S5 Report

CONFIDENTIAL

Case Report Form

TITLE

COMPARISON OF A SERUM PROCALCITONIN (PRO-CT) GUIDED TREATMENT PLAN WITH THE STANDARD GUIDELINE RECOMMENDED ANTIBIOTIC TREATMENT PLAN FOR PATIENTS HOSPITALIZED WITH A DIAGNOSIS OF EXACERBATION OF COPD

Centre No.:

Patient's initials:

Screening No.:

Randomisation No.:

FINAL VERSION: SEPTEMBER 27, 2006

|____|



Andomisation no.

INSTRUCTIONS

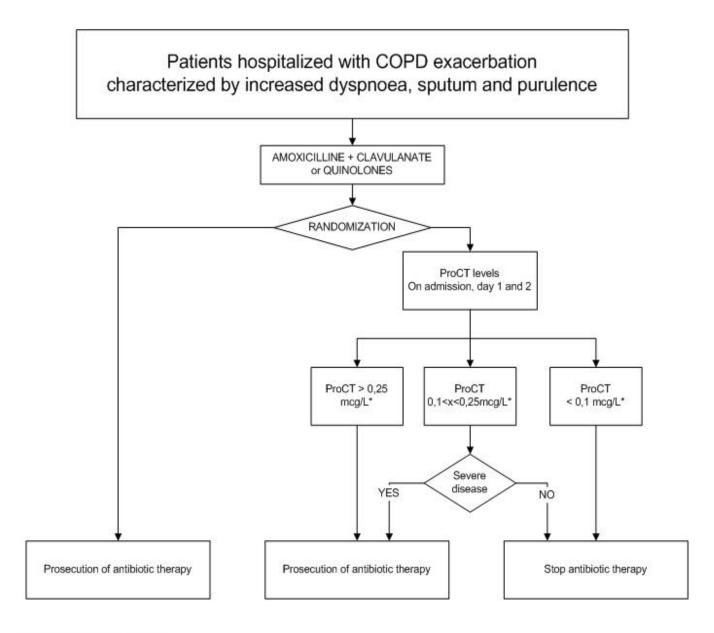
Please complete each form; date and sign the Investigator's Statement at the end of each visit as indicated in a legible manner. The use of a black ball point pen is recommended. If a change is necessary to any entry, cross it out with a single line, write in the correction and give reason for the change. Initial and date the correction.

Do not leave any questions unanswered. Please write the explanation beside any blank spaces.

Flow chart

	Hospitalization						
	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7
	Day 0	Day 1	Day 2 Randomisation	At hospital discharge e/o day 10	Day 30	Day 90	Day 180
Informed	Х						
Consent							
Medical history	х						
Physical examination	х	х	Х	Х	X	Х	х
Vital signs	х	х	X	Х	Х	х	х
Body	Х	х	х	Х			
temperature							
Medication	X	X	X	X	Х	X	X
Pulmonary x-ray	Х						
Spirometry	Х			Х	Х	х	х
Sputum collection	х			х	Х		х
ECG	х						
Inclusion / exclusion criteria	х						
Questionnaire for quality of life	х			x	x	X	X
Pharmaco- economy questionnaire	х			x	x	X	X
Haematology	Х		x (if abnormal at day 0)	Х		X	
Blood chemistry	Х		x (if abnormal at day 0)	Х		х	
CRP, SAA and RANTES	Х	X	X	Х	х	х	x
PTX3 and IL- 1 decoy	х			Х		X	
Pro-ct levels	х	X	X	X	Х	х	Х
Arterial blood gases	X	X	X	X	X	X	X
Treatment compliance	X	X	X	Х			
Adverse event	x	x	x	X	x	x	x
Auverse event	л	Λ	Λ	л	Λ	Λ	Λ

Study Design



* On admission, day 1 and day 2

Centre No. Screen. No.	Randomisation No. F	Pat. Init.		
		1	Family name	Name

VISIT 1 – Day 0
Visit date at D D M M Y Y At
Participation agreement attestation:
I the undersigned, Doctor, certify that the patient's written informed
consent form has been read, understood, approved and signed by the patient after having
received information.
Date of written informed consent signature:
Investigator's Signature:
The informed consent form must be signed before any procedure related to the study.

Centre No. _	Screen. No. _	Randomisation No.	Pat. Init.		
				Family name	Name

VISIT 1 – Day 0

Visit date		_	_	.			at	.		
	D	D	М	М	Y	Y	ł	HOUR	MINUTES	

	INCLUSION CRITERIA	Yes	No
1.	Male and female patients who give written informed consent		•
2.	Age: adults > 18 years old		•*
3.	Diagnosis of COPD according to GOLD guidelines: FEV1/FVC < 70% with FEV1 < 80% of predicted		*
4.	History of cigarette smoking		*
5.	Diagnosis of COPD exacerbation: defined as acute-onset dyspnoea and/or cough associated with purulent sputum production (Anthonisen's criteria); requiring, according to guidelines (GOLD 2005), treatment with antibiotic; requiring hospitalisation		•

Any NO* leads to immediate exclusion from the study.

Fill in the "Investigator's statement" at the end of visit 1 and the "Study Conclusion Summary/Wihtdrawal/Drop-out Form".

	EXCLUSION CRITERIA	Yes	No	NA
1.	Female subjects: pregnant, lactating mother or lack of efficient contraception in a subject with child-bearing potential (e.g. contraceptive methods other than oral contraceptives, IUD, tubal ligature)	•		
2.	Diagnosis of asthma	*		
3.	Coexisting medical conditions: unstable concomitant cardiovascular, renal, hepatic, gastrointestinal, neurological, endocrine, metabolic, musculo- skeletal, neoplastic, respiratory or other clinically significant disease (Patients with stable and well controlled hypertension or diabetes maybe included in the study)	•*		
4.	Clinical significant laboratory abnormalities indicating unstable concomitant disease	*		
5.	Patients in whom survival for at least 1 year is unlikely	•*		
6.	Inability to give informed consent	•		
υ.				

Any YES* leads to immediate exclusion from the study.

Fill in the "Investigator's statement" at the end of visit 1 and the "Study Conclusion Summary/Wihtdrawal/Drop-out Form".

Centre No. Screen. No.	_ Randomisation No. Pat. Init.	
		Comilia nome Nome

VISIT 1 – Day 0	
	Visit date at _ _ _ _ _ _ _ _ _ _ _
DEN	MOGRAPHIC DATA
_	
Age years old	Date of Birth
Sex: 1) 🖵 Male	Height (cm) _ .
2) 🖵 Female	Weight (Kg) _ _
If the patient is a female	
Is she of childbeari	ng potential? 1) INO 2) Yes
1) If no:	
1) Post menop the last perio	ausal (two years after 🔲 od)
2) Surgically st	erilised
3) Other:	
Specify:	
2) If yes:	
1) Tubal Ligatu	
2) Using oral o	estro-progestatives
3) Using intra u	uterine-device (IUD)
4) Other:	
Specify:	
	pearing potential must use an effective ethod. If not, the patient cannot be

Centre No. _ S	creen. No. _	Randomisation No. _	Pat. Init.	.	
			Fami	ly name	Name

VISIT 1 – Day 0

 Visit date

 at

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 MINUTES

MEDICAL AND SURGICAL HISTORY AND CONCOMITANT DISEASES

Does the patient have a <u>relevant</u> medical and/or surgical history, and/or <u>relevant</u> concomitant diseases? (including clinically significant laboratory values)

□ No □ Yes*

*If yes, fill in this table.

Medical or surgical history and/or concomitant diseases	Start Date DD / MM / YY	End date DD / MM / YY	On going
1. COPD			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			

Centre No. _ \$	Screen. No.	Randomisation No.	Pat. Init.		_
				Family name	Name

VISIT 1 - Day 0

Visit date |___|_||__| at |_ __||_ D м р HOUR MINUTES

MEDICATION FOR CONDITIONS OTHER THAN COPD

Is the patient under ANY medication for any medical condition other than COPD?

Yes* _|

*If YES please complete the following table, specifying ALL medication taken by the patient for ANY medical condition except COPD, at the time of enrolment in the study

Trade	Indication	Poso	Posology		Administration (DD/MM/YY)	
name		Dose/day	Unit	_	Start date	End date (or ONGOING)

MEDICATION FOR STABLE COPD

Is the patient under pharmacologic treatment for stable COPD?

Yes*

*If YES please complete the following table, specifying any medication taken by the patient for stable COPD, at the time of enrolment in the study

Trade	Indication	Posology		Route	Adminis (DD/MN	
name indication	Indication	Dose/day	Unit		Start date	End date (or ONGOING)

Centre No. _ Sc	creen. No.	Randomisation No. _	_ Pat. Init.		
				Family name	Name

VISIT 1 – Day 0

 Visit date

 at

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 HOUR
 MINUTES

Yes*

HOME MEDICATION FOR THE CURRENT COPD EXACERBATION

Did the patient take ANY medication for the current COPD exacerbation <u>before</u> hospital admission (for example, any antibiotics taken at home before hospital admission)?

🖵 No

*If YES please complete the following table, specifying any medication taken by the patient for the current COPD exacerbation at home (before hospital admission)

Trade	Indication	Poso	Posology		Administration (DD/MM/YY)	
name		Dose/day	Unit		Start date	End date (or ONGOING)

HISTORY OF CURRENT COPD EXACERBATION

Please indicate when the first sign/symptom of the current COPD exacerbation began (DD/MM/YY):

|____| |____| |____|

What were the characteristics of the current COPD exacerbation? Please indicate:

	Sign/symptom		Comments:
1.	Fever	□ Yes □ No	
2.	Dyspnoea	□ Yes □ No	
3.	Cough	□ Yes □ No	
4.	Sputum	□ Yes □ No	
5.	Sputum purulence	□ Yes □ No	
6.	Wheezing	□ Yes □ No	
7.	Other (specify)	□ Yes □ No	

Centre No. Screen. No. Randomis	ation No. _ Pat. Init. _
	Family name Name

VISIT 1 – Day 0

Visit date	_	_	_				at	
	D	D	М	М	Y	Y	HOUR	MINUTES

PHYSICAL EXAMINATION					
Physical examination	Status	Comments: if "abnormal" specify:			
	Abnormal				
Cardiovascular system	Normal				
	Not done				
Respiratory system	Abnormal				
(except COPD)	Normal				
	Not done				
	Abnormal				
Lymphatic system	Normal				
	Not done				
Neurological-locomotor	Abnormal				
	Normal				
system	Not done				
	Abnormal				
Skin	Normal				
	Not done				
	Abnormal				
Endocrine	Normal				
	Not done				
Ear-nose-throat	Abnormal				
	Normal				
system	Not done				
Ontralmalagiaal	Abnormal				
Ophtalmological	Normal				
system	Not done				
Gastrointestinal	Abnormal				
	Normal				
system	Not done				
Othoro	Abnormal				
Others	Normal				
	Not done				

If an abnormality is clinically significant, please complete the 'Medical and surgical history and Concomitant Diseases' form on page 4.

Centre No.	Centre No. Screen. No. _ Randomisation No. Pat. Init.					
VISIT 1 – Da	y 0					
		Visit date at D D M Y Y HOUR MINUTES				
		SMOKING HABITS				
Information on the	e patient:					
Never smoked						
Former-smoker		Start date Stop date _				
Smoker		Start date _				
For former-smokers and smokers: Number packs year						
 Reminder: 1 pack year = 20 cigarettes/day for 1 year or equivalent. Calculation: PACK-YEARS = (number of cigarettes smoked per day) × (years smoked) 20 						

VITAL SIGNS				
Body temperature _ . °C				
	OD PRESSURE hHg)	SITTING HEART RATE (bpm)		
Systolic	Diastolic			

Centre No. _	Screen. No.	_ Randomisation No.		
VISIT 1 – Day 0				
	Vi	isit date	at	
		D D M M	Y Y	HOUR MINUTES
	LAB	ORATORY TESTS		
	Collect blood sample	e for haematology and blood	chemistry	
	(LC	CAL LABORATORY)		
Haematology tests	*		-	Significant **
Haemoglobin (mmol/	′L)	.	Yes 	No
Haematocrit (L/L)		. 		
RBC (10 ¹² /L)		.		
WBC (10 ⁹ /L)				
WBC (differential counts)	Neutrophils (%)	.		
	Eosinophils (%)			
	Basophils (%)			
	Monocytes (%)			
	Lymphocytes (%)			
Platelet (10 ⁹ /L)				
Blood Chemistry te	sts *			
Alkaline Phosphatas	e (U/L)			
AST (SGOT) (U/L)		.		
ALT (SGPT) (U/L)				
BUN/blood urea (mm	nol/L)	.		
Creatinine Kinase (U	/L)	.		
Creatinine (µmol/L)		.		
Gamma-GT (U/L)		. ·		
Sodium (mmol/L)		.		
Potassium (mmol/L)		.		
Glucose (mmol/L)		·		
* to be filled in as se	oon as results are av	ailable		
** For the out of rang	ge values, please spo	ecify if the abnormality is clin	nically or not	clinically significant

Laboratory results need to be stored in the patient's file

Г

Centre No. _ Screen. No. _	Randomisation No.	Pat. Init. _	
		Family name	Name

VISIT 1 – Day 0					
Visit date at D D M M Y HOUR MINUTES					
Pro-calcitonin (pro-ct)					
Has the blood sample been taken for the pro-ct analysis?					
Yes No					
If Yes, refer to the Study Procedures Handbook for handling and storage.					
If No, please specify why:					
Please fill in as soon as the results are available:					
Pro-calcitonin (mcg/L) I_I_I.I_II					

C-reactive protein (CRP), serum amyloid (SAA) and RANTES				
Has the blood sample	been taken for the CRP, SAA and RANTES analysis?			
	Yes No			
If Yes, refer to the Stu	idy Procedures Handbook for handling and storage.			
If No, please specify v	If No, please specify why:			
Please fill in as soon a CRP (mg/L)	as the results are available:			
SAA (mg/L)	II.II			
RANTES (mcg/L)	II.II			

PTX-3 and IL1 decoy				
Has the blood sample been taken for the PTX-3 and II	_1 decoy analysis?			
Yes No				
If Yes, refer to the Study Procedures Handbook for ha	If Yes, refer to the Study Procedures Handbook for handling and storage.			
If No, please specify why:				
Please fill in as soon as the results are available:				
PTX-3 (ng/ml) II_I_I_I_I				
IL1 decoy (ng/ml) IIII.II				

Centre No. Screen. No. _	Randomisation No. Pa	at. Init. _	
		Family name	Name

VISIT 1 – Day 0
Visit date at D D M M Y HOUR MINUTES
PULMONARY X-RAY
Has a pulmonary X-ray been obtained? Yes D No D
If YES: X ray was: Normal 🖵 Abnormal 🖵
If "Abnormal", please specify:
If not obtained, specify why:

QUESTIONNAIRES	FOR RESPIRATORY SYMPTOMS/QUALITY OF LIFE
SF36 score:	total III
BDI score:	total II
TDI score:	total II
CCIQ Score:	total III

PHARMACOECONOMIC QUESTIONNAIRE

Please remind to fill in the pharmacoeconomic questionnaire and enclose it in the plastic envelope.

	SPIROMETRY				
•	• SPIROMETRY: from 3 acceptable spirometric manoeuvres record the highest FEV ₁ and FVC, irrespective of the manoeuvre (curve) they come from.				
	date at HOUR MINUTES				
	FVC , litre				
FEV1		, litre			
FEV1 predicted normal value		, litre [ERS standards]			
FEV1 (% predicted normal value)		% of predicted value			
	FEV₁/FVC (%)	, %			

Centre No. _ Screen. No. _	Randomisation No.	Pat. Init.		_
			Family name	Name

VISIT 1 – Day 0					
Visit date at D D M Y HOUR MINUTES					
	MICROBI	OLOG	Y		
	Yes		No		
Sputum collection performed:					
If YES, specify volume of sputum co		lml	-		
If NO, specify why		•			
······································					
Results from local laboratory:					
Bacteriology:					
Identified microorganism #1:					
Identified microorganism #2:					
Identified microorganism #3:			_ CFU/ml:		
Serology for Intracellular pathoge	ens:				
Has the sample for serology for intra		ns been	obtained? Yes 🔲 No 🗖		
If Yes, please complete below:	1				
Was serology positive for Mycoplas	ma pneumonia	e? Yes [
If YES, indicate: IgM:					
igo:	_ ,				
Was serology positive for Chlamyd i	ia? Yes 🔲 🛛 No				
If YES, indicate: IgM:					
	_ ,				
	_ 11				
Was serology positive for Legionella pneumophila? Yes D No D					
If YES, indicate:					
P	OSITIVE	NEGA	TIVE		
Legionella pneumophila IgM					
Legionella pneumophila IgG					

Centre No. Screen. No. Randomisation No.	Pat.	Family name	 Name
VISIT 1 – Day 0			
Visit date 	 N Y Y		_ MINUTES
MICROBIOLOGY (conti	nued)		
Has the sample for respiratory viruses RT-PCR analysis bee	n collected a	nd stored at -	-80°C?
		Yes 🗖	No 🗖
If YES , specify volume stored at -80°C for RT-PCR: ,	ml		
Please remember to label the sample with the patient's ID number and store it at -80°C, as described in the Study Procedures Handbook.			
Has the sample for inflammatory cell counts been collected?	Yes 🗖	No 🗖	
Were the slides prepared and stored at -20°C?	Yes 🗖	No 🗖	
If YES: how many slides were prepared?			

ARTERIAL BLOOD GASES				
	Yes	Νο		
	_			
Arterial blood gas analysis performed:				
If YES: patient was under O ₂ therapy?				
If patient was under O ₂ therapy please indicate:				
- how many L/min:	,			
- how many hours/day:				
If arterial blood gas analysis was performed, indicate	e:			
pH: ,				
PaO _{2:} mmHg				
PaCO _{2:} mmHg				
SO _{2:} %				
HCO3 ^{-:} mmol/L				

Centre No. _	Screen. No. _	Randomisation No.	_ Pat. Init.		
			Fami	ly name	Name

VISIT 1 – Day 0	
Visit date	at
D	D M M Y Y HOUR MINUTES
ECG (12-lead	
Has an ECG recording been obtained? Yes <pre>D</pre> No <pre>D</pre>	
If No specify why:	
If YES, please complete the following table and file the	
RECORDING	COMMENTS (if any)
Normal	
Abnormal (not clinically significant)	
Abnormal (clinically significant)	1
and surgical history and Concomitant Diseases' form on page 4)	
ANTIBIOTIC TREATMEN	FADMINISTRATION
- Indicate the antibiotic prescribed to the patient of	during the current hospitalization (choose one):
Amoxicilline + Clavulanate D OR Quinol	ones 🗖 (specify kind)
- Indicate route of administration (choose one):	per os D intravenous D
 record dosage of administered antibiotic: 	
- Indicate start date of antibiotic (DD/MM/YY):	

HOSPITAL MEDICATION

Please record in the following table ALL medication (steroid treatment, bronchodilators, any other therapy prescribed) to the patient during the current hospitalization (except antibiotic treatment, since it was already indicated above)

Trade name Indication		Posology		Route	Administration (DD/MM/YY)	
name	mulcation	Dose/day	Unit		Start date	End date (or ONGOING)

Centre No. _ Screen. No.	. Ra	ndomisation N	o. Pat. I	nit. Family name Name
VISIT 1 – Day 0				
	Visit d	ate □ □	 MYY	
ADVERSE E	EVENTS re	lated to a	ntibiotic treat	tment
Did any advarge event related to antibiotic treatment ecour on day 02		C Yes		
Did any adverse event related to antibiotic treatment occur on day 0?				D No
If Yes, please complete the report it immediately to the Dir CROM (see Study Procedures)	ezione Sanita Handbook for	ria of the Ho	ospital and to s).	
	Yes	No		
Is patient compliant:				
If "No", please specify:				
IN	VESTIGAT	OR'S STA	TEMENT	

I confirm that the data herein is a true complete and accurate reflection of this subject participation	n
the study, according to the protocol procedures.	

Investigator's name:	
Investigator's signatu	ıre:
Date:	

Centre No. Screen. No. Randomisation No. Pat. Init. _					
VISIT 2 – Day 1					
Visit date					
Has the patient withdrawn prematurely from the study?	☐ Yes ☐ No				
If Yes, please fill in the "Investigator's statement" at the end of visit 2 and the "Study Conclusion Summary/Wihtdrawal/Drop-out Form" .					
ADVERSE EVENTS related to antibiotic treatment	ment				
Did only advance event related to entiblicitic treatment ecour cines the	C Yes				
Did any adverse event related to antibiotic treatment occur since the last visit?	🖵 No				
If Yes, please complete the appropriate "adverse event" page and report it immediately to the Direzione Sanitaria of the Hospital and to CROM (see Study Procedures Handbook for instructions).					

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Centre No.	Scı	reen. No.	_	Randomisation No.	 Pat. Init.	_	
						Family name	Name

VISIT 2 – Day 1

 Visit date

 at

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 M
 Y
 Y
 HOUR
 MINUTES

OCCUF		/ENTS			
PLEASE COMPLE	TE THE FOL	LOWING TABLE:			
Did the patient require <u>ventilatory support</u> since the last visit?	Yes* No	If YES, specify reason(s) for ventilatory support need:			
<u>*If YES: please add ventilatory support information in</u> <u>the "medication since the last visit" section on page</u> <u>18.</u>		If YES, please indicate date when ventilatory support began since last visit (DD/MM/YY):			
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	☐ Yes ☐ No	Image:			
Did the patient have any episode(s) of <u>pulmonary embolism</u> since the last visit?	Yes No	If YES indicate date of onset of pulmonary embolism since last visit (DD/MM/YY):			
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary edema since the last visit?	☐ Yes ☐ No	If YES, specify kind of cardiovascular event(s):			
Did the patient have any episodes of pneumonia since the last visit?	YesNo	If YES indicate date of onset of pneumonia since last visit (DD/MM/YY):			
Did the patient have <u>any other significant</u> occurring event since the last visit?	YesNo	If YES, specify event(s):			
Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?					
		No 🗖 Yes* 🗖			
* If YES please fax a copy of this page to CR	OM as indi	cated in the Study Procedures Handbook.			

Centre No. _ S	creen. No. _	Randomisation No. _	Pat. Init.	.	
			Fami	ly name	Name

VISIT 2 – Day 1

Visit date |____|__|__|__|__| at |___||__|__|

MEDICATION SINCE THE LAST VISIT

Has any medication been instituted, stopped and/or modified (dose change) since the last visit?

No Yes

If YES please complete the following details, including only medications **instituted**, **stopped and/or modified** (dose change) since the last visit.

Trade		Posology		Route	Administration (DD/MM/YY)	
name	Indication	Dose/day	Unit		Start date	End date (or ONGOING)

Centre No. Screen. No. Randomisation No. _ _	Pat. Init. _		
	Family r	ame Name	

VISIT 2 – Day 1

		Visit date at D D M M Y HOUR MINUTES
	PHY	SICAL EXAMINATION
Physical examination	Status	Comments: if "abnormal" specify:
Cardiovascular system	 Abnormal Normal Not done 	
Respiratory system (except COPD)	 Abnormal Normal Not done 	
Lymphatic system	AbnormalNormalNot done	
Neurological-locomotor system	AbnormalNormalNot done	
Skin	AbnormalNormalNot done	
Endocrine	AbnormalNormalNot done	
Ear-nose-throat system	AbnormalNormalNot done	
Ophtalmological system	AbnormalNormalNot done	
Gastrointestinal system	AbnormalNormalNot done	
Others	AbnormalNormalNot done	

VITAL SIGNS						
Body temperature .						
	DOD PRESSURE nHg)	SITTING HEART RATE (bpm)				
Systolic	Diastolic					

Centre No. _ Screen. No. _ Randomisation No.		Pat. Init. _		_
		Fa	mily name	Name

VISIT 2 – Day 1	
Visit dat	e at D D M M Y Y HOUR MINUTES
Pro-calcit	onin (pro-ct)
Has the blood sample been taken for the pro-ct a	nalysis?
Yes	No
If Yes, refer to the Study Procedures Handbook for	or handling and storage.
If No, please specify why:	
Please fill in as soon as the results are available:	
Pro-calcitonin (mcg/L) I_I_I	_11

C-reactive protein (CRP), serum amyloid (SAA) and RANTES									
Has the blood sample	Has the blood sample been taken for the CRP, SAA and RANTES analysis?								
	Yes No								
If Yes, refer to the Stud	ly Procedures Handbook for handling and storage.								
If No, please specify w	hy:								
Please fill in as soon a	Please fill in as soon as the results are available:								
CRP (mg/L)	II.II								
SAA (mg/L)	II.II								
RANTES (mcg/L)	II.II								

Centre No. Screen. No.	Randomisation No. _	Pat. Init.	
		Family nam	e Name

_									
VISIT 2 – Day 1									
	Visit date								
	D D	M M	Y Y	HOUR	MINUTES				
ARTERIAL BLOOD GASES									
	Ye	NG	No						
Arterial blood gas analysis performed:		_							
	-	-	_						
If YES : patient was under O ₂ therapy?	_								
If patient was under O2 therapy pleas	e indicate:								
- how	many L/min: ,								
- how	many hours/day: _								
If arterial blood gas analysis was perfor	med, indicate:								
pH: ,									
PaO _{2:} mmHg									
PaCO _{2:} mmHg									
SO _{2:} %									
HCO3 ^{-:} mmol/L									

COMPLIANCE						
	Yes	No				
Is patient compliant:						
If "No", please specify:						

	INVESTIGATOR'S STATEMENT
I confirm that the data hereir the study, according to the p	n is a true complete and accurate reflection of this subject participation in protocol procedures.
Investigator's name:	
Investigator's signatur	e:
Date:	

Centre No. Screen. No. _ Randomisation No. _ Pat. In	it. Family name Name
VISIT 3 – Day 2	
Visit date	at HOUR MINUTES
Has the patient withdrawn prematurely from the study?	C Yes
	D No
If Yes, please fill in the "Investigator's statement " at the end of visit 3 and the "Study Conclusion Summary/Wihtdrawal/Drop-out Form ".	
ADVERSE EVENTS related to antibiotic treat	ment
Did any adverse event related to antibiotic treatment occur since the	C Yes
last visit?	D No
If Yes, please complete the appropriate "adverse event" page and	

If Yes, please complete the appropriate "adverse event" page and report it immediately to the Direzione Sanitaria of the Hospital and to CROM (see Study Procedures Handbook for instructions).

Centre No.	Scı	reen. No.	_	Randomisation No.	 Pat. Init.	_	
						Family name	Name

VISIT 3 – Day 2

Visit date				.	.	_	at	
	D	D	м	М	Y	Y	HOUR	MINUTES

OCCURRING EVENTS					
PLEASE COMPLE	TE THE FOL	LOWING TABLE:			
Did the patient require <u>ventilatory support</u> since the last visit?	☐ Yes* ☐ No	If YES, specify reason(s) for ventilatory support need:			
*If YES: please add ventilatory support information in the "medication since the last visit" section on page 24.		If YES, please indicate date when ventilatory support began since last visit (DD/MM/YY):			
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for admission to ICU: If YES, please indicate date of admission to ICU since last visit (DD/MM/YY):			
Did the patient have any episode(s) of pulmonary embolism since the last visit?	☐ Yes ☐ No	If YES indicate date of onset of pulmonary embolism since last visit (DD/MM/YY):			
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary edema since the last visit?	☐ Yes ☐ No	If YES, specify kind of cardiovascular event(s):			
Did the patient have any episodes of pneumonia since the last visit?	YesNo	If YES indicate date of onset of pneumonia since last visit (DD/MM/YY):			
Did the patient have <u>any other significant</u> occurring event since the last visit?	☐ Yes ☐ No	If YES, specify event(s):			
Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?					
No Yes* * If YES please fax a copy of this page to CROM as indicated in the Study Procedures Handbook.					
		Page 23 of 85			

Centre No. _	Screen. No.	Randomisation No. _	Pat. Init.	.	
			Famil	ly name	Name

VISIT 3 – Day 2

 Visit date

 at

 D
 D
 M
 Y
 Y
 HOUR
 MINUTES

MEDICATION SINCE THE LAST VISIT

Has any medication been instituted, stopped and/or modified (dose change) since the last visit?

No Yes

If YES please complete the following details, including only medications instituted, stopped and/or modified (dose change) since the last visit.

Trade		Posology		Route	Administration (DD/MM/YY)	
name Indication	Dose/day	Unit		Start date	End date (or ONGOING)	

Centre No.	Screen. No.	 Randomisation No.	 Pat. Init.		_
				Family name	Name

VISIT 3 – Day 2

		Visit date at D D M Y HOUR MINUTES					
PHYSICAL EXAMINATION							
Physical examination	Status	Comments: if "abnormal" specify:					
Cardiovascular system	 Abnormal Normal Not done 						
Respiratory system (except COPD)	 Abnormal Normal Not done 						
Lymphatic system	 Abnormal Normal Not done 						
Neurological-locomotor system	 Abnormal Normal Not done 						
Skin	 Abnormal Normal Not done 						
Endocrine	 Abnormal Normal Not done 						
Ear-nose-throat system	 Abnormal Normal Not done 						
Ophtalmological system	 Abnormal Normal Not done 						
Gastrointestinal system	AbnormalNormalNot done						
Others	 Abnormal Normal Not done 						

VITAL SIGNS							
Body temperature .							
	DOD PRESSURE mHg)	SITTING HEART RATE (bpm)					
Systolic	Diastolic						

Centre No. Scree	n. No. _	Randomisation No.	_ Pat. Init.	·	_
				Family name	Name

VISIT 3 – Day 2				
	Visit	t date	at	_
		D D M M	Y Y HOUR MINUTES	
	LABO	RATORY TESTS		
Collect blood sample for haematology and blood chemistry. (LOCAL LABORATORY) - Only those parameters (if any) which were abnormal at Visit 1				
Haematology tests * Clinically Significant ** Yes No				
Haemoglobin (mmol/	L)			
Haematocrit (L/L)		.		
RBC (10 ¹² /L)		.		
WBC (10 ⁹ /L)				
WBC (differential counts)	Neutrophils (%)	.		
	Eosinophils (%)	.		
	Basophils (%)	.		
	Monocytes (%)	.		
	Lymphocytes (%)	·		
Platelet (10 ⁹ /L)				
Blood Chemistry te	sts *			
Alkaline Phosphatase	e (U/L)	.		
AST (SGOT) (U/L)		.		
ALT (SGPT) (U/L)		.		
BUN/blood urea (mm	iol/L)	.		
Creatinine Kinase (U	/L)	.		
Creatinine (µmol/L)				
Gamma-GT (U/L)		·		
Sodium (mmol/L)				
Potassium (mmol/L)		.		
Glucose (mmol/L)		.		
* to be filled in as soon as results are available				
** For the out of rang	ge values, please speci	fy if the abnormality is cli	nically or not clinically signific	ant

Laboratory results need to be stored in the patient's file

Centre No. Screen. No. Randomisation No.	Pat. Init.		_
		Family name	Name

VISIT 3 – Day 2
Visit date at D D M M Y HOUR MINUTES
Pro-calcitonin (pro-ct)
as the blood sample been taken for the pro-ct analysis?
Yes No
Yes, refer to the Study Procedures Handbook for handling and storage.
No, please specify why:
Please fill in as soon as the results are available:
Pro-calcitonin (mcg/L) I_I_I.I_I

C-reactive protein (CRP), serum amyloid (SAA) and RANTES							
Has the blood sample b	been taken for the CRP, SAA and RANTES analysis?						
	Yes No						
If Yes, refer to the Study	dy Procedures Handbook for handling and storage.						
If No, please specify wh	'hy:						
Please fill in as soon as	Please fill in as soon as the results are available:						
CRP (mg/L)	III.II						
SAA (mg/L)	ll.ll						
RANTES (mcg/L)	ll.ll						

Centre No. Screen. No.	<pre> Randomisation No. </pre>	_ Pat. Init. Family name Name					
VISIT 3 – Day 2							
	Visit date	at M Y Y HOUR MINUTES					
ARTERIAL BLOOD GASES							
	Yes	Νο					
Arterial blood gas analysis performed:							
If YES: patient was under O ₂ therapy?							
If patient was under O2 therapy please	indicate:						
- how n	nany L/min: ,						
- how n	nany hours/day:	_					
If arterial blood gas analysis was perform	ned, indicate:						
pH: ,							
PaO _{2:} mmHg							
PaCO _{2:} mmHg							
SO _{2:} %							
HCO3 ^{-:} mmol/L							

COMPLIANCE					
Is patient compliant:	Yes	No			
If "No", please specify:					

Centre No. Screen. No. Randomisation No. Pat. Ini	t. _	
	Family name	Name

Visit date	
Can the subject be randomised? Procentral Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been	VISIT 3 – Day 2
TO BE FILLED ON DAY 2 Can the subject be randomised? Yes Yes If Yes, indicate randomisation number: The patient has been randomized to (indicate ONLY ONE): Pro-CT arm Standard treatment arm Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been	
TO BE FILLED ON DAY 2 Can the subject be randomised? Yes Yes If Yes, indicate randomisation number: The patient has been randomized to (indicate ONLY ONE): Pro-CT arm Standard treatment arm Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been	
 Can the subject be randomised? Yes Yes No If Yes, indicate randomisation number: The patient has been randomized to (indicate ONLY ONE): Pro-CT arm Standard treatment arm Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been 	
Yes No If Yes, indicate randomisation number: The patient has been randomized to (indicate ONLY ONE): Pro-CT arm Standard treatment arm Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been	TO BE FILLED ON DAY 2
If Yes, indicate randomisation number: • The patient has been randomized to (indicate ONLY ONE):	Can the subject be randomised?
 The patient has been randomized to (indicate ONLY ONE): Pro-CT arm Standard treatment arm Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been 	
 The patient has been randomized to (indicate ONLY ONE): Pro-CT arm Standard treatment arm Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been 	
 Pro-CT arm Standard treatment arm Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been 	If Yes, indicate randomisation number:
☐ Standard treatment arm Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been	• The patient has been randomized to (indicate ONLY ONE):
Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been	Pro-CT arm
University of Padua. Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been	Standard treatment arm
	Remember to send the 3 pro-CT samples (day 0, day 1 and day 2) to the Central Laboratory, University of Padua.
	Shipping is via courier and takes place on day 2 as soon as the last pro-CT sample has been
Refer to the Study Procedures Handbook for instructions on shipment.	Refer to the Study Procedures Handbook for instructions on shipment.

INVESTIGATOR'S STATEMENT

I confirm that the data herein is a true complete and accurate reflection of this subject participation in	۱
the study, according to the protocol procedures.	

Investigator's name:

Investigator's signature:

Date:

						L
D	D	M	M	Ϋ́	Y	

Centre No. _ Screen. No. _	Randomisation No.	Pat. Init. _	
		Family na	ame Name

VISIT 4 – At discharge and / or at day 10	
Visit date	at HOUR MINUTES
Has the patient withdrawn prematurely from the study?	☐ Yes ☐ No
If Yes, please fill in the " Investigator's statement " at the end of visit 4 and the " Study Conclusion Summary/Wihtdrawal/Drop-out Form ".	
Has the patient been discharged from the Hospital?	☐ Yes ☐ No
If Yes, please specify the date: _ _ _ _ _ _ _ _ _ _ _ _	
ADVERSE EVENTS related to antibiotic treat	ment

Did any adverse event related to antibiotic treatment occur since the last visit?	☐ Yes ☐ No
If Yes, please complete the appropriate "adverse event" page and report it immediately to the Direzione Sanitaria of the Hospital and to CROM (see Study Procedures Handbook for instructions).	

Centre No. Screen. No. Randomisation No. _	Pat.	lnit.	_
		Family name	Name

VISIT 4 – At discharge and / or at day 10

 Visit date

 at

 D
 D
 M
 M
 Y
 Y
 HOUR
 MINUTES

OCCURRING EVENTS				
PLEASE COMPLE	TE THE FOL	LOWING TABLE:		
Did the patient require <u>ventilatory support</u> since the last visit?	Yes* No	If YES, specify reason(s) for ventilatory support need:		
<u>*If YES: please add ventilatory support information in the "medication since the last visit" section on page 32.</u>		If YES, please indicate date when ventilatory support began since last visit (DD/MM/YY):		
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	Yes No	If YES, specify reason(s) for admission to ICU:		
Did the patient have any episode(s) of pulmonary embolism since the last visit?	YesNo	If YES indicate date of onset of pulmonary embolism since last visit (DD/MM/YY):		
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary edema since the last visit?	☐ Yes ☐ No	If YES, specify kind of cardiovascular event(s):		
Did the patient have any episodes of pneumonia since the last visit?	YesNo	If YES indicate date of onset of pneumonia since last visit (DD/MM/YY):		
Did the patient have <u>any other significant</u> occurring event since the last visit?	☐ Yes ☐ No	If YES, specify event(s):		
Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?				
		No 🗖 Yes* 🗖		
* If YES please fax a copy of this page to CR	OM as indic	cated in the Study Procedures Handbook.		

Centre No. Screen. No. Randomisation No.		Pat. Init.	_		
			Family name	Name	

VISIT 4 -	- At discharg	e and / or a	at day 10					
	Visit date at D M M Y Y HOUR MINUTES							
	MF		SINCE T	HE LAST	VISIT			
	MEDICATION SINCE THE LAST VISIT Has any medication been instituted, stopped and/or Image: No Image: Yes** modified (dose change) since the last visit?* Image: No Image: Yes**							
** If YES ple	* please remember to include information on any change to antibiotic treatment ** If YES please complete the following details, including only medications instituted, stopped and/or modified (dose change) since the last visit.							
Trade		Poso	logy	Route	Admini: (DD/M			
name	Indication	Dose/day	Unit	_	Start date	End date (or ONGOING)		

MEDICATION AT HOSPITAL DISCHARGE

When the patient is discharged: please record in the following table <u>all</u> medication prescribed to the patient at the time of hospital discharge, including therapy for stable COPD and any other therapy the patient will take after leaving the hospital

Trade name	Indication	Posology		Route	Administration (DD/MM/YY)	
		Dose/day	Unit		Start date	End date (or ONGOING)

Centre No. _	_ Screen. No. _	 Randomisation No.	 Pat. Init.		_
				Family name	Name

VISIT 4 – At discharge and / or at day 10								
		Visit date at D D M Y Y HOUR MINUTES						
PHYSICAL EXAMINATION								
Physical examination	Status	Comments: if "abnormal" specify:						
Cardiovascular system	 Abnormal Normal Not done 							
Respiratory system (except COPD)	 Abnormal Normal Not done 							
Lymphatic system	 Abnormal Normal Not done 							
Neurological-locomotor system	 Abnormal Normal Not done 							
Skin	 Abnormal Normal Not done 							
Endocrine	 Abnormal Normal Not done 							
Ear-nose-throat system	AbnormalNormalNot done							
Ophtalmological system	 Abnormal Normal Not done 							
Gastrointestinal system	AbnormalNormalNot done							
Others	 Abnormal Normal Not done 							

VITAL SIGNS							
Body temperature .							
	DOD PRESSURE mHg)	SITTING HEART RATE (bpm)					
Systolic	Diastolic						

VISIT 4 – At discharge and / or at day 10						
	Vis	sit date	at			
		D D M M Y	Y Y HOUR MINUTES			
	LABC	DRATORY TESTS				
	-	for haematology and blood	d chemistry			
	(LOC	CAL LABORATORY)				
Haematology tests * Clinically Significant **						
			Yes No			
Haemoglobin (mmol/	L)					
Haematocrit (L/L)						
RBC $(10^{12}/L)$						
WBC (10 ⁹ /L)	Noutrophile (9/)					
WBC (differential counts)						
	Eosinophils (%) Basophils (%)					
	Monocytes (%)					
	Lymphocytes (%)					
Platelet (10 ⁹ /L)	Lymphocytes (76)					
		II				
Blood Chemistry te	sts *					
Alkaline Phosphatas	e (U/L)	.				
AST (SGOT) (U/L)						
ALT (SGPT) (U/L)						
BUN/blood urea (mm	iol/L)	.				
Creatinine Kinase (U	/L)					
Creatinine (µmol/L)						
Gamma-GT (U/L)						
Sodium (mmol/L)		·				
Potassium (mmol/L)		.				
Glucose (mmol/L)		.				
* to be filled in as soon as results are available						
** For the out of range values, please specify if the abnormality is clinically or not clinically significant						

Centre No. |____ Screen. No. |____ Randomisation No. |____ Pat. Init. |____ |__ |___

Laboratory results need to be stored in the patient's file

Centre No. _ Se	creen. No. _	Randomisation No. _	Pat. Init.]]]	_
			F	Family name	Name

VISIT 4 – At discharge and / or at day 10							
Visit date at D D M M Y HOUR MINUTES							
Pro-calcitonin (pro-ct)							
Has the blood sample been taken for the pro-ct analysis?							
Yes No							
If Yes, refer to the Study Procedures Handbook for handling and storage.							
If No, please specify why:							
Please fill in as soon as the results are available:							
Pro-calcitonin (mcg/L) I_I_I_I.I_I							

C-reactive protein (CRP), serum amyloid (SAA) and RANTES						
Has the blood sample	e been taken for the CRP, SAA and RANTES analysis?					
	Yes No					
If Yes, refer to the Study Procedures Handbook for handling and storage.						
If No, please specify	why:					
Please fill in as soon	as the results are available:					
CRP (mg/L)	II.II					
SAA (mg/L)						
RANTES (mcg/L)						

PTX-3 and IL1 decoy							
Has the blood sample been taken for the P	TX-3 and IL1 decoy analysis?						
Yes No							
If Yes, refer to the Study Procedures Hand	If Yes, refer to the Study Procedures Handbook for handling and storage.						
If No, please specify why:							
Please fill in as soon as the results are available:							
PTX-3 (ng/ml) II	l.ll						
IL1 decoy (ng/ml) II	l.ll						

Centre No. _	Screen. No.	_	Randomisation No.		Pat. Init.				
						Family name		Name	

VISIT 4 – At discharge and / or at day 10

 Visit date

 at

 D
 D
 M
 M
 Y
 Y
 HOUR
 MINUTES

QUESTIONNAIRES FOR RESPIRATORY SYMPTOMS/QUALITY OF LIFE

SF36 score:

BDI score:

TDI score:

total I____I___I total I____I___I total I____I___I

CCIQ Score: total I ___ I ___ I

PHARMACOECONOMIC QUESTIONNAIRE

Please remind to fill in the pharmacoeconomic questionnaire and enclose it in the plastic envelope.

	SPIROMETRY							
•	SPIROMETRY: from 3 acceptable spirometric manoeuvres record the highest FEV ₁ and FVC, irrespective of the manoeuvre (curve) they come from.							
	date at HOUR	II MINUTES						
	FVC	, litre						
	FEV1	, litre						
	FEV1 predicted normal value	, litre [ERS standards]						
	FEV1 (% predicted normal value)	% of predicted value						
	FEV₁/FVC (%)	, %						

Centre No. Scree	n. No. _	Randomisation No.	_ Pat. Init.	·	_
				Family name	Name

VISIT 4 – At discharge	and / or at	day 10						
Visit date at D M M Y HOUR MINUTES								
	MICR	OBIOLOO	jΥ					
		Yes	No					
Sputum collection performed:								
If YES, specify volume of sputu	m collected:	, ml						
If NO, specify why								
Results from local laboratory:								
Bacteriology:								
Identified microorganism #1:			CFU/ml:					
Identified microorganism #2:								
Identified microorganism #3:	Identified microorganism #3: CFU/mI:							
Serology for Intracellular pat	hogens:							
Has the sample for serology for	· intracellular pa	thogens bee	n obtained? Yes 📮 No 📮					
If Yes, please complete below	v:							
Was serology positive for Myco	plasma pneun	n oniae ? Yes	No D					
If YES, indicate: IgM	: ,							
IgG	: ,							
Was serology positive for Chla	mydia? Yes 🖵	No 🗖						
If YES, indicate: IgM	: ,	1						
, i i i i i i i i i i i i i i i i i i i	: , ,							
Was serology positive for Legi	onella pneumo	phila? Yes 🕻						
If YES, indicate:								
	POSITIVE	NEGA	ATIVE					
Legionella pneumophila IgM			נ					
Legionella pneumophila IgG			נ					

Centre No. Screen. No. Randomisati	ion No. Pat. Init. _	
	Family name Name	

VISIT 4 – At discharge and / or at day 10							
Visit date	 M Y Y	at HOUR	_ MINUTES				
MICROBIOLOGY (conti	nued)						
Has the sample for respiratory viruses RT-PCR analysis been	n collected a	ind stored at -	–80°C?				
		Yes 🗖	No 🗖				
If YES, specify volume stored at -80°C for RT-PCR: ,	ml						
Please remember to label the sample with the patient's ID number and store it at -80°C, as described in the Study Procedures Handbook.							
Has the sample for inflammatory cell counts been collected?	Yes 🗖	No 🗖					
Were the slides prepared and stored at -20°C?	Yes 🗖	No 🗖					
If YES: how many slides were prepared?							

Centre No. Screen. No.	Randomisation No.	Pat. Init.		
		Famil	y name	Name

VISIT 4 – At discharge and / or at day 10					
Visit da		 M Y Y	at		
ARTERIAL	BLOOD GAS	DE9			
	Yes	No			
Arterial blood gas analysis performed:					
If YES: patient was under O ₂ therapy?					
If patient was under O2 therapy please indicat	e:				
- how many L/	min: ,				
- how many ho	ours/day:	_			
If arterial blood gas analysis was performed, ind pH: , PaO _{2:} mmHg PaCO ₂ : mmHg SO ₂ : % HCO ₃ ^{-:} mmol/L	licate:				
COM	PLIANCE				

	CON	IPLIANCE		
	Yes	No		
Is patient compliant:				
If "No", please specify:				

INVESTIGATOR'S STATEMENT

I confirm that the data herein is a true complete and accurate reflection of this subject participation in the study, according to the protocol procedures.

Investigator's name:	
Investigator's signatu	re:
Date:	 D D M M Y Y

Centre No. Screen. No. Randomisation No. Pat.	nit. Family name Name
VISIT 5 – Day 30	
Visit date	at HOUR MINUTES
Has the patient withdrawn prematurely from the study?	C Yes
	No No
If Yes, please fill in the "Investigator's statement" at the end of visit 5 and the "Study Conclusion Summary/Wihtdrawal/Drop-out Form".	
Has the patient been discharged from the Hospital?*	C Yes
	No No
If Yes, please specify the date:	
* please complete only if patient had not been discharged by Visit 4	

Centre No. _	_ Screen. No.	Randomisation No.	_ Pat. Init	.	_
				Family name	Name

VISIT 5 – Day 30

Visit date					_	_	at	
	D	D	М	М	Y	Y	HOUR	MINUTES

OCCURRING EVENTS						
PLEASE COMPLETE THE FOLLOWING TABLE:						
Did the patient have at least one COPD exacerbation* since the last visit? (*defined as: - worsening of respiratory symptoms requiring treatment with antibiotics and/or systemic steroids since last visit - and/or new hospital admission for a COPD exacerbation since last visit - and/or need for ventilatory support or intubation, or death since last visit)	☐ Yes ☐ No	If YES indicate date(s) of onset of new COPD exacerbation(s) since last visit (DD/MM/YY): 1) 2) 3)				
Was the patient hospitalized <u>for a new</u> <u>COPD exacerbation</u> since the last visit?	☐ Yes ☐ No	If YES indicate date(s) of new hospitalization(s) for COPD exacerbation(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from				
Was the patient hospitalized <u>for any other</u> <u>cause</u> (except COPD) since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for hospitalization(s): If YES, please indicate date(s) of new hospitalization(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from to to 2) from to to				
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for admission(s) to ICU:				

Centre No. _	Screen. No. _	Randomisation No.	Pat. Init.		
			F	amily name	Name

VISIT 5 – Day 30

Visit date					_	_	at	
	D	D	М	Μ	Y	Y	HOUR MINU	JTES

OCCURRING EVENTS (continued)			
	YesNo	If YES indicate date(s) of onset of episode(s) of pulmonary embolism since last visit (DD/MM/YY):	
Did the patient have any episode(s) of pulmonary embolism since the last visit?		1)	
		2) _	
	☐ Yes	If YES, specify kind of cardiovascular	
	🖵 No	event(s):	
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary		If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY):	
edema since the last visit?		1)	
		2)	
	☐ Yes	3) If YES indicate date(s) of onset of pneumonia	
		since last visit (DD/MM/YY):	
Did the patient have any episodes of	D No	1)	
pneumonia since the last visit?		2)	
		3)	
	Yes	If YES, specify event(s):	
	🖵 No		
Did the patient have any other significant		If YES indicate date(s) of onset of new	
<u>occurring event</u> since the last visit?		event(s) since last visit (DD/MM/YY):	
		1)	
		2)	
		3)	

Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?

No 🖸 Yes* 🗖

* If YES please fax a copy of pages 41-42 to CROM as indicated in the Study Procedures Handbook.

Centre No. Screen. No. Randomisation No. Pat. Init. _								
VISIT 5 -	- Day 30							
		Visi	t date □	 D M M Y	at ⁄ Y F	 HOUR MINUTES		
	ME	DICATION	SINCE T	HE LAST	VISIT			
	edication been in lose change) sind				🗖 No	C Yes		
	se complete the fo dified (dose chang			nly medicatio	<i>ก</i> ร instituted, ร	stopped		
					Administration			
Trade		Poso	Posology Ro		(DD/M	(DD/MM/YY)		
name	Indication	Dose/day	Unit		Start date	End date (or ONGOING)		

Г

Centre No. Screen. No. Randomisation No.	Pat. Init. _	
	Family na	ame Name

VISIT 5 – Day 30

		Visit date at D D M Y Y HOUR MINUTES
	PHY	SICAL EXAMINATION
Physical examination	Status	Comments: if "abnormal" specify:
Cardiovascular system	AbnormalNormalNot done	
Respiratory system (except COPD)	AbnormalNormalNot done	
Lymphatic system	 Abnormal Normal Not done 	
Neurological-locomotor system	AbnormalNormalNot done	
Skin	AbnormalNormalNot done	
Endocrine	AbnormalNormalNot done	
Ear-nose-throat system	AbnormalNormalNot done	
Ophtalmological system	 Abnormal Normal Not done 	
Gastrointestinal system	AbnormalNormalNot done	
Others	AbnormalNormalNot done	

VITAL SIGNS				
SITTING BLOOD PRESSURE (mmHg)		SITTING HEART RATE (bpm)		
Systolic	Diastolic			

Centre No. _ Screen. No. _ Randomisation No.		Pat. Init. _		_
		Fa	mily name	Name

VISIT 5 – Day 30				
Visit d	date at D M M Y HOUR MINUTES			
Pro-calc	lcitonin (pro-ct)			
Has the blood sample been taken for the pro-c	ct analysis?			
Yes	No			
If Yes, refer to the Study Procedures Handbook for handling and storage.				
If No, please specify why:				
Please fill in as soon as the results are available:				
Pro-calcitonin (mcg/L) I_I_I.	l.ll			

C-reactive protein (CRP), serum amyloid (SAA) and RANTES			
Has the blood sample	been taken for the CRP, SAA and RANTES analysis?		
	Yes No		
If Yes, refer to the Study Procedures Handbook for handling and storage.			
If No, please specify w	hy:		
Please fill in as soon as the results are available:			
CRP (mg/L)	ll.ll		
SAA (mg/L)	lll		
RANTES (mcg/L)			

Centre No. Screen. No.		Randomisation No.	Pat. Init.		
			F	amily name	Name

VISIT 5 - Day 30

 Visit date

 at

 D
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 M
 M
 Y
 Y
 HOUR
 MINUTES

QUESTIONNAIRES FOR RESPIRATORY SYMPTOMS/QUALITY OF LIFE

SF36 score:

BDI score:

TDI score:

total I___I___I total I___I___I total I___I___I

CCIQ Score: total I___I___I

PHARMACOECONOMIC QUESTIONNAIRE

Please remind to fill in the pharmacoeconomic questionnaire and enclose it in the plastic envelope.

	SPIROMETRY				
•	SPIROMETRY: from 3 acceptable spirometric manoeuvres record the highest FEV ₁ and FVC, irrespective of the manoeuvre (curve) they come from.				
	date at				
	FVC	, litre			
FEV1		, litre			
FEV1 predicted normal value		, litre [ERS standards]			
FEV1 (% predicted normal value)		% of predicted value			
	FEV₁/FVC (%)	, %			

Centre No. _ Screen. No. _	<u> </u> R	andomisation No.	Pat. Init.		_
				Family name	Name

VISIT 5 – Day 30			
	Visit date _	_ at	
	MICROBIOLO		
	WICKOBIOLC		
	Yes	No	
Sputum collection performed:			
If YES, specify volume of sputum	collected: , ml		
If NO, specify why			
Results from local laboratory:			
Bacteriology: Identified microorganism #1:			
Identified microorganism #2:			
Identified microorganism #3:			
Serology for Intracellular patho	gens:		
Has the sample for serology for in	tracellular pathogens be	en obtained? Yes 📮 No 📮	
If Yes, please complete below:			
Was serology positive for Mycopl	asma pneumoniae ? Ye	es 🖬 No 🗖	
If YES, indicate: IgM: _	,		
-			
Was serology positive for <u>Chlamy</u>	r <u>dia</u> ? Yes 📮 No 🗖		
If YES, indicate: IgM: _	,		
	,		
Was serology positive for Legionella pneumophila? Yes D No D			
If YES, indicate:			
	POSITIVE NEO	GATIVE	
Legionella pneumophila IgM			
Legionella pneumophila IgG			

		Family name	Name
VISIT 5 – Day 30			
Visit date □ □ M	 M Y Y	at HOUR	_ MINUTES
MICROBIOLOGY (contin	nued)		
Has the sample for respiratory viruses RT-PCR analysis been	n collected a	and stored at -	-80°C?
		Yes 🗖	No 🗖
If YES , specify volume stored at -80°C for RT-PCR: ,	ml		
Please remember to label the sample with the patient's ID numb	per and store	e it at -80°C, a	as described
in the Study Procedures Handbook.			
Has the sample for inflammatory cell counts been collected?	Yes 🗖	No 🗖	
Were the slides prepared and stored at -20°C?	Yes 🗖	No 🗖	
If YES: how many slides were prepared?			

Centre No. Scree	n. No. _	Randomisation No.	_ Pat. Init.	·	_
				Family name	Name

VISIT 5 – Day 30							
	Visit date _						
	D	D M	M Y Y	HOUR MINUTES			
ARTERIAL BLOOD GASES							
	,	Yes	Νο				
Arterial blood gas analysis performed:							
If YES: patient was under O ₂ therapy?							
If patient was under O2 therapy pleas	e indicate:						
- how	many L/min:	,					
- how	many hours/day:	_	_				
If arterial blood gas analysis was perfor	med, indicate:						
pH: ,							
PaO _{2:} mmHg							
PaCO _{2:} mmHg							
SO _{2:} %							
HCO3 ^{-:} mmol/L							

INVESTIGATOR'S STATEMENT

I confirm that the data herein is a true complete and accurate reflection of this subject participation in the study, according to the protocol procedures.

Investigator's name:	
Investigator's signature:	
Date:	 D D M M Y Y

Centre No. _ Screen. No. _	Randomisation No. _	Pat. Init.		
		Famil	y name	Name

	CLINICAL STATUS				
Collect information on	Status	Comments: if "abnormal" specify:			
1. Cardiovascular system	 Abnormal Normal Not done 				
2. Respiratory system (except COPD)	 Abnormal Normal Not done 				
3. Lymphatic system	 Abnormal Normal Not done 				
4. Neurological- locomotor system	 Abnormal Normal Not done 				
5. Skin	 Abnormal Normal Not done 				
6. Endocrine	 Abnormal Normal Not done 				
7. Ear-nose-throat system	 Abnormal Normal Not done 				
8. Ophtalmological system	 Abnormal Normal Not done 				
9. Gastrointestinal system	 Abnormal Normal Not done 				
10. Others	 Abnormal Normal Not done 				

Centre No. Screen. No.	Randomisation No. Pat. Init.		
		Family name	Name

 Visit date

 at

 D
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 Y
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 HOUR
 MINUTES

OCCURRING EVENTS					
PLEASE COMPLE	TE THE FOL	LOWING TABLE:			
Did the patient have at least one COPD exacerbation* since the last visit? (*defined as: - worsening of respiratory symptoms requiring treatment with antibiotics and/or systemic steroids since last visit - and/or new hospital admission for a COPD exacerbation since last visit - and/or need for ventilatory support or intubation, or death since last visit)	☐ Yes ☐ No	If YES indicate date(s) of onset of new COPD exacerbation(s) since last visit (DD/MM/YY): 1) 2) 3)			
Was the patient hospitalized <u>for a new</u> <u>COPD exacerbation</u> since the last visit?	☐ Yes ☐ No	If YES indicate date(s) of new hospitalization(s) for COPD exacerbation(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from			
Was the patient hospitalized <u>for any other</u> <u>cause</u> (except COPD) since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for hospitalization(s): If YES, please indicate date(s) of new hospitalization(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from to to 2) from to to			
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for admission(s) to ICU: If YES, please indicate date(s) of admission(s) to ICU since last visit (from DD/MM/YY to DD/MM/YY): 1) from to 2) from to to			

Centre No. _ Scre	een. No. _	Randomisation No. _	Pat. In	it.	_
				Family name	Name

 Visit date

 at

OCCURRING EVENTS (continued)					
Did the patient have any episode(s) of <u>pulmonary embolism</u> since the last visit?	☐ Yes ☐ No	If YES indicate date(s) of onset of episode(s) of pulmonary embolism since last visit (DD/MM/YY): 1) 2)			
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary edema since the last visit?	☐ Yes ☐ No	3)			
Did the patient have any episodes of pneumonia since the last visit?	Yes No	3)			
Did the patient have <u>any other significant</u> occurring event since the last visit?	☐ Yes ☐ No	If YES, specify event(s): If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY): 1) 2) 3)			

Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?

No 🖵 Yes* 🗖

* If YES please fax a copy of pages 51-52 to CROM as indicated in the Study Procedures Handbook.

Centre No. Screen. N	o.	Randomisation No.	 Pat. Init.	_	_
			Fam	ily name	Name

TELEPHONE CONTACT – Day 60								
Visit date _ _ I at I D M M Y HOUR MINUTES								
	MEDICATION SINCE THE LAST VISIT							
Has any medication been instituted, stopped and/or INO Yes								
	e complete the fo ified (dose chang			ly medication	es instituted, s	topped		
					Adminis	stration		
Trade		Poso	ogy	Route	(DD/MM/YY)			
name	Indication	Dose/day	Unit	-	Start date	End date (or ONGOING)		

PHARMACOECONOMIC QUESTIONNAIRE

Please remind to fill in the pharmacoeconomic questionnaire and enclose it in the plastic envelope

INVESTIGATOR'S S	STATEMENT
-------------------------	-----------

I con	firm that the data herein i	is a true complete and accurate reflection of this subject participation in
the s	tudy, according to the pro	ptocol procedures.
	Investigator's name:	
	Investigator's signature:	
	Date:	

Centre No. Screen. No. _ Randomisation No. _ Pat. In	it. Family name Name
VISIT 6 – Day 90	
Visit date	at HOUR MINUTES
Has the patient withdrawn prematurely from the study?	🖵 Yes
	□ No
If Yes, please fill in the "Investigator's statement" at the end of visit 6 and the "Study Conclusion Summary/Wihtdrawal/Drop-out Form" .	

Centre No. _	_ Screen. No.	Randomisation No.	_ Pat. Init	.	_
				Family name	Name

VISIT 6 – Day 90

Visit date							at	
	D	D	М	М	Y	Y	HOUR	MINUTES

OCCURRING EVENTS						
PLEASE COMPLE	PLEASE COMPLETE THE FOLLOWING TABLE:					
Did the patient have at least one COPD exacerbation* since the last visit? (*defined as: - worsening of respiratory symptoms requiring treatment with antibiotics and/or systemic steroids since last visit - and/or new hospital admission for a COPD exacerbation since last visit - and/or need for ventilatory support or intubation, or death since last visit)	☐ Yes ☐ No	If YES indicate date(s) of onset of new COPD exacerbation(s) since last visit (DD/MM/YY): 1) 2) 3)				
Was the patient hospitalized <u>for a new</u> <u>COPD exacerbation</u> since the last visit?	☐ Yes ☐ No	If YES indicate date(s) of new hospitalization(s) for COPD exacerbation(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from				
Was the patient hospitalized <u>for any other</u> <u>cause</u> (except COPD) since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for hospitalization(s): If YES, please indicate date(s) of new hospitalization(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from to to 2) from to to				
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for admission(s) to ICU:				

Centre No. _ S	Screen. No.	Randomisation No. _	_ Pat. Ini	L.	_
				Family name	Name

VISIT 6 – Day 90

Visit date					.		at
	D	D	М	М	Y	Y	HOUR MINUTES

OCCURRING	EVENTS	6 (continued)
	YesNo	If YES indicate date(s) of onset of episode(s) of pulmonary embolism since last visit (DD/MM/YY):
Did the patient have any episode(s) of <u>pulmonary embolism</u> since the last visit?		1) 2)
		2) 3)
	Yes No	If YES, specify kind of cardiovascular event(s):
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary		If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY):
edema since the last visit?		1) 2)
	Yes No	3) If YES indicate date(s) of onset of pneumonia since last visit (DD/MM/YY):
Did the patient have any episodes of pneumonia since the last visit?		1)
		2) 3)
	□ Yes □ No	If YES, specify event(s):
Did the patient have <u>any other significant</u> occurring event since the last visit?		If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY): 1) 2) 3)

Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?

No 🖸 Yes* 🗖

* If YES please fax a copy of pages 55-56 to CROM as indicated in the Study Procedures Handbook.

Centre No.	Screen. No.	Randomisation No.	Pat. Init.	_	
			Fam	nily name	Name

VISIT 6 - Day 90 Visit date |___|__|__|__|___ ___ at |____| |___| **MEDICATION SINCE THE LAST VISIT** Has any medication been instituted, stopped and/or **No V**es modified (dose change) since the last visit? If YES please complete the following details, including only medications instituted, stopped and/or modified (dose change) since the last visit. Administration Trade Posology Route (DD/MM/YY) Indication name Unit Start date End date Dose/day (or ONGOING)

Centre No.	Screen. No.	 Randomisation No.	 Pat. Init.		_
				Family name	Name

VISIT 6 – Day 90

		Visit date at D M M Y Y HOUR MINUTES			
PHYSICAL EXAMINATION					
Physical examination	Status	Comments: if "abnormal" specify:			
Cardiovascular system	 Abnormal Normal Not done 				
Respiratory system (except COPD)	 Abnormal Normal Not done 				
Lymphatic system	 Abnormal Normal Not done 				
Neurological-locomotor system	 Abnormal Normal Not done 				
Skin	 Abnormal Normal Not done 				
Endocrine	 Abnormal Normal Not done 				
Ear-nose-throat system	 Abnormal Normal Not done 				
Ophtalmological system	 Abnormal Normal Not done 				
Gastrointestinal system	 Abnormal Normal Not done 				
Others	 Abnormal Normal Not done 				

VITAL SIGNS			
	D OD PRESSURE nHg <i>)</i>	SITTING HEART RATE (bpm)	
Systolic	Diastolic		

VISIT 6 – Day 9	0		
	Visi	t date	at
		RATORY TESTS	- h - m - la tra
		or haematology and blood AL LABORATORY	cnemistry.
Haematology tests	*		Clinically Significant **
Haemoglobin (mmol/	1)		Yes No
Haematocrit (L/L)	L)		
RBC (10 ¹² /L)			
WBC (10 ⁹ /L)			
WBC (differential counts)	Neutrophils (%)		
	Eosinophils (%)		
	Basophils (%)		
	Monocytes (%)		
	Lymphocytes (%)		
Platelet (10 ⁹ /L)			
Blood Chemistry te	sts *		
Alkaline Phosphatase	e (U/L)		
AST (SGOT) (U/L)			
ALT (SGPT) (U/L)			
BUN/blood urea (mm	nol/L)	.	
Creatinine Kinase (U	/L)	·	
Creatinine (µmol/L)		·	
Gamma-GT (U/L)		.	
Sodium (mmol/L)		.	
Potassium (mmol/L)		.	
Glucose (mmol/L)		.	
* to be filled in as so	oon as results are avai	lable	
			nically or not clinically signific
	je valace, picase spec		iouny of not on nouny signino

Laboratory results need to be stored in the patient's file

Centre No. Screen. No. _	Randomisation No.	Pat. Init. _	
		Family name	Name

VISIT 6 – Day 90				
	Visit o	late	_	at HOUR MINUTES
	Dre cel			
	Pro-cal	citonin (p	pro-ct)	
Has the blood sample been take	n for the pro-c	t analysis?		
	Yes	No		
If Yes, refer to the Study Procedu	ures Handboo	k for handlir	ng and storage.	
If No, please specify why:				
Please fill in as soon as the resul	ts are availab	le:		
Pro-calcitonin (mcg/L)	II.	III		

C-reactiv	e protein (CRP), serum amyloid (SAA) and RANTES
Has the blood sample	been taken for the CRP, SAA and RANTES analysis?
	Yes No
If Yes, refer to the Stu	dy Procedures Handbook for handling and storage.
If No, please specify w	/hy:
	is the results are available:
CRP (mg/L)	
SAA (mg/L)	
RANTES (mcg/L)	ll.ll.ll

	PTX-3 ar	nd IL1 decoy
Has the blood sample been taken	for the PTX-3	and IL1 decoy analysis?
	Yes	No
If Yes, refer to the Study Procedure	es Handbook	for handling and storage.
If No, please specify why:		
Please fill in as soon as the results	are available	:
PTX-3 (ng/ml) II	II.I	II
IL1 decoy (ng/ml) II	II.I	II

Centre No. Screen. No. _ Ran	domisation No. _ Pat. Init.]	
	Family r	name Name	

VISIT 6 - Day 90

 Visit date

 at

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 HOUR
 MINUTES

QUESTIONNAIRES FOR RESPIRATORY SYMPTOMS/QUALITY OF LIFE

SF36 score:

BDI score:

TDI score:

total I___I__I total I___I__I total I___I__I

CCIQ Score: total I___I___I

PHARMACOECONOMIC QUESTIONNAIRE

Please remind to fill in the pharmacoeconomic questionnaire and enclose it in the plastic envelope.

	SPIROMETRY			
•	SPIROMETRY: from 3 acceptable spirometric manoeuvres record the highest FEV ₁ and FVC, irrespective of the manoeuvre (curve) they come from.			
	date at HOUR	 MINUTES		
	FVC	, litre		
	FEV1	, litre		
	FEV ₁ predicted normal value	, litre [ERS standards]		
Γ	FEV1 (% predicted normal value)	% of predicted value		
	FEV₁/FVC (%)	, %		

Centre No. Screen. No. Randomisation No. Pat. Init.		_
F	amily name	Name

VISIT 6 – Day 90						
Visit da	nte					
		1 Y Y	HOUR MINUTES			
ARTERIAL	ARTERIAL BLOOD GASES					
	Yes	No				
		_				
Arterial blood gas analysis performed:						
If YES: patient was under O ₂ therapy?						
If patient was under O2 therapy please indicat	e:					
- how many L/	min: ,					
- how many ho	ours/day:					
If arterial blood gas analysis was performed, ind	licate:					
рН: ,						
PaO _{2:} mmHg						
PaCO _{2:} mmHg						
SO _{2:} %						
HCO3 ^{-:} mmol/L						

INVESTIGATOR'S STATEMENT

I confirm that the data herein is a true complete and accurate reflection of this subject participation in the study, according to the protocol procedures.

Invest	igator's name:	
Invest	igator's signature:	
Date:		

Centre No. _ Screen. No. _	Randomisation No.	Pat. Init.	_
		Family name	Name

 Visit date

 at

 D
 D
 M
 Y
 Y
 HOUR
 MINUTES

CLINICAL STATUS			
Collect information on	Status	Comments: if "abnormal" specify:	
1. Cardiovascular system	 Abnormal Normal Not done 		
2. Respiratory system (except COPD)	 Abnormal Normal Not done 		
3. Lymphatic system	 Abnormal Normal Not done 		
4. Neurological- locomotor system	 Abnormal Normal Not done 		
5. Skin	 Abnormal Normal Not done 		
6. Endocrine	 Abnormal Normal Not done 		
7. Ear-nose-throat system	 Abnormal Normal Not done 		
8. Ophtalmological system	 Abnormal Normal Not done 		
9. Gastrointestinal system	 Abnormal Normal Not done 		
10. Others	 Abnormal Normal Not done 		

Centre No. Screen. No. Randomisation No.). _	Pat. Init.	_
		Family na	me Name

 Visit date

 at

 D
 D
 M
 M
 Y
 HOUR
 MINUTES

OCCURRING EVENTS				
PLEASE COMPLETE THE FOLLOWING TABLE:				
Did the patient have at least one COPD exacerbation* since the last visit? (*defined as: - worsening of respiratory symptoms requiring treatment with antibiotics and/or systemic steroids since last visit - and/or new hospital admission for a COPD exacerbation since last visit - and/or need for ventilatory support or intubation, or death since last visit) Was the patient hospitalized for a new COPD exacerbation since the last visit?	 Yes No Yes No 	If YES indicate date(s) of onset of new COPD exacerbation(s) since last visit (DD/MM/YY): 1) 2) 3) 3) 4 3) 4 4 5 5 6 7 7 8 9 10 11 12 13 14 15 15 16 17 18 19 11 11 12 12 13 14 15 15 16 17 18 19 10 10 11 12 13 14 15 16 17 18 19 10 </td		
Was the patient hospitalized <u>for any other</u> <u>cause</u> (except COPD) since the last visit?	Yes No	If YES, specify reason(s) for hospitalization(s): If YES, please indicate date(s) of new hospitalization(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from to to 2) from to to		
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for admission(s) to ICU:		

Centre No. _ Screen. No. _ Randomisa	ion No. Pat. Init. _	
	Family name Name	

 Visit date

 at

OCCURRING EVENTS (continued)				
Did the patient have any episode(s) of <u>pulmonary embolism</u> since the last visit?	☐ Yes ☐ No	If YES indicate date(s) of onset of episode(s) of pulmonary embolism since last visit (DD/MM/YY): 1) 2) 3)		
	Yes No	If YES, specify kind of cardiovascular event(s):		
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary edema since the last visit?		If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY): 1) 2) 3)		
Did the patient have any episodes of <u>pneumonia</u> since the last visit?	☐ Yes ☐ No	If YES indicate date(s) of onset of pneumonia since last visit (DD/MM/YY): 1) 2) 3)		
Did the patient have <u>any other significant</u> occurring event since the last visit?	☐ Yes ☐ No	If YES, specify event(s):		

Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?

No 🖸 Yes* 🗖

* If YES please fax a copy of pages 64-65 to CROM as indicated in the Study Procedures Handbook.

Centre No. Screen. No. Randomisation No. Pat. Init.		
	Family name	Name

MEDICATION SINCE THE LAST VISIT

TELEPHONE CONTACT – Day 120

Visit date |___|__|__|__|__|

Ves

MINUTES

HOUR

at |

Has any medication been instituted, stopped and/or modified (dose change) since the last visit?

If YES please complete the following details, including only medications **instituted**, **stopped and/or modified** (dose change) since the last visit.

Trade name Indication		Poso	Posology		Administration (DD/MM/YY)	
		Dose/day	Unit		Start date	End date (or ONGOING)

PHARMACOECONOMIC QUESTIONNAIRE

Please remind to fill in the pharmacoeconomic questionnaire and enclose it in the plastic envelope.

INVESTIGATOR'S STATEMENT

I confirm that the data herein i	s a true complete and accurate reflection of this subject participation in
the study, according to the pro	ptocol procedures.
Investigator's name:	
Investigator's signature:	
Date:	

Centre No. _ Screen. No. _	Randomisation No. _	Pat. Init.		
		Famil	y name	Name

 Visit date

 at

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 HOUR
 MINUTES

CLINICAL STATUS			
Collect information on	Status	Comments: if "abnormal" specify:	
1. Cardiovascular system	 Abnormal Normal Not done 		
2. Respiratory system (except COPD)	 Abnormal Normal Not done 		
3. Lymphatic system	 Abnormal Normal Not done 		
4. Neurological- locomotor system	 Abnormal Normal Not done 		
5. Skin	 Abnormal Normal Not done 		
6. Endocrine	 Abnormal Normal Not done 		
7. Ear-nose-throat system	 Abnormal Normal Not done 		
8. Ophtalmological system	 Abnormal Normal Not done 		
9. Gastrointestinal system	 Abnormal Normal Not done 		
10. Others	 Abnormal Normal Not done 		

Centre No. Screen. No. Randomisation No. Pat. Init.		_
F	amily name	Name

 Visit date

 at

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 HOUR
 MINUTES

OCCURRING EVENTS				
PLEASE COMPLE	TE THE FOL	LOWING TABLE:		
Did the patient have at least one COPD exacerbation* since the last visit? (*defined as: - worsening of respiratory symptoms requiring treatment with antibiotics and/or systemic steroids since last visit - and/or new hospital admission for a COPD exacerbation since last visit - and/or need for ventilatory support or intubation, or death since last visit)	Yes No	If YES indicate date(s) of onset of new COPD exacerbation(s) since last visit (DD/MM/YY): 1) 2) 3)		
Was the patient hospitalized <u>for a new</u> <u>COPD exacerbation</u> since the last visit?	YesNo	If YES indicate date(s) of new hospitalization(s) for COPD exacerbation(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from		
Was the patient hospitalized <u>for any other</u> <u>cause</u> (except COPD) since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for hospitalization(s): If YES, please indicate date(s) of new hospitalization(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from to to 2) from to to		
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for admission(s) to ICU:		

Centre No. _	Screen. No. _ _	_ Randomisation No.		Pat. Init.			
					Family name	Name	э

TELEPHONE CONTACT – Day 150

 Visit date

 at

OCCURRING EVENTS (continued)						
Did the patient have any episode(s) of <u>pulmonary embolism</u> since the last visit?	YesNo	If YES indicate date(s) of onset of episode(s) of pulmonary embolism since last visit (DD/MM/YY): 1) 2)				
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary edema since the last visit?	☐ Yes ☐ No	3) If YES, specify kind of cardiovascular event(s): If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY): 1) 2) 3)				
Did the patient have any episodes of <u>pneumonia</u> since the last visit?	☐ Yes ☐ No	If YES indicate date(s) of onset of pneumonia since last visit (DD/MM/YY): 1) 2) 3)				
Did the patient have <u>any other significant</u> occurring event since the last visit?	☐ Yes ☐ No	If YES, specify event(s): If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY): 1) 2) 3)				

Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?

No 🖵 Yes* 🗖

* If YES please fax a copy of pages 68-69 to CROM as indicated in the Study Procedures Handbook.

Centre No. Screen. No. Randomisation No. Pat. Init.									
TELEPH	TELEPHONE CONTACT – Day 150								
	Visit date at D M M Y HOUR MINUTES								
	MEDICATION SINCE THE LAST VISIT								
	edication been in lose change) sind				🗖 No	C Yes			
	If YES please complete the following details, including only medications instituted, stopped and/or modified (dose change) since the last visit.								
Trade		Poso	logy	Route	Administration (DD/MM/YY)				
name	Indication	Dose/day	Unit		Start date	End date (or ONGOING)			
	1								

PHARMACOECONOMIC QUESTIONNAIRE

Please remind to fill in the pharmacoeconomic questionnaire and enclose it in the plastic envelope.

INVESTIGATOR'S STATEMENT	
--------------------------	--

I confirm that the data herein is a true complete and accurate reflection of this subject participation in						
the study, according to the protocol procedures.						
Investigator's name:						
Investigator's signature:						
Date:						

Centre No. Screen. No. Randomisation No. Pat. Init. _					
VISIT 7 – Day 180					
Visit date at D D M M Y HOUR MINUTES					
Has the patient withdrawn prematurely from the study?					
D No					
If Yes, please fill in the " Investigator's statement " at the end of visit 7 and the " Study Conclusion Summary/Wihtdrawal/Drop-out Form".					

Centre No. _	_ Screen. No.	Randomisation No.	_ Pat. Init	.	_
				Family name	Name

Visit date				.	.	_	at	
	D	D	М	М	Y	Y	HOUR M	INUTES

OCCURRING EVENTS						
PLEASE COMPLE	TE THE FOL	LOWING TABLE:				
Did the patient have at least one COPD exacerbation* since the last visit? (*defined as: - worsening of respiratory symptoms requiring treatment with antibiotics and/or systemic steroids since last visit - and/or new hospital admission for a COPD exacerbation since last visit - and/or need for ventilatory support or intubation, or death since last visit)	☐ Yes ☐ No	If YES indicate date(s) of onset of new COPD exacerbation(s) since last visit (DD/MM/YY): 1) 2) 3)				
Was the patient hospitalized <u>for a new</u> <u>COPD exacerbation</u> since the last visit?	☐ Yes ☐ No	If YES indicate date(s) of new hospitalization(s) for COPD exacerbation(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from				
Was the patient hospitalized <u>for any other</u> <u>cause</u> (except COPD) since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for hospitalization(s): If YES, please indicate date(s) of new hospitalization(s) since last visit (from DD/MM/YY to DD/MM/YY): 1) from to to to 2) from to to to				
Was the patient admitted to an Intensive Care Unit <u>for any cause</u> since the last visit?	☐ Yes ☐ No	If YES, specify reason(s) for admission(s) to ICU:				

Centre No. _ S	Screen. No.	Randomisation No. _	_ Pat. Ini	L.	_
				Family name	Name

Visit date					_	_	at	
	D	D	М	Μ	Y	Y	HOUR	MINUTES

OCCURRING EVENTS (continued)						
	YesNo	If YES indicate date(s) of onset of episode(s) of pulmonary embolism since last visit (DD/MM/YY):				
Did the patient have any episode(s) of <u>pulmonary embolism</u> since the last visit?		1)				
		2) _				
	C Yes	If YES, specify kind of cardiovascular				
	🗖 No	event(s):				
Did the patient have any <u>cardiovascular</u> events, including acute onset pulmonary		If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY):				
edema since the last visit?		1)				
		2)				
		3)				
	□ Yes □ No	If YES indicate date(s) of onset of pneumonia since last visit (DD/MM/YY):				
Did the patient have any episodes of pneumonia since the last visit?		1)				
		2)				
	_	3)				
	□ Yes	If YES, specify event(s):				
	🗖 No					
Did the patient have <u>any other significant</u> <u>occurring event</u> since the last visit?		If YES indicate date(s) of onset of new event(s) since last visit (DD/MM/YY):				
		1)				
		2)				
		3)				

Has the patient experienced <u>at least one</u> of the above events <u>since the last visit</u> (i.e. did you answer YES to any of the above questions)?

No 🖸 Yes* 🗖

* If YES please fax a copy of pages 72-73 to CROM as indicated in the Study Procedures Handbook.

Centre No. Screen. No. Randomisation No. Pat. Init.									
VISIT 7 – Day 180									
Visit date at D D M M Y HOUR MINUTES									
MEDICATION SINCE THE LAST VISIT									
		DICATION	SINCE I	HE LASI	VI5I I				
	edication been ins lose change) sind				🗖 No	C Yes			
If YES please complete the following details, including only medications instituted, stopped and/or modified (dose change) since the last visit.									
					Admini	stration			
Trade		Posology		Route	(DD/MM/YY)				
name	ame Indication	Dose/day	Unit		Start date	End date (or ONGOING)			

Γ

Centre No.	Screen. No.	 Randomisation No.	 Pat. Init.		_
				Family name	Name

		Visit date at D M M Y HOUR MINUTES						
PHYSICAL EXAMINATION								
Physical examination	Status	Comments: if "abnormal" specify:						
Cardiovascular system	 Abnormal Normal Not done 							
Respiratory system (except COPD)	 Abnormal Normal Not done 							
Lymphatic system	 Abnormal Normal Not done 							
Neurological-locomotor system	 Abnormal Normal Not done 							
Skin	 Abnormal Normal Not done 							
Endocrine	 Abnormal Normal Not done 							
Ear-nose-throat system	 Abnormal Normal Not done 							
Ophtalmological system	 Abnormal Normal Not done 							
Gastrointestinal system	AbnormalNormalNot done							
Others	 Abnormal Normal Not done 							

VITAL SIGNS							
	OOD PRESSURE nHg)	SITTING HEART RATE (bpm)					
Systolic Diastolic							

Centre No. _ Screen. No. _ Randomisation No.		Pat. Init. _		_
		Fa	mily name	Name

C-reactive protein (CRP), serum amyloid (SAA) and RANTES							
Has the blood sample been taken for the CRP, SAA and RANTES analysis?							
Yes No							
If Yes, refer to the Study	If Yes, refer to the Study Procedures Handbook for handling and storage.						
If No, please specify wh	y:						
Please fill in as soon as the results are available:							
CRP (mg/L)							
SAA (mg/L)	III.II						
RANTES (mcg/L)	II.II						

Centre No.	Screen. No.	Randomisation No.	Pat. Init. _		
			Fa	amily name	Name

 Visit date

 at

 D
 D
 M
 M
 Y
 HOUR
 MINUTES

QUESTIONNAIRES FOR RESPIRATORY SYMPTOMS/QUALITY OF LIFE

SF36 score:

BDI score:

TDI score:

total I total I total I I I

total I___I___I CCIQ Score:

PHARMACOECONOMIC QUESTIONNAIRE

Please remind to fill in the pharmacoeconomic questionnaire and enclose it in the plastic envelope.

SPIROMETRY

For this visit, please obtain a complete spirometry. •

SPIROMETRY: from 3 acceptable spirometric manoeuvres record the highest FEV₁ and FVC, irrespective of the manoeuvre (curve) they come from.

date |___| |__| |__| at |__| |__| HOUR MINUTES

FVC	, litre
FEV1	, litre
FEV1 predicted normal value	, litre [ERS standards]
FEV1 (% predicted normal value)	% of predicted value
FEV₁/FVC (%)	, %
RV	, litre
RV (% predicted normal value)	, %
TLC	, litre
TLC (% predicted normal value)	, %
RV/TLC (%)	, %
KCO	, ml/min/mmHg/l
KCO (% predicted normal value)	, %

Centre No. _ Screen. No. _	<u> </u> Ra	andomisation No.	Pat. Init.		_
				Family name	Name

VISIT 7 – Day 180	VISIT 7 – Day 180						
			at M Y Y HOUR MINUTES				
	MICROBI	OLOGY					
	Yes	Ν	0				
Sputum collection performed:							
If YES, specify volume of sputum col	lected: .	l ml					
If NO, specify why		-					
Results from local laboratory:							
Bacteriology:							
Identified microorganism #1:							
Identified microorganism #2:							
Identified microorganism #3:			CFU/ml:				
Serology for Intracellular pathoger	าร:						
Has the sample for serology for intra	cellular pathoge	ns been o	btained? Yes 📮 No 🗖				
If Yes, please complete below:							
Was serology positive for Mycoplasi	<u>ma pneumoniae</u>	e? Yes 🗖	No 🗖				
If YES, indicate: IgM:],						
IgG:	,						
Was serology positive for Chlamydia	? Yes 📮 No						
If YES, indicate: IgM:	,						
lgG: ∣	,						
Was serology positive for Legionella pneumophila? Yes D No D							
If YES, indicate:							
PC	OSITIVE	NEGATI	VE				
Legionella pneumophila IgM							
Legionella pneumophila IgG							

		Family name	Name			
VISIT 7 – Day 180						
Visit date D D M M	 Y Y	at	 MINUTES			
MICROBIOLOGY (continu	ued)					
Has the sample for respiratory viruses RT-PCR analysis been o	collected a	nd stored at -	-80°C?			
		Yes 🗖	No 🗖			
If YES, specify volume stored at -80°C for RT-PCR: , ml						
Please remember to label the sample with the patient's ID number in the Study Procedures Handbook.	er and store	it at -80°C, a	s described			
Has the sample for inflammatory cell counts been collected? Y	Yes 🗖	No 🗖				
Were the slides prepared and stored at -20°C?	Yes 🗖	No 🗖				
If YES: how many slides were prepared?						

Centre No. |____ Screen. No. |____ Randomisation No. |____ Pat. Init. |____ |_ |__ |___

Centre No. Screen. No. Randomisation No.	Pat. Init. _	
	Family name	Name

VISIT 7 – Day 180							
v	/isit date	_ _	at				
	D D M	M Y	Y HOUR MINUTES				
ARTERIAL BLOOD GASES							
	Yes	No					
Arterial blood gas analysis performed:							
If YES: patient was under O ₂ therapy?							
If patient was under O2 therapy please	indicate:						
- how m	any L/min: ,	-					
- how m	any hours/day:						
If arterial blood gas analysis was performe	ed, indicate:						
pH: ,							
PaO _{2:} mmHg							
PaCO _{2:} mmHg							
SO _{2:} %							
HCO3 ^{-:} mmol/L							

INVESTIGATOR'S STATEMENT

I confirm that the data herein is a true complete and accurate reflection of this subject participation in the study, according to the protocol procedures.

Investigator's name:	
Investigator's signature	
Date:	

SECTION A

ADVERSE EVENT, SPECIFY	SERIOUS	REASON (several statements are possible)	DATE OF ONSET	DATE OF END	SEVERITY	RELATIONSHIP	ACTION TAKEN (several statements are possible)	OUTCOME OF EVENT
Please, list ONE event per line	1. No 2. Yes	 Fatal Life-threatening Inpatient hospitalisation or prolonged inpatient hospitalisation Permanent or significant disability / Incapacity Congenital anomaly / Birth defect May require medical intervention to prevent the above outcomes 	(dd mm yy)	(dd mm yy)	 Mild Moderate Severe 	 Certain/Definite Probable/Likely Possible Doubtful/Unlikely Not available Not assessable Not related 	drug(s)	 Recovered Recovered with sequelae Not yet recovered Death: drug may be contributory Death: due to adverse event Death: unrelated to drug Unknown
1.		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	//	//				$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
2.		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	//	//				$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
3.		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	//	//				$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
4.		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	//	//				1 2 3 4 5 6 7
5.		1 2 3 4 5 6	/	//		1 2 3 4 5 6 7		1 2 3 4 5 6 7

ADVERSE EVENT(S) REPORT FORM

FILL IN THE REASON FOR SERIOUSNESS AND THE COMPLEMENTARY PAGE FOR SERIOUS ADVERSE EVENTS AND REPORT BOTH PAGES TO CROM AND THE DIREZIONE SANITARIA OF THE HOSPITAL WITHIN A WORKING DAY (SEE STUDY PROCEDURES HANDBOOK FOR INSTRUCTIONS).

Date: / /

Investigator's Signature:

Centre No. ____ Screening No. ____ Randomisation No. ____ Visit No. ____ Patient's Initials |

Family name . Name

Centre No.	L	I I	

Screening No. |____ Randomisation No. |__ |__ Visit No. |___ |

Patient's Initials

Family name . Name _

COMPLEMENTARY PAGE FOR THE SERIOUS ADVERSE EVENT(S)

SECTION B

FURTHER DETAILS OF AD	FURTHER DETAILS OF ADVERSE EVENT									
REPORT TYPE	CODE BROKEN	OCCURRED	SE EVENT	re of Birth (dd/mm/yy)	AGE (years)	SEX				
Initial 🔲 Follow-up 🗌	Yes 🗌 🛛 No 🗌]				Male 🗌 🛛 Female 🗌				
CONCOMITANT DISEASE((S)			MEDICAL HISTORY	_	·				
		L. P. Mar familie	Della de es	Deute of a decision of the	Transferrent datas	Querrante				
SUSPECTED DRUG(S)		Indication for use	Daily dose	Route of administration	Treatment dates (dd/mm/yyyy)	Comments				
					From/ To/					
					From/ To/					
DECHALLENGE AND REC	HALLENGE	Did suspect study drug (s) discontinue? Yes No NA	Did reaction abate Yes	te after stopping study drug(s)?	Was/were study drug(s) readministered? Yes No NA	Did reaction reappear after reintroduction? Yes No NA				
CONCOMITANT MEDICATI (Tradename/Generic name)		Indication for use	Daily dose	Route of administration	Treatment dates (dd/mm/yyyy)	Comments				
					From/ To/	/				
					From/ To/					
	I(S) FOR SERIOU Intercurrent dise Concomitant dru	ease 🔲 Study drug	Date of death (do		of hospital report, autopsy report, death	certificate, if available):				

Date:___/__/

Investigator's Signature:_____

Contro No. I. I.		Randomisation No.	
Centre No.	Screening No.	Randomisation No.	Visit No. F

Patient's Initials |___| |__| |___| Family name Name

COMPLEMENTARY PAGE FOR THE SERIOUS ADVERSE EVENT(S)

SECTION B

FURTHER DETAILS OF ADVERSE EVENT								
REPORT TYPE	CODE BROKEN	COUNTRY WHERE THE ADVERS	SE EVENT	DATE O	F BIRTH (dd/mm/yy)	AGE (years)	SEX	
Initial 🗌 Follow-up 🗌	Yes 🗌 🛛 No 🗌						N	lale 🗌 🛛 Female 🗌
CONCOMITANT DISEASE	(S)			8	MEDICAL HISTORY			
SUSPECTED DRUG(S)		Indication for use	Daily dos	se	Route of administration	Treatment dates (dd/mm/yyyy)		Comments
						From/ To/	/	
						From/ To/		
DECHALLENGE AND REC	HALLENGE	Did suspect study drug (s) discontinue? Yes No NA	Did reaction	n abate afte Yes 🔲 N	er stopping study drug(s)?	Was/were study drug(s) readministered? Yes No NA	Did reacti ץ	on reappear after reintroduction? ′es
CONCOMITANT MEDICAT (Tradename/Generic name)		Indication for use	Daily dos	se	Route of administration	Treatment dates (dd/mm/yyyy)		Comments
						From/ To/	/	
						From/ To/		
POSSIBLE EXPLANATION Underlying disease Concomitant disease	Intercurrent dis	ease 🔲 Study drug	Date of de	ath (dd/mr		of hospital report, autopsy report, death e specify:	certificate, if	available):

Date:___/__/___

Investigator's Signature:____

Centre N		L	
	IU.		

Patient's Initials |_

Family name . Name _

COMPLEMENTARY PAGE FOR THE SERIOUS ADVERSE EVENT(S)

SECTION B

FURTHER DETAILS OF A								
	DVERGE ETE							
REPORT TYPE	CODE BROKEN	N COUNTRY WHERE THE ADVERS	SE EVENT	DATE OF	BIRTH (dd/mm/yy)	AGE (years)	SEX	
		OCCURRED						
Initial 🔲 Follow-up 🗌	Yes 🗌 🛛 No 🗌						M	lale 🗌 🛛 Female 🗌
CONCOMITANT DISEASE	(S)				MEDICAL HISTORY			
SUSPECTED DRUG(S)		Indication for use	Daily dos	<u> </u>	Route of administration	Treatment dates		Comments
SUSPECIED DRUG(S)			Daily uos	e	Roule of autimistration	(dd/mm/yyyy)		Comments
				 				
						From/ To/	/	
						From/ To/	/	
			Did reactiv				Did raaati	
DECHALLENGE AND REC	HALLENGE	Did suspect study drug (s) discontinue? Yes No NA			r stopping study drug(s)?	Was/were study drug(s) readministered? Yes No NA	Did reaction Y	ion reappear after reintroduction? ⁄es
		Indication for use	Daily dos	e	Route of administration	Treatment dates		Comments
(Tradename/Generic name))					(dd/mm/yyyy)		
						From / / To /		
						From/ To/	/	
						From/ To/	/	
POSSIBLE EXPLANATION	N(S) FOR SERIOU	JS ADVERSE EVENT				y of hospital report, autopsy report, death	certificate, if	available):
Underlying disease [Concomitant disease]	Intercurrent dise		Date of dea	ath (dd/mm/	n/yy):// disease	e specify:		
							_	

Date: /___/

Investigator's Signature:

Centre No.	_	Screen.	No.		 Randomisation No. _	 	Pat. Init.				
								Family nam	ne	Name	

STUDY	CONCLUSION SUMMARY/WI	THDRAWAL/DROP-OUT FORM
Did the patient	complete the study?	No
Date of las	t study treatment (antibiotic) intake: _	
If Yes:	Date of study completion:	
If No:	- Date of withdrawal:	
	- Reason for the withdrawal:	
	Did not satisfy all inclusion/exc Specify:	usion criteria
	 Protocol violation 	
	Specify:	
	Adverse event (noted on adver	se event page)
	Death	
	Specify cause of death:	
	Withdrawal of consent	
	Pregnancy	
	Insufficient therapeutic response	se 🗖
	Lost to follow-up visit	
	Poor compliance	
	Other reason(s)	
	Specify:	

INVESTIGATOR'S STATEMENT

I confirm that the data herein is a true complete and accurate reflection of this subject participation in the study, according to the protocol procedures.

Investigator's name:	
Investigator's signatur	e:
Date:	