Clinical trial results:
Trial of Optimal Therapy for Pseudomonas Eradication in Cystic Fibrosis

Summary

EudraCT number	2009-012575-10
Trial protocol	GB SE IT
Global end of trial date	10 April 2018

Results information

Result version number	v1 (current)
This version publication date	10 April 2019
First version publication date	10 April 2019
Summary attachment (see zip file)	Protocol Amendments V2.0, V4.0 and V6.0 (Protocol Amendments V2.0 V4.0 and V6.0.docx)

Trial information

Trial identification

Sponsor protocol code	CH/2007/2661

Additional study identifiers

ISRCTN number	ISRCTN02734162
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Funder reference: HTA 07/51/01

Notes:

Sponsors

Sponsor organisation name	University Hospitals Bristol NHS Foundation Trust
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2018
Global end of trial reached?	Yes
Global end of trial date	10 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This trial assessed whether fourteen days intravenous ceftazidime with tobramycin is superior to three months (12 weeks) oral ciprofloxacin. Both treatment regimes were in conjunction with three months (12 weeks) nebulised colistin.

Primary outcome:
Successful eradication of P. aeruginosa infection at three months (12 weeks) after allocated treatment had started, remaining infection free through to 15 months (60 weeks) after the start of allocated treatment.

Protection of trial subjects:

There were no formal accountability measures required for the trial. TORPEDO-CF has put the following measures in place to safeguard the safety of trial participants:
- Participant completed treatment diaries to record treatment compliance
- Collection of unused trial IMP
- Collection of packaging of used IMP
- Verbal interview conducted by the PI at the 3 month follow-up visit
- Local procedures should be used if a manufacturer issues a recall

Background therapy:

Participants recruited into the study were randomised to one of the following treatment arms:

Arm A: 14 days* intravenous (IV) antibiotics as follows:

- Ceftazidime 150 milligram (mg)/kilogram (kg)/day, in 3 divided doses (maximum of 3 grams (g) three times daily (tds)). Some centres used a once daily continuous infusion (where the maximum daily dose would usually be 6g/day) or twice daily regimen for ceftazidime.
These centres continued to use this regimen for the study and followed their local dosing guidelines.

- Tobramycin 10mg/kg/day once daily (od) (maximum 660mg /day). Some centres used a twice daily or three times daily regimen for tobramycin. These centres continued to use their current regimen for the study and should follow their local dosing guidelines. Therapeutic drug monitoring should be used to guide tobramycin dosing as per national guidelines (https://www.cysticfibrosis.org.uk/media/82010/CD_Antibiotic_treatment_for_CF_May_09.pdf) and usual clinic procedures.

*Recommended treatment duration should be 14 days, minimum treatment duration should be no less than 10 days

Arm B: 3 months oral ciprofloxacin twice daily (bd). (Ciprofloxacin dose will be 20 mg/kg twice daily (maximum 750mg twice daily. This is in line with the BNF for children (http://bnfc.org/bnfc/). Some clinicians prefered to use a lower dose of 15mg/kg twice daily for children under 5 years, as used in national CF guidelines (https://www.cysticfibrosis.org.uk/media/82010/CD_Antibiotic_treatment_for_CF_May_09.pdf).

randomised treatment. Colistin dose was as recommended by the UK CF Trust: 1,000,000 units twice daily for children aged ≤ 2 years and 2,000,000 units twice daily for children aged > 2 years and adults. If the colistin was administered via an I-neb a lower dose of 1,000,000 units twice daily for all ages should be used.

Evidence for comparator:

The rationale for choosing fourteen days of intravenous treatment and for choosing three months for oral treatment is that both of these are standard practice for many UK CF centres identified in the HTA feasibility study and both are standard recommendations within the published UK guideline and believed to represent current best practice.

Actual start date of recruitment	18 June 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 284
Country: Number of subjects enrolled	Italy: 2
Worldwide total number of subjects	286
EEA total number of subjects	286

Notes:

Subjects enrolled per age group

In utero	3
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	70
Children (2-11 years)	161
Adolescents (12-17 years)	37
Adults (18-64 years)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

60 UK based centres and 1 centre based in Italy took part in the trial. The first patient was randomised on 5th October 2010 and the last patient was randomised on 27th January 2017.

Pre-assignment

Screening details:

There were 1522 screenings from 1308 patients for eligibility and of those 554 were ineligible, 193 were not approached, 489 didn't provide consent and 3 patients were excluded but no reason was given. 286 patients were randomised into the trial.

(Note that patients could be screened more than once)

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Randomisation lists were generated in a 1:1 ratio using simple block randomisation with random variable block lengths. Factors within the protocol that were used to stratify randomisation were not disclosed to prevent prediction in this open trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Intravenous (IV) antibiotics

Arm description:

14 days IV antibiotics; Ceftazidime and Tobramycin alongside three months of nebulised Colistin

Arm type	Experimental
Investigational medicinal product name	Ceftazidime
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Ceftazidime 150 milligram (mg)/kilogram (kg)/day, in 3 divided doses (maximum of 3 grams (g) three times daily (tds)). Some centres used a once daily continuous infusion (where the maximum daily dose would usually be 6g/day) or twice daily regimen for ceftazidime.

Investigational medicinal product name	Tobramycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Tobramycin 10mg/kg/day once daily (od) (maximum 660mg /day). Some centres used a twice daily or three times daily regimen for tobramycin.

Investigational medicinal product name	Colistin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

3 months (12 weeks) of nebulised colistin in conjunction to the randomised treatment. Colistin dose was

as recommended by the UK CF Trust: 1,000,000 units twice daily for children aged ≤ 2 years and 2,000,000 units twice daily for children aged > 2 years and adults. If the colistin is administered via an I-neb a lower dose of 1,000,000 units twice daily for all ages was used.

Arm title	Oral antibiotic therapy
Arm description:	
3 months (12 weeks) of oral ciprofloxacin alongside 3 months (12 weeks) of nebulised colistin.	
Arm type	Active comparator
Investigational medicinal product name	Ciprofloxacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules and solvent for oral suspension, Tablet
Routes of administration	Oral use
Dosage and administration details:	
3 months (12 weeks) oral ciprofloxacin twice daily (bd). (Ciprofloxacin dose was 20 mg/kg twice daily (maximum 750mg twice daily. Some clinicians could use a lower dose of 15mg/kg twice daily for children under 5 years, as used in national CF guidelines.	
Investigational medicinal product name	Colistin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use
Dosage and administration details:	
3 months (12 weeks) of nebulised colistin in conjunction to the randomised treatment. Colistin dose was as recommended by the UK CF Trust: 1,000,000 units twice daily for children aged ≤ 2 years and 2,000,000 units twice daily for children aged > 2 years and adults. If the colistin is administered via an I-neb a lower dose of 1,000,000 units twice daily for all ages was used.	

Number of subjects in period 1	Intravenous (IV) antibiotics	Oral antibiotic therapy
Started	137	149
Completed	137	148
Not completed	0	1
Unable to obtain PI sign-off	-	1

Period 2

Period 2 title	Follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Blinding implementation details:	
See blinding details for the baseline period.	

Arms

Are arms mutually exclusive?	Yes

Arm title	Intravenous (IV) antibiotics

Arm description:

14 days IV antibiotics; Ceftazidime and Tobramycin alongside three months nebulised Colistin

Arm type	Experimental
Investigational medicinal product name	Ceftazidime
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ceftazidime 150 milligram (mg)/kilogram (kg)/day, in 3 divided doses (maximum of 3 grams (g) three times daily (tds)). Some centres used a once daily continuous infusion (where the maximum daily dose would usually be 6g/day) or twice daily regimen for ceftazidime.

Investigational medicinal product name	Tobramycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tobramycin 10mg/kg/day once daily (od) (maximum 660mg /day). Some centres used a twice daily or three times daily regimen for tobramycin.

Investigational medicinal product name	Colistin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

3 months (12 weeks) of nebulised colistin in conjunction to the randomised treatment. Colistin dose was as recommended by the UK CF Trust: 1,000,000 units twice daily for children aged ≤ 2 years and 2,000,000 units twice daily for children aged > 2 years and adults. If the colistin is administered via an I-neb a lower dose of 1,000,000 units twice daily for all ages was used.

Arm title	Oral antibiotic therapy

Arm description:

3 months (12 weeks) of oral ciprofloxacin alongside 3 months (12 weeks) of nebulised colistin.

Arm type	Active comparator
Investigational medicinal product name	Ciprofloxacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 months (12 weeks) oral ciprofloxacin twice daily (bd). (Ciprofloxacin dose was 20 mg/kg twice daily (maximum 750mg twice daily. Some clinicians preferred to use a lower dose of 15mg/kg twice daily for children under 5 years, as used in national CF guidelines.

Investigational medicinal product name	Colistin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

3 months (12 weeks) of nebulised colistin in conjunction to the randomised treatment. Colistin dose was as recommended by the UK CF Trust: 1,000,000 units twice daily for children aged ≤ 2 years and 2,000,000 units twice daily for children aged > 2 years and adults. If the colistin is administered via an I-neb a lower dose of 1,000,000 units twice daily for all ages was used.

Number of subjects in period 2	Intravenous (IV) antibiotics	Oral antibiotic therapy
Started	137	148
Completed	132	132
Not completed	5	16
Consent withdrawn by subject	1	4
Adverse event, non-fatal	-	1
Other	1	2
Lost to follow-up	3	9

Baseline characteristics

Reporting groups	
Reporting group title	Intravenous (IV) antibiotics
Reporting group description:	
14 days IV antibiotics; Ceftazidime and Tobramycin alongside three months of nebulised Colistin	
Reporting group title	Oral antibiotic therapy
Reporting group description:	
3 months (12 weeks) of oral ciprofloxacin alongside 3 months (12 weeks) of nebulised colistin.	

Reporting group values	Intravenous (IV) antibiotics	Oral antibiotic therapy	Total
Number of subjects	137	149	286
Age categorical			
PLEASE NOTE THAT THE AGE FOR 3 PARTICIPANTS COULD NOT BE CALCULATED AND THEREFORE DATA WAS UNOBTAINABLE FOR THESE PARTICIPANTS. THE TABLE TITLED 'AGE GROUP BREAKDOWN FOR TRIAL' IN THE SECTION 'TRIAL INFORMATION' HAS THESE 3 PARTICIPANTS ADDED IN THE 'IN UTERO' SECTION TO ALLOW RESULTS TO BE POSTED ONTO EUDRACT. AGE DATA ARE ONLY AVAILABLE FOR 283 PARTICIPANTS IN THE TRIAL.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	42	28	70
Children (2-11 years)	71	90	161
Adolescents (12-17 years)	18	19	37
Adults (18-64 years)	6	9	15
From 65-84 years	0	0	0
85 years and over	0	0	0
Missing	0	2	2
Not recorded	0	1	1
Gender categorical Units: Subjects			
Female	74	81	155
Male	63	67	130
Not recorded	0	1	1
Pseudomonas status Units: Subjects			
Free	56	55	111
Naïve	81	93	174
Not recorded	0	1	1
Genotype Units: Subjects			
Delta F508/ Delta F508	70	90	160
Delta F508/other	40	43	83
Delta F508/unknown	4	5	9
other/other	12	7	19
Diagnosis not based on genetics	10	3	13

Unknown whether diagnosis based on genetics	1	0	1
Not recorded	0	1	1
Pulmonary exacerbation			
Units: Subjects			
Yes	18	17	35
No	119	131	250
Not recorded	0	1	1
Candida detected			
Units: Subjects			
Yes	11	17	28
No	126	131	257
Not recorded	0	1	1
MRSA detected			
Units: Subjects			
Yes	0	2	2
No	137	146	283
Not recorded	0	1	1
Burkholderia cepacia detected			
Units: Subjects			
Yes	0	0	0
No	137	148	285
Not recorded	0	1	1
Aspergillus detected			
Units: Subjects			
Yes	2	2	4
No	135	146	281
Not recorded	0	1	1
Other micro-organism detected			
Units: Subjects			
Yes	26	31	57
No	111	117	228
Not recorded	0	1	1
BMI z-score (paediatric)			
Units: z-score			
arithmetic mean	0.3	0.3	
standard deviation	± 1	± 0.9	-
BMI (adults)			
Units: (m/kg^2)			
arithmetic mean	24.6	23.2	
standard deviation	± 1.8	± 2.3	-
Time from PsA isolation to treatment initiation			
Units: (days)			
arithmetic mean	9	7	
standard deviation	± 5	± 5	-
%predicted FEV1			
Units: FEV1 %predicted			
arithmetic mean	86.6	85.7	
standard deviation	± 15.8	± 16	-
%predicted FVC			
Units: FVC %predicted			

arithmetic mean	92.2	95.1	
standard deviation	± 15.5	± 14.5	-
%predicted FEF25-75			
Units: FEF25-75 %predicted			
arithmetic mean	72.7	70.6	
standard deviation	± 26.6	± 30.3	-
Oxygen saturation			
Units: (%)			
arithmetic mean	97.7	97.7	
standard deviation	± 1.4	± 1.7	-

End points

End points reporting groups

Reporting group title	Intravenous (IV) antibiotics
Reporting group description:	
14 days IV antibiotics; Ceftazidime and Tobramycin alongside three months of nebulised Colistin	
Reporting group title	Oral antibiotic therapy
Reporting group description:	
3 months (12 weeks) of oral ciprofloxacin alongside 3 months (12 weeks) of nebulised colistin.	
Reporting group title	Intravenous (IV) antibiotics
Reporting group description:	
14 days IV antibiotics; Ceftazidime and Tobramycin alongside three months nebulised Colistin	
Reporting group title	Oral antibiotic therapy
Reporting group description:	
3 months (12 weeks) of oral ciprofloxacin alongside 3 months (12 weeks) of nebulised colistin.	

Primary: Primary efficacy assessment - Successful eradication of P. aeruginosa three months after the start of treatment, remaining infection free through to 15 months after the start of treatment

End point title	Primary efficacy assessment - Successful eradication of P. aeruginosa three months after the start of treatment, remaining infection free through to 15 months after the start of treatment
End point description:	
End point type	Primary
End point timeframe:	
3 months after the start of treatment through to 15 months after the start of treatment .	

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	130		
Units: Subjects				
Successful eradication	55	68		
Unsuccessful eradication	70	62		

Statistical analyses

Statistical analysis title	Successful eradication from 3 months to 15 months
Statistical analysis description:	
The number of patients who were classified as (a) a success and (b) failure for the primary outcome (and percentages) were presented for each treatment arm. The relative risk together with 95% confidence interval was reported along with a two-sided p-value from a chi-squared test.	
Comparison groups	Oral antibiotic therapy v Intravenous (IV) antibiotics

Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.184
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.09

Primary: Primary efficacy assessment - Successful eradication of P. aeruginosa three months after the start of treatment, remaining infection free through to 15 months after the start of treatment

End point title	Primary efficacy assessment - Successful eradication of P. aeruginosa three months after the start of treatment, remaining infection free through to 15 months after the start of treatment

End point description:

End point type	Primary

End point timeframe:

From 3 months after the start of treatment to 15 months after the start of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	116		
Units: Subjects				
Successful eradication	97	111		
Unsuccessful eradication	13	5		

Statistical analyses

Statistical analysis title	Unsuccessful eradication at 3 months
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	226
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.037
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	2.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	7.44

Primary: Primary efficacy assessment – Sensitivity analysis 6: no T15 window (Post hoc)

End point title	Primary efficacy assessment – Sensitivity analysis 6: no T15 window (Post hoc)

End point description:

End point type	Primary

End point timeframe:

From 3 months after the start of treatment to 15 months after the start of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	144		
Units: Subjects				
Successful eradication	58	70		
Unsuccessful eradication	78	74		

Statistical analyses

Statistical analysis title	Sensitivity analysis 6

Statistical analysis description:

The relative risk with 95% CI was presented. A chi-squared test will be used to calculate a p-value for this relative risk.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	280
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.317
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.13

Secondary: Time to reoccurrence of original P.aeruginosa infection - unknown strains assumed to be same as baseline

End point title	Time to reoccurrence of original P.aeruginosa infection - unknown strains assumed to be same as baseline

End point description:

End point type	Secondary

End point timeframe:

3 months to 24 months. Only patients who have a baseline sample and at least one sample post three months will be included in this analysis.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	148		
Units: Subjects				
Reoccurence of original P.aeruginosa infection	74	66		
Censored	63	82		

Statistical analyses

Statistical analysis title	Time to reoccurrence of original P.aeruginosa

Statistical analysis description:

Difference between the two treatment arms was tested using the log-rank test. Cox proportional hazards regression was used to calculate a hazard ratio with 95% CI, comparing the IV treatment group to oral, – unknown strains assumed to be same as baseline.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.061
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.91

Secondary: Time to reoccurrence of original P.aeruginosa infection - unknown

strains assumed to be different to baseline	
End point title	Time to reoccurrence of original P.aeruginosa infection - unknown strains assumed to be different to baseline

End point description:

End point type	Secondary

End point timeframe:

From 3 to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	148		
Units: Subjects				
Reoccurence of original P.aeruginosa infection	21	14		
Censored	116	134		

Statistical analyses

Statistical analysis title	Time to reoccurrence of original P.aeruginosa

Statistical analysis description:

Difference between the two treatment arms was tested using the log-rank test. Cox proportional hazards regression was used to calculate a hazard ratio with 95% CI, comparing the IV treatment group to oral, – unknown strains assumed to be differnt than baseline.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	3.64

Secondary: Re-infection with a different strain of P.aeruginosa	
End point title	Re-infection with a different strain of P.aeruginosa

End point description:

End point type	Secondary

End point timeframe:

From baseline to 15 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	17		
Units: Subjects				
Same genotype	19	12		
Different genotype	6	5		

Statistical analyses

Statistical analysis title	Re-infection with a different strain

Statistical analysis description:

The relative risk together with 95% confidence interval was reported along with a two-sided p-value from a chi-squared test.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.733
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.25

Secondary: Post hoc analysis – Genotyping results

End point title	Post hoc analysis – Genotyping results

End point description:

End point type	Secondary

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	22		
Units: Subjects				
Same genotype	20	13		
Different genotype	8	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Lung function - FEV1% predicted

End point title	Lung function - FEV1% predicted

End point description:

End point type	Secondary

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[1]	70[2]		
Units: FEV1% predicted				
arithmetic mean (standard deviation)				
Baseline	86.6 (± 15.8)	85.7 (± 16.0)		
3 Months (11-13 weeks)	86.3 (± 18.6)	81.9 (± 15.6)		
15 Months (59-62 weeks)	89.5 (± 18.2)	82.3 (± 18.9)		
24 Months (95-97 weeks)	83.8 (± 13.7)	79.8 (± 15.0)		

Notes:

[1] - At baseline n=67, T3 n=25, T15 n=32, T24 n= 11

[2] - At baseline n=70, T3 n=28, T15 n=32 , T24 n=17

Statistical analyses

Statistical analysis title	FEV1 % predicted - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	137
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.008
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	3.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	6.53

Statistical analysis title	FEV1 % predicted - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.184
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	2.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	5.14

Statistical analysis title	FEV1 % predicted - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures will be fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	137
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.705
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.45
upper limit	5.1

Statistical analysis title	FEV1 % predicted - treat difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a continuous variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	137
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.019
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	3.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	5.8

Secondary: Lung function - FVC% predicted

End point title	Lung function - FVC% predicted

End point description:

End point type	Secondary

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67[3]	70[4]		
Units: FVC% predicted				
arithmetic mean (standard deviation)				
Baseline	92.2 (± 15.5)	95.1 (± 14.5)		
3 Months (11-13 weeks)	89.7 (± 19.3)	88.9 (± 16.2)		
15 months (59-62 weeks)	91.4 (± 18.4)	89.4 (± 18.8)		
24 Months (95-97 weeks)	89.4 (± 15.4)	91.8 (± 20.4)		

Notes:

[3] - At baseline n=67, T3 n= 25, T15 n=32 and T24 n=11

[4] - At baseline n=70, T3 n=28, T15 n=32 and T24 n=17

Statistical analyses

Statistical analysis title	FVC % predicted - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	137
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.008
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	3.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	6.69

Statistical analysis title	FVC % predicted - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0396
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	3.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	6.14

Statistical analysis title	FVC % predicted - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	137
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.216
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	2.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.52
upper limit	6.73

Statistical analysis title	FVC % predicted - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a continuous variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	137
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.009
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	3.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	6.21

Secondary: Lung function - FEF25-75% predicted

End point title	Lung function - FEF25-75% predicted

End point description:

End point type	Secondary

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[5]	53[6]		
Units: FEF25-75% predicted				
arithmetic mean (standard deviation)				
Baseline	72.7 (± 26.6)	70.6 (± 30.3)		
3 Months (11-13 weeks)	84.0 (± 23.5)	70.6 (± 25.1)		
15 Months (59-62 weeks)	77.2 (± 28.0)	68.1 (± 21.5)		
24 Months (95-97 weeks)	58.3 (± 23.1)	58.9 (± 13.3)		

Notes:

[5] - At baseline n=44, T3 n=18, T15 n=26 and T24 n=7

[6] - At baseline n=53, T3 n=20, T15 n=21 and T24 n=12

Statistical analyses

Statistical analysis title	FEV25-75% predicted - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	97
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.274
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	3.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.99
upper limit	10.52

Statistical analysis title	FEV25-75% predicted - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived

from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.345
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	3.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.74
upper limit	10.66

Statistical analysis title	FEV25-75% predicted - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	97
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.505
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	3.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.29
upper limit	12.76

Statistical analysis title	FEV25-75% predicted - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a continuous variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	97
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.269
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	3.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.82
upper limit	10.11

Secondary: Oxygen saturation

End point title	Oxygen saturation

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118[7]	133[8]		
Units: Percentage				
arithmetic mean (standard deviation)				
baseline	97.7 (± 1.4)	97.7 (± 1.7)		
3 months (11-13 weeks)	97.6 (± 1.5)	98.2 (± 1.6)		
15 months (59-62 weeks)	97.8 (± 1.5)	97.9 (± 1.4)		
24 months (95-97 weeks)	97.9 (± 1.1)	97.6 (± 1.8)		

Notes:

[7] - At baseline n=118, T3 n= 42 , t15 n=48 and T24 n=17

[8] - At baseline n=133, T3 n=53, T15 n=46 and T24 n=26

Statistical analyses

Statistical analysis title	O2 Saturation - 3 month treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	251
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.728
Method	Mixed models analysis
Parameter estimate	3 Month Treatment difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.3

Statistical analysis title	O2 Saturation - 15 month treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.709
Method	Mixed models analysis
Parameter estimate	15 Month Treatment difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.29

Statistical analysis title	O2 Saturation - Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a continuous variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	251
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.686
Method	Mixed models analysis
Parameter estimate	Treatment difference
Point estimate	0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.27

Statistical analysis title	O2 Saturation - 24 Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	251
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.79
Method	Mixed models analysis
Parameter estimate	24 month Treatment difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.4

Secondary: Growth and nutritional status - Height z-scores

End point title	Growth and nutritional status - Height z-scores

End point description:

End point type	Secondary

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[9]	131[10]		
Units: Height z-scores				
arithmetic mean (standard deviation)				
Baseline	-0.4 (± 1.0)	-0.4 (± 1.0)		
3 Months (11-13 weeks)	-0.2 (± 1.0)	-0.2 (± 1.0)		
15 Months (59-62 weeks)	-0.2 (± 1.0)	-0.1 (± 0.9)		
24 Months (95-97 weeks)	-0.5 (± 0.8)	-0.7 (± 0.6)		

Notes:

[9] - At baseline n=125, T3 n=32, T15 n=36 and T24 n=13

[10] - At baseline n=131, T3 n=47, T15 n=32 and T24 n=16

Statistical analyses

Statistical analysis title	Height z-scores - 3 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures will be fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	256
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.952
Method	Mixed models analysis
Parameter estimate	3 Month treatment difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.05

Statistical analysis title	Height z-scores - 15 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.572
Method	Mixed models analysis
Parameter estimate	15 Month treatment difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.07

Statistical analysis title	Height z-scores - 24 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	256
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.543
Method	Mixed models analysis
Parameter estimate	24 Month treatment difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.11

Statistical analysis title	Height z-scores - Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a continuous variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	256
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.939
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.05

Secondary: Growth and nutritional status - Weight z-scores

End point title	Growth and nutritional status - Weight z-scores

End point description:

End point type	Secondary

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102[11]	109[12]		
Units: Weight z-scores				
arithmetic mean (standard deviation)				
Baseline	0.0 (± 1.1)	0.0 (± 0.9)		
3 Months (11-13 weeks)	0.2 (± 1.2)	0.2 (± 0.9)		
15 Months (59-62 weeks)	0.1 (± 1.1)	0.3 (± 0.8)		
24 Months (95-97 weeks)	0.1 (± 0.7)	-0.4 (± 0.8)		

Notes:

[11] - At baseline n=102, T3 n=30, T15 n=27, T24 n=12

[12] - At baseline n=109, T3 n=37, T15 n=23, T24 n=11

Statistical analyses

Statistical analysis title	Weight z-scores - 3 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	211
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.988
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.06

Statistical analysis title	Weight z-scores - 15 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived

from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.794
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.11

Statistical analysis title	Weight z-scores - 24 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	211
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.78
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.18

Statistical analysis title	Weight z-scores - Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a continuous variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	211
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.987
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.06

Secondary: Growth and nutritional status - BMI z-scores

End point title	Growth and nutritional status - BMI z-scores

End point description:

End point type	Secondary

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[13]	131[14]		
Units: BMI z-scores				
arithmetic mean (standard deviation)				
Baseline	0.3 (± 1.0)	0.3 (± 0.9)		
3 Months (11-13 weeks)	0.3 (± 1.0)	0.2 (± 1.0)		
15 Months (59-62 weeks)	0.4 (± 1.1)	0.2 (± 1.1)		
24 Months (95-97 weeks)	0.5 (± 0.7)	0.0 (± 0.8)		

Notes:

[13] - At baseline n=125, T3 n=32, T15 n=36 and T24 n=13

[14] - At baseline n=131, T3 n=47, T15 n=32 and T24 n=16

Statistical analyses

Statistical analysis title	BMI z-score - 3 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	256
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.767
Method	Mixed models analysis
Parameter estimate	3 Month Treatment Difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.06

Statistical analysis title	BMI z-score - 15 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.912
Method	Mixed models analysis
Parameter estimate	15 Month Treatment Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.16

Statistical analysis title	BMI z-score - 24 Month Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	256
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.854
Method	Mixed models analysis
Parameter estimate	24 Month Treatment Difference
Point estimate	0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.26

Statistical analysis title	BMI z-score - Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a continuous variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	256
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.774
Method	Mixed models analysis
Parameter estimate	Treatment Difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.06

Secondary: Growth and nutritional status - BMI

End point title	Growth and nutritional status - BMI

End point description:

End point type	Secondary

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[15]	10[16]		
Units: m/kg^2				
arithmetic mean (standard deviation)				
Baseline	24.2 (± 1.9)	22.9 (± 2.4)		
3 Months (11-13 weeks)	23.1 (± 2.7)	21.0 (± 0.6)		
15 Months (59-62 weeks)	26.4 (± 1.4)	22.2 (± 1.4)		
24 Months (95-97 weeks)	25.2 (± 1.1)	22.8 (± 2.8)		

Notes:

[15] - At baseline n=7, T3 n=2, T15 n=2 and T24 n=2

[16] - At baseline n=10, T3 n=2, T15 n=3 and T24 n=3

Statistical analyses

Statistical analysis title	BMI - 3 Month Treat Diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	17
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.067
Method	Mixed models analysis
Parameter estimate	3 Month Treatment Difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.03

Statistical analysis title	BMI - 15 Month Treat Diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	Mixed models analysis
Parameter estimate	15 Month Treatment Difference
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	-0.08

Statistical analysis title	BMI - Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a continuous variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	17
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.02
Method	Mixed models analysis
Parameter estimate	Treatment Difference
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	-0.09

Statistical analysis title	BMI - 24 Month Treat Diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a continuous variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	17
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.093
Method	Mixed models analysis
Parameter estimate	24 Month Treatment Difference
Point estimate	-0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.01
upper limit	0.16

Secondary: Number of pulmonary exacerbations - median number of exacerbations during the 15 months following treatment commencement

End point title	Number of pulmonary exacerbations - median number of

	exacerbations during the 15 months following treatment commencement

End point description:

End point type	Secondary

End point timeframe:

From baseline to 15 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	146		
Units: Number of pulmonary exacerbations				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 1)		

Statistical analyses

Statistical analysis title	Mann–Whitney U test

Statistical analysis description:

A Mann-Whitney U-test will test whether the distribution of number of exacerbations is the same in each treatment arm

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.09
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of pulmonary exacerbations - Number of participants experiencing at least one exacerbation during the first 15 months of follow up

End point title	Number of pulmonary exacerbations - Number of participants experiencing at least one exacerbation during the first 15 months of follow up

End point description:

End point type	Secondary

End point timeframe:

From baseline to 15 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	146		
Units: Subjects				
0 exacerbations	99	94		
>=1 exacerbations	38	52		

Statistical analyses

Statistical analysis title	Chi-squared test

Statistical analysis description:

The number and percentage of patients experiencing at least one exacerbation in each treatment arm was reported. Treatment groups were compared using the chi-squared test.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.155
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.1

Secondary: Admission to hospital - Number of participants experiencing at least one hospital stay during the first 3 months of treatment

End point title	Admission to hospital - Number of participants experiencing at least one hospital stay during the first 3 months of treatment

End point description:

End point type	Secondary

End point timeframe:

First 3 months of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	143		
Units: Subjects				
0 Hospital Stays	110	128		
>=1 Hospital Stay	25	15		

Statistical analyses

Statistical analysis title	Admission to hospital - 3 months of treatment
Statistical analysis description: Number of participants experiencing at least one hospital stay during the first 3 months of treatment	
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.057
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	3.2

Secondary: Admission to hospital - Number of participants experiencing at least one hospital stay during the 12 months following treatment

End point title	Admission to hospital - Number of participants experiencing at least one hospital stay during the 12 months following treatment
End point description:	
End point type	Secondary
End point timeframe: 12 months following treatment.	

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	136		
Units: Subjects				
0 Hospital Stays	89	75		
>=1 Hospital Stay	40	61		

Statistical analyses

Statistical analysis title	Admission to hospital - 12 months
Statistical analysis description:	
Number of participants experiencing at least one hospital stay during the 12 months following treatment.	
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.95

Secondary: Admission to hospital - Number of participants experiencing at least one hospital stay between 15 and 24 months

End point title	Admission to hospital - Number of participants experiencing at least one hospital stay between 15 and 24 months
End point description:	
Number of participants experiencing at least one hospital stay between 15 months and 24 months.	
End point type	Secondary
End point timeframe:	
Between 15 months and 24 months.	

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	107		
Units: Subjects				
0 Hospital Stays	72	66		
>=1 Hospital Stay	33	41		

Statistical analyses

Statistical analysis title	Admission to hospital - 15-24 months
Statistical analysis description:	
Number of participants experiencing at least one hospital stay between 15 months and 24 months	
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.293
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.19

Secondary: Number of days spent as an inpatient in hospital - During treatment phase

End point title	Number of days spent as an inpatient in hospital - During treatment phase
End point description:	
End point type	Secondary
End point timeframe:	
From baseline to 3 months.	

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	143		
Units: Days				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Length of stay in days during the treatment phase
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.066
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of days spent as an inpatient in hospital - During the 12 months post treatment phase

End point title	Number of days spent as an inpatient in hospital - During the 12 months post treatment phase

End point description:

End point type	Secondary

End point timeframe:

12 months post treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	136		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 3)	0 (0 to 13)		

Statistical analyses

Statistical analysis title	Length of stay during 12 months post treatment

Statistical analysis description:

Length of stay in days during the 12 months post treatment phase.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of days spent as an inpatient in hospital - between 15 and 24 months follow up

End point title	Number of days spent as an inpatient in hospital - between 15 and 24 months follow up

End point description:

End point type	Secondary

End point timeframe:

Between 15 and 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	102		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 2.8)	0 (0 to 4)		

Statistical analyses

Statistical analysis title	Length of stay 15-24 months
Statistical analysis description:	
Length of stay in days, between 15 and 24 months follow up.	
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.261
Method	Wilcoxon (Mann-Whitney)

Secondary: CFQ - Physical functioning – Self Report

End point title	CFQ - Physical functioning – Self Report
End point description:	
End point type	Secondary
End point timeframe:	
Basline to 24 months	

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53[17]	61[18]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	80.70 (± 19.8)	81 (± 17.4)		
3 months (11-13 weeks)	85.5 (± 15.1)	78.1 (± 20)		
15 months (59-62 weeks)	83 (± 18)	85.5 (± 14.7)		
24 months (95-97 weeks)	84.2 (± 14.6)	86.2 (± 16.7)		

Notes:

[17] - The number of patients at base line was 53, 49 at 3 months, 50 at 15 months and 44 at 24 months.
[18] - The number of patients at baseline was 61, 56 at 3 months, 50 at 15 months and 45 at 24 months

Statistical analyses

Statistical analysis title	Physical functioning (Self-report) - 3 Month Diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups at T3 (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.056
Method	Mixed models analysis
Parameter estimate	Mean difference at 3 months
Point estimate	6.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	13.44

Statistical analysis title	Physical functioning (Self-report) - 15 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups at T15 (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.292
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	-3.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.41
upper limit	3.16

Statistical analysis title	Physical functioning (Self-report) - 24 Month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups at T24 (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.793
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.15
upper limit	8.03

Statistical analysis title	Physical functioning (Self-report) - Treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable . The following was reported: mean (SD) for each treatment group; mean (95% CI) and difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.538
Method	Mixed models analysis
Parameter estimate	Treatment Difference
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.57
upper limit	6.8

Secondary: CFQ - Role/school functioning – Self Report

End point title	CFQ - Role/school functioning – Self Report

End point description:

End point type	Secondary

End point timeframe:

baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[19]	18[20]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	83.33 (± 19.06)	91.20 (± 10.87)		
3 months (11-13 weeks)	87.82 (± 15.82)	85.12 (± 21.73)		
15 months (59-62 weeks)	96.21 (± 8.63)	88.33 (± 11.70)		
24 months (95-97 weeks)	94.44 (± 8.94)	93.06 (± 9.29)		

Notes:

[19] - At baseline n=14, at T3 n=13, at T15 n=11 and at T24 n=12

[20] - At baseline n=18, T3 n= 14, T15 n=15 and T24 n=12

Statistical analyses

Statistical analysis title	Role/school functioning (Self-report)-3 Month diff

Statistical analysis description:

A mixed-effects model for repeated measures will be fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.181
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	8.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.42
upper limit	22.26

Statistical analysis title	Role/school functioning (Self-report)15 treat diff

Statistical analysis description:

A mixed-effects model for repeated measures will be fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.267
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	7.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.21
upper limit	21.52

Statistical analysis title	Role/school functioning (Self-report)24 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.328
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	6.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.39
upper limit	21.33

Statistical analysis title	Role/school functioning (Self-report) -treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.204
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	8.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	20.89

Secondary: CFQ - Vitality – Self Report

End point title	CFQ - Vitality – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[21]	18[22]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	50.60 (± 24.56)	63.89 (± 20.21)		
3 Months (11-13 weeks)	68.59 (± 17.06)	64.88 (± 21.48)		
15 Months (59-62 weeks)	74.24 (± 17.26)	66.67 (± 18.90)		
24 Months (95-97 weeks)	72.92 (± 18.84)	73.61 (± 16.60)		

Notes:

[21] - At baseline n=14, T3 n=13, T15 n=11 and T24 n=12

[22] - At baseline n=18, T3 n=14, T15 n=15 and T24 n=12

Statistical analyses

Statistical analysis title	Vitality (Self Report) - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.182
Method	Mixed models analysis
Parameter estimate	3 Month Treatment Difference
Point estimate	9.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.56
upper limit	22.69

Statistical analysis title	Vitality (Self Report) - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.373
Method	Mixed models analysis
Parameter estimate	15 Month Treatment Difference
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.88
upper limit	17.69

Statistical analysis title	Vitality (Self Report) - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.132
Method	Mixed models analysis
Parameter estimate	24 Month Treatment Difference
Point estimate	10.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.27
upper limit	23.41

Statistical analysis title	Vitality (Self Report) - Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.191
Method	Mixed models analysis
Parameter estimate	Treatment Difference
Point estimate	6.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.67
upper limit	17.45

Secondary: CFQ - Emotional functioning – Self Report

End point title	CFQ - Emotional functioning – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53[23]	61[24]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	78.8 (± 16.5)	76.7 (± 14.5)		
3 Months (11-13 weeks)	78.1 (± 15.1)	77.1 (± 14.8)		
15 Months (59-62 weeks)	80.8 (± 14.3)	79 (± 13.6)		
24 Months (95-97 weeks)	80.3 (± 14.1)	78.1 (± 13.5)		

Notes:

[23] - At baseline n=53, T3 n=49, T15 n=50 and T24 n=44

[24] - At baseline n=56, T3 n=49, T15 n=50 and T24 n=45

Statistical analyses

Statistical analysis title	Emotional functioning (Self-report) - 3 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.977
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.06
upper limit	4.91

Statistical analysis title	Emotional functioning (Self-report) -15 month diff

Statistical analysis description:

A mixed-effects model for repeated measure was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.589
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	-1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.39
upper limit	4.22

Statistical analysis title	Emotional functioning (Self-report) -24 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.964
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.19
upper limit	5.91

Statistical analysis title	Emotional functioning (Self-report) - Treat Diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.807
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.78
upper limit	3.73

Secondary: CFQ - Social functioning – Self Report

End point title	CFQ - Social functioning – Self Report

End point description:

End point type	Secondary

End point timeframe:

baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53[25]	61[26]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	73 (± 17.6)	73.7 (± 15.3)		
3 Months (11-13 weeks)	75.5 (± 16.5)	72.2 (± 16.3)		
15 Months (59-62 weeks)	74.4 (± 18.1)	73.8 (± 15.5)		
24 Weeks (95-97 weeks)	77.8 (± 13.9)	73 (± 15.8)		

Notes:

[25] - At baseline n=53, T3 n=49, T15 n=49 and T24 n=44

[26] - At baseline n=61, T3 n=56 , T15 n=50 and T24 n=45

Statistical analyses

Statistical analysis title	Social functioning (Self-report) - 3 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.311
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	2.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.82
upper limit	8.78

Statistical analysis title	Social functioning (Self-report) - 15 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.498
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	2.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.03
upper limit	8.25

Statistical analysis title	Social functioning (Self-report) - 24 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.159
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	4.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.72
upper limit	10.34

Statistical analysis title	Social functioning (Self-report) - Treatment Diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. . The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.138
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	3.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	7.36

Secondary: CFQ - Body Image – Self Report

End point title	CFQ - Body Image – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52[27]	61[28]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	90.4 (± 16.8)	86.3 (± 17.6)		
3 Months (11-13 weeks)	90 (± 16.2)	86.4 (± 16.4)		
15 Months (59-62 weeks)	88.2 (± 20)	86.4 (± 17.7)		
24 Months (95-97 weeks)	90.4 (± 12)	88.4 (± 18.3)		

Notes:

[27] - At baseline n=52, T3 n= 49, T15 n=50 and T24 n=43

[28] - At baseline n=61, T3 n=56, T15 n=50 and T24 n=45

Statistical analyses

Statistical analysis title	Body image (Self-report) - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	113
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.443
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	2.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.51
upper limit	7.97

Statistical analysis title	Body image (Self-report) - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.309
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	-4.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.78
upper limit	3.77

Statistical analysis title	Body image (Self-report) - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	113
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.986
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.58
upper limit	7.45

Statistical analysis title	Body image (Self-report) - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable.The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	113
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.931
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.43
upper limit	4.48

Secondary: CFQ - Eating Problems – Self Report

End point title	CFQ - Eating Problems – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53[29]	61[30]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	91 (± 16.5)	84.9 (± 19.7)		
3 Months (11-13 weeks)	86.5 (± 18.8)	82.1 (± 20.5)		
15 Months (59-62 weeks)	88.3 (± 17.4)	86.4 (± 17.3)		
24 Months (95-97 weeks)	92.6 (± 13.6)	87.4 (± 15.6)		

Notes:

[29] - At baseline n=53, T3 n=49, T15 n=50 and T24 n=44

[30] - At baseline n=61, T3 n=56, T15 n=50 and T24 n=45

Statistical analyses

Statistical analysis title	Eating problems (Self-report) - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.453
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	2.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.12
upper limit	9.16

Statistical analysis title	Eating problems (Self-report) - 15 month treat dif

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.903
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.78
upper limit	6

Statistical analysis title	Eating problems (Self-report) -24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.31
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	3.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.47
upper limit	10.81

Statistical analysis title	Eating problems (Self-report) -treatment diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.506
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	1.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.27
upper limit	6.58

Secondary: CFQ - Treatment Burden – Self Report

End point title	CFQ - Treatment Burden – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52[31]	61[32]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	77.4 (± 21.7)	74.1 (± 18.5)		
3 Months (11-13 weeks)	71.9 (± 25.4)	70.7 (± 21.9)		
15 Months (59-62 weeks)	76.4 (± 18.7)	71.1 (± 20.5)		
24 Months (95-97 weeks)	77.3 (± 20.3)	74.8 (± 20.3)		

Notes:

[31] - At baseline n=52, T3 n=49, T15 n=50 and T24 n=43

[32] - At baseline n=61, T3 n=56, T15 n=50 and T24 n=45

Statistical analyses

Statistical analysis title	Treatment burden (Self-report) -3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	113
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.244
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	4.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.42
upper limit	13.27

Statistical analysis title	Treatment burden (Self-report)-15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.532
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	2.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.19
upper limit	11.92

Statistical analysis title	Treatment burden (Self-report)-24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	113
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.343
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	4.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.07
upper limit	14.43

Statistical analysis title	Treatment burden (Self-report)- Treatment diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	113
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.167
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	4.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	10.27

Secondary: CFQ - Health Perceptions – Self Report

End point title	CFQ - Health Perceptions – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[33]	18[34]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	65.87 (± 27.38)	70.99 (± 16.23)		
3 Months (11-13 weeks)	78.21 (± 20.84)	67.46 (± 27.38)		
15 Months (59-62 weeks)	80.81 (± 19.30)	71.11 (± 25.13)		
24 Weeks (95-97 weeks)	72.22 (± 24.39)	69.44 (± 20.17)		

Notes:

[33] - At baseline n=14, T3 n=13, T15 n=11 and T24 n=12

[34] - At baseline n=18, T3 n=14, T15 n= 15 and T24 n=12

Statistical analyses

Statistical analysis title	Health perceptions (Self-report)-3 month treat dif

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.045
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	18.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	36.42

Statistical analysis title	Health perceptions (Self-report)-15 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.583
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	5.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.72
upper limit	23.84

Statistical analysis title	Health perceptions (Self-report)-24 month diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.544
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	6.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.89
upper limit	27.54

Statistical analysis title	Health perceptions (Self-report)-treatment diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.13
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	12.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.96
upper limit	28.88

Secondary: CFQ - Weight – Self Report

End point title	CFQ - Weight – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[35]	17[36]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	85.71 (± 25.2)	78.43 (± 35.24)		
3 Months (11-13 weeks)	94.44 (± 19.25)	92.86 (± 19.30)		
15 Months (59-62 weeks)	93.94 (± 13.48)	84.44 (± 21.33)		
24 Months (95-97 weeks)	88.89 (± 25.95)	80.56 (± 26.43)		

Notes:

[35] - At baseline n=14, T3 n= 12, T15 n=11 and T24 n=12

[36] - At baseline n=17, T3 n=14 , T15 n=15, T24 n=12

Statistical analyses

Statistical analysis title	Weight (self report) - 3 Month treatment diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Oral antibiotic therapy v Intravenous (IV) antibiotics

Number of subjects included in analysis	31
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.725
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	2.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.06
upper limit	17.08

Statistical analysis title	Weight (self report) - 15 Month treatment diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.888
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.02
upper limit	21.83

Statistical analysis title	Weight (self report) - 24 Month treatment diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	31
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.842
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	2.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.8
upper limit	30.17

Statistical analysis title	Weight (self report) - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	31
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.603
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.29
upper limit	12.29

Secondary: CFQ - Respiratory Symptoms – Self Report

End point title	CFQ - Respiratory Symptoms – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 Months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53[37]	61[38]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	67.0 (± 20.2)	70.5 (± 18.5)		
3 Months (11-13 weeks)	76.8 (± 19.8)	77 (± 15.9)		
15 Months (59-62 weeks)	80.4 (± 15.7)	78.4 (± 16)		
24 Months (95-97 weeks)	83.2 (± 13.4)	82.3 (± 13.4)		

Notes:

[37] - At baseline n=53, T3 n=48, T15 n=49 and T24 n=44

[38] - At baseline n=61, at T3 n=48 , at T15 n=50 and T24 n=44

Statistical analyses

Statistical analysis title	Resp Symp Self Report - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.606
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.06
upper limit	8.64

Statistical analysis title	Resp Symp Self Report -15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.374
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	2.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.44
upper limit	9.08

Statistical analysis title	Resp Symp Self Report -24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.53
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	2.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.47
upper limit	8.64

Statistical analysis title	Resp Symp Self Report -treat diff

Statistical analysis description:

A mixed-effects model for repeated measures wsa fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.344
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.47
upper limit	7.01

Secondary: CFQ - Digestive Symptoms – Self Report

End point title	CFQ - Digestive Symptoms – Self Report

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 Months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53[39]	61[40]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	78.4 (± 25.3)	74.5 (± 22.3)		
3 Months (11-13 weeks)	75.7 (± 29.1)	74.2 (± 24.8)		
15 Months (59-62 weeks)	80.1 (± 24.1)	80.2 (± 22.3)		
24 Months (95-97 weeks)	78.6 (± 23.3)	83.2 (± 17.2)		

Notes:

[39] - At baseline n=53, T3 n=47, T15 n=48 and T24 n=42

[40] - At baseline n=61, T3 n=56, T15 n=50 and T24 n=45

Statistical analyses

Statistical analysis title	Digestive (Self report) - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.551
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	2.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.3
upper limit	11.75

Statistical analysis title	Digestive (Self report) -15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived

from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.998
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.95
upper limit	9.93

Statistical analysis title	Digestive (Self report) - treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.987
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.23
upper limit	6.33

Statistical analysis title	Digestive (Self report) - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	114
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.581
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	-2.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.44
upper limit	6.45

Secondary: CFQ - Physical functioning – Parent/Carer

End point title	CFQ - Physical functioning – Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 Months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[41]	42[42]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	82.9 (± 18.3)	85.9 (± 14.3)		
3 Months (11-13 weeks)	90.1 (± 10.5)	84 (± 15.1)		
15 Months (59-62 weeks)	82.2 (± 20.9)	86.8 (± 15.6)		
24 Months (95-97 weeks)	82.8 (± 22)	89.2 (± 14.4)		

Notes:

[41] - At baseline n=37, T3 n=38 , T15 n= 42, T24 n=32

[42] - At baseline n=42, T3 n=39, T15 n=32 and T24 n=33

Statistical analyses

Statistical analysis title	Phys Fn - Parent/Carer - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.033
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	6.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	11.85

Statistical analysis title	Phys Fn - Parent/Carer - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.223
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	-5.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.55
upper limit	3.22

Statistical analysis title	Phys Fn - Parent/Carer - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.342
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	-4.63

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.29
upper limit	5.03

Statistical analysis title	Phys Fn - Parent/Carer - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.191
Method	Mixed models analysis
Parameter estimate	treat difference
Point estimate	3.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	9.09

Secondary: CFQ - Role/school functioning – Parent/Carer

End point title	CFQ - Role/school functioning – Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[43]	42[44]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	70.1 (± 27.1)	66.3 (± 21.4)		
3 Months (11-13 weeks)	73 (± 25.1)	66.7 (± 21)		
15 Months (59-62 weeks)	67.1 (± 29.3)	69.8 (± 22.3)		
24 Months (95-97 weeks)	72.2 (± 25.9)	78.1 (± 21.4)		

Notes:

[43] - At baseline n= 36, T3 =37, T15 n=42 and T24 n=32

[44] - At baseline n=42, T3 n=39, T15 n=32 and T24 n=33

Statistical analyses

Statistical analysis title	Role/School - P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.238
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	5.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.69
upper limit	14.64

Statistical analysis title	Role/School - P/C - treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.845
Method	Mixed models analysis
Parameter estimate	treat diff
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.49
upper limit	6.15

Statistical analysis title	Role/School - P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.738
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	-1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.22
upper limit	7.28

Statistical analysis title	Role/School - P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.318
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	-5.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.09
upper limit	4.97

Secondary: CFQ - Vitality– Parent/Carer

End point title	CFQ - Vitality– Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[45]	41[46]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	63.9 (± 17.4)	67 (± 16.8)		
3 Months (11-13 weeks)	67.1 (± 13.8)	62.2 (± 15.8)		
15 Months (59-62 weeks)	65.4 (± 18.1)	66.7 (± 18.4)		
24 Months (95-97 weeks)	66.5 (± 17.1)	68.3 (± 14.8)		

Notes:

[45] - At baseline n=37, T3 n=38, T15 n=42 and T24 n=31

[46] - At baseline n=41, T3 n=39 , T15 n=32 and T24 n=33

Statistical analyses

Statistical analysis title	Vitality - P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.059
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	6.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	13.32

Statistical analysis title	Vitality - P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived

from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.923
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.36
upper limit	8.48

Statistical analysis title	Vitality - P/C - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable.The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.208
Method	Mixed models analysis
Parameter estimate	treat diff
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	9.5

Statistical analysis title	Vitality - P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.913
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.84
upper limit	10.98

Secondary: CFQ - Emotional functioning – Parent/Carer

End point title	CFQ - Emotional functioning – Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[47]	42[48]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	77.2 (± 16.6)	80.3 (± 17)		
3 Months (11-13 weeks)	80.7 (± 14.2)	75.9 (± 18.1)		
15 Months (59-62 weeks)	79.9 (± 15.4)	79.6 (± 15.8)		
24 Months (95-97 weeks)	83.1 (± 14.1)	88.1 (± 10.5)		

Notes:

[47] - At baseline n=36, T3 n=37, T15 n= 42, t24 n=32

[48] - At baseline n=42, T3 n=39, T15 n=32 adn T24 n=33

Statistical analyses

Statistical analysis title	Emotional - P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.069
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	5.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	12.4

Statistical analysis title	Emotional - P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.339
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	3.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.56
upper limit	10.2

Statistical analysis title	Emotional - P/C - treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.166
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	3.47

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.48
upper limit	8.41

Statistical analysis title	Emotional - P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.668
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	-1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.55
upper limit	6.16

Secondary: CFQ - Body Image – Parent/Carer

End point title	CFQ - Body Image – Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 Months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[49]	42[50]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	75.3 (± 21.4)	72.5 (± 24.3)		
3 Months (11-13 weeks)	78.2 (± 22.5)	72.9 (± 24.4)		
15 Months (59-62 weeks)	71.8 (± 28)	76 (± 22.9)		
24 months (95-97 weeks)	71.9 (± 25.6)	82.5 (± 23.7)		

Notes:
[49] - At baseline n=36, T3 n=36 , T15 n=42 and T24 n=32
[50] - At baseline n=42, T3 n=39, T15 n=32, and T24 n=33

Statistical analyses

Statistical analysis title	Body Image - P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Oral antibiotic therapy v Intravenous (IV) antibiotics
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.555
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	2.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.28
upper limit	11.59

Statistical analysis title	Body Image - P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.922
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	-0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.03
upper limit	10.9

Statistical analysis title	Body Image - P/C - treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.644
Method	Mixed models analysis
Parameter estimate	treat diff
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	10.28

Statistical analysis title	Body Image - P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.679
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.81
upper limit	14.97

Secondary: CFQ - Eating Problems– Parent/Carer

End point title	CFQ - Eating Problems– Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[51]	41[52]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	77 (± 29.7)	78.9 (± 25.3)		
3 Months (11-13 weeks)	78.9 (± 26.7)	72.6 (± 22.8)		
15 Months (59-62 weeks)	77.8 (± 27.9)	78.6 (± 22.5)		
24 Months (95-97 weeks)	78.1 (± 24.1)	82.3 (± 19.4)		

Notes:

[51] - Baseline n=37, T3 n=34 , T15 n=39 and T24 n=32

[52] - At baseline n=41, T3 n=39, T15 n=32 and T24 n=32

Statistical analyses

Statistical analysis title	Eating Problem P/C - 3 Month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.3
Method	Mixed models analysis
Parameter estimate	3 month treatment difference
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.19
upper limit	13.39

Statistical analysis title	Eating Problem P/C - 15 Month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived

from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.174
Method	Mixed models analysis
Parameter estimate	15 month treatment difference
Point estimate	6.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.78
upper limit	15.08

Statistical analysis title	Eating Problem P/C - 24 Month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.732
Method	Mixed models analysis
Parameter estimate	24 month treatment difference
Point estimate	-1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.18
upper limit	9.31

Statistical analysis title	Eating Problem P/C - Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable . The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.138
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	4.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	9.44

Secondary: CFQ - Treatment Burden – Parent/Carer

End point title	CFQ - Treatment Burden – Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[53]	42[54]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	57.8 (± 20.8)	55.4 (± 23.4)		
3 Months (11-13 weeks)	59.3 (± 24.3)	51.6 (± 23.8)		
15 Months (59-62 week)	57.7 (± 23.6)	54.2 (± 20.9)		
24 Months (95-97 weeks)	58.3 (± 22.9)	57.9 (± 21.8)		

Notes:

[53] - At baseline n=37, T3 n=37, T15 n=42, T24 n=32

[54] - At baseline n=42, T3 n=39, T15 n=32, T24 n=33

Statistical analyses

Statistical analysis title	Treatment Burden P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.718
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	1.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.94
upper limit	12.92

Statistical analysis title	Treatment Burden P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.96
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.25
upper limit	10.69

Statistical analysis title	Treatment Burden P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.966
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	0.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.12
upper limit	10.57

Statistical analysis title	Treatment Burden P/C - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.862
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.08
upper limit	8.44

Secondary: CFQ - Health Perceptions – Parent/Carer

End point title	CFQ - Health Perceptions – Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36[55]	42[56]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	71.6 (± 21)	70.1 (± 18.3)		
3 Months (11-13 weeks)	69.9 (± 20)	70.1 (± 18.4)		
15 Months (59-62 weeks)	67.9 (± 17.6)	74.7 (± 15.5)		
24 Months (95-97 weeks)	72.2 (± 23.1)	79.8 (± 17.7)		

Notes:

[55] - At baseline n=36, T3 n=36, T15 n=42, T24 n=32

[56] - At bseline n=42, T3 n=39, T15 n=32, T24 n=33

Statistical analyses

Statistical analysis title	Health Perceptions P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.988
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.37
upper limit	9.23

Statistical analysis title	Health Perceptions P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	-7.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.09
upper limit	0.6

Statistical analysis title	Health Perceptions P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.297
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	-6.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.6
upper limit	6.07

Statistical analysis title	Health Perceptions P/C - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.115
Method	Mixed models analysis
Parameter estimate	treat diff
Point estimate	-4.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.88
upper limit	1.1

Secondary: CFQ - Weight – Parent/Carer

End point title	CFQ - Weight – Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[57]	42[58]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	64 (± 31.8)	69.8 (± 32.8)		
3 Months (11-13 weeks)	70.3 (± 33.1)	62.2 (± 30.6)		
15 Months (59-62 weeks)	64.2 (± 35.3)	69.8 (± 30.9)		
24 Months (95-97 weeks)	64.6 (± 35.9)	69.7 (± 36.7)		

Notes:

[57] - At baseline n=37, T3 n=37, T15 n=41 and T24 n=32

[58] - At baseline n=42, T3 n=37, T15 n=32 and T24 n=33

Statistical analyses

Statistical analysis title	Weight - P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.294
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	7.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.78
upper limit	22.1

Statistical analysis title	Weight - P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived

from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.886
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	-1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.63
upper limit	15.26

Statistical analysis title	Weight - P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.492
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	7.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.27
upper limit	27.33

Statistical analysis title	Weight - P/C - treatment difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.247
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	6.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	17.25

Secondary: CFQ - Respiratory Symptoms– Parent/Carer

End point title	CFQ - Respiratory Symptoms– Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[59]	42[60]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	68.6 (± 20.9)	73.5 (± 21.9)		
3 Months (11-13 weeks)	82.1 (± 18.1)	79.1 (± 19.5)		
15 Months (59-62 weeks)	76.1 (± 18.2)	82.6 (± 14.9)		
24 Months (95-97 weeks)	78.3 (± 20.2)	82 (± 16.3)		

Notes:

[59] - At baseline n=37, T3 n=37, T15 n=41 and T24 n=32

[60] - At baseline n=42, T3 n=39, T15 n=32 and T24 n=33

Statistical analyses

Statistical analysis title	Resp Symp P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.39
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	4.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.36
upper limit	13.58

Statistical analysis title	Resp Symp P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.432
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	-3.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.71
upper limit	5.06

Statistical analysis title	Resp Symp P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.728
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	-2.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.15
upper limit	9.93

Statistical analysis title	Resp Symp P/C - treament difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Oral antibiotic therapy v Intravenous (IV) antibiotics
Number of subjects included in analysis	79
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.885
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.01
upper limit	6.06

Secondary: CFQ - Digestive symptoms – Parent/Carer

End point title	CFQ - Digestive symptoms – Parent/Carer

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[61]	41[62]		
Units: CFQ Score				
arithmetic mean (standard deviation)				
Baseline	70.9 (± 22.6)	74 (± 19.5)		
3 Months (11-13 weeks)	76.8 (± 20)	74.5 (± 13.2)		
15 months (59-62 weeks)	77.2 (± 18.7)	73.6 (± 20.5)		
24 Weeks (95-97 weeks)	76.4 (± 16.2)	79.5 (± 17.4)		

Notes:
[61] - At baseline n=37, T3 n=34 , T15 n=39 and T24 n=32
[62] - At baseline n=41, T3 n=39, T15 n=32 and T24 n=32

Statistical analyses

Statistical analysis title	Digestive - P/C - 3 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.474
Method	Mixed models analysis
Parameter estimate	3 month treat diff
Point estimate	2.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.71
upper limit	10.03

Statistical analysis title	Digestive - P/C - 15 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.405
Method	Mixed models analysis
Parameter estimate	15 month treat diff
Point estimate	3.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	11.98

Statistical analysis title	Digestive - P/C - 24 month treat diff

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group, time-point as a categorical variable and an interaction term (treatment group*time). The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.725
Method	Mixed models analysis
Parameter estimate	24 month treat diff
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.12
upper limit	11.62

Statistical analysis title	Digestive - P/C - Treatment Difference

Statistical analysis description:

A mixed-effects model for repeated measures was fitted, with an unstructured covariance matrix. The baseline measurement of the domain was fitted as a covariate along with treatment group and time-point as a categorical variable. The following was reported: mean (SD) for each treatment group; mean (95% CI) difference between treatment groups (derived from the model); and a p-value of the treatment effect

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.389
Method	Mixed models analysis
Parameter estimate	treatment difference
Point estimate	2.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	8.61

Secondary: Number of patients with at least one positive result of MRSA by 3 months

End point title	Number of patients with at least one positive result of MRSA by

	3 months

End point description:

No analysis was possible due to there being 0 events in the IV group.

End point type	Secondary

End point timeframe:

Baseline to three months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	145		
Units: Subjects				
0 Culture	136	144		
>= 1 culture	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with at least one positive result of Burkholderia cepacia complex (BC) by 3 months

End point title	Number of patients with at least one positive result of Burkholderia cepacia complex (BC) by 3 months

End point description:

No analysis was possible due to there being 0 events in the Oral group.

End point type	Secondary

End point timeframe:

Baseline to three months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	144		
Units: Subjects				
0 culture	135	144		
>=1 culture	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with at least one positive result of Candida by 3

months

End point title	Number of patients with at least one positive result of Candida by 3 months

End point description:

End point type	Secondary

End point timeframe:

Baseline to 3 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	146		
Units: Subjects				
0 culture	111	119		
>=1 culture	26	27		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result were presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared test (or if necessary Fisher's exact test) was used to test for a difference between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	283
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.917
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.67

Secondary: Number of patients with at least one positive result of Aspergillus by 3 months

End point title	Number of patients with at least one positive result of Aspergillus by 3 months

End point description:

End point type	Secondary

End point timeframe: Baseline to 3 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	144		
Units: Subjects				
0 culture	130	139		
>=1 culture	6	5		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk
Statistical analysis description: For each microorganism, the number and percentage with at least one positive result waspresented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared tests (or if necessary Fisher's exact test) was used to test for differences between treatment groups.	
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	280
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.686
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	4.07

Secondary: Number of patients with at least one positive result of MRSA by 15 months

End point title	Number of patients with at least one positive result of MRSA by 15 months
End point description:	
End point type	Secondary
End point timeframe: Baseline to 15 months	

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	140		
Units: Subjects				
0 culture	131	138		
>=1 culture	4	2		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result was presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared tests (or if necessary Fisher's exact test) was used to test for differences between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	275
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.441
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	2.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	11.14

Secondary: Number of patients with at least one positive result of Burkholderia cepacia complex (BC) by 15 months

End point title	Number of patients with at least one positive result of Burkholderia cepacia complex (BC) by 15 months

End point description:

End point type	Secondary

End point timeframe:

Baseline to 15 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	139		
Units: Subjects				
0 culture	133	135		
>= 1 culture	2	4		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result was presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared tests (or if necessary Fisher's exact test) was used to test for differences between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.684
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	2.76

Secondary: Number of patients with at least one positive result of Candida by 15 months

End point title	Number of patients with at least one positive result of Candida by 15 months

End point description:

End point type	Secondary

End point timeframe:

Baseline to 15 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	142		
Units: Subjects				
0 culture	81	87		
>=1 cultures	55	55		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result was presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared test (or if necessary Fisher's exact test) was used to test for a difference between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.771
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.4

Secondary: Number of patients with at least one positive result of Aspergillus by 15 months

End point title	Number of patients with at least one positive result of Aspergillus by 15 months

End point description:

End point type	Secondary

End point timeframe:

baseline to 15 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	139		
Units: Subjects				
0 culture	121	119		
>=1 cultures	14	20		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result will be presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared test (or if necessary Fisher's exact test) will be used to test for a difference between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.313
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.37

Secondary: Number of patients with at least one positive result of MRSA by 24 months

End point title	Number of patients with at least one positive result of MRSA by 24 months

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	133		
Units: Subjects				
0 culture	130	129		
>=1 cultures	2	4		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result was presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared test (or if necessary Fisher’s exact test) was used to test for a difference between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.684
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	2.7

Secondary: Number of patients with at least one positive result of Burkholderia cepacia complex (BC) by 24 months

End point title	Number of patients with at least one positive result of Burkholderia cepacia complex (BC) by 24 months

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	133		
Units: Subjects				
0 culture	130	129		
>=1 cultures	2	4		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result was presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared test (or if necessary Fisher’s exact test) was used to test for a difference between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.684
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	2.7

Secondary: Number of patients with at least one positive result of Candida by 24 months

End point title	Number of patients with at least one positive result of Candida by 24 months

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Subjects				
0 culture	76	81		
>=1 culture	59	56		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result was presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared test (or if necessary Fisher’s exact test) was used to test for a difference between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.637
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.41

Secondary: Number of patients with at least one positive result of Aspergillus by 24 months

End point title	Number of patients with at least one positive result of Aspergillus by 24 months

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	134		
Units: Subjects				
0 culture	114	111		
>=1 cultures	20	23		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

For each microorganism, the number and percentage with at least one positive result was presented split by treatment arm, and a relative risk and 95% confidence interval calculated. Chi-squared test (or if necessary Fisher’s exact test) was used to test for a difference between treatment groups.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.618
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.51

Secondary: Carer Burden - Median number of days absence during the 15 months following randomisation

End point title	Carer Burden - Median number of days absence during the 15 months following randomisation

End point description:

End point type	Secondary

End point timeframe:

Randomisation until 15 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	139		
Units: Days				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 1)		

Statistical analyses

Statistical analysis title	Secondary Outcome - Median

Statistical analysis description:

The number of days spent absent from work or education was presented as a median with 95% confidence interval for each treatment arm, together with the interquartile range, min and max. A Mann Whitney test was used to detect differences in the distributions of carer burden between the two treatment groups

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.616 [63]
Method	Wilcoxon (Mann-Whitney)

Notes:

[63] - The median and 95% Confidence Interval for each group was 0 (0,0). The minimum and maximum for the IV and oral group resepectively were 0 and 24 and 0 and 98.

Secondary: Carer Burden - Number of carers experiencing at least one episode of absence during the first 15 months of follow up

End point title	Carer Burden - Number of carers experiencing at least one episode of absence during the first 15 months of follow up

End point description:

End point type	Secondary

End point timeframe:

Baseline to 15 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	139		
Units: Subjects				
0 absence	87	90		
>=1 absence	44	49		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

Whether carers have been absent from education or work or not during the first 15 months post randomisation, was analysed using a relative risk, presented with a 95% confidence interval and a chi squared test.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.774
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.22

Secondary: Participant burden - Median number of days absence during the 15 months following treatment randomisation

End point title	Participant burden - Median number of days absence during the

	15 months following treatment randomisation

End point description:

End point type	Secondary

End point timeframe:

Baseline to 15 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	140		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 6.2)	0 (0 to 10)		

Statistical analyses

Statistical analysis title	Secondary Outcome - Median

Statistical analysis description:

The number of days spent absent from work or education will be presented as a median with 95% confidence interval for each treatment arm, together with the interquartile range, min and max. A Mann Whitney test was used to detect differences in the distributions of carer burden between the two treatment groups

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.263 [64]
Method	Wilcoxon (Mann-Whitney)

Notes:

[64] - The median and 95% CI for the IV group was 0 (0,2) and for the oral group was 1 (0,3). The minimum and maximum for the IV group was 0 and 56 and was 0 and 113 for the oral group.

Secondary: Participant burden - Number of participants experiencing at least one episode of absence during the first 15 months of follow up

End point title	Participant burden - Number of participants experiencing at least one episode of absence during the first 15 months of follow up

End point description:

End point type	Secondary

End point timeframe:

baseline to 15 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	140		
Units: Subjects				
0 absence	66	64		
>=1 absence	65	76		

Statistical analyses

Statistical analysis title	Secondary Outcome - Relative Risk

Statistical analysis description:

Whether participants have been absent from education or work or not during the first 15 months post randomisation, was analysed using a relative risk, presented with a 95% confidence interval and a chi squared test.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.442
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.41

Secondary: Number of days spent as an inpatient in hospital during treatment phase - Sensitivity Analysis 1

End point title	Number of days spent as an inpatient in hospital during treatment phase - Sensitivity Analysis 1

End point description:

End point type	Secondary

End point timeframe:

treatment phase

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	143		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Sens 1 - Length of stay - tmt phase

Statistical analysis description:

The number of patients with hospital stays and their median, interquartile range and minimum and maximum total length of stay was calculated for each treatment arm and each time-period. A Mann-Whitney test was be used to detect differences between treatment groups for each time-period of interest.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of days spent as an inpatient in hospital during 12 months post treatment- Sensitivity Analysis 1

End point title	Number of days spent as an inpatient in hospital during 12 months post treatment- Sensitivity Analysis 1

End point description:

End point type	Secondary

End point timeframe:

12 month post treatment phase

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	136		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 2)	0 (0 to 12.5)		

Statistical analyses

Statistical analysis title	Sens 1 - Length of stay - 12 months post treat

Statistical analysis description:

The number of patients with hospital stays and their median, interquartile range and minimum and maximum total length of stay was calculated for each treatment arm and each time-period. A Mann-

Whitney test was used to detect differences between treatment groups for each time-period of interest.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of days spent as an inpatient in hospital between 15 and 24 months - Sensitivity Analysis 1

End point title	Number of days spent as an inpatient in hospital between 15 and 24 months - Sensitivity Analysis 1

End point description:

End point type	Secondary

End point timeframe:

between 15 and 24 months follow up

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	101		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 3)		

Statistical analyses

Statistical analysis title	Sens 1 - Length of stay - 15-24mths

Statistical analysis description:

The number of patients with hospital stays and their median, interquartile range and minimum and maximum total length of stay was calculated for each treatment arm and each time-period. A Mann-Whitney test was used to detect differences between treatment groups for each time-period of interest.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.273
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of days spent as an inpatient in hospital during treatment phase

- Sensitivity Analysis 2

End point title	Number of days spent as an inpatient in hospital during treatment phase - Sensitivity Analysis 2

End point description:

End point type	Secondary

End point timeframe:

treatment phase

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	143		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Sens 2 - length of stay - tmt phase

Statistical analysis description:

The number of patients with hospital stays and their median, interquartile range and minimum and maximum total length of stay was calculated for each treatment arm and each time-period. A Mann-Whitney test was used to detect differences between treatment groups for each time-period of interest.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of days spent as an inpatient in hospital during 12 months post treatment- Sensitivity Analysis 2

End point title	Number of days spent as an inpatient in hospital during 12 months post treatment- Sensitivity Analysis 2

End point description:

End point type	Secondary

End point timeframe:

12 months post treatment phase

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	136		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 13)		

Statistical analyses

Statistical analysis title	Sens 2 - length of stay - 12 months post

Statistical analysis description:

The number of patients with hospital stays and their median, interquartile range and minimum and maximum total length of stay was calculated for each treatment arm and each time-period. A Mann-Whitney test was used to detect differences between treatment groups for each time-period of interest.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of days spent as an inpatient between 15 and 24 months- Sensitivity Analysis 2

End point title	Number of days spent as an inpatient between 15 and 24 months- Sensitivity Analysis 2

End point description:

End point type	Secondary

End point timeframe:

between 15 and 24 months follow up

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	102		
Units: days				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 3)		

Statistical analyses

Statistical analysis title	Sens 2 - Length of Stay - 15-24 months

Statistical analysis description:

The number of patients with hospital stays and their median, interquartile range and minimum and maximum total length of stay was calculated for each treatment arm and each time-period. A Mann-

Whitney test was used to detect differences between treatment groups for each time-period of interest.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.574
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of patients with at least one positive result of another organism during the study

End point title	Number of patients with at least one positive result of another organism during the study

End point description:

End point type	Secondary

End point timeframe:

Baseline to 24 months

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	148		
Units: Subjects				
Aeromonas	3	1		
Acinetobacter	15	7		
Achromobacter	2	4		
Chryseobacterium	2	2		
Coliform (genera other than those listed separatel	9	10		
Elizabethkingia	0	2		
Enterobacter	10	7		
Escherichia (specifically E. coli)	6	5		
Haemophilus	44	39		
Klebsiella	7	11		
Moraxella	9	5		
Mycobacterium	1	3		
Ochrobactrum	2	0		
Pantoea	2	0		
Pseudomonas (species other than P. aeruginosa)	10	10		
Serratia	5	3		
Staphylococcus	60	63		
Stenotrophomonas	7	10		
Streptococcus	15	20		
Unspecified/unidentified/commencals	11	7		
Other	9	2		
Fusarium	1	0		
Rhodotorula	0	1		

Scedosporium	0	2		
Yeasts (other than Candida)	19	13		
Adenovirus	1	2		
Enterovirus	3	3		
Influenza viruses	3	3		
Metapneumovirus	2	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Primary efficacy assessment – Sensitivity analysis 1: All patients followed up past 3 months but with no 15 month sample classified as successes

End point title	Primary efficacy assessment – Sensitivity analysis 1: All patients followed up past 3 months but with no 15 month sample classified as successes

End point description:

End point type	Other pre-specified

End point timeframe:

3 months after the start of treatment to 15 months after the start of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	144		
Units: Subjects				
Successful eradication	66	82		
Unsuccessful eradication	70	62		

Statistical analyses

Statistical analysis title	Sensitivity analysis 1
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	280
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.159
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.07

Other pre-specified: Primary efficacy assessment – Sensitivity analysis 2 – All patients followed up past 3 months but with no 15-month sample classified as failures

End point title	Primary efficacy assessment – Sensitivity analysis 2 – All patients followed up past 3 months but with no 15-month sample classified as failures

End point description:

End point type	Other pre-specified

End point timeframe:

From 3 months after the start of treatment to 15 months after the start of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	144		
Units: Subjects				
Successful eradication	55	68		
Unsuccessful eradication	81	76		

Statistical analyses

Statistical analysis title	Sensitivity analysis 2

Statistical analysis description:

Primary efficacy assessment – Sensitivity analysis 2: All patients followed up past 3 months but with no 15-month sample classified as failures.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	280
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.253
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.12

Other pre-specified: Sensitivity analysis 3 – All patients followed up for more than 15 months but with no 15-month sample classified as success/failure in accordance with the next sample taken after the 15-month window

End point title	Sensitivity analysis 3 – All patients followed up for more than 15 months but with no 15-month sample classified as success/failure in accordance with the next sample taken after the 15-month window

End point description:

End point type	Other pre-specified

End point timeframe:

From 3 months after the start of treatment to 15 months after the start of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	144		
Units: Subjects				
Successful eradication	66	81		
Unsuccessful eradication	70	63		

Statistical analyses

Statistical analysis title	Sensitivity analysis 3

Statistical analysis description:

Primary efficacy assessment – Sensitivity analysis 3: All patients followed up for more than 15 months but with no 15-month sample classified as success/failure in accordance with the next sample taken after the 15-month window.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	280
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.196
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.08

Other pre-specified: Primary efficacy assessment – Sensitivity analysis 4: Centre effect

End point title	Primary efficacy assessment – Sensitivity analysis 4: Centre effect

End point description:

The model with site as a random effect was not statistically different to the model without a random effect.

End point type	Other pre-specified

End point timeframe:

From 3 months after the start of treatment to 15 months after the start of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	130		
Units: Subjects	55	68		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Primary efficacy assessment – Sensitivity analysis 5: T3 and T15 extended to +10 weeks (Post hoc) - successful eradication

End point title	Primary efficacy assessment – Sensitivity analysis 5: T3 and T15 extended to +10 weeks (Post hoc) - successful eradication

End point description:

End point type	Other pre-specified

End point timeframe:

From 3 months after the start of treatment to 15 months after the start of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	139		
Units: Subjects				
Successful eradication	61	73		
Unsuccessful eradication	71	66		

Statistical analyses

Statistical analysis title	Sensitivity analysis 5 - Successful eradication

Statistical analysis description:	
Sensitivity analysis 5: T3 and T15 extended to +10 weeks (Post hoc)	
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	271
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.299
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.12

Other pre-specified: Primary efficacy assessment – Sensitivity analysis 5: T3 and T15 extended to +10 weeks (Post hoc) - unsuccessful eradication

End point title	Primary efficacy assessment – Sensitivity analysis 5: T3 and T15 extended to +10 weeks (Post hoc) - unsuccessful eradication

End point description:

End point type	Other pre-specified

End point timeframe:

Number of participants who had unsuccessful eradication at their three-month visit (T3 extended to +10 weeks (Post hoc)).

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	135		
Units: Subjects				
Successful eradication	102	123		
Unsuccessful eradication	22	12		

Statistical analyses

Statistical analysis title	Sensitivity analysis 5 - Unsuccessful eradication

Statistical analysis description:

Number of participants who had unsuccessful eradication at their three-month visit (T3 extended to +10 weeks (Post hoc)).

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	259
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.035
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	3.86

Other pre-specified: Sensitivity analysis: Time to reoccurrence of original P.aeruginosa infection (Those with reoccurrence but unknown strain assumed to be same as baseline and T0 adjusted to be date of treatment commencement rather than date of randomisation)

End point title	Sensitivity analysis: Time to reoccurrence of original P.aeruginosa infection (Those with reoccurrence but unknown strain assumed to be same as baseline and T0 adjusted to be date of treatment commencement rather than date of randomisation)

End point description:

End point type	Other pre-specified

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	148		
Units: Subjects				
Reoccurrence of original P.aeruginosa infection	74	66		
Censored	63	82		

Statistical analyses

Statistical analysis title	Sensitivity analysis
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.92

Other pre-specified: Sensitivity analysis: Time to reoccurrence of original P.aeruginosa infection (Those with reoccurrence but unknown strain assumed to be different to baseline and T0 adjusted to be date of treatment commencement rather than date of randomisation)

End point title	Sensitivity analysis: Time to reoccurrence of original P.aeruginosa infection (Those with reoccurrence but unknown strain assumed to be different to baseline and T0 adjusted to be date of treatment commencement rather than date of randomisation)

End point description:

End point type	Other pre-specified

End point timeframe:

From baseline to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	148		
Units: Subjects				
Reoccurence of original P.aeruginosa infection	21	14		
Censored	116	134		

Statistical analyses

Statistical analysis title	Sensitivity analysis
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy

Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	3.64

Other pre-specified: Additional analysis 1: Time to first pulmonary exacerbation

End point title	Additional analysis 1: Time to first pulmonary exacerbation
End point description:	

End point type	Other pre-specified
End point timeframe:	
From baseline to 24 months.	

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	148		
Units: Subjects				
Number of patients who had pulmonary exacerbation	48	63		
Censored	89	85		

Statistical analyses

Statistical analysis title	Time to first pulmonary exacerbation
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.06

Other pre-specified: Additional analysis 2: At least one exacerbation during the treatment phase

End point title	Additional analysis 2: At least one exacerbation during the treatment phase

End point description:

End point type	Other pre-specified

End point timeframe:

Treatment phase.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	144		
Units: Subjects				
0 exacerbations	127	129		
>=1 exacerbations	8	15		

Statistical analyses

Statistical analysis title	1+ exacerbations during the treatment phase

Statistical analysis description:

The number and percentage of patients experiencing at least one exacerbation in each treatment arm was reported. Treatment groups were compared using the chi-squared test.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	279
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.173
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	1.3

Other pre-specified: Additional analysis 2: At least one exacerbation during the first year following treatment

End point title	Additional analysis 2: At least one exacerbation during the first year following treatment

End point description:

End point type	Other pre-specified

End point timeframe:

From 3 months to 15 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	136		
Units: Subjects				
0 exacerbations	100	90		
>=1 exacerbations	31	46		

Statistical analyses

Statistical analysis title	1+ exacerbations between 3-15 months

Statistical analysis description:

The number and percentage of patients experiencing at least one exacerbation in each treatment arm was reported. Treatment groups were compared using the chi-squared test.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.067
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.03

Other pre-specified: Additional analysis 2: At least one exacerbation during the second year following treatment

End point title	Additional analysis 2: At least one exacerbation during the second year following treatment

End point description:

End point type	Other pre-specified

End point timeframe:

From 15 months to 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	103		
Units: Subjects				
0 exacerbations	85	77		
>=1 exacerbations	14	26		

Statistical analyses

Statistical analysis title	1+ exacerbations between 15-24 months

Statistical analysis description:

The number and percentage of patients experiencing at least one exacerbation in each treatment arm was reported. Treatment groups were compared using the chi-squared test.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.01

Other pre-specified: Sensitivity analysis - Admission to hospital - Number of participants experiencing at least one hospital stay during the first 3 months of treatment

End point title	Sensitivity analysis - Admission to hospital - Number of participants experiencing at least one hospital stay during the first 3 months of treatment

End point description:

End point type	Other pre-specified

End point timeframe:

First 3 months of treatment.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	143		
Units: Subjects				
0 Hospital Stays	111	134		
>=1 Hospital Stay	24	9		

Statistical analyses

Statistical analysis title	Admission to hospital - 3 months of treatment
Statistical analysis description:	
The secondary outcome analysis was ran under the assumption that where there is uncertainty about which period hospital stay occurred in, all reported hospital stay occurs in the time-period least likely.	
Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	2.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.36
upper limit	5.86

Other pre-specified: Sensitivity analysis - Number of participants experiencing at least one hospital stay during the 12 months following treatment

End point title	Sensitivity analysis - Number of participants experiencing at least one hospital stay during the 12 months following treatment
End point description:	
End point type	Other pre-specified
End point timeframe:	
12 months following treatment.	

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	136		
Units: Subjects				
0 Hospital Stays	90	73		
>=1 Hospital Stay	39	63		

Statistical analyses

Statistical analysis title	Admission to hospital - 12 months

Statistical analysis description:

The secondary outcome analysis was ran under the assumption that where there is uncertainty about which period hospital stay occurred in, all reported hospital stay occurs in the time-period least likely.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.9

Other pre-specified: Sensitivity analysis - Admission to hospital - Number of participants experiencing at least one hospital stay between 15 months and 24 months

End point title	Sensitivity analysis - Admission to hospital - Number of participants experiencing at least one hospital stay between 15 months and 24 months

End point description:

End point type	Other pre-specified

End point timeframe:

Between 15 and 24 months.

End point values	Intravenous (IV) antibiotics	Oral antibiotic therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	108		
Units: Subjects				
0 Hospital Stays	70	67		
>=1 Hospital Stay	34	41		

Statistical analyses

Statistical analysis title	Admission to hospital - 15-24 months

Statistical analysis description:

The secondary outcome analysis was ran under the assumption that where there is uncertainty about which period hospital stay occurred in, all reported hospital stay occurs in the time-period least likely.

Comparison groups	Intravenous (IV) antibiotics v Oral antibiotic therapy
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.422
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.24

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Only AEs occuring from commencement of allocated treatment until 28 days after cessation of allocated treatment were reported during the trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	Intravenous (IV) antibiotics
Reporting group description: -	
Reporting group title	Oral antibiotic therapy

Reporting group description: -

Serious adverse events	Intravenous (IV) antibiotics	Oral antibiotic therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 126 (7.94%)	14 / 146 (9.59%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Catheter management			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Distal intestinal obstruction syndrome			
subjects affected / exposed	2 / 126 (1.59%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	0 / 126 (0.00%)	3 / 146 (2.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung consolidation			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety	Additional description: Event was that after 5 weeks on trial developed voices in his head and obsessive behaviours and anxiety at night.		
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			

subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	0 / 126 (0.00%)	3 / 146 (2.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Intravenous (IV) antibiotics	Oral antibiotic therapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 126 (50.79%)	75 / 146 (51.37%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Administration site bruise			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Administration site pain			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Adverse drug reaction			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Catheter site related reaction			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Influenza like illness			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Pyrexia			

subjects affected / exposed	2 / 126 (1.59%)	7 / 146 (4.79%)	
occurrences (all)	2	7	
Swelling			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Cough			
subjects affected / exposed	22 / 126 (17.46%)	23 / 146 (15.75%)	
occurrences (all)	26	28	
Epistaxis			
subjects affected / exposed	1 / 126 (0.79%)	2 / 146 (1.37%)	
occurrences (all)	1	2	
Haemoptysis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Pharyngeal oedema			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	5 / 126 (3.97%)	8 / 146 (5.48%)	
occurrences (all)	5	8	
Sputum increased			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Wheezing			

subjects affected / exposed	3 / 126 (2.38%)	6 / 146 (4.11%)	
occurrences (all)	3	6	
Psychiatric disorders			
Enuresis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Product issues			
Device occlusion			
subjects affected / exposed	2 / 126 (1.59%)	0 / 146 (0.00%)	
occurrences (all)	2	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Blood glucose increased			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Chest X-ray abnormal			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Enterobacter test positive			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Haemophilus test positive			
subjects affected / exposed	2 / 126 (1.59%)	0 / 146 (0.00%)	
occurrences (all)	2	0	
Klebsiella test positive			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Pseudomonas test			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Pseudomonas test positive			
subjects affected / exposed	1 / 126 (0.79%)	2 / 146 (1.37%)	
occurrences (all)	1	2	
Pulmonary function test			

subjects affected / exposed	0 / 126 (0.00%)	2 / 146 (1.37%)	
occurrences (all)	0	2	
Pulmonary function test decreased			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Stenotrophomonas test positive			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Streptococcus test positive			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 126 (0.79%)	2 / 146 (1.37%)	
occurrences (all)	1	2	
Skull fracture			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Sunburn			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Wrist fracture			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Febrile convulsion			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	2 / 126 (1.59%)	0 / 146 (0.00%)	
occurrences (all)	3	0	
Lethargy			

subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Ear pain			
subjects affected / exposed	0 / 126 (0.00%)	2 / 146 (1.37%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 126 (0.79%)	2 / 146 (1.37%)	
occurrences (all)	1	2	
Abdominal pain upper			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	5 / 126 (3.97%)	3 / 146 (2.05%)	
occurrences (all)	6	3	
Distal intestinal obstruction syndrome			
subjects affected / exposed	2 / 126 (1.59%)	3 / 146 (2.05%)	
occurrences (all)	2	3	
Haematemesis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Pancreatitis			

subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Paraesthesia oral			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Rectal haemorrhage			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Tongue discolouration			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	3 / 126 (2.38%)	0 / 146 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Dry skin			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Onychoclasis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Petechiae			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Photosensitivity reaction			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	2 / 126 (1.59%)	1 / 146 (0.68%)	
occurrences (all)	2	1	

Skin discolouration			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Polyuria			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 126 (0.00%)	3 / 146 (2.05%)	
occurrences (all)	0	3	
Back pain			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Flank pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Limb discomfort			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Pain in extremity			

subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Infections and infestations			
Bacterial disease carrier			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Candida infection			
subjects affected / exposed	1 / 126 (0.79%)	5 / 146 (3.42%)	
occurrences (all)	1	5	
Conjunctivitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Eczema infected			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Eye infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Foot and mouth disease			
subjects affected / exposed	0 / 126 (0.00%)	2 / 146 (1.37%)	
occurrences (all)	0	2	
Gastroenteritis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Haemophilus infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	2	0	
Infectious mononucleosis			

subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	3 / 126 (2.38%)	6 / 146 (4.11%)	
occurrences (all)	4	6	
Lower respiratory tract infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Mycobacterium avium complex infection			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Pseudomonas infection			
subjects affected / exposed	7 / 126 (5.56%)	2 / 146 (1.37%)	
occurrences (all)	7	2	
Respiratory tract infection			
subjects affected / exposed	1 / 126 (0.79%)	2 / 146 (1.37%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			

subjects affected / exposed	11 / 126 (8.73%)	2 / 146 (1.37%)	
occurrences (all)	15	3	
Urinary tract infection			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Varicella			
subjects affected / exposed	3 / 126 (2.38%)	1 / 146 (0.68%)	
occurrences (all)	3	1	
Viral infection			
subjects affected / exposed	1 / 126 (0.79%)	1 / 146 (0.68%)	
occurrences (all)	1	1	
Vulvovaginal candidiasis			
subjects affected / exposed	2 / 126 (1.59%)	0 / 146 (0.00%)	
occurrences (all)	2	0	
Nasal vestibulitis			
subjects affected / exposed	1 / 126 (0.79%)	0 / 146 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Vitamin A deficiency			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	
Vitamin E deficiency			
subjects affected / exposed	0 / 126 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2010	V2.0 (15/2/2010): A complete list of amendments and clarifications have been attached in a seperate document.
01 September 2010	V3.0 (1/9/2010) Page Number Amendment Comment Throughout Updated version and date; correction of typographical errors 5 Addition of Miss Joanne Eatock, Senior Data Manager 9 Updated the table of contents 11 List of abbreviations updated Throughout Clarification text added to Exclusion criteria 4. 'Please note, short courses of oral ciprofloxacin or intravenous antibiotics (with an anti-pseudomonal spectrum of action) are not an exclusion unless they are given to treat proven infections with P. aeruginosa' Throughout Primary endpoint text amended from 'Successful eradication of P. aeruginosa infection at three months post randomisation, remaining infection free through to 15 months post randomisation' changed to read 'Successful eradication of P. aeruginosa infection at three months post treatment, remaining infection free through to 15 months post treatment' Throughout Secondary endpoint 8 changed from 'Number of days spent as inpatient in hospital over the three-month period post-treatment and between three months and 15 months post-treatment (other than 14 days spent on initial IV treatment)' to 'Number of days spent as inpatient in hospital over the three-month period post-randomisation and between three months and 15 months post-randomisation (other than 14 days spent on initial IV treatment)' 16 Section 1.3 text 'post randomisation' changed to 'post treatment' 21 Section 4.3.3 text ' Premature Discontinuation' changed to 'Withdrawal' 22 Details for the web randomisation system changed 23 Section 6.1 text 'designed as a' replaced with 'a phase IV' 23-30 Formal accountability procedures for the trial along with labelling requirements removed and section updated to detail informal accountability introduced to monitor treatment compliance 31-32 Section 35 Addition of guidance table for administration of Questionnaire Booklets 41 Change to the wording of the CACE study to reflect changes in the ethics approved protocol 43 Section 8.4 tex
13 December 2010	V4.0 (13/12/2010) A complete list of amendments and clarifications have been attached in a seperate document

11 January 2012	V5.0 (11/01/2012) Page Number Amendment Comment Throughout Updated version and date; correction of typographical errors 24 Section 6.3.3 changed from 'Home Care companies can be used to provide Home IVs only if the CTU is provided with a copy of the companies MIAIMP licence as part of the green light process.' to 'Homecare companies can be used. Homecare companies that reconstitute intravenous medicines centrally and supply reconstituted injectables directly to patient's home must be a registered pharmacy. In addition, the IMPs shall be dispensed to a subject in accordance with a prescription given by an authorised health care professional and labelled in accordance with the requirements that apply to dispensed relevant medicinal products.'
17 October 2013	V6.0 (17/10/2013) : A complete list of amendments and clarifications have been attached in a seperate document.
12 August 2014	V7.0 (12/08/2014) Page Number Amendment Comment Throughout Updated version and date Throughout Updated contact details 9 - 10 Updated table of contents Throughout Replacement of Medicines for Children Research Network with Medicines for Children Throughout Participating sites to include international sites Throughout Addition of University of Liverpool as Co-Sponsor; they will act as sole sponsor for international sites 11 Study period changed from 6 years and 3 months to 8 years and 7 months 22 Section 4.3.1 changed requirement for follow-up via GP where the participant moves to a non-particpiating site. Replaced with: "Where this is not possible, if the participant is still happy for their data to be collected, the recruiting centre should make every effort to obtain data collected as part of routine care from the centre that is now responsible for the participants care." 39 Section 7.6 Added sentence: "At the time of database lock, data entry privileges are withdrawn from the trial database." 61 Section 14 Details of financial arrangements removed, described separately in the contracts.

23 December 2015	V8.0 (23/12/2015) Page Number Amendment Comment Throughout Updated version and date 9 - 10 Updated table of contents Throughout Clarifying follow-up period; patients who start randomised treatment before 1st January 2016 will continue follow-up for 24 months, patients who start randomised treatment on or after 1st January 2016 will continue follow-up for 15 months. 27 Text changed from "Ceftazidime 150 milligram (mg)/kilogram (kg)/day, in 3 divided doses (maximum of 3 grams (g) three times daily (tds)). Some centres may use a twice daily regimen for ceftazidime. These centres may continue to use this regimen for the study and should follow their local dosing guidelines." To "Ceftazidime 150 milligram (mg)/kilogram (kg)/day, in 3 divided doses (maximum of 3 grams (g) three times daily (tds)). Some centres may use a once daily continuous infusion (where the maximum daily dose would usually be 6g/day) or twice daily regimen for ceftazidime. These centres may continue to use this regimen for the study and should follow their local dosing guidelines." 42 Clarification of genotyping arrangement outside the UK - 45 Corrected typrographical error inserting "serious" in section 9.5 to correct text to say "Expectedness should be assessed for all serious adverse reactions" 63 Removed reference to supllementary document describing indemnity arrnagemnets for non-Uk sites. Replaced with "Equivalent cover to that provided by the Clinical Negligence Scheme for UK Trusts should be confirmed to be in place for non-UK sites during site suitability assessment and cover summarised in the sponsor-site contract."
12 December 2016	V9.0 (12/10/2016) Page Number Amendment Comment Throughout Updated version and date 11 Updated number of patients to be enrolled

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported