zinforo® in the clinical management of the patients hospitalized for CAP or cSSTI, details on pre-Zinforo treatment, Zinforo treatment as well as post-Zinforo antibiotic treatment will be summarized to describe line of therapy, monotherapy vs. combination therapy, etc (see related endpoints described in section 5.1.7). Proportion of patients with a clinical response, clinical cure and clinical failure in response to Zinforo® treatment will be summarized. Using the endpoints outlined in section 5.1.3, the clinical outcomes (e.g. hospital readmission, mortality) of patients hospitalized for CAP or cSSTI after starting Zinforo will be summarized and stratified by clinical response. Treatment modification Zinforo® and reasons for treatment modification will be described for the CAP and cSSTI patient cohorts, using the endpoints collected as described in section 5.1.4. Healthcare resource utilization will be described for patients hospitalized for CAP or cSSTI after starting Zinforo® and stratified by clinical response, using the appropriate endpoints as described in section 5.1.8.

7.1.5 INTERIM ANALYSIS

One interim analysis will be performed on all validated and locked patient data within the EDC. The time frame for the interim database lock and interim analysis will be based on Pfizer's internal needs and dissemination plans. The interim analysis will be performed on the full set of planned analyses. Due to the purely descriptive nature of the study no further considerations on issues such as alpha spending are required. The final analyses will be performed after completion of data collection and subsequent data base lock.

8 LIST OF TABLES AND TABLE SHELLS

8.1.1 ANALYSES OF PATIENTS WITH CAP

8.1.2 CHARACTERISTICS OF PATIENTS WITH CAP

Table 1. Demographic characteristics of included CAP patients at index hospitalization

CAP Demographic characteristics	All CAP patients (N=XX)	
	n	%
Age		
<90 years		
≥ 90 years		
If <90 years,		
Mean (SD)		
Median (Min Max)		
<65 years		
≥ 65 years		
Sex		
Male		
Female		
Race, Ethnicity		
White, Caucasian		
Black/African-American/Caribbean		
Latin-American		
Asian		
Middle Eastern		
Mixed		
Other		
Not available		
Country		
France		
Greece		
Italy		
Spain		
Russia		
Brazil		
Columbia		
Mexico		

CAP Demographic characteristics	All CAP patients (N=XX) n	%
Height (cm)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Weight (kg)		
Mean (SD)		
Median (Min-Max)		
Unknown		
BMI		
Mean (SD)		
Median (Min-Max)		
Unknown		
Type of residence/cohabitation *(pre index if changed after discharge)*		
Nursing home or extended care facility		
Living independently		
Living with care support (family, friend, hired support)		
Other		
Unknown		
Smoking habits		
Non-smoker		
Ex-smoker (stopped ≥ 365 days ago)		
Occasional smoker (less than 1 tobacco product per day)		
Habitual smoker (1 or more tobacco products per day)		
Unknown		

Abbreviations: n=number; SD = Standard deviation

Table 2. Medical history in patients with CAP

Medical history	All CAP patients (N=XX) n	%
Medical condition(s) at index hospitalization		
None		
AIDS/HIV infection		
If HIV infected: Controlled with HAART		
Yes (n, % of HIV infected)		
No (n, % of HIV infected)		
Unknown (n, % of HIV infected)		
Alcohol abuse		
Cancer/malignancy		
Cerebrovascular disease		
Chronic dialysis within the past 30 days		
Chronic obstructive pulmonary disease		
Chronic renal disease		
Congestive heart failure		
Decompensated cirrhosis		
Diabetes mellitus		
Immunosuppressive disease		
Influenza		
Injection drug use		
End stage liver disease		
Peripheral vascular disease		
Respiratory disease		
Other relevant condition(s) or disease(s) requiring chronic drug treatment.		
Unknown		

Abbreviations: AIDS/ HIV: acquired immunodeficiency syndrome/ human immunodeficiency virus, HAART: highly active antiretroviral therapy

Table 3. Hospitalization and treatments in the 3 months prior to index hospitalization in patients with CAP

Prior hospitalization	All CAP patients (N=XX) n %
Hospitalization for any reason in the 3 months before index hospitalization	
Yes	
No	
Unknown	
If hospitalized	
Duration of hospitalization previous to index	
Mean (SD)	
Median (Min-Max)	
Invasive major surgical treatment in the 3 months before index	
Yes	
No	
Unknown	
Therapies received in the 3 months before index	
Antimicrobial (e.g. antibiotics, antivirals)	
Immunosuppressors/ immunomodulators	
Anticoagulants	
Non-steroid anti-inflammatory agents (NSAIs)	
Home infusion therapy	
Home wound care provided by a medical professional	
None	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 4. Diagnostics in patients with CAP

CAP Diagnostic	All CAP patients (N=XX) n %
Radiographic findings in tests for CAP	
Infiltrate	
Consolidation	
Pleural effusion	
Other findings	
Unknown	
None of the above	
Triggering signs and symptoms at CAP diagnosis	
New or increased cough	
Purulent sputum or change in sputum character	
Auscultatory findings consistent with pneumonia	
Dyspnea, tachypnea, or hypoxemia (O2 saturation < 90% on room air or pO2 < 60 mmHg)	
Fever (>38 °C oral; > 38.5 °C rectally or tympanically) or hypothermia (< 35 °C)	
WBC count > 10,000 cells/mm³ or < 4,500 cells/mm³	
Unknown	
None of the above	
Criteria for severe CAP	
Yes	
No	
Unknown	
Prognostic scoring system used	
PORT Score / Pneumonia Severity Index	
Mean (SD)	
Median (Min-Max)	
CURB-65	
Mean (SD)	
Median (Min-Max)	
Other	
None	
Unknown	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation. O2: oxygen, pO2: oxygen partial pressure, WBC: white blood cells, PORT: Pneumonia Severity Index, CURB-65: Confusion, Blood urea, Respiratory rate, Blood pressure, age ≥65

Table 5. Diagnosis and infection details in patients with CAP

CAP Time of infection	All CAP patients (N=XX) n %
Time of CAP diagnosis	
Prior to index hospitalization	
Days prior to index hospitalization	
Mean (SD)	
Median (Min-Max)	
During index hospitalization	
Unknown	
Recurrent CAP infection	
Yes	
No	
Unknown	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 6. Microbiological findings in patients with CAP

CAP Microbiological findings	All CAP patients (N=XX) n %
Microbiological CAP diagnosis positive for	
Streptococcus pneumonia	
Multidrug resistant S. pneumoniae	
Penicillin resistant S. pneumoniae	
Escherichia coli	
Mycoplasma pneumonia	
Chlamydophila pneumonia	
Haemophilus influenza	
H. Parainfluenzae	
Legionella spp.	
Staphylococcus aureus	
Methicillin resistance Staphylococcus aureus	
Methicillin susceptible S. aureus	
Gram-negative bacilli	
Moraxella catarrhalis	
Coxiella burnetii	
Kiebsiella pneumonia	
Other enterobacteria	
Pseudomonas aeruginosa	
Aspirative pneumonia	
Other microorganism	
Unknown	
None of the above	
Investigation conducted for positive microbiological CAP diagnosis	
Sputum examination	
Blood culture	
Bronchoalveolar lavage or bronchial brush examination	
Pleural fluid sample examination	
Legionella antigen test in urine	
Pneumococcal antigen test in urine	
Other	
Unknown	
None of the above	

Table 7. Additional tests and vaccination status in patients with CAP

CAP test and vaccination	All CAP patients (N=XX) n	%
PCF determination of H1N1 influence virus performed		
Yes		
No		
Unknown		
If yes:		
Positive		
Negative		
Influenza vaccination received within the 12 months pre index hospitalization		
Yes		
No		
Unknown		
Pneumococcal vaccination received		
Yes		
No		
Unknown		
Biomarkers used to monitor the clinical evolution of the patient		
CRP		
Procalcitonin		
Other biomarker		
Unknown		
None of the above		

Abbreviation: CRP: c-reactive protein

8.1.3 HEALTHCARE RESOURCE USE FOR PATIENTS WITH CAP STARTING ZINFORO

Table 8. Utilization during index hospitalization in patients with CAP

Resource utilization	All CAP patients (N=XX) n %
Duration of index hospitalization (days)	
Mean (SD)	
Median (Min-Max)	
Duration of days in ICU	
Mean (SD)	
Median (Min-Max)	
Quick sepsis-related organ failure assessment (qSOFA) conducted	
Yes	
No	
Unknown	
If qSOFA was conducted	
(n, % of qSOFA assessed)	
Glasgow coma scale <15	
Systolic blood pressure <100 mmHg	
High respiration rate (≥ 22 breaths per minute)	
Patient required isolation	
Yes	
No	
Unknown	
If patient isolated:	
Duration of isolation (days)	
Mean (SD)	
Median (Min-Max)	
Unknown	

Abbreviations: ICU: intensive care unit; Max: maximum; Min: minimum; qSOFA: Quick sepsis-related organ failure assessment; SD: standard deviation.

Table 9. Hospitalisation cost in patients with CAP

Hospital Cost	All CAP patients (N=XX) n %
Hospital Cost - standard hospital (local currency)	
Mean (SD)	
Median (Min-Max)	
Hospital Cost - advanced level (local currency)	
Mean (SD)	
Median (Min-Max)	
Hospital Cost - standard hospital (USD)	
Mean (SD)	
Median (Min-Max)	
Hospital Cost - advanced level (USD)	
Mean (SD)	
Median (Min-Max)	

Abbreviations: USD: US Dollars, Max: maximum; Min: minimum; SD: standard deviation.

Table 10. Utilization during index hospitalization by response status in patients with CAP

Resource utilization	CAP responders (N=XX)		CAP non-responders (N=XX)	
	n	%	n	%
Duration of index hospitalization (days)				
Mean (SD)				
Median (Min-Max)				
Duration of days in ICU				
Mean (SD)				
Median (Min-Max)				
Quick sepsis-related organ failure assessment (qSOFA) conducted				
Yes				
No				
Unknown				
If qSOFA was conducted (n, % of qSOFA assessed)				
Glasgow coma scale <15				
Systolic blood pressure <100 mmHg				
High respiration rate (≥ 22 breaths per minute)				
Patient required isolation				
Yes				
No				
Unknown				
If patient isolated:				
Duration of isolation (days)				
Mean (SD)				
Median (Min-Max)				
Unknown				

Table 11. Hospitalisation cost by response status in patients with CAP

Hospital Cost	CAP responders (N=XX)		CAP non-responders (N=XX)	
	n	%	n	%
Hospital Cost- standard hospital (local currency)				
Mean (SD)				
Median (Min-Max)				
Hospital Cost- advanced level (local currency)				
Mean (SD)				
Median (Min-Max)				
Hospital Cost- standard hospital (USD)				
Mean (SD)				
Median (Min-Max)				
Hospital Cost- advanced level (USD)				
Mean (SD)				
Median (Min-Max)				

Abbreviations: USD: US Dollars, Max: maximum; Min: minimum; SD: standard deviation.

Table 12. Ventilation and parenteral nutrition in patients with CAP

Ventilation and parenteral nutrition	All CAP patients (N=XX) n %
Patient required mechanical ventilation	
Yes	
No	
Unknown	
If patient received ventilation:	
Type of ventilation	
Invasive ventilation (n, % ventilated)	
Duration of invasive ventilation (days)	
Mean (SD)	
Median (Min-Max)	
Non-invasive ventilation (n, % ventilated)	
Duration of non-invasive ventilation (days)	
Mean (SD)	
Median (Min-Max)	
Including high flow oxygen therapy	
Yes (n, % ventilated)	
No (n, % ventilated)	
Unknown (n, % ventilated)	
Patient received parenteral nutrition	
Yes	
No	
Unknown	
If Yes:	
Duration of parenteral nutrition (days)	
Mean (SD)	
Median (Min-Max)	
Unknown	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 13. Treatments received during index hospitalization in patients with CAP

Treatments received	All CAP patients (N=XX) n %
Treatment received during index hospitalization?	
Surgery related to the infection	
Surgery unrelated to the infection	
Blood pressure support	
If blood pressure support received:	
Fluid resuscitation (n,% blood pressure support)	
Vasopressors (n,% blood pressure support)	
Invasive procedures (n,% blood pressure support)	
Unknown	
Other	
None of the above	

Table 14. Complications during index hospitalization in patients with CAP

Complications	All CAP patients (N=XX) n	%
Renal failure necessitating renal replacement		
Yes		
No		
Unknown		
If renal replacement :		
Duration of therapy (days)		
Mean (SD)		
Median (Min-Max)		
Renal replacement after first dose of Zinforo		
Yes (n,% with renal replacement)		
No (n,% with renal replacement)		
Unknown (n,% with renal replacement)		
Serum creatinine at the first Zinforo dose (mg/dL)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Complications developed during index hospitalization		
Sepsis		
Severe sepsis		
Septic shock		
Unknown		
None of the above		

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 15. Dosages of Zinforo and other antibiotics in patients with CAP

Complications	All CAP patients (N=XX) n	%
Total number of doses of Zinforo administered		
Mean (SD)		
Median (Min-Max)		
Total number doses of other antibiotics administered in combination with Zinforo		
Mean (SD)		
Median (Min-Max)		
Total number of doses of other antibiotics administered post Zinforo treatment		
Mean (SD)		
Median (Min-Max)		

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 16. Resource use post index hospitalization in patients with CAP

Resource utilization post index	All CAP patients (N=XX) n %
Home-based care received through a health-care agency (e.g. for wounds, intravenous infusions)	
Yes	
No	
Unknown	
If home based care received ,	
Duration of home-based care (days)	
Mean (SD)	
Median (Min-Max)	
Re-hospitalized within 30 days of initial discharge	
Yes	
No	
Unknown	
If re-hospitalized,	
Number of re-hospitalizations	
Mean (SD)	
Median (Min-Max)	
Duration of all hospitalizations	
Mean (SD)	
Median (Min-Max)	
Admission reason:	
For index infection (n,% of re-hospitalizations)	
For other reason (n,% of re-hospitalizations)	
Unknown (n,% of re-hospitalizations)	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

8.1.4 PHYSICIANS USE OF ZINFORO® (AND OTHER ANTIBIOTICS) DURING INDEX HOPSPITALIZATION IN PATIENTS WITH CAP

Table 17. Pre Zinforo treatment- Summary across all treatment lines in patients with CAP

Antibiotic treatment pre Zinforo	All CAP patients (N=XX) n %
Antibiotic treatment for the index infection received prior to Zinforo	
Yes	
No	
Pre Zinforo treatment received	
Aminoglycoside	
Betalactam	
Carbapenem	
Ceftriaxone	
Cephalosporins	
Glycopeptide	
Macrolide	
Betalactam /Combination	
Quinolone	
Sulfonamide	
Clindamycin	
Linezolid	
Other antibiotic agent	
Unknown	
Line of therapy	
First	
Second	
Third	
Fourth	
Number of pre Zinforo lines of therapy	
Mean (SD)	
Median (Min-Max)	
Route of administration	
Oral	
Intra-venous	
Intra-muscular	
Subcutaneous	
Unknown	

Antibiotic treatment pre Zinforo	All CAP patients (N=XX) n %
Duration of pre Zinforo treatment (days)	
Mean (SD)	
Median (Min-Max)	
Treatment type	
Empiric	
Definitive/Specific	
Unknown	
Number of administrations	
Mean (SD)	
Median (Min-Max)	
Number of doses administered	
Mean (SD)	
Median (Min-Max)	
Administration location	
ICU	
General ward	
At home	
Out patient	
Medical setting	
Unknown	
Treatment modification	
Yes	
No	
Unknown	
If yes:	
Time to treatment modification from initial dose	
Reason for treatment modification	
Treatment response	
Time to clinical response	
Clinical failure details	
Daily dose unit	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 18. Pre Zinforo treatment by line of treatment in patients with CAP

Pre Zinforo treatment	Line of treatment			
	1st Line N, %	2nd Line N, %	3rd Line N, %	4th Line N, %
Aminoglycoside				
Betalactam				
Carbapenem				
Ceftriaxone				
Cephalosporins				
Glycopeptide				
Macrolide				
Betalactam /Combination				
Quinolone				
Sulfonamide				
Clindamycin				
Linezolid				
Other antibiotic agent				
Unknown				

Table 19. Zinforo treatment during index hospitalization in patients with CAP

Zinforo treatment	All CAP patients (N=XX) n	%
Zinforo line of therapy		
First		
Second		
Third		
Fourth		
Duration of Zinforo treatment (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Time from admission to 1st dose (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Time from symptom onset to 1st dose (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Treatment type		
Empiric		
Definitive/Specific		
Unknown		
Daily dose (mg/kg)		
Mean (SD)		
Median (Min-Max)		
Number of infusions per day		
Mean (SD)		
Median (Min-Max)		
Unknown		
Administration location		
ICU		
General ward		
At home		
Out-patient setting		
Medical clinic		
Unknown		

Abbreviations: ICU: intensive care unit; Max: maximum; Min: minimum; SD: standard deviation.

Table 20. Zinforo administered in combination therapy in patients with CAP

Antibiotic treatments given in combination with Zinforo	All CAP patients (N=XX) n %
Zinforo as Mono/ Combination treatment	
Monotherapy	
Combination therapy	
Unknown	
If administered in combination:	
Antibiotic treatment received	
Aminoglycoside	
Betalactam	
Carbapenem	
Ceftriaxone	
Cephalosporins	
Glycopeptide	
Macrolide	
Betalactam /Combination	
Quinolone	
Sulfonamide	
Clindamycin	
Linezolid	
Other antibiotic agent	
Unknown	
Route of administration	
Oral	
Intra-venous	
Intra-muscular	
Subcutaneous	
Unknown	
Duration of combination treatment (days)	
Mean (SD)	
Median (Min-Max)	
Unknown	
Number of doses administered	
Mean (SD)	
Median (Min-Max)	
Unknown	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 21. Zinforo treatment and concomitant therapy in patients with CAP

Therapies concomitant to Zinforo	All CAP patients (N=XX) n %
Concomitant therapy given	
Yes	
No	
If concomitant therapy "yes"	
Therapy received	
Immunosuppressors/ Immunomodulators	
Anticoagulants	
Non-steroidal anti-inflammatory agents (NSAIs)	
Chemotherapeutic agents	
Other	
Unknown	

8.1.5 TREATMENT RESPONSE TO ZINFORO® IN PATIENTS WITH CAP

Table 22. Response to Zinforo treatment in patients with CAP

Treatment response	All CAP patients (N=XX) n %
Zinforo treatment response	
Clinical response	
Clinical failure	
Time to clinical response	
Mean (SD)	
Median (Min-Max)	
Unknown	
Zinforo early treatment response	
Response ≤4 days	
Response >4 days	
No response	
Unknown	
Clinical cure achieved	
Yes	
No	
Time to clinical cure	
Mean (SD)	
Median (Min-Max)	
Unknown	
Clinical stability achieved	
Time to clinical stability	
Mean (SD)	
Median (Min-Max)	
Unknown	
Clinical improvement achieved	
Time to clinical improvement	
Mean (SD)	
Median (Min-Max)	
Unknown	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

8.1.6 ADDITIONAL CLINICAL OUTCOMES IN PATIENTS WITH CAP

Table 23. Additional clinical outcomes in response to Zinforo treatment in patients with CAP

Additional clinical outcomes	All CAP patients (N=XX) n %
Discharge status	
Died in the hospital	
Discharged to a nursing home or extended care facility	
Discharged to independent living (with or without support)	
Other	
Unknown	
Vital status at end of follow up	
Patient is still alive	
Patient is deceased	
If deceased	
Duration of days from discharge until death(days)	
Mean (SD)	
Median (Min-Max)	
Unknown	
Minimum inhibitory concentrations (MIC) of antibacterial drugs assessed	
Yes	
No	
Unknown	
If assessed	
Day of assessment since index hospitalization	
Mean (SD)	
Median (Min-Max)	
MIC of ceftaroline for all isolated pathogens	
MIC of oxacillin, vancomycin, linezolid, and daptomycin for S. aureus	
MIC of ceftriaxone for MSSA	
MIC of penicillin and ceftriaxone for S. pneumonia	

Abbreviations: Max: maximum; MIC: minimum inhibitory concentrations; Min: minimum; SD: standard deviation.

8.1.7 TREATMENT MODIFICATIONS / ADVERSE EVENTS IN PATIENTS WITH CAP

Table 24. Clinical failure with Zinforo in patients with CAP

Clinical failure with Zinforo	All CAP patients (N=XX) n	%
Etiology of clinical failure		
Failure related to CAP		
Failure unrelated to CAP		
Unknown		
Reason for clinical failure		
Treatment modification due to AE		
Time to modification (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Drug-drug interaction		
Insufficient response		
Death due to index infection		
Time to death due to infection (days)		
Mean (SD)		
Median (Min-Max)		
Death due to other		
Relapse or recurrence		
Time to relapse/recurrence:		
Mean (SD)		
Median (Min-Max)		
Unknown		

Abbreviations: AE: adverse events; Max: maximum; Min: minimum; SD: standard deviation.

Table 25. Clinical failure with Zinforo due to adverse events in patients with CAP

Clinical failure to Zinforo due to AEs	All CAP patients (N=XX)	
	n	%
AE causing Zinforo discontinuation		
Infections and infestations		
Clostridium difficile colitis		
Other		
Blood and lymphatic system disorders		
Activated partial thromboplastin time (aPTT) prolonged		
Agranulocytosis		
Anaemia		
Eosinophilia		
International normalized ratio (INR) increased		
Leucopenia		
Neutropenia		
Prothrombin time (PT) prolonged		
Thrombocytopenia		
Other		
Immune system disorders		
Anaphylaxis		
Hypersensitivity (e.g. urticarial, lip and face swelling)		
Pruritus		
Rash		
Other		
Nervous system disorders		
Dizziness		
Headache		
Other		
Vascular disorders		
Phlebitis		
Other		
Gastrointestinal disorders		
Abdominal pain		
Diarrhea		
Nausea		
Vomiting		
Other		
Hepatobiliary disorders		
Increased transaminases		
Other		
Renal urinary disorders		
Blood creatinine increased		
Other		
General disorders and administrative site conditions		
Infusion site reaction (e.g. erythema, phlebitis, pain)		
Pyrexia		
Other		
Investigations		

Clinical failure to Zinforo due to AEs	All CAP patients (N=XX) n %
Coombs direct test positive	
Other	
Unknown	

Abbreviations: AE: adverse events, aPTT: activated partial thromboplastin time

Table 26. Seriousness of adverse events in patients with CAP

Clinical failure to Zinforo	All CAP patients (N=XX) n %
Serious AE at Zinforo discontinuation	
Yes	
No	
Unknown	
Seriousness criteria applied (for AEs indicated as serious)	
Resulted in death	
Life-threatening	
Hospitalization/prolongation of hospitalization	
Persistent/significant disability/incapacity	
Congenital anomaly/birth defect	
Important medical event	
None of the above	
Unknown	

Abbreviations: AE: adverse event.

Table 27. Post Zinforo treatment- Summary across all lines in patients with CAP

Antibiotic treatment post Zinforo	All CAP patients (N=XX) n %
Antibiotic treatment received for index infection after Zinforo	
Yes	
No	
Post Zinforo treatment received	
Aminoglycoside	
Betalactam	
Carbapenem	
Ceftriaxone	
Cephalosporins	
Glycopeptide	
Macrolide	
Betalactam /Combination	
Quinolone	
Sulfonamide	
Clindamycin	
Linezolid	
Other antibiotic agent	
Unknown	
Line of therapy	
First	
Second	
Third	
Fourth	
Number of post Zinforo lines of therapy	
Mean (SD)	
Median (Min-Max)	
Route of administration	
Oral	
Intra-venous	
Intra-muscular	
Subcutaneous	
Unknown	
Duration from Zinforo discontinuation to initiation of new treatment (days)	
Mean (SD)	
Median (Min-Max)	
Unknown	
Duration of treatment (days)	

Antibiotic treatment post Zinforo	All CAP patients (N=XX) n %
Mean (SD)	
Median (Min-Max)	
Unknown	
Treatment type	
Empiric	
Definitive/Specific	
Unknown	
Number of administrations	
Mean (SD)	
Median (Min-Max)	
Number of doses administered	
Mean (SD)	
Median (Min-Max)	
Administration location	
ICU	
General ward	
Unknown	
Reason for switch	
Lack of efficacy of previous treatment	
Side effect of previous treatment	
Drug interaction of previous treatment	
Results of susceptibility test/pathogen identification	
Special population with renal impairment	
Other	
Unknown	

Abbreviations: ICU: intensive care unit; Max: maximum; Min: minimum; SD: standard deviation.

Table 28. Response to post-Zinforo treatment in patients with CAP

Post Zinforo treatment response	All CAP patients (N=XX) n %
Treatment response to post- Zinforo treatment	
Clinical response	
Clinical failure	
Unknown	
Clinical cure achieved	
Yes	
No	
Unknown	
If clinical failure to post–Zinforo treatment	
Treatment modification due to adverse event	
Drug-drug interaction	
Insufficient response	
Relapse/reoccurrence	
Death due to infection	
Death due to other	
Unknown	

8.1.8 ANALYSES OF CSSTI PATIENTS

8.1.9 PATIENT CHARACTERISTICS IN PATIENTS WITH CSSTI

Table 29. Demographic characteristics of included cSSTI patients at index hospitalization

Demographic characteristics	All cSSTI patients (N=XX)	
	n	%
Age		
<90 years		
≥ 90 years		
If <90 years,		
Mean (SD)		
Median (Min Max)		
<65 years		
≥ 65 years		
Sex		
Male		
Female		
Race, Ethnicity		
White, Caucasian		
Black/African-American/Caribbean		
Latin-American		
Asian		
Middle Eastern		
Mixed		
Other		
Not available		
Country		
France		
Greece		
Italy		
Spain		
Russia		
Brazil		
Columbia		
Mexico		
Height (cm)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Weight (kg)		
Mean (SD)		
Median (Range)		
Unknown		
BMI		
Mean (SD)		
Median (Min-Max)		

Demographic characteristics	All cSSTI patients (N=XX) n	%
Unknown		
Type of residence/cohabitation *(pre index if changed after discharge)*		
Nursing home or extended care facility		
Living independently		
Living with care support (family, friend, hired support)		
Other		
Unknown		
Smoking habits		
Non-smoker		
Ex-smoker (stopped ≥ 365 days ago)		
Occasional smoker (less than 1 tobacco product per day)		
Habitual smoker (1 or more tobacco products per day)		
Unknown		

Abbreviations: Max: maximum; Min: minimum; SD: Standard deviation

Table 30. Medical history in patients with cSSTI

Medical history	All cSSTI patients (N=XX)	
	n	%
Medical condition(s) the patient presented at index visit hospitalization		
None		
AIDS/HIV infection		
If HIV infected: Controlled with HAART		
Yes (n, % HIV infected)		
No (n, % HIV infected)		
Unknown (n, % HIV infected)		
Alcohol abuse		
Cancer/malignancy		
Cerebrovascular disease		
Chronic dialysis within the past 30 days		
Chronic obstructive pulmonary disease		
Chronic renal disease		
Congestive heart failure		
Decompensated cirrhosis		
Diabetes mellitus		
Immunosuppressive disease		
Influenza		
Injection drug use		
End stage liver disease		
Peripheral vascular disease		
Respiratory disease		
Other relevant condition(s) or disease(s) requiring chronic drug treatment.		
Unknown		

Abbreviations: AIDS/ HIV acquired immunodeficiency syndrome/ human immunodeficiency virus, HAART highly active antiretroviral therapy.

Table 31. Hospitalization and treatments in the 3 months prior to index hospitalization in patients with cSSTI

Prior hospitalization	All cSSTI patients (N=XX) n %
Hospitalization for any reason in the 3 months before index hospitalization	
Yes	
No	
Unknown	
If hospitalized	
Duration of Hospitalization previous to index	
Mean (SD)	
Median (Min-Max)	
Invasive major surgical treatment in the 3 months before index	
Yes	
No	
Unknown	
Therapies received in the 3 months before index	
Antimicrobial (e.g. antibiotics, antivirals)	
Immunosuppressors/ immunomodulators	
Anticoagulants	
Non-steroid anti-inflammatory agents (NSAIs)	
Home infusion therapy	
Home wound care provided by a medical professional	
None	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 32. cSSTI Characteristics

Characteristics	All cSSTI patients (N=XX)	
	n	%
Lesions involved in the patient's cSSTI		
Abscess		
Cellulitis/fasciitis		
Post-traumatic wound		
Post-surgical wound		
Decubitus ulcer		
Diabetic leg ulcer		
Peripheral vascular disease ulcer		
Burn		
Bite		
Unknown		
None of the above		
Body areas involved in cSSTI		
Head		
Hand		
Upper extremities		
Lower extremities		
Thorax		
Abdomen		
Genitalia		
Unknown		
Muscle		
Unknown		
Extension of the skin infection (cm^2)		
<5 cm2		
5-10 cm2		
10-50 cm2		
>50 cm2		
Unknown		
Level of infection		
Superficial		
Deep incisional		
Organ or space infection		
Unknown		
Anatomical structures affected		
Epithelium		
Epidermis		
Dermis		
Subcutaneous fat		

Characteristics	All cSSTI patients (N=XX)	
	n	%
Fascia		
Muscle		
Unknown		

Table 33. Diagnosis and infection details in patients with cSSTI

Characteristics	All cSSTI patients (N=XX)	
	n	%
Time of cSSTI diagnosis		
Prior to index hospitalization		
Days prior to index hospitalization		
Mean (SD)		
Median (Min-Max)		
During index hospitalization		
Days prior after hospitalization (admission)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Recurrent cSSTI infection		
Yes		
No		
Unknown		

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 34. cSSTI Diagnostics

Diagnostic criteria	All cSSTI patients (N=XX) n	%
Triggering signs and symptoms for cSSTI at diagnosis		
Purulent or seropurulent drainage/discharge		
Bullae		
Erythema		
Fluctuance		
Heat/localized warmth		
Pain/tenderness to palpitation		
Swelling/induration		
Skin necrosis		
Systemic signs of cSSTI at diagnosis		
Temperature > 38◦C		
White blood cell count > 10,000/mm3 or < 4,500/mm3 or immature neutrophilis >10%		
Septic shock		
Organ dysfunction		
Unknown		
None of the above		
Tests conducted for cSSTI diagnosis		
Blood cultures		
Superficial swab and culture		
Needle aspiration		
Skin biopsy		
Surgical sample		
X-ray		
Ultrasound		
CT/MRI		
Unknown/not performed		
Microbiological cSSTI diagnosis positive for		
Methicillin resistance Staphylococcus aureus		
Methicillin susceptible S. aureus (MSSA)		
Staphylococcus coagulase negative		
Vancomycin Intermediate S. aureus (VISA)		
Streptococcus pneumonia		
Multidrug resistant S. pneumoniae (MDRSP)		
Penicillin resistant S. pneumoniae (PRSP)		
Beta-hemolytic Streptococci		
Streptococcus pyogenes		
Streptococcus agalactiae		
Enterococcus faecalis		
Enterococcus faecium		
Gram-negative bacilli		
Non-fermenting enterobacteria		

Diagnostic criteria	All cSSTI patients (N=XX)	
	n	%
Clostirdium spp.		
Other strict anaerobic bacteria		
Other microorganism		
Mixed flora		
Unknown		
None of the above		

8.1.10 HEALTHCARE RESOURCE USE FOR CSSTI PATIENTS STARTING ZINFORO

Table 35. Utilization during index hospitalization in patients with cSSTI

Resource utilization	All cSSTI patients (N=XX) n %
Duration of index hospitalization (days)	
Mean (SD)	
Median (Min-Max)	
Duration of days in ICU	
Mean (SD)	
Median (Min-Max)	
Quick sepsis-related organ failure assessment (qSOFA) conducted	
Yes	
No	
Unknown	
If qSOFA was conducted	
(n, % of qSOFA assessed)	
Glasgow coma scale <15	
Systolic blood pressure <100 mmHg	
High respiration rate (≥ 22 breaths per minute)	
Patient required isolation	
Yes	
No	
Unknown	
If patient isolated:	
Duration of isolation (days)	
Mean (SD)	
Median (Min-Max)	
Unknown	

Abbreviations: ICU: intensive care unit; Max: maximum; Min: minimum; qSOFA: Quick sepsis-related organ failure assessment; SD: standard deviation.

Table 36. Hospitalisation cost in patients with cSSTI

Hospital Cost	All cSSTI patients (N=XX) n %
Hospital Cost - standard hospital (local currency)	
Mean (SD)	
Median (Min-Max)	
Hospital Cost - advanced level (local currency)	
Mean (SD)	
Median (Min-Max)	
Hospital Cost - standard hospital (USD)	
Mean (SD)	
Median (Min-Max)	
Hospital Cost - advanced level (USD)	
Mean (SD)	
Median (Min-Max)	

Abbreviations: USD: US Dollars, Max: maximum; Min: minimum; SD: standard deviation.

Table 37. Utilization during index hospitalization by response status in patients with cSSTI

Resource utilization	cSSTI responders (N=XX)		cSSTI non-responders (N=XX)	
	n	%	n	%
Duration of index hospitalization (days)				
Mean (SD)				
Median (Min-Max)				
Duration of days in ICU				
Mean (SD)				
Median (Min-Max)				
Quick sepsis-related organ failure assessment (qSOFA) conducted				
Yes				
No				
Unknown				
If qSOFA was conducted (n, % of qSOFA assessed)				
Glasgow coma scale <15				
Systolic blood pressure <100 mmHg				
High respiration rate (≥ 22 breaths per minute)				
Patient required isolation				
Yes				
No				
Unknown				
If patient isolated:				
Duration of isolation (days)				
Mean (SD)				
Median (Min-Max)				
Unknown				

Table 38. Hospitalisation cost by response status in patients with cSSTI

Hospital Cost	cSSTI responders (N=XX)		cSSTI non-responders (N=XX)	
	n	%	n	%
Hospital Cost- standard hospital (local currency)				
Mean (SD)				
Median (Min-Max)				
Hospital Cost- advanced level (local currency)				
Mean (SD)				
Median (Min-Max)				
Hospital Cost- standard hospital (USD)				
Mean (SD)				
Median (Min-Max)				
Hospital Cost- advanced level (USD)				
Mean (SD)				
Median (Min-Max)				

Abbreviations: USD: US Dollars, Max: maximum; Min: minimum; SD: standard deviation.

Table 39. Ventilation and parenteral nutrition in patients with cSSTI

Ventilation and parenteral nutrition	All cSSTI patients (N=XX) n %
Patient required mechanical ventilation	
Yes	
No	
Unknown	
If patient received ventilation:	
Type of ventilation	
Invasive ventilation (n, % ventilated)	
Duration of invasive ventilation (days)	
Mean (SD)	
Median (Min-Max)	
Non-invasive ventilation (n, % ventilated)	
Duration of non-invasive ventilation (days)	
Mean (SD)	
Median (Min-Max)	
Including high flow oxygen therapy	
Yes (n, % ventilated)	
No (n, % ventilated)	
Unknown (n, % ventilated)	
Patient received parenteral nutrition	
Yes	
No	
Unknown	
If Yes:	
Duration of parenteral nutrition (days)	
Mean (SD)	
Median (Min-Max)	
Unknown	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 40. Treatments received during index hospitalization in patients with cSSTI

Treatments received	All cSSTI patients (N=XX) n %
Treatment received during index hospitalization	
Surgery related to the infection	
Surgery unrelated to the infection	
Blood pressure support	
If blood pressure support received:	
Fluid resuscitation (n,% blood pressure support)	
Vasopressors (n,% blood pressure support)	
Invasive procedures (n,% blood pressure support)	
Unknown	
Other	
None of the above	

Table 41. Complications during index hospitalization in patients with cSSTI

Complications	All cSSTI patients (N=XX) n %
Renal failure necessitating renal replacement	
Yes	
No	
Unknown	
If renal replacement :	
Duration of therapy (days)	
Mean (SD)	
Median (Min-Max)	
Renal replacement after first dose of Zinforo	
Yes (n,% with renal replacement)	
No (n,% with renal replacement)	
Unknown (n,% with renal replacement)	
Serum creatinine at the first Zinforo dose (mg/dL)	
Mean (SD)	
Median (Min-Max)	
Unknown	
Complications developed during index hospitalization	
Sepsis	
Severe sepsis	
Septic shock	
Unknown	
None of the above	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 42. Dosages of Zinforo and other antibiotics in patients with cSSTI

Complications	All cSSTI patients (N=XX) n %
Total number of doses of Zinforo administered	
Mean (SD)	
Median (Min-Max)	
Total number doses of other antibiotics administered in combination with Zinforo	
Mean (SD)	
Median (Min-Max)	
Total number of doses of other antibiotics administered post Zinforo treatment	
Mean (SD)	
Median (Min-Max)	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 43. Resource use post index hospitalization in patients with cSSTI

Resource utilization post index hospitalization	All cSSTI patients (N=XX) n %
Home-based care received through a health-care agency (e.g. for wounds, intravenous infusions)	
Yes	
No	
Unknown	
If home based care received ,	
Duration of home-based care (days)	
Mean (SD)	
Median (Min-Max)	
Re-hospitalized within 30 days of initial discharge	
Yes	
No	
Unknown	
If re-hospitalized,	
Number of re-hospitalizations	
Mean (SD)	
Median (Min-Max)	
Duration of all hospitalizations	
Mean (SD)	
Median (Min-Max)	
Admission reason:	
For index infection (n,% of re-hospitalizations)	
For other reason (n,% of re-hospitalizations)	
Unknown (n,% of re-hospitalizations)	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

8.1.11 PHYSICIANS USE OF ZINFORO® (AND OTHER ANTIBIOTICS) DURING INDEX HOPSPITALIZATION IN PATIENTS WITH CSSTI

Table 44. Pre Zinforo treatment- Summary across all treatment lines in patients with cSSTI

Antibiotic treatment pre Zinforo	All cSSTI patients (N=XX) n %
Antibiotic treatment for the index infection received prior to Zinforo	
Yes	
No	
Pre Zinforo treatment received	
Aminoglycoside	
Betalactam	
Carbapenem	
Ceftriaxone	
Cephalosporins	
Glycopeptide	
Macrolide	
Betalactam /Combination	
Quinolone	
Sulfonamide	
Clindamycin	
Linezolid	
Other antibiotic agent	
Unknown	
Line of therapy	
First	
Second	
Third	
Fourth	
Number of pre Zinforo lines of therapy	
Mean (SD)	
Median (Min-Max)	
Route of administration	
Oral	
Intra-venous	
Intra-muscular	
Subcutaneous	
Unknown	

Antibiotic treatment pre Zinforo	All cSSTI patients (N=XX) n %
Duration of pre Zinforo treatment (days)	
Mean (SD)	
Median (Min-Max)	
Treatment type	
Empiric	
Definitive/Specific	
Unknown	
Number of administrations	
Mean (SD)	
Median (Min-Max)	
Number of doses administered	
Mean (SD)	
Median (Min-Max)	
Administration location	
ICU	
General ward	
At home	
Out patient	
Medical setting	
Unknown	
Treatment modification	
Yes	
No	
Unknown	
If yes:	
Time to treatment modification from initial dose	
Reason for treatment modification	
Treatment response	
Time to clinical response	
Clinical failure details	
Daily dose unit	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 45. Pre Zinforo treatment by line of treatment in patients with cSSTI

Pre Zinforo treatment	Line of treatment			
	1st Line N, %	2nd Line N, %	3rd Line N, %	4th Line N, %
Aminoglycoside				
Betalactam				
Carbapenem				
Ceftriaxone				
Cephalosporins				
Glycopeptide				
Macrolide				
Betalactam /Combination				
Quinolone				
Sulfonamide				
Clindamycin				
Linezolid				
Other antibiotic agent				
Unknown				

Table 46. Zinforo treatment during index hospitalization in patients with cSSTI

Zinforo treatment	All cSSTI patients (N=XX) n	%
Zinforo line of therapy		
First		
Second		
Third		
Fourth		
Duration of Zinforo treatment (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Time from admission to 1st dose (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Time from symptom onset to 1st dose (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Treatment type		
Empiric		
Definitive/Specific		
Unknown		
Daily dose (mg/kg)		
Mean (SD)		
Median (Min-Max)		
Number of infusions per day		
Mean (SD)		
Median (Min-Max)		
Unknown		
Administration location		
ICU		
General ward		
At home		
Out-patient setting		
Medical clinic		
Unknown		

Abbreviations: ICU: intensive care unit; Max: maximum; Min: minimum; SD: standard deviation.

Table 47. Zinforo administered in combination therapy in patients with cSSTI

Antibiotic treatments given in combination with Zinforo	All cSSTI patients (N=XX) n %
Zinforo as Mono/ Combination treatment	
Monotherapy	
Combination therapy	
Unknown	
If administered in combination:	
Antibiotic treatment received	
Aminoglycoside	
Betalactam	
Carbapenem	
Ceftriaxone	
Cephalosporins	
Glycopeptide	
Macrolide	
Betalactam /Combination	
Quinolone	
Sulfonamide	
Clindamycin	
Linezolid	
Other antibiotic agent	
Unknown	
Route of administration	
Oral	
Intra-venous	
Intra-muscular	
Subcutaneous	
Unknown	
Duration of combination treatment (days)	
Mean (SD)	
Median (Min-Max)	
Unknown	
Number of doses administered	
Mean (SD)	
Median (Min-Max)	
Unknown	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

Table 48. Zinforo treatment and concomitant therapy in patients with cSSTI

Therapies concomitant to Zinforo	All cSSTI patients (N=XX) n %
Concomitant therapy given	
Yes	
No	
If concomitant therapy "yes"	
Therapy received	
Immunosuppressors/ Immunomodulators	
Anticoagulants	
Non-steroidal anti-inflammatory agents (NSAIs)	
Chemotherapeutic agents	
Other	
Unknown	

8.1.12 TREATMENT RESPONSE TO ZINFORO® IN PATIENTS WITH CSSTI

Table 49. Response to Zinforo treatment in patients with cSSTI

Treatment response	All cSSTI patients (N=XX) n %
Zinforo treatment response	
Clinical response	
Clinical failure	
Time to clinical response	
Mean (SD)	
Median (Min-Max)	
Unknown	
Zinforo early treatment response	
Response ≤3 days	
Response >3days	
No response	
Unknown	
Clinical cure achieved	
Yes	
No	
Time to clinical cure	
Mean (SD)	
Median (Min-Max)	
Unknown	
Reduction of ≥20% from baseline area achieved	
Time to ≥20% reduction from baseline area	
Mean (SD)	
Median (Min-Max)	
Unknown	
Cessation of spread measured by total infection area	
Time to cessation of spread	
Mean (SD)	
Median (Min-Max)	
Unknown	
Cessation of spread measured by infection length and width	
Time to cessation of spread	
Mean (SD)	
Median (Min-Max)	
Unknown	

Abbreviations: Max: maximum; Min: minimum; SD: standard deviation.

8.1.13 ADDITIONAL CLINICAL OUTCOMES IN PATIENTS WITH CSSTI

Table 50. Additional clinical outcomes in response to Zinforo treatment in patients with cSSTI

Additional clinical outcomes	All cSSTI patients (N=XX) n %
Discharge status	
Died in the hospital	
Discharged to a nursing home or extended care facility	
Discharged to independent living (with or without support)	
Other	
Unknown	
Vital status at end of follow up	
Patient is still alive	
Patient is deceased	
If deceased	
Duration of days from discharge until death(days)	
Mean (SD)	
Median (Min-Max)	
Unknown	
Minimum inhibitory concentrations (MIC) of antibacterial drugs assessed	
Yes	
No	
Unknown	
If assessed	
Day of assessment since index hospitalization	
Mean (SD)	
Median (Min-Max)	
MIC of ceftaroline for all isolated pathogens	
MIC of oxacillin, vancomycin, linezolid, and daptomycin for S. aureus	
MIC of ceftriaxone for MSSA	
MIC of penicillin and ceftriaxone for S. pneumonia	

Abbreviations: Max: maximum; MIC: minimum inhibitory concentrations; Min: minimum; SD: standard deviation.

8.1.14 TREATMENT MODIFICATIONS / ADVERSE EVENTS IN PATIENTS WITH CSSTI

Table 51. Clinical failure with Zinforo in patients with cSSTI

Clinical failure with Zinforo	All cSSTI patients (N=XX) n	%
Etiology of clinical failure		
Failure related to cSSTI		
Failure unrelated to cSSTI		
Unknown		
Reason for clinical failure		
Treatment modification due to AE		
Time to modification (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Drug-drug interaction		
Insufficient response		
Death due to index infection		
Time to death due to infection (days)		
Mean (SD)		
Median (Min-Max)		
Death due to other		
Relapse or recurrence		
Time to relapse/recurrence:		
Mean (SD)		
Median (Min-Max)		
Unknown		

Abbreviations: AE: adverse events; Max: maximum; Min: minimum; SD: standard deviation.

Table 52. Clinical failure with Zinforo due to adverse events in patients with cSSTI

Clinical failure to Zinforo due to AEs	All cSSTI patients (N=XX)	
	n	%
AE causing Zinforo discontinuation		
Infections and infestations		
Clostridium difficile colitis		
Other		
Blood and lymphatic system disorders		
Activated partial thromboplastin time (aPTT) prolonged		
Agranulocytosis		
Anaemia		
Eosinophilia		
International normalized ratio (INR) increased		
Leucopenia		
Neutropenia		
Prothrombin time (PT) prolonged		
Thrombocytopenia		
Other		
Immune system disorders		
Anaphylaxis		
Hypersensitivity (e.g. urticarial, lip and face swelling)		
Pruritus		
Rash		
Other		
Nervous system disorders		
Dizziness		
Headache		
Other		
Vascular disorders		
Phlebitis		
Other		
Gastrointestinal disorders		
Abdominal pain		
Diarrhea		
Nausea		
Vomiting		
Other		
Hepatobiliary disorders		
Increased transaminases		
Other		
Renal urinary disorders		
Blood creatinine increased		
Other		
General disorders and administrative site conditions		
Infusion site reaction (e.g. erythema, phlebitis, pain)		
Pyrexia		
Other		
Investigations		

Clinical failure to Zinforo due to AEs	All cSSTI patients (N=XX) n %
Coombs direct test positive	
Other	
Unknown	

Abbreviations: AE: adverse events, aPTT: activated partial thromboplastin time

Table 53. Seriousness of adverse events in patients with cSSTI

Clinical failure to Zinforo	All cSSTI patients (N=XX) n %
Serious AE at Zinforo discontinuation	
Yes	
No	
Unknown	
Seriousness criteria applied (for AEs indicated as serious)	
Resulted in death	
Life-threatening	
Hospitalization/prolongation of hospitalization	
Persistent/significant disability/incapacity	
Congenital anomaly/birth defect	
Important medical event	
None of the above	
Unknown	

Abbreviations: AE: adverse event.

Table 54. Post Zinforo treatment- Summary across all lines in patients with cSSTI

Antibiotic treatment post Zinforo	All cSSTI patients (N=XX) n	%
Antibiotic treatment received for index infection after Zinforo		
Yes		
No		
Post Zinforo treatment received		
Aminoglycoside		
Betalactam		
Carbapenem		
Ceftriaxone		
Cephalosporins		
Glycopeptide		
Macrolide		
Betalactam /Combination		
Quinolone		
Sulfonamide		
Clindamycin		
Linezolid		
Other antibiotic agent		
Unknown		
Line of therapy		
First		
Second		
Third		
Fourth		
Number of post Zinforo lines of therapy		
Mean (SD)		
Median (Min-Max)		
Route of administration		
Oral		
Intra-venous		
Intra-muscular		
Subcutaneous		
Unknown		
Duration from Zinforo discontinuation to initiation of new treatment (days)		
Mean (SD)		
Median (Min-Max)		
Unknown		
Duration of treatment (days)		

Antibiotic treatment post Zinforo	All cSSTI patients (N=XX) n %
Mean (SD)	
Median (Min-Max)	
Unknown	
Treatment type	
Empiric	
Definitive/Specific	
Unknown	
Number of administrations	
Mean (SD)	
Median (Min-Max)	
Number of doses administered	
Mean (SD)	
Median (Min-Max)	
Administration location	
ICU	
General ward	
Unknown	
Reason for switch	
Lack of efficacy of previous treatment	
Side effect of previous treatment	
Drug interaction of previous treatment	
Results of susceptibility test/pathogen identification	
Special population with renal impairment	
Other	
Unknown	

Abbreviations: ICU: intensive care unit; Max: maximum; Min: minimum; SD: standard deviation.

Table 55. Response to post-Zinforo treatment in patients with cSSTI

Post Zinforo treatment response	All cSSTI patients (N=XX) n %
Treatment response to post- Zinforo treatment	
Clinical response	
Clinical failure	
Unknown	
Clinical cure achieved	
Yes	
No	
Unknown	
If clinical failure to post–Zinforo treatment	
Treatment modification due to adverse event	
Drug-drug interaction	
Insufficient response	
Relapse/reoccurrence	
Death due to infection	
Death due to other	
Unknown	

9 REFERENCES

1. Martinez R, Reyes S, Lorenzo MJ, Menendez R. Impact of guidelines on outcome: the evidence. *Semin Respir Crit Care Med.* 2009;30(2):172-178.
2. Welte T. Managing CAP patients at risk of clinical failure. *Respir Med.* 2015;109(2):157-169.
3. Personne V, Chevalier J, Buffel du Vaure C, Partouche H, Gilberg S, de Pouvourville G. CAPECO: Cost evaluation of community acquired pneumonia managed in primary care. *Vaccine.* 2016;34(19):2275-2280.
4. Rozenbaum MH, Mangen MJ, Huijts SM, van der Werf TS, Postma MJ. Incidence, direct costs and duration of hospitalization of patients hospitalized with community acquired pneumonia: A nationwide retrospective claims database analysis. *Vaccine.* 2015;33(28):3193-3199.
5. Kolditz M, Tesch F, Mocke L, Hoffken G, Ewig S, Schmitt J. Burden and risk factors of ambulatory or hospitalized CAP: A population based cohort study. *Respir Med.* 2016;121:32-38.
6. Schnoor M, Hedicke J, Dalhoff K, Raspe H, Schafer T, group Cs. Approaches to estimate the population-based incidence of community acquired pneumonia. *J Infect.* 2007;55(3):233-239.
7. Ramirez JA, Anzueto AR. Changing needs of community-acquired pneumonia. *J Antimicrob Chemother.* 2011;66 Suppl 3:iii3-9.
8. Blasi F, Garau J, Medina J, et al. Current management of patients hospitalized with community-acquired pneumonia across Europe: outcomes from REACH. *Respir Res.* 2013;14:44.
9. Capelastegui A, Espana PP, Bilbao A, et al. Etiology of community-acquired pneumonia in a population-based study: link between etiology and patients characteristics, process-of-care, clinical evolution and outcomes. *BMC Infect Dis.* 2012;12:134.
10. Dryden MS. Complicated skin and soft tissue infection. *J Antimicrob Chemother.* 2010;65 Suppl 3:iii35-44.
11. Raghavan M, Linden PK. Newer treatment options for skin and soft tissue infections. *Drugs.* 2004;64(15):1621-1642.
12. Tognetti L, Martinelli C, Berti S, et al. Bacterial skin and soft tissue infections: review of the epidemiology, microbiology, aetiopathogenesis and treatment: a collaboration between dermatologists and infectivologists. *J Eur Acad Dermatol Venereol.* 2012;26(8):931-941.
13. Hatoum HT, Akhras KS, Lin SJ. The attributable clinical and economic burden of skin and skin structure infections in hospitalized patients: a matched cohort study. *Diagn Microbiol Infect Dis.* 2009;64(3):305-310.

14. Talan DA, Salhi BA, Moran GJ, et al. Factors associated with decision to hospitalize emergency department patients with skin and soft tissue infection. *West J Emerg Med.* 2015;16(1):89-97.
15. Lodise TP, Fan W, Sulham KA. Hospital admission patterns in adult patients with skin and soft tissue infections: Identification of potentially avoidable hospital admissions through a retrospective database analysis. *Hosp Pract (1995).* 2015;43(3):137-143.
16. Garau J, Ostermann H, Medina J, et al. Current management of patients hospitalized with complicated skin and soft tissue infections across Europe (2010-2011): assessment of clinical practice patterns and real-life effectiveness of antibiotics from the REACH study. *Clin Microbiol Infect.* 2013;19(9):E377-385.
17. Lipsky BA, Weigelt JA, Gupta V, Killian A, Peng MM. Skin, soft tissue, bone, and joint infections in hospitalized patients: epidemiology and microbiological, clinical, and economic outcomes. *Infect Control Hosp Epidemiol.* 2007;28(11):1290-1298.
18. File TM, Jr., Low DE, Eckburg PB, et al. FOCUS 1: a randomized, double-blinded, multicentre, Phase III trial of the efficacy and safety of ceftaroline fosamil versus ceftriaxone in community-acquired pneumonia. *J Antimicrob Chemother.* 2011;66 Suppl 3:iii19-32.
19. Low DE, File TM, Jr., Eckburg PB, et al. FOCUS 2: a randomized, double-blinded, multicentre, Phase III trial of the efficacy and safety of ceftaroline fosamil versus ceftriaxone in community-acquired pneumonia. *J Antimicrob Chemother.* 2011;66 Suppl 3:iii33-44.
20. Ramani A, Udeani G, Evans J, et al. Contemporary use of ceftaroline fosamil for the treatment of community-acquired bacterial pneumonia: CAPTURE study experience. *Journal of chemotherapy (Florence, Italy).* 2014;26(4):229-234.
21. Eckberg PF, D. Llorens, L. Smith, A. Witherell, G. Laudano, J. Thye, D. Day 4 clinical response of ceftaroline for community-acquired bacterial pneumonia. *Infectious Diseases in Clinical Practice.* 2012;20(4):254-260.
22. File TM, Jr., Wilcox MH, Stein GE. Summary of ceftaroline fosamil clinical trial studies and clinical safety. *Clin Infect Dis.* 2012;55 Suppl 3:S173-180.
23. Wilcox MH, Corey GR, Talbot GH, et al. CANVAS 2: the second Phase III, randomized, double-blind study evaluating ceftaroline fosamil for the treatment of patients with complicated skin and skin structure infections. *J Antimicrob Chemother.* 2010;65 Suppl 4:iv53-iv65.
24. Corey GR, Wilcox MH, Talbot GH, et al. CANVAS 1: the first Phase III, randomized, double-blind study evaluating ceftaroline fosamil for the treatment of patients with complicated skin and skin structure infections. *J Antimicrob Chemother.* 2010;65 Suppl 4:iv41-51.
25. Corey GR, Wilcox M, Talbot GH, et al. Integrated analysis of CANVAS 1 and 2: phase 3, multicenter, randomized, double-blind studies to evaluate the safety and efficacy of ceftaroline versus vancomycin plus aztreonam in complicated skin and skin-structure infection. *Clin Infect Dis.* 2010;51(6):641-650.

26. Dryden M, Zhang Y, Wilson D, Iaconis JP, Gonzalez J. A Phase III, randomized, controlled, non-inferiority trial of ceftaroline fosamil 600 mg every 8 h versus vancomycin plus aztreonam in patients with complicated skin and soft tissue infection with systemic inflammatory response or underlying comorbidities. *J Antimicrob Chemother.* 2016;71(12):3575-3584.