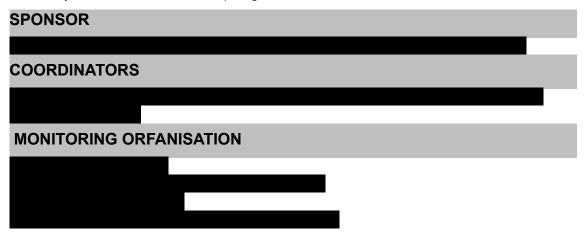
Phase II multicenter clinical trial to evaluate the efficacy and safety of ibrutinib in combination with rituximab, gemcitabine, oxaliplatin, and dexamethasone followed by ibrutinib as maintenance treatment in patients with diffuse large B-cell lymphoma refractory to the treatment or relapsing, non-candidates to receive a TACM.

STATISTICAL ANALYSIS REPORT

26th of April 2021 (version 1.0)

TITLE

Phase II multicenter clinical trial to evaluate the efficacy and safety of ibrutinib in combination with rituximab, gemcitabine, oxaliplatin, and dexamethasone followed by ibrutinib as maintenance treatment in patients with diffuse large B-cell lymphoma refractory to the treatment or relapsing, non-candidates to receive a TACM.



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LIST OF ABBREVIATIONS

Abbreviations AE CR eCRF ECOG EFS GEL/TAMO HLA LDCBG LNH NA ND OR OS PET PR PD PFS R-GEMOX SAE SD	Term explanationAdverse EventComplete responseCase Report FormEastern Cooperative Oncology GroupEvent Free SurvivalGrupo Español de Linfoma/Trasplante Autólogo de Médula ÓseaHuman Leukocyte AntigenLinfoma difuso de células B grandesLinfoma no HodgkinNot aplicableNot DoneOverall ResponseOverall ResponseProgression diseaseProgression free SurvivalRituximab-GEMOXSerious Adverse EventStable Disease
-	
UK	Unknown

1. DEFINITIONS

1.1. POPULATIONS FOR ANALYSIS

The analysis populations are defined as:

- **Population of all treated patients**: defined as all patients receiving at least 1 dose of study drug.

- **Population with evaluable response**: defined as all patients with measurable disease at baseline, receiving at least 1 dose of study drug, and having at least 1 adequate post-baseline disease evaluation. An adequate disease assessment is defined as having sufficient evidence to correctly indicate whether or not disease progression has occurred. Patients who have died from progression are also considered to have had an adequate evaluation.

- **Safety population:** defined as all patients receiving at least 1 dose of study drug, which is the same definition as for the population of all treated patients.

1.2. EFFICACY ANALYSIS

Efficacy analysis: final analysis of the primary endpoint, ORR (CR + PR) after 4 cycles, can be carried out 4 months after the last patient was enrolled, and will be based on the population of all treated patients. Response rates with confidence intervals (95% interval) will be presented. The TRG will be evaluated in accordance with local and centralized PET / CT evaluations.

Overall survival, PFS, event-free survival, and duration of response are defined as follows (Cheson et al., 2007):

Overall survival (OS): defined as the time between entry into the trial and death from any cause. It will be analyzed using the Kaplan-Meier method. Data on patients withdrawn from the study or unavailable for follow-up will be censored on the date of the last contact.

Progression-free survival (PFS). It is defined as the time elapsed from the inclusion of the first patient in the study until the progression of the disease or death from any cause.

Event-free survival (EFS). It is defined as the time elapsed from inclusion in the trial to lymphoma progression, treatment failure, or death from any cause. It will be analyzed using the Kaplan-Meier method.

Duration of response. It will be calculated from the date there is an indication of CR or PR to the date of disease recurrence or progression. It will be analyzed using the Kaplan-Meier method.

2. RESULTS

2.1. POPULATIONS

2.1.1. Patients registered in the eCRF

Table 1. Patients registered by hospital

		Ν	%			
Hospital						
	Total					
	Yes					
Analyzable	Νο					
-	Total					

2.1.2. Analyzable patients

Table 2. Not analyzable patients

No.	Study Subject ID	Hospital	Reason

Table 3. Analyzable patient by hospital

	·····	Analyzable					
			No	Ye	es	Т	otal
		Ν	%	Ν	%	Ν	%
Hospital							
	Total						

2.1.3. Analysis populations

Table 4. Analysis population					
		Ν	%		
Treated patient	Yes				
population	Total				
Available reenance -	Yes				
Available response - patient population -	No				
patient population	Total				
Reason considered At least one post-baseline evaluation					
response not Death due to progression					
available	Total				

Table 5. List of patients excluded from Available response patient population

	Study Subject ID	Hospital	Available response Reason considered patient population response available (or not)	Overall survival	Reason of Death	Specify reason of Death
1						
2						
3						
4						

2.2. BASELINE CHARACTERISTICS

Table 6. Gender				
N %				
	Male			
Gender (Baseline)	Female			
	Total			

Table 7. Age							
	Ν	Mean	SD	Median	Min	Мах	
Age (years)							

Vital signs						
		Table 8.	Vital sig	ns 1		
	Ν	Mean	SD	Median	Min	Мах
Systolic blood pressure						
(Baseline)						
Diastolic blood pressure						
(Baseline)						
Temperature (Baseline)						
Weight (Baseline)						
Height (Baseline)						

Table 9. Vital signs 2						
		Ν	%			
	0					
ECOG (Basalina)	1					
ECOG (Baseline)	2					
	Total					
	Yes					
B symptoms (Baseline)	No					
	Total					
Pre-existing condition,	Yes					
relevant signs or	No					
symptoms (Baseline)	Total					

All relevant previous events are listed in ANNEX 1: RELEVANT PREVIOUS EVENTS (page 40), and the following table contains those events present in at least 5% of the patients.

Table 10. Most frequent relevant previous events (present in at least 5% of
patients)

	IN
Relevant	
previous events	
•••••	

Table 11. Previous medication					
N %					
Draviaua	Yes				
Previous medication	No				
medication	Total				

All previous medications are listed in ANNEX 2: PREVIOUS MEDICATION (page 40), and the following table contains those medications present in at least 5% of the patients.

Table 12. Most frequent previous medication (present in at least 5% of patients)

	IN
Previous	
medication	

...

...

2.3. DIAGNOSIS

Table 13. Time from diagnosis and age at diagnosis						
	Ν	Mean	SD	Median	Min	Max
Time from diagnosis to study						
inclusion (months)						
Age at diagnosis						

Table 14. Local histological diagnosis, centralized and agreement N

	inetere grear e	nagriosis, centralizea a	na agreenie	
			Ν	%
	LDCBG w	ithout specification		
Histological subtype at		Others ¹		
diagnosis, <u>local</u> (Baseline)	LDC	BG specified ²		
(Baseline)		Total		
2: LDC	BG specified	LDCGB rich in T		
	1: Others	Follicular lymphoma		
			Ν	%
	LDCBG w	ithout specification		
Histological subtype at		Others ³		
diagnosis, <u>centralized</u>		NA		
review (Baseline)		ND		
		Total		
		CD5+ B lymphoma		
		Could not be		
		determined with		
	3: Others	submitted sample		
		MO cylinder biopsy		
		without evidence of		
		neoplastic infiltration		
			N	%
		No		
Agreement in histology a	at diagnosis	Yes		
		Total		

Table 15. Patients without agreement in Histological type at diagnosis

	Study Subject ID	Hospital	Diagnosis date (Baseline)	Histological subtype at diagnosis, local (Baseline)	Histological subtype at diagnosis, centralized review (Baseline)	Agreement in histology at diagnosis
1						_
2						
3						
4						

1.1.1. Diagnosis: Immunohistochemical type of LDCBG

		N	%
luumunahistaahamiaal —	no-CGB		
Immunohistochemical -	Others		
type at diagnosis, – local (Baseline)	UK		
iocal (Baseline)	Total		
	CGB		
Immunohistochemical	no-CGB		
type of LDCBG at	NA		
diagnosis, centralized	ND		
review (Baseline)	UK		
	Total		
_	Non-CGB local and centralized		
A groom ont in _	Non-CGB local and CGB centralized		
Agreement in – immunohistochemical –	Non-CGB local and missing centralized		
at diagnosis –	Missing local and centralized		
	Other local and missing centralized		
	Total		
Agreement in	Yes		
immunohistochemical	No		
at diagnosis	Total		

Table 16. Immunohistochemical type of LDCBG at diagnosis

Table 17. Patients without agreement in Immunohistochemical type of LDCBG at diagnosis

	Study Subject ID	Hospital	Diagnosis date (Baseline)	Immunohistochemical agreement at diagnosis (Yes/No)	Immunohistochemical agreement at diagnosis
1					
2					
3					
4					
5					

1.1.2. Diagnosis: Other histological data

Other histological data at diagnosis.

Table 18. Other histological data

		Ν	%
	ABC		
	Not done		
Nanostring result at	NA		
diagnosis (Baseline)	ND		
	UK		
	Total		
	1		
	I		
Lymphoma stage at	III		
diagnosis (Baseline)	IV		
	ND		

	1117	
	UK	
	Total	
	0	
	1	
	2	
ECOG diagnosis —— (Baseline) ——	3	
(Baseinie)	ND	
	UK	
	Total	
	Normal	
	Increased	
LDH at diagnosis —— (Baseline) ——	ND	
(Daseine)	UK	
	Total	
	0-1	
	2	
	3	
IPI diagnosis	4	
(Baseline)	5	
	ND	
	UK	
	Total	

1.1.3. Current lymphoma exploration

Table 19. Current lymphoma exploration

		Ν	%
	Yes		
Adenopathy (Baseline)	No		
	Total		
Specify adenopathy	Example: Bilateral supraclavicular, Axillary, mediastinal,		
(Baseline)	hilar		
(Daseline)	Total		
Honotomogaly	Yes		
Hepatomegaly (Baseline)	No		
(Dasenne)	Total		
Splanomogoly	Yes		
Splenomegaly (Baseline)	No		
(Baseline)	Total		
Lymphomotous	Yes		
Lymphomatous involvement (Baseline)	No		
	Total		
Specify Lymphomatous	Example: Bone, liver and bone marrow		
involvement (Baseline)	Total		

1.1.4. Current stage: Rebiopsy and other current results

Table 20. Histological, molecular and current stage

		N %
	Yes	
Rebiopsy (Baseline)	No	
	Total	
	CGB	
	ABC	
	Not done	
Current nanostring result	NA	
(Baseline) ———	ND	
	UK	
	Total	
	I	
	III	
Current lymphoma clinical	IV	
stage (Baseline)	NA	
	ND	
	UK	
	Total	
	Yes	
Current Dana mamou hianau	No	
Current Bone marrow biopsy	NA	
(Baseline)	ND	
(Daseille)	UK	
	Total	
	Yes	
	No	
Current cytometry involvement	NA	
(Baseline)	ND	
	UK	
	Total	

1.1.5. Current histology	: diagnosis and agreement		
Table 21. (Current Histological subtype		
		Ν	%
	LDCBG without specification		
	LDCBG specified		
Current, <u>local</u> histological subtype (Baseline)	NA		
	ND		
	UK		
	Total		
Specify other histological	Example: LDCBG gastric		
subtypes current, local (Baseline)	Total		
	LDCBG without specification		
Current histological subtype,	Others		
<u>centralized review</u> (Baseline)	NA		
	ND		

	UK	
	Total	
Specify other surrent histolesical	Example: Lymphoma B of the marginal	
Specify <u>other</u> current histological subtypes, centralized review	zone/Lymphoma B with plasmocellular	
	differentiation	
(Baseline)	Total	
Current concordance in Histology	Νο	
at diagnosis	Yes	
	Total	

Table 22. Patients without agreement in current histology diagnosis

Study Subject ID	Hospital	Current, local histological subtype (Baseline)	Specify other histological subtypes current, local (Baseline)	Current histological subtype, centralized review (Baseline)	Specify other current histological subtypes, centralized review (Baseline)
1					
2					
3					

1.1.6. Current Immunohistochemistry: diagnosis and agreement

		Ν	%
	no-CGB		
Current	NA		
immunohistochemical	ND		
type, <u>local</u> (Baseline)	UK		
	Total		
	CGB		
Immunohistochemical	no-CGB		
type of current	NA		
LDCBG, <u>centralized</u>	ND		
review (Baseline)	UK		
	Total		
Current	Νο		
immunohistochemical	Yes		
agreement	Total		

Table 23. Agreement current immunohistochemical diagnosis

Table 24. Patients without agreement in current immunohistochemical diagnosis

Study Subject ID	Hospital	Current immunohistochemica agreement	Current al immunohistochemical type, local (Baseline)	Immunohistochemical type of current LDCBG, centralized review (Baseline)
1				
2				
3				
4				

1.1.7. Global diagnosis

		Ν	%
Global <u>local</u>	no-CGB		
diagnosis	Total		
	no-CGB		
	CGB		
Global	LDCBG without specification		
<u>centralized</u>	Others: Follicular lymphoma, Lymphoma B with plasmocellular differentiation		
diagnosis	ND		
	UK		
	Total		
Global	No		
	Yes		
agreement	Total		

Table 25. Agreement current immunohistochemical diagnosis

Table 26. Patients without agreement in current immunohistochemical diagnosis

Study Subject ID	Hospital	Global local diagnosis	Global centralized diagnosis
1			
2			
3			

1.2. PREVIOUS TREATMENTS LYMPHOMA

		<u>. p</u>				
					Ν	%
			1			
			2			
Number of previous treatment lines (Baseline)		s	3			
			4			
			5			
			Tota	l		
	Ν	Mean	SD	Media	n Min	Max
Number of previous treatment						
lines (Baseline)						

Table 27. Number of previous treatment lines

Table 28. Previous treatment: 1st line

		Ν	%
	CR		
	PR		
Best response previous	SD		
treatment line 1	PD		
(Baseline)	ND		
	UK		
	Total		
	Yes		
Relapse or previous	No		
progression line 1	NA		
(Baseline)	ND		
	Total		
First line treatment	Example: R- CHOP, Rituximab, Splenectomy		
(Baseline)	Total		

Table 29. Previous treatment: 2nd line

		N	%
	CR		
	PR		
Best response	SD		
previous ——— treatment line 2 ———	PD		
(Baseline) ———	NA		
(Daseille)	UK		
	Total		
	Yes		
Relapse or	No		
previous ——— progression line ———	NA		
2 (Baseline)	UK		
	Total		
Second line	NA		
treatment	Example: R-ESHAP, R-DHAP		
(Baseline)	Total		

Table 30. Previous treatment: 3rd line

		Ν	%
	PR		
Best response	SD		
previous	PD		
treatment line 3	NA		
(Baseline)	UK		
	Total		
Relapse or	Yes		
previous _	No		
progression line	NA		
3 (Baseline)	Total		
Third line	NA		
treatment	Example: BeGEV + Transplant		
(Baseline)	Total		

Table 31. Previous treatment: 4th line

		Ν	%
Best response previous treatment line 4 (Baseline) -	PR		
	PD		
	NA		
	UK		
	Total		
Relapse or previous	Yes		
progression line 4	NA		
(Baseline)	Total		
Fourth line treatment	NA		
Fourth line treatment	Example: Prednisone + Brentuximab		
(Baseline)	Total		

1.3. AUTOLOGOUS STEM CELL TRANSPLANT

Table 32. Autologous stem cell transplant

		Ν	%
	Yes		
Autotransplantation —	Νο		
(Baseline) —	Total		
	1st CR		
	1st PR		
Situation	2nd CR		
autotransplantation	2nd PR		
(Baseline)	Others		
	NA		
	Total		
Specify other	Example: PD located in right axillar region		
(Baseline)	Total		
	CR		
	PR		
Best response —— autotransplantation ——	PD		
(Baseline)	NA		
	UK		
	Total		

	Example: 0, 3, 6, 9	
Response duration	NA	
(Baseline)	UK	
	Total	
Delense er	Yes	
Relapse or - progression (Baseline) -	NA	
progression (Baseline)	Total	

Table 33. Response duration (autologous stem cell transplant)

	Ν	Mean	SD	Median	Min	Max
Response duration (Baseline)						

1.4. ALEOGENIC TRANSPLANT HEMATOPOIETIC PROGENITORS

 Table 34. Allogenic transplant hematopoietic progenitors

 N
 %

Allotransplant (Baseline) <u>No</u> Total

1.5. EXTRANODAL AND NODAL AFFECTATION

Table 35. Extranodal Affectation

		Ν	%
	Yes		
Extranodal affectation	No		
at diagnosis - (Baseline) -	ND		
(Baselille)	Total		
	ND		
Locations extranodals - (Baseline) -	Example: 0, 1, 2, 3		
(Baselille)	Total		
Specify extranodal	Example: Bone, Lung, Bone marrow		
affectation (Baseline)	Total		

Table 36. Nodal Affectation

		Ν	%
Nodal	Yes		
affectation at	Νο		
diagnosis	ND		
(Baseline)	Total		
Nodal	ND		
locations	Example: 0, 1, 2, 3		
(Baseline)	Total		
Specify nodal	Example: Bilateral adrenal burky mass, Retroperitoneal		
affectation (Baseline)	Total		

1.6. BASELINE ANALYTICS

1.6.1. HEMOGRAM

Table 37. Baseline analytics: Hemogram

	Ν	Mean	SD	Median	Min	Max
Hemoglobin Value (Baseline)						
Leukocytes Value (Baseline)						
Lymphocytes Value (Baseline)						
Monocytes Value (Baseline)						
Eosinophils Value (Baseline)						
Neutrophils Value (Baseline)						
Platelets Value (Baseline)						

1.6.2. BIOCHEMISTRY

Table 38. Baseline analytics: Biochemistry

	Ν	Mean	SD	Median	Min	Мах
Creatinine Value (Baseline)						
Urea Value (Baseline)						
Urate Value (Baseline)						
Sodium Value (Baseline)						
Potassium Value (Baseline)						
Calcium Value (Baseline)						
Glucose Value (Baseline)						
Protein Value (Baseline)						
Albumin Value (Baseline)						
LDH Value (Baseline)						
Gamma globulin Value (Baseline)						
Meta2-seric microglobulin Value (Baseline)						
OSTP/ALT Value (Baseline)						
OSOT/AST Value (Baseline)						
FA Value (Baseline)						
GGT Value (Baseline)						
BIL Value (Baseline)						
IgG Determination Value (Baseline)						
IgA Determination Value (Baseline)						
IgM Determination Value (Baseline)						

1.6.3. COAGULATION TEST Table 39. Baseline analytics: Coagulation test N Mean SD Median Min Max TTP Value (Baseline) TP Value (Baseline) Fibrinogen Value (Baseline)

1.6.4. IPI

Table 40. Baseline analytics: IPI

				Ν		%
		0				
IPI (Baseline)		1				
		2				
		3				
		4				
		5				
		UK				
		Total				
	N	Mean	SD	Median	Min	Мах
IPI (Baseline)						

1.6.5. LYMPHOMA SITUATION

Table 41. Baseline analytics: Lymphoma situation

		Ν	%
	Partial Response		
Oltreation	Refractory disease		
Situation	Relapse early untreated (<1 year after diagnosis)		
lymphoma (Baseline)	Relapse late untreated		
(Dasenne)	UK		
	Total		

1.6.6. SEROLOGY

Table 42. Baseline analytics: Serology

		Ν	%
HIV antibodies	Negative		
(Baseline)	Total		
	Positive		
Hepatitis C	Negative		
(Baseline)	UK		
	Total		
	Negative		
RNA VHC	NA		
(Baseline) -	ND		
(Daseille)	UK		
	Total		
	Positive		
	Negative		
Hho A a (Bosolino)	NA		
HbsAg (Baseline) -	ND		
_	UK		
	Total		

	Positive	
	Negative	
Anti Hbc	ND	
(Baseline)	UK	
	Total	
	Positive	
A with Lille a	Negative	
Anti Hbs	ND	
(Baseline)	UK	
	Total	
	Positive	
	Negative	
DNA VHB	NA	
(Baseline)	ND	
	UK	
	Total	

1.7. OTHER TESTS

1.7.1. OTHER TESTS: PREGNANCY

Table 43. Other test: Pregnancy

		Ν	%
	Negative		
	NA		
Pregnancy test at inclusion (Baseline)	ND		
	UK		
	Total		

1.7.2. OTHER TESTS: CARDIOLOGY TEST

Table 44. Other test: Cardiology test

		Ν	%
	Without significative alterations		
	Significative alterations		
ECG at inclusion	NA		
(Baseline)	ND		
	UK		
	Total		
	Yes		
Cardiac	No		
ventricular	NA		
ejection fraction	ND		
(Baseline)	UK		
	Total		
	Ecocardio		
Taabaiawa FF —	MUGA		
Technique FE —	NA		
(Baseline) —	ND		
	Total		
Result FE	Normal		
(Baseline)	Total		

Table 45. Comorbidities que		N	%
	Yes		
CRS-G comorbidity scale has been done	No		
(Baseline)	Total		
	Example: 0, 1		
Hearth (Baseline)	Total		
	Example: 0, 1		
Hypertension (Baseline)	Total		
	Example: 0, 1		
Hematopoietic vascular (Baseline)	Total		
	Example: 0, 1		
Respiratory (Baseline)	Total		
	Example: 0, 1		
ORL (Baseline)	Total		
	Example: 0, 1		
Upper GI apparatus (Baseline)	Total		
	Example: 0, 1		
Lower GI apparatus (Baseline)	Total		
	Example: 0, 1		
Liver (Baseline)	Total		
	Example: 0, 1		
Renal (Baseline)	Total		
	Example: 0, 1		
Genitourinary (Baseline)	Total		
	Example: 0, 1		
Skeletal muscle (Baseline)	Total		
	Example: 0, 1		
Nervous system (Baseline)	Total		
Endocrine-metabolic system and breast	Example: 0, 1		
(Baseline)	Total		
	Example: 0, 1		
Psychiatric problems (Baseline)	Total		
	Yes		
	No		
GAH (Baseline)	NA		
	ND		
	Total		

1.7.3. OTHER TESTS: COMORBIDITIES QUESTIONNAIRE

Table 45. Comorbidities questionnaire: Item results

Table 46. Comorbidities questionnaire: Scores

		Ν	%
Number of categories that have scored: of the total	Example: 0, 1		
of 14 categories, count those that have not received a score of 0	Total		
Total score (adding all the points)	Example: 0, 1		
	Total		
Severity index (total score/number of categories	Example: 0, 1		
that have scored)	Total		

Number of categories that have scored with a		Example: 0, 1					
score>=3		Total					
Number of categories that have scored with score		Example: 0, 1					
4		Total					
	Ν	Mean	SD	Med	dian	Min	Max
Score > 0 (Baseline)							
Score (Baseline)							
Severity index (Baseline)							

1.8. TREATMENT COMPLIANCE

Table 47. Treatment compliance Induction: Received cycles/completed

		Ν	%
Number of induction evolopy received	Example: 1.00, 2.00		
Number of induction cycles received -	Total		
Number of induction cycles received	Example: 1.00, 2.00		
complete (according to protocol)	Total		
	Νο		
Patients with delayed induction cycles	Yes		
	Total		
% of induction cycles received complete	% of induction cycles		
(according to protocol)	received		
,	Total		
Number of induction cycles received _	Example: 1.00, 2.00		
with delay	Total		
% of induction cycles received with	% of induction cycles		
delay -	received with delay.00		
	Total	_	
	Not delayed cycle due to		
No. of induction cycles delayed due to _	hematological toxicity		
hematological toxicity	Example: 1.00, 2.00	_	
	Total		
	N Mean SD Me	edian I	Min Max
Number of induction cycles received			
Number of induction cycles received			
complete (according to protocol)			
complete (according to protocol) % of induction cycles received complete			
complete (according to protocol) % of induction cycles received complete (according to protocol) Number of induction cycles received with delay			
complete (according to protocol)% of induction cycles received complete (according to protocol)Number of induction cycles received with delay% of induction cycles received with delay			
complete (according to protocol)% of induction cycles received complete (according to protocol)Number of induction cycles received with delay% of induction cycles received with delayNo. of induction cycles delayed due to			
complete (according to protocol)% of induction cycles received complete (according to protocol)Number of induction cycles received with delay% of induction cycles received with delayNo. of induction cycles delayed due to hematological toxicity			
complete (according to protocol)% of induction cycles received complete (according to protocol)Number of induction cycles received with delay% of induction cycles received with delayNo. of induction cycles delayed due to hematological toxicity	rutinib dosage		
complete (according to protocol)% of induction cycles received complete (according to protocol)Number of induction cycles received with delay% of induction cycles received with delayNo. of induction cycles delayed due to hematological toxicity	utinib dosage	N	%
complete (according to protocol)% of induction cycles received complete (according to protocol)Number of induction cycles received with delay% of induction cycles received with delayNo. of induction cycles delayed due to hematological toxicity	rutinib dosage 560mg/day	N	%
complete (according to protocol)% of induction cycles received complete (according to protocol)Number of induction cycles received with delay% of induction cycles received with delayNo. of induction cycles delayed due to hematological toxicity	560mg/day 420mg/day	N	%
complete (according to protocol) % of induction cycles received complete (according to protocol) Number of induction cycles received with delay % of induction cycles received with delay No. of induction cycles delayed due to hematological toxicity Table 48. Ibi	560mg/day	N	%
complete (according to protocol) % of induction cycles received complete (according to protocol) Number of induction cycles received with delay % of induction cycles received with delay No. of induction cycles delayed due to hematological toxicity Table 48. Ibi Minimum dose of ibrutinib received per	560mg/day 420mg/day 280mg/day Total	N	%
complete (according to protocol) % of induction cycles received complete (according to protocol) Number of induction cycles received with delay % of induction cycles received with delay No. of induction cycles delayed due to hematological toxicity Table 48. Ibi Minimum dose of ibrutinib received per	560mg/day 420mg/day 280mg/day	N	%
complete (according to protocol) % of induction cycles received complete (according to protocol) Number of induction cycles received with delay % of induction cycles received with delay No. of induction cycles delayed due to hematological toxicity Table 48. Ibi Minimum dose of ibrutinib received per	560mg/day 420mg/day 280mg/day Total	N	%

Table 49. Treatment duration						
	Ν	Mean	SD	Median	Min	Max
Treatment duration (months)						

1.9. END OF TREATMENT

	Table 50. End of treatment		
		Ν	%
Treatment ends	Yes		
freatment enus	Total		
	Progression		
	Unacceptable toxicity		
Reason end of	End of maintenance		
treatment (End of	Investigator criteria		
treatment)	Patient withdrawal of continuing with treatment		
	Others		
	Total		
Specify	Example: Allogeneic transplant, Cardiac		
Other/Unacceptable	complications		
toxicity or Investigator criteria	Total		

1.10. EFFICACY: RESPONSE

1.10.1. SUMMARY RESPONSE AT 4TH CYCLE AND AFTER INDUCTION IN TREATED PATIENTS

Table 51. Summary of local response in the 4th cycle, 6-8th cycles in localevaluation (treated patients) and ORR

	After 4th cycle N (%)	After induction N (%)	ORR (as Best Overall Response)
Complete response (CR)			
Partial response (PR)			
Global response (GR=CR+PR)			
Stable disease (SD)			
Progression			
Not evaluated due to lack of follow-up at cycle 6-8			
Not evaluated due to other reasons			
Total			

1.10.2. RESPONSE AT 4TH CYCLE IN TREATED PATIENTS

Table 52. Response at 4th cycle in local evaluation (treated patients)

	N (%, CI 95%)
	14 (70, 01 30 70)
CR	
PR	
SD	
Progression	
Study ends due to Exitus without CT scan 4th cycle	
Study ends due to IC withdrawal without CT scan 4th cycle	
Total	
PR or CR	
No PR or CR	
Total	
	PR SD Progression Study ends due to Exitus without CT scan 4th cycle Study ends due to IC withdrawal without CT scan 4th cycle Total PR or CR No PR or CR

Table 53. Response at 4th cycle in centralized evaluation (treated patients)

		N (%, CI 95%)
	CR	
	PR	
Centralized	SD	
evaluation	Progression	
CT scan 4th	Study ends due to Exitus without CT scan 4th cycle	
cycle	Study ends due to IC withdrawal without CT scan 4th cycle	
	Without centralized response CT scan 4th cycle (local available)	
	Total	
CR or PR at	PR or CR	
4th cycle in	No PR or CR	
centralized	Without centralized response CT scan 4th cycle (local available)	
evaluation	Total	

1.10.3. RESPONSE AT 4TH CYCLE IN PATIENTS FROM AVAILABLE RESPONSE POPULATION

Table 54. Response at 4th cycle in local evaluation (evaluable assessment)

		N (%, CI 95%)
	CR	
	PR	
Local –	SD	
evaluation CT —	Progression	
scan 4th cycle –	Study ends for Exitus without CT scan 4th cycle	
	Total	
CR or PR at 4th	PR or CR	
cycle in local	No PR or CR	
evaluation	Total	

		N (%, CI 95%)
	CR	
	PR	
Centralized	SD	
evaluation CT scan 4th	Progression	
	Study ends for Exitus without CT scan 4th cycle	
cycle -	Without centralized response CT scan 4th cycle (local available)	
	Total	
CR or PR at	PR or CR	
4th cycle in	No PR or CR	
centralized	Without centralized evaluation	
evaluation	Total	

Table 55. Response at 4th cycle in centralized evaluation (evaluable assessment)

1.10.4. RESPONSE AT 6-8TH CYCLE IN TREATED PATIENTS

Table 56. Response at 6-8th cycle in local evaluation (treated patients) N (%, CI 95%) CR PR SD Local Progression evaluation CT Study ends for Exitus without CT scan 6-8th cycle scan 6-8th cycle Study ends for IC withdrawal without CT scan 6-8th cycle Without CT scan 6-8th cycle due to lack of follow-up Total PR or CR CR or PR at No PR or CR 6-8th cycle in Without CT scan at 6-8th cycle due to lack of follow-up local evaluation · Total

Table 57. Response at 6-8th cycle in centralized evaluation (treated patients)

		N (%, CI 95%)
	Positive*	
	Negative*	
	Progression in PET-TAC 4th cycle centralized (without evaluation	
Centralized	at 6-8th cycle)	
evaluation	Ends study due to Exitus without CT-scan 6-8th cycle	
CT scan	Ends study due to withdrawal of IC without CT-scan 6-8th cycle	
6-8th cycle	Without CT-scan 6-8th cycle due to lack of follow-up	
	Without centralized evaluation 6-8th cycle (local available)	
	Without centralized evaluation 6-8th cycle	
	Total	
CR or PR at	Positive (Response)*	
6-8th cycle in	Negative (No response)*	
centralized	Without CT scan at 6-8th	
evaluation	Total	64

1.10.5. RESPONSE AT 6-8TH CYCLE IN PATIENTS FROM AVAILABLE RESPONSE POPULATION

Table 58. Response at 6-8th cycle in local evaluation (evaluable assessment)

		N (%, CI 95%)
_	CR	
Level	PR	
Local	SD	
evaluation · CT scan ·	Progression	
6-8th cycle	Study ends for Exitus without CT scan 6-8th cycle	
0-otil cycle	Without CT scan 6-8th cycle due to lack of follow-up	
	Total	
CR or PR at	PR or CR	
6-8th cycle _ in local	No PR or CR	
	Without CT scan at 6-8th cycle due to lack of follow-up	
evaluation	Total	

Table 59. Response at 6-8th cycle in centralized evaluation (evaluable assessment)

		N (%, CI 95%)
	Positive*	
	Negative*	
O a se tura lima al	Progression in PET-TAC 4th cycle centralized (without evaluation	
Centralized	at 6-8th cycle)	
evaluation CT scan	Ends study due to Exitus without CT-scan 6-8th cycle	
6-8th cycle	Without CT-scan 6-8th cycle due to lack of follow-up	
o-otti cycle	Without centralized evaluation 6-8th cycle (local available)	
	Without centralized evaluation 6-8th cycle	
	Total	
CR or PR at	Positive (Response)*	
6-8th cycle in	Negative (No response)*	
centralized	Without CT scan at 6-8th	
evaluation	Total	

1.1.1. ORR IN TREATED PATIENTS

Table 60. ORR in local evaluations (treated patients)

		N (%, CI 95%)
	CR	
	PR	
	SD	
Best Overall	Relapse	
Response (including	Progression	
CT-scans after	Study ends due to Exitus without CT scan 4th cycle and	
EOT)	after	
EOT)	Study ends due to IC withdrawal without CT scan 4th cycle	
	and after	
	Total	

BOR: CR or PR	No
(including	Yes
CT-scans after EOT)	Total

Table 61. ORR in centralized evaluations (treated patients)

		N (%, CI 95%)
BOR: CR or PR as Positive/Negative* -	No	
(including CT-scans	Yes	
after EOT)	Total	

1.10.6. ORR IN PATIENTS FROM AVAILABLE RESPONSE POPULATION

Table 62. ORR in local evaluations (evaluable assessment)

		N (%, CI 95%)
	CR	
Dest Oserall	PR	
Best Overall	SD	
Response (including	Relapse	
CT-scans after	Progression	
EOT)	Study ends due to Exitus without CT scan 4th cycle and	
201)	after	
	Total	
BOR: CR or PR	No	
(including	Yes	
CT-scans after EOT)	Total	

Table 63. ORR in centralized evaluations (evaluable assessment)

		N (%, CI 95%)
BOR: CR or PR as	No	
Positive/Negative* (including CT-scans	Yes	
after EOT) centralized	Total	

1.1	1.1.	OVERAL		L IN TREATED	PATIENTS	
		Table 64.	Overall su	rvival in treated	patients	
Estimate	d OS	N events	N at risk	% patients without exitus	CI 95%	% with exitus
at 6 mo	nths					
at 12 mo	onths					
at 24 mo	onths					
		N events (%)	Median	Min-Max	Standard error	CI 95%
Estimate	d OS					
	Table 6	5. Overall surv	rival in treat	ed patients: Event		eason ⁄‹; CI 95%)
					•	
	Alive					
Overall	<u>Alive</u> Deatl					
Overall survival	Death Total	ו				
	Death Total Lymp	า ohoma/Progres	ssion			
	Death Total Lymp Toxic	n ohoma/Progres sity	ssion			
survival	Death Total Lymp Toxic Other	n bhoma/Progres ity rs	ssion			
survival Death	Death Total Lymp Toxic Other	n ohoma/Progres sity	ssion			
survival Death	Death Total Lymp Toxic Other Not s Total eath	n ohoma/Progres ity rs pecified				
survival Death reason	Death Total Lymp Toxic Other Not s Total eath	n ohoma/Progres ity rs pecified		, Nosocomial resp	iratory infection	
survival Death reason Specify de	Death Total Lymp Toxic Other Not s Total eath	n ohoma/Progres ity rs pecified Example: CAR	T-T therapy		-	
survival Death reason Specify de	Death Total Lymp Toxic Other Not s Total eath	n ohoma/Progres ity rs pecified Example: CAR	T-T therapy	time in treated pa	atients	on
survival Death reason Specify de reason	Death Total Lymp Toxic Other Not s Total eath E	n ohoma/Progres ity rs pecified Example: CAR	T-T therapy 5. Follow-up	time in treated pa	atients	<u>N (%)</u> on edian (Min-Max)
survival Death reason Specify de reason	Death Total Lymp Toxic Other Not s Total eath E	n ohoma/Progres ity rs pecified Example: CAR Table 66	T-T therapy 5. Follow-up	time in treated pa	atients	on

Table 67	7. Overall surv	ival in co	mplete responders	(treated p	atients)
Estimated OS	N events	N at risk	% patients without Death	CI 95%	% with Death
at 6 months					
at 12 months					
at 24 months					
	N events (%)	Median	Min-Max	Standard error	CI 95%
Estimated OS					

Table 68. Overall survival in complete responders (treated patients): Events and death reason

N (%; CI 95%)

Overall	Vivo
	Death
survival	Total
Death	Lymphoma/Progression
Death	Others
reason	Total
Specify de	eath N (%)
reason	Example: Respiratory insufficiency due to progression
	Table 69. Follow-up time complete responders (treated patients)
	N Mean (SE) Median (Min-Max)
Time unt	il evitus or last follow-up (from inclusion)

Time until exitus or last follow-up (from inclusion)

1.1.1. OVERALL SUVIVAL IN AVAILABLE RESPONSE POPULATION

Table 70. Overall survival in available response population

Estimated OS	N events	N at risk	% patients without exitus	CI 95%	% with Death
at 6 months					
at 12 months					
at 24 months					
	N events (%)	Median	Min-Max	Standard error	CI 95%
Estimated OS					

Table 71. Overall survival in available response population: Events and death reason

N	10/	CI	95%)
	/0,	UI.	JJ /0)

	Viv	10
Overall survival	De	ath
Survivai	То	tal
	Ly	mphoma/Progression
Death	Ot	hers
reason	No	t specified
	То	tal
Specify de	ath	N (%)
Specify de reason	am	Example: CART-T therapy, Respiratory insufficiency due to progression…
		Table 72. Follow-up time in available response population
		N Mean (SE) Median (Min-Max)
Time unt	il exit	us or last follow-up (from inclusion)

1.1.1.1 OVERALL SUVIVAL IN COMPLETE RESPONDERS (AVAILABLE RESPONSE POPULATION)

Table 73. Overall survival in complete responders (available response population)

Estimated OS	N events	N at risk	% patients without exitus	CI 95%	% with exitus		
at 6 months							
at 12 months							
at 24 months							
	N events (%)	Median	Min-Max	Standard error	CI 95%		
Estimated OS							

Table 74. Overall survival in complete responders (available response population):Events and death reason

		N (%; CI 95%)
	Viv	0
Overall	De	ath
survival	Tot	al
Deeth	Lyı	nphoma/Progression
Death	Oth	ners
reason	Tot	al
		N (%)
Specify de	ath	Others: Probable septic shock with multi-organ failure
reason		(post-haploidentical transplantation)
		Others: Respiratory insufficiency due to progression
Tabl	le 75.	Follow-up time complete responders (available response population)
		N Mean (SE) Median (Min-Max)

Time until exitus or last follow-up (from inclusion)

1.11.2. PROGRESSION FREE SURVIVAL IN TREATED PATIENTS

	Table 76. Progression Free Survival in treated patients					
Estimated PFS	N events	N at risk	% of patients without PFS	CI 95%	% with PD	
at 6 months						
at 12 months						
at 24 months						
	N (%)	Median	Min-Max	Standard error	CI 95%	
Estimated PFS						

Tab	<u>le 77. PFS in t</u>	reated patient	ts: Events and PD	assessment	
				N (%; C	CI 95%)
	Vivo sin PD				
Progression Free	PD				
Survival	Death				
	Total				
PD assessment				N (%)
	PD assessm	ent			
1.11.2.1		PFS IN CO PATIENTS)	OMPLETE RES	PONDERS	(TREATED
Table 78. Pr	ogression Fre	e Survival in o	complete respond	ers (treated pa	itients)
Estimated PFS	N events	N at risk	% of patients without PFS	CI 95%	% with PI
at 6 months					
at 12 months					
at 24 months					
	N (%)	Median	Min-Max	Standard error	CI 95%
Estimated PFS					
Table 79. PFS i		sponders (trea	ated patients): Eve	ents and PD as N (%; C	
	<u>Vivo sin PD</u>				
Progression Free	PD				
Survival	Death				
	Total				
				N (%)

PD assessment

1.11.3. PROGRESSION FREE SURVIVAL IN AVAILABLE RESPONSE POPULATION

Table 8	0. Progression	Free Surviva	al in available resp	onse populatio	on
Estimated PFS	N events	N at risk	% of patients without PFS	CI 95%	% with PD
at 6 months					
at 12 months					
at 24 months					
	N (%)	Median	Min-Max	Standard error	CI 95%
Estimated PFS					

Table 81. PFS in available response population: Events and PD assessment

		N (%; CI 95%)
	Vivo sin PD	
Progression Free	PD	
Survival	Death	
	Total	
		N (%)
PD assessment	PD assessment	

1.11.3.1 PFS IN COMPLETE RESPONDERS (AVAILABLE RESPONSE POPULATION)

Table 82. Progression Free Survival in complete responders (available response nonulation)

Estimated PFS	N events	N at risk	% of patients without PFS	CI 95%	% with PE
at 6 months					
at 12 months					
at 24 months					
	N (%)	Median	Min-Max	Standard error	CI 95%
Estimated PFS					

Table 83. PFS in complete responders (available response population): Events and PD assessment

		N (%; CI 95%)
	Vivo sin PD	
Progression Free Survival	PD	
	Death	
	Total	
		N (%)
PD assessment	PD assessment	

1.11.4. EVENT FREE SURVIVAL IN TREATED PATIENTS

Estimated EFS	N events	N at risk	% patients without event	CI 95%	% patients with event
at 6 months					
at 12 months					
at 24months					
	N (%)	Median	Min-Max	Standard error	CI 95%
Estimated EFS					

Table 85. EFS in treated patients: Events

		N (%; CI 95%)
	Alive (without event)	
	PD	
Type of events	Death	
	Therapeutic failure (Toxicity)	
	Total	

1.11.4.1 EFS IN COMPLETE RESPONDERS (AVAILABLE RESPONSE POPULATION)

	Table 86. EFS in	available res	ponse population		
Estimated EFS	N events	N at risk	% patients without event	CI 95%	% patients with event
at 6 months					
at 12 months					
at 24months					
	N (%)	Median	Min-Max	Standard error	CI 95%
Estimated EFS					

	Table 87. EFS in available response popul	ation: Events
		N (%; CI 95%)
	Alive (without event)	
	PD	
Type of events	Death	
	Therapeutic failure (Toxicity)	
	Total	

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1.11.5. **RESPONSE DURATION IN TREATED PATIENTS**

Table 88. TAC at which the CR or PR is reached (treated patients)

%

Median (Min-Max)

Ν

Mean (SD)

 TAC at which the CR
 Cycle X

 or PR is reached
 Total

Table 89. Response duration (treated patients)

Time since CR/PR until PD/exitus or censored

1.11.5.1 PFS FROM RESPONSE (CR or PR) IN TREATED PATIENTS

Ν

Table 90. PFS from response until PD/exitus (estimated by Kaplan-Meier) (in treated

Estimated PFS from response	N events	patients N at risk	s) % of patients without event	CI 95%	% of patients with event
at 6 months			Without event		ovent
at 12 months					
at 24 months					
	N (%)	Median	Min-Max	Standard error	CI 95%
Estimated PFS from response					

Table 91. PFS from response (in treated patients): Events	
---	--

		N (%; CI 95%)
	Alive without PD	
PFS from response	PD	
events	Exitus without previous PD	
	Total	
Dto with roomonoo	No	
Pts with response	Yes	
longer than 12m	Total	

1.1.1.COMPLETE RESPONSE DURATION IN TREATED PATIENTS

Table 92. TAC at which the CR is reached (treated patients)

		Ν	%
TAC at which the CR	Cycle X		
is reached	Total		

			N Mean (SD)	Median (Mi	n-Max)
Time since CR until PD/	exitus or cen	sored			
1.1.1.1		S FROM <u>C</u> EATED PA	<u>OMPLETE RES</u> TIENTS	<u>SPONSE</u> IN	
Table 94. PFS from Cl	R until PD/exi	itus (estimat			
Estimated PFS from CR	N events	N at risk	% of patients without event	CI 95%	of patients event
at 6 months					
at 12 months					
at 24 months					
	N (%)	Median	Min-Max	Standard	CI 95%
Estimated PFS from CR				error	
Estimated FFS Irom CR					
Table 9	5. PFS from	response (ir	treated patients)	: Events	
			N	(%; CI 95%)	
	Alive with	out PD			
PFS from CR	PD				
events		nout previou	IS PD		
	Total				
Pts with CR long	er No				
than 12m	Yes Total				
PARTI/ PATIEN	AL RES ITS	PONSE	DURATION	I IN TR	EATED
PATIEN	ITS TAC at whic ich the PR _		reached (treate N		EATED
PATIENTable 96.TAC at wh	TAC at whic ich the PR _ ched	th the PR is Cycle Tota	reached (treate N X I (treated patients	ed patients) %	
PATIEN Table 96. TAC at wh is read	TAC at whic ich the PR _ ched Table 97. PF	th the PR is Cycle Tota R duration	reached (treate N X	ed patients) %	
PATIENTable 96.TAC at wh	TAC at whic ich the PR _ ched Table 97. PF	th the PR is Cycle Tota R duration	reached (treate N X I (treated patients	ed patients) %	
PATIEN Table 96. TAC at wh is read	ITS TAC at whic ich the PR ched Table 97. PF exitus or cen	th the PR is Cycle Tota R duration sored	reached (treate N X I (treated patients	ed patients) % 5) Median (Mi	n-Max)
Table 96. TAC at wh is rea Time since PR until PD/	ITS TAC at whic ich the PR ched Table 97. PF exitus or cen PFS PAT	th the PR is Cycle Tota R duration sored S FROM <u>P</u> TENTS	ed by Kaplan-Mei	ed patients) % % Median (Mi DNSE IN TRE	n-Max) ATED patients)
PATIEN Table 96. TAC at wh is rea Time since PR until PD/ 1.1.1.2	ITS TAC at whic ich the PR ched Table 97. PF exitus or cen PFS PAT	th the PR is Cycle Tota R duration sored S FROM <u>P</u> TENTS	reached (treate N X I (treated patients N Mean (SD)	ed patients) % % Median (Mi DNSE IN TRE	n-Max)

at 24 months				Standard	
	N (%)	Median	Min-Max	error	CI 95%
stimated PFS from PR					
Table 99	. PFS from	response (in	treated patients): Events	
			I	N (%; CI 95%)	
DES from DD	PD			N (%; CI 95%)	
PFS from PR		hout previous		N (%; CI 95%)	
PFS from PR events		hout previous		N (%; CI 95%)	_
events	Death with Total	hout previous		N (%; CI 95%)	
	Death with Total	hout previous		N (%; CI 95%)	

1.2. SAFETY: TOXICITY

Total

As per protocol, the following definition is used to determine which adverse events are considered as toxicities:

"Adverse event related to drug use

An adverse event is considered to be drug-related if the attribution is possible, probable, or very probable, based on the definitions provided below. (see page 54 of the protocol)".

Table 10	0. Toxicities
	N (%, IC 95%)
	Νο
AE	Yes
	Total
Toxicity: AE related to the	No
treatment (possible, probable or definitively)	Yes
	Total
	Νο
AE grade ≥3	Yes
	Total
	No
Hematological Toxicity	Yes
	Total
	Yes
SAE	Νο
	Total

T I I 400 **T**

1.2.1. MOST FREQUENT ADVERSE EVENTS AND TOXICITIES

The following table shows the most frequent Adverse events taking a threshold of 5% and in overall and also taking into account the treatment phase at the date that the AEs first appeared.

Table 101. Most frequent AEs with 5% threshold				
	Induction	Maintenance	Start day missing	Total
	N (%)	N (%)	N (%)	N (%)
Example: Platelet count decreased, Neutrophil count decreased				

The following table shows the most frequent **Toxicities** taking a threshold of 5% and in overall and also taking into account the treatment phase at the date that the AEs first appeared.

Table 102. Most frequent Toxicities with 5% threshold					
	Inductio	Maintenanc	Start day missing	Total	
	n	n e Start day missing		TOtal	
	N (%)	N (%)	N (%)	N (%)	
Example: Diarrhea, Anemia					

The following table shows the most frequent **Toxicities** taking a threshold of 5%, according to their maximum grade in overall:

Table 103. Grades of most frequent Toxicities with 5% threshold. Overall
--

	No	G-UK	G-1	G-2	G-3	G-4	Total
	N (%)						
Example: Nausea, Anemia							

Table 104. Grades of most frequent Toxicities (5% threshold). Induction phase.							
	No	G-UK	G-1	G-2	G-3	G-4	Total
	N (%)						
Example: Nausea, Anemia							

Table 105. Grades of most frequent Toxicities (5% threshold). Maintenance phase. No G-UK G-1 G-2 G-3 G-4 Total N (%) Example: Nausea, Anemia...

1.1.1. HEMATOLOGICAL AND NON-HEMTOLOGICAL TOXICITIES

The following table shows all the hematological toxicities (with maximum grade) taking into account the treatment phase at the date that the AEs first appeared.

Table 106. List of all hematological toxicities

	Inductio n	Maintenance	Total
	N (%)	N (%)	N (%)
Example: Anemia - Grade 1, Lymphocyte count decreased - Grade 2			

The following table shows all the non-haematological toxicities with maximum grade \geq 3, taking into account the treatment phase at the date that the AEs first appeared.

Table 107. List of non-hematological toxicities G≥3							
	Inductio	Inductio Maintenanc					
	n	е	Total				
	N (%)	N (%)	N (%)				

The following table shows all the non-haematological toxicities with their maximum grades, taking into account the treatment phase at the date that the AE first appeared.

Table 108. List of non-hematological t	oxicities any	y grade		
	Induction	Maintenanc	AE start day missing	Total
	N (%)	N (%)	N (%)	N (%)
Example: Abdominal pain - Grade 2, Anorexia - Grade 2				
1.1.1. SAES				
Table 109. List of non-hematologic	al toxicities	G≥3		
		Induction I	Maintenance	Total
		N (%)	N (%)	N (%)
Example: Abdominal pain - Grade 3. Anemia - Grade 3. Vomiting - Grade 3				

Table 110. List of all adverse events reported as SAEs

Study Subject ID	Hospital	AE with grade	Date AE start Date AE end	Continuing at the end of study	AE related with treatment (possible /probable/ definitely)	Status	AEs according to treatment

2. ANNEXES

2.1. ANNEX 1: RELEVANT PREVIOUS EVENTS

Table 111. List of all relevant previous events

Ν

Ν

Relevant

previous Example: Arterial hypertension, Acute cholecystitis, Dyslipidemia...

2.2. ANNEX 2: PREVIOUS MEDICATION

Table 112. List of all previous medication

Previous	Example: Acetylsalicylic acid, Omeprazole,	
medication	Trimethoprim/sulfamethoxazole	

2.3. ANNEX 3: ALL TOXICITIES

	Table 113. List of all toxicities								
Study Subjec t ID	Hospital	AE with grade	Date AE start	Date AE end	Continuing at the end of study	SAE	Status	Hematological AE	AEs according to treatment