



## Clinical trial results:

### A Phase 1, Open-label, Single-Dose Study to Assess the Pharmacokinetics, Safety and Tolerability of Ceftazidime-Avibactam (CAZ-AVI) in Children From 3 Months to Less Than 18 Years of age who are Hospitalised and Receiving Systemic Antibiotic Therapy for Suspected or Confirmed Nosocomial Pneumonia, Including Ventilator-Associated Pneumonia

#### Summary

EudraCT number	2018-002841-12
Trial protocol	SK GB EE GR NL IT
Global end of trial date	07 May 2021

#### Results information

Result version number	v1 (current)
This version publication date	05 April 2022
First version publication date	05 April 2022

#### Trial information

##### Trial identification

Sponsor protocol code	C3591025
-----------------------	----------

##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04040621
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

##### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001313-PIP01-12
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 September 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	07 May 2021
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To characterize the pharmacokinetics (PK) of a single intravenous dose of CAZ-AVI in pediatric subjects aged 3 months to less than 18 years who are receiving systemic antibiotic therapy for suspected or confirmed nosocomial pneumonia, including ventilator-associated pneumonia.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	China: 2
Country: Number of subjects enrolled	Taiwan: 2
Worldwide total number of subjects	4
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2
Children (2-11 years)	2
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Hospitalised pediatric subjects who were receiving systemic antibiotic therapy for suspected or confirmed nosocomial pneumonia (NP), including ventilator-associated pneumonia (VAP) were enrolled.

### Pre-assignment

Screening details:

Only 4 subjects were enrolled before trial was stopped prematurely. Data cannot be reported per cohort as planned because doing so would risk re-identification of subjects. Thus, to avoid this potential risk, only disposition and baseline characteristics data are reported for all subjects as 1 reporting group and no data for endpoints are reported.

### Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

<b>Arm title</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)
------------------	--

Arm description:

Subjects received 50 milligram (mg)/kilogram (kg) of CAZ and 12.5 mg/kg of AVI intravenously.

Arm type	Experimental
Investigational medicinal product name	CAZ-AVI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 50 mg/kg of CAZ and 12.5 mg/kg of AVI intravenously.

<b>Number of subjects in period 1</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)
Started	4
Completed	4

## Baseline characteristics

### Reporting groups

Reporting group title	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)
-----------------------	--

Reporting group description:

Subjects received 50 milligram (mg)/kilogram (kg) of CAZ and 12.5 mg/kg of AVI intravenously.

Reporting group values	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)	Total	
Number of subjects	4	4	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	2	2	
Children (2-11 years)	2	2	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender Categorical Units: Subjects			
Female	1	1	
Male	3	3	
Race Units: Subjects			
Black or African American	0	0	
American Indian or Alaska Native	0	0	
Asian	4	4	
Native Hawaiian or Other Pacific Islander	0	0	
White	0	0	
Mixed Race	0	0	
Not reported	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	4	4	
Not reported	0	0	

## End points

### End points reporting groups

Reporting group title	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)
Reporting group description: Subjects received 50 milligram (mg)/kilogram (kg) of CAZ and 12.5 mg/kg of AVI intravenously.	

### Primary: Plasma Concentration Time Summary for Ceftazidime and Avibactam

End point title	Plasma Concentration Time Summary for Ceftazidime and Avibactam <sup>[1]</sup>
-----------------	--

End point description:

Pharmacokinetics (PK) analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[2]</sup>			
Units: nanogram per milliliter				
geometric mean (geometric coefficient of variation)	()			

Notes:

[2] - Data cannot be reported because doing so would risk re-identification of subjects.

### Statistical analyses

No statistical analyses for this end point

### Primary: Area Under the Curve From Time Zero to Extrapolated Infinite Time of CAZ-AVI (AUCinf)

End point title	Area Under the Curve From Time Zero to Extrapolated Infinite Time of CAZ-AVI (AUCinf) <sup>[3]</sup>
-----------------	--

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. AUCinf = AUClast + (Clast\*/ kel), where Clast\* is the estimated concentration at the time of the last quantifiable concentration and kel is the terminal phase rate constant calculated by a linear regression of the log-linear concentration-time curve. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[4]</sup>			
Units: nanogram*hour per milliliter				
geometric mean (geometric coefficient of variation)	( )			

Notes:

[4] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

## Primary: Area Under the Plasma Concentration-Time Profile From Time 0 to 8 Hours (AUC0-8 hours)

End point title	Area Under the Plasma Concentration-Time Profile From Time 0 to 8 Hours (AUC0-8 hours) <sup>[5]</sup>
-----------------	---

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8 hours post dose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[6]</sup>			
Units: nanogram*hour per milliliter				
geometric mean (geometric coefficient of variation)	( )			

Notes:

[6] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

**Primary: Area Under the Concentration-Time Profile From Time 0 to Time to Last Quantifiable Concentration (AUClast) of CAZ-AVI**

End point title	Area Under the Concentration-Time Profile From Time 0 to Time to Last Quantifiable Concentration (AUClast) of CAZ-AVI <sup>[7]</sup>
-----------------	--

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[8]</sup>			
Units: nanogram*hour per milliliter				
geometric mean (geometric coefficient of variation)	()			

Notes:

[8] - Data cannot be reported because doing so would risk re-identification of subjects.

**Statistical analyses**

No statistical analyses for this end point

**Primary: Time to Last Quantifiable Plasma Concentration (Tlast) of CAZ-AVI**

End point title	Time to Last Quantifiable Plasma Concentration (Tlast) of CAZ-AVI <sup>[9]</sup>
-----------------	--

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[10]</sup>			
Units: hour				



median (full range (min-max))	( to )			
-------------------------------	--------	--	--	--

Notes:

[10] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

## Primary: Maximum Observed Plasma Concentration (Cmax) of CAZ-AVI

End point title	Maximum Observed Plasma Concentration (Cmax) of CAZ-
-----------------	--

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[12]</sup>			
Units: nanogram per milliliter				
geometric mean (geometric coefficient of variation)	( )			

Notes:

[12] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

## Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax) of CAZ-AVI

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) of CAZ-AVI <sup>[13]</sup>
-----------------	---

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[14]</sup>			
Units: hour				
median (full range (min-max))	( to )			

Notes:

[14] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

## Primary: Termination Elimination Half-Life (t<sub>1/2</sub>) of CAZ-AVI

End point title	Termination Elimination Half-Life (t <sub>1/2</sub> ) of CAZ-AVI <sup>[15]</sup>
-----------------	--

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. t<sub>1/2</sub> = Loge(2)/kel. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[16]</sup>			
Units: hour				
median (standard deviation)	( )			

Notes:

[16] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

## Primary: Clearance (CL) of CAZ-AVI

End point title	Clearance (CL) of CAZ-AVI <sup>[17]</sup>
-----------------	---

End point description:

Drug clearance is a quantitative measure of the rate at which a drug substance is removed from the blood (rate at which a drug is metabolised or eliminated by normal biological processes). Clearance obtained after intravenous infusion dose (apparent clearance) is influenced by the fraction of the dose absorbed.  $CL = \text{Dose}/AUC_{inf}$ . PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[18]</sup>			
Units: liter per hour				
geometric mean (geometric coefficient of variation)	()			

Notes:

[18] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

## Primary: Volume of Distribution of CAZ-AVI

End point title	Volume of Distribution of CAZ-AVI <sup>[19]</sup>
-----------------	---

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available.  $V_{ss} = CL \times MRT$ ,  $MRT = AUMC_{inf}/AUC_{inf} - (\text{infusion time}/2)$ ,  $AUMC_{inf} = AUMC_{last} + (t \times C_{est1}/k_{el}) + (C_{est1}/k_{el}^2)$ ,  $1C_{est} = e^{(-K_{el} \times T_{last})} \times K_{el}C_0$ , where  $C_0$  is the back-extrapolated concentration at time zero. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[20]</sup>			
Units: liter				
geometric mean (geometric coefficient of variation)	()			

of variation)

Notes:

[20] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

### Primary: Volume of Distribution During Terminal Phase (V<sub>z</sub>) of CAZ-AVI

End point title	Volume of Distribution During Terminal Phase (V <sub>z</sub> ) of CAZ-
-----------------	--

End point description:

PK analysis set included all subjects who received a complete IV study dose of CAZ-AVI and had at least 1 ceftazidime and/or avibactam plasma measurement available.  $V_z = \text{Dose}/(\text{AUC}_{\text{inf}} \times \text{kel})$ . Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 1: 2, 2.25, 2.5, 3, 3.5, 4, 5, 6, 8, 12, 13, 24 hours post dose

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[22]</sup>			
Units: liter				
geometric mean (geometric coefficient of variation)	( )			

Notes:

[22] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)
-----------------	--

End point description:

An Adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Safety set included all subjects who had received any amount of IV study dose of CAZ AVI. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Secondary
----------------	-----------

End point timeframe:  
Baseline up to 28 days after last dose of study treatment

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[23]</sup>			
Units: Subjects				

Notes:

[23] - Data cannot be reported because doing so would risk re-identification of subjects.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Death and Discontinuations due to Adverse Events (AEs)

End point title	Number of Subjects With Death and Discontinuations due to Adverse Events (AEs)
-----------------	--

End point description:

An Adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Safety set included all subjects who had received any amount of IV study dose of CAZ AVI. Data cannot be reported because doing so would risk re-identification of subjects.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline up to 28 after last dose of study treatment

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[24]</sup>			
Units: Subjects				

Notes:

[24] - Data cannot be reported because doing so would risk re-identification of subjects.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Clinically Significant Physical Examination Abnormalities

End point title	Number of Subjects With Clinically Significant Physical
-----------------	---

End point description:

Parameters assessed for physical examination included: body weight and height. Abnormality was judged by investigator. Safety set included all subjects who had received any amount of IV study dose of CAZ-AVI. Data cannot be reported because doing so would risk re-identification of subjects.

End point type Secondary

End point timeframe:

Baseline, Day 3 (48 hours post dose on Day 1)

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[25]</sup>			
Units: Subjects				

Notes:

[25] - Data cannot be reported because doing so would risk re-identification of subjects.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Clinically Significant Abnormal Laboratory Values

End point title Number of Subjects With Clinically Significant Abnormal Laboratory Values

End point description:

Following parameters were analysed for laboratory examination: Clinical Chemistry-sodium, potassium, chloride, bicarbonate, creatinine, blood urea nitrogen, glucose-non fasting, calcium, phosphorus, magnesium, alkaline phosphatase, gamma glutamyl transferase, aspartate transaminase, alanine transaminase, creatinine kinase, lactate dehydrogenase, indirect bilirubin, total bilirubin; Hematology-hematocrit, hemoglobin, RBC, WBC, neutrophils, lymphocytes, monocytes, eosinophils, basophils, neutrophils immature, platelets, mean cell volume, mean cell hemoglobin,  $\beta$ - human chorionic gonadotropin (hCG) pregnancy test (blood or urine) for females; Urinalysis- appearance (color, clarity), bilirubin, glucose, ketones leukocyte esterase, nitrite, pH, protein, specific gravity, urobilinogen, microscopic (RBC, WBC, casts, crystals, bacteria, yeast, parasites). Safety set. Data cannot be reported because doing so would risk re-identification of subjects.

End point type Secondary

End point timeframe:

Baseline up to Day 3 (48 hours post dose on Day 1)

<b>End point values</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[26]</sup>			
Units: Subjects				

---

Notes:

[26] - Data cannot be reported because doing so would risk re-identification of subjects.

---

### **Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Up to 48 hours after the end of infusion

Adverse event reporting additional description:

Data cannot be reported because doing so would risk re-identification of subjects.

Assessment type	Non-systematic
-----------------	----------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24.1
--------------------	------

### Reporting groups

Reporting group title	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)
-----------------------	--

Reporting group description:

Subjects received 50 mg/kg of CAZ and 12.5 mg/kg of AVI intravenously.

<b>Serious adverse events</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	All Enrolled Subjects: Ceftazidime-Avibactam (CAZ-AVI)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Data cannot be reported per cohort as planned because doing so would risk re-identification of subjects.



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
07 May 2021	Following approval of the HAP/VAP indication in pediatric subjects in the EU in October 2020 based on extrapolation of efficacy and, based on subsequent regulatory consultations as well as slow enrollment, the sponsor made the decision to terminate the study and analyze the current dataset. This decision was not due to safety concerns.	-

Notes:

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Only 4 subjects were enrolled in this study, with each enrolled in a different cohort. Endpoints and AE data were not reported by cohort as planned in the protocol because doing so would risk re-identification of the individual subjects.

Notes: