LyMa101

Phase II study to evaluate the efficacy of upfront obinutuzumab in mantle cell lymphoma patients treated by DHAP followed by autologous transplantation plus obinutuzumab maintenance then MRD driven maintenance

Statistical Analysis Plan

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1.0	11JAN2019	Samuel GRIOLET		
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LIST OF ABBREVIATIONS

AE	Adverse Event
AEPI	Adverse Event of Particular Interest
AESI	Adverse Event of Specific Interest
ASCT	Autologous Stem Cell Transplant
BM	Bone Marrow
BSA	Body Surface Area
CHOP	Cyclophosphamide, doxorubicin, vincristine, and prednisone
CI	Confidence Interval
CR	Complete Response
CRR	Complete Response Rate
CRu	Complete Response unconfirmed
CT	Computed Tomography
CTCAE	Common Terminology Criteria for Adverse Events
DOR	Duration Of Response
ECOG	Eastern Cooperative Oncology Group
EFS	Event-Free Survival
FLIPI	Follicular Lymphoma International Prognostic Index
G-CSF	Granulocyte Colony-Stimulating Factor
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
IRR	Infusion Related Reaction
LDH	Lactic DeHydrogenase
MCL	Mantle Cell Lymphoma
MRD	Minimal Residual Disease
NCI	National Cancer Institute
ND	Not Done
NHL	Non-Hodgkin's Lymphoma
ORR	Overall response Rate
OS	Overall Survival
PD	Progressive Disease
PET	^{18}F-FDG Positron Emission Tomography
PFS	Progression Free Survival
PI	Principal Investigator
PPD	Percentage of Planned Dose
PR	Partial Response
PS	Performance Status
PT	Preferred Term
QoL	Quality Of Life
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Stable Disease
SOC	System Organ Class
OPM	Other Primary Malignancy

1 INTRODUCTION

This document describes the statistical analyses and the different layouts for tables and listings to be produced for the protocol **LyMa101** titled "*Phase II study to evaluate the efficacy of upfront obinutuzumab in mantle cell lymphoma patients treated by DHAP followed by autologous transplantation plus obinutuzumab maintenance then MRD driven maintenance*".

One interim analyse for the primary criterion is planned for this study.

The statistical analysis plan (SAP) provides a comprehensive and detailed description of the strategy, rationale, and statistical methods to be applied to assess the efficacy and safety of Obinutuzumab (GA101), in patients with previously untreated MCL treated by DHAP.

The purpose of the SAP is to ensure the credibility of the study findings by pre-specifying the statistical approaches for all data analysis before database lock.

The SAP is finalized and signed prior to the clinical database lock.

2 INVESTIGATIONAL PLAN

2.1 Rationale

Achievement and preservation of minimal residual disease (MRD) response is the strongest independent predictor of prognosis in MCL patients. By using MRD status as tool for treatment selection, treatment should be focused to achieve and maintain a maximum MRD response to improve outcome. (Pott Blood 2010, Abstract ASH 2014).

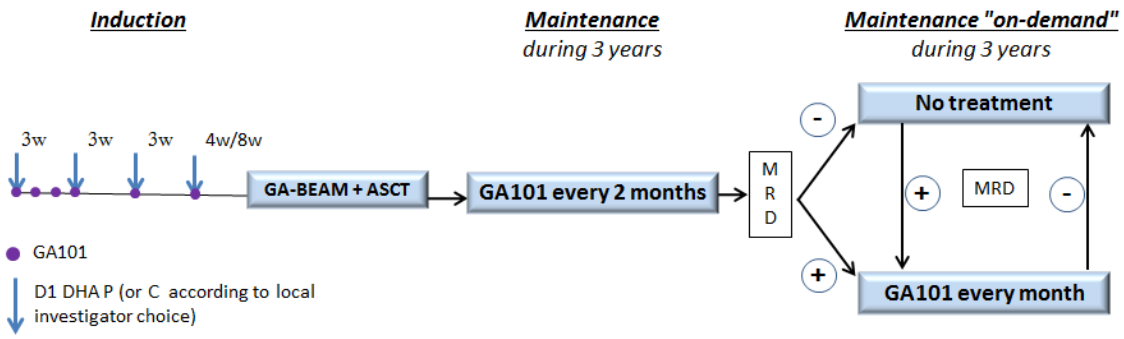
Because of the economic constraints of maintenance therapy, preemptive treatment using rituximab based on MRD relapse should be evaluated and might be effective at preventing clinical relapse. Indeed, it has been shown in 32 MCL patients that MRD-based preemptive rituximab therapy restored a PCR-negative state in 81% of cases, of whom 38% subsequently relapsed clinically at a median time of 3.9 years (Andersen JCO 2009, Geisler BJH 2012). Pre-emptive treatment may thus prevent relapse in at least some patients and may prove to be a more cost effective strategy. Use of pre-emptive treatment requires definition of molecular relapse, which is classically based on a progressive rise in MRD levels in three consecutive samples, which can be increasingly closely spaced.

The gold standard for monitoring MRD in MCL is real-time quantitative polymerase chain reaction (RQ-PCR) amplification of clonal immunoglobulin heavy chain (IgH) VDJ or IgH-BCL1 rearrangements, which are informative in 90% and 40% of patients respectively (Pott Blood 2006, Andersen JCO 2009). RQ-PCR strategies are sufficiently sensitive (minimum 0.01%) and specific for MRD quantification in around 85% of MCL patients. These strategies are, however, long, complex and associated with a significant grey zone of non-quantifiable positivity, Below the Quantitative Range (BQR). The quantifiable range (QR) should ideally be at least 0.01% (10E-4), but this is not achieved in 20-25% of samples (Cheminant et al. submitted). For these reasons, RQ-PCR is increasingly challenged by multicolor Flow cytometry (MFC) or droplet digital PCR (ddPCR).

Approximately 10% of MCL patients are not accessible to RQ-PCR MRD with acceptable sensitivity and QR. A proportion of these cases become accessible to MRD assessment by MFC (Cheminant, submitted) or by PCR quantification relative to patient specific plasmid calibrators (Gimenez et al. BJH 2012). The use of MRD results for patient stratification obviously requires maximal informativity. Therefore, the present project will also investigate complementary techniques, including MFC, ddPCR and/or plasmid calibrators.

During follow-up, the percentage of MRD positive samples was approximately 20-25% during the first 3 years, and less than 20% at later time points (Pott ASH 2014 abstract 147). Among patients with clinical relapses, it has been shown that clinical relapse is strongly associated with MRD positivity. In an analysis of the EU-MCL network, only 13% of MCL patients were peripheral blood (PB)-negative (Pott ASH 2014 abstract 147), whereas this will be the predominant source of material for MRD analysis in the proposed study, for ease of sampling, patient comfort and because informativity is comparable to bone marrow analysis, particularly at later time points.
To the present trial will determine what proportion of patients' clinical relapse is preceded by molecular relapse and with what delay. In the EU-MCL studies, the latency between the first positive MRD and the clinical relapse varies greatly between patients. The median latency for prediction by RQ-PCR when any increase to at least 2 positive triplicates was considered as MRD relapse was 22.5 months [range 1-48m] and 5 months [range 2-11m] when only results above 0.01% were considered positive, with no difference between RQ-PCR and MFC quantification (Cheminant et al. submitted).

2.2 Study Design



3 STUDY OBJECTIVES AND ENDPOINTS

3.1 Objectives

3.1.1 Primary objective

The primary objective of the study is to evaluate the efficacy of upfront Obinutuzumab (GA101) at the molecular level (MRD) in bone marrow after induction, after the 4 cycles or at premature discontinuation, in patients with previously untreated MCL treated by DHAP..

3.1.2 Secondary objectives

The secondary objectives of the study are:

- To evaluate the efficacy of the obinutuzumab in patients with MCL treated by DHAP before ASCT, after ASCT and every 6 months in terms of clinical response (Cheson 99) and MRD plus in terms of FDG-PET before and after ASCT
- To evaluate PFS, Overall survival at study end
- To evaluate the incidence of stem cell collection failure after obinutuzumab-DHAP = GA-DHAP
- To evaluate MRD negativity after 3 years of maintenance and maintenance “on-demand”
- To evaluate PET results after 3 years of maintenance
- Duration of MRD negativity
- To evaluate tolerability of obinutuzumab at induction and then “on-demand”

3.1.3 Exploratory objectives

The exploratory objectives of the study is:

- To determine baseline prognostic factors on PFS and OS

3.2 Evaluation endpoints

3.2.1 Primary efficacy endpoint

The primary endpoint is the Molecular residual disease (MRD) negativity after induction. Assessment of MRD will be based on molecular level in BM according to EU MCL network guidelines. Patient without MRD assessment (due to whatever reason) will be considered as MRD positive.
This endpoint will be analyzed on efficacy set (ES) and also on modified efficacy set (mES) as sensitivity analysis.

3.2.2 Secondary efficacy endpoints

The following secondary efficacy endpoints will be analyzed using appropriate statistical methods.

3.2.2.1 Secondary efficacy endpoint 1

Response according to Cheson 99 and overall response rate after 3 years of maintenance

Response after 3 years of maintenance will be evaluated. Assessment of response will be based on the International Workshop to Standardize Response criteria for NHL (Criteria for evaluation of response in Non-Hodgkin's lymphoma (Cheson, 1999)). Patient without response assessment (due to whatever reason) will be considered as non-responder. Overall (CR/PR) response rate will be also presented.

An additional analysis will be performed considering as non-responders all patients who relapsed or died during treatment phase even if they were prematurely treatment discontinued as responder during treatment phase.

This endpoint will be analyzed on efficacy set (ES) and on safety set (SS).

3.2.2.2 Secondary efficacy endpoint 2

PET result after 3 years of maintenance

PET result after 3 years of maintenance will be evaluated. Assessment of PET will be based on Lugano 2014 criteria (according to Cheson & Al. J. Clinic Oncol 2015). See Appendix C (Reponse criteria for lymphoma – Lugano classification).

This endpoint will be analyzed on efficacy set (ES) and on safety set (SS).

3.2.2.3 Secondary efficacy endpoint 3

MRD after 3 years of maintenance and after maintenance "on demand"

Molecular residual disease (MRD) after 3 years of maintenance and after maintenance "on demand" will be evaluated. Assessment of MRD will be based on molecular level in BM according to EU MCL network guidelines. Patient without MRD assessment (due to whatever reason) will be considered as MRD positive.

This endpoint will be analyzed on efficacy set (ES).

3.2.2.4 Secondary efficacy endpoint 4

PFS

PFS is defined as the time from inclusion into the study to the first observation of documented disease progression or death due to any cause. If a subject has not progressed or died, PFS will be censored at the time of last visit with adequate assessment.

This endpoint will be analyzed on efficacy set (ES) and on safety set (SS).

3.2.2.5 Secondary efficacy endpoint 5

OS

Overall survival will be measured from the date of inclusion to the date of death from any cause. Alive patients will be censored at their last contact date.

This endpoint will be analyzed on efficacy set (ES) and on safety set (SS).

3.2.2.6 Secondary efficacy endpoint 6

Stem cell collection failure

Stem cell collection failure will be evaluated after induction.
This endpoint will be analyzed on efficacy set (ES) and on safety set (SS).

3.2.2.7 Secondary efficacy endpoint 7

Duration of MRD negativity

Duration of MRD negativity is defined as the time from the date of attainment the first negative MRD to the date of positive MRD. Duration or MRD negativity would be assessed for patients with at least one MRD negativity and as survival endpoint. For patients achieving a negative MRD but who have not positive MRD or not MRD assessment at the time of analysis, duration of MRD negativity will be censored on the date of last MRD assessment.
This endpoint will be analyzed on efficacy set (ES).

3.2.3 Secondary safety endpoints

Summary of study drug administration including treatment duration and average dose will be displayed.

Number, frequency, reasons for premature treatment discontinuation and study discontinuation will be summarized.

Adverse events, clinical laboratory measurements will be described.

AEs will be classified using the latest version of Medical Dictionary for Drug Regulatory Activities (MedDRA) coding system at the time of database lock. The severity of the toxicities will be graded according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) whenever possible. Subsets of AEs to be summarized include serious, NCI CTCAE grade severities, suspected treatment-related, and events that resulted in withdrawal of investigational product. The most severe grade of each preferred term for a patient will be utilized for summaries of adverse events by NCI CTCAE grade.

All AEs and SAEs will be described by system organ class and preferred term (a patient having the same event more than once will be counted only once) by period. Focus on AEs leading to death, Aes leading to discontinuation from treatment and AEs of special interest (i.e Tumor Lysis Syndrom) will also be displayed in a separate table and listing.

All deaths will be listed and summarized by cause of death and narratives of death will be also presented.

This endpoint will be performed on safety set (SS).

3.2.4 Exploratory endpoints

The following exploratory endpoint will be summarized using appropriate statistical methods.

Baseline prognostic factors on PFS and OS

A dedicated analysis on survival (PFS/OS) will be performed in order to determined baseline prognostic factors. The implemented method will take into account the specificities of on-demand treatment during the second maintenance period.

3.3 Follow-up duration

The follow-up duration is defined as the time between the inclusion date and the last contact date. Follow-up duration is based on OS and calculated with a reverse Kaplan-Meier method. Deceased patients are censored at the date of death.

3.4 Extent of exposure

- Treatment duration
- Total dose
- % planned dose

4 STATISTICAL CONSIDERATIONS

4.1 Sample size calculation

Hypothesis:

We expect to have an increase of 15% of the MRD negativity in bone marrow (BM) rate for patients treated with GA-DHAP.

Based on the interim results of LYMA presented at ASH 2014, the MRD negativity rate were 65% (Legouill, ASH 2014). Nevertheless, in the LYMA study, the MRD has been assessed after 4 cycles of DHAP only for patient that completed the 4 cycles. Therefore this rate does not take into account the rate of patients who progressed on treatment or took R-CHOP because of insufficient response. If we take into account these patients considering them as non responder patients and based on the LYSA/LYSARC experience, then the MRD negativity rate of all patients in the LYMA may be around 55%. Considering that these patients will also be included in the LyMa101 we have to take into account a rate of 55% of MRD negativity instead of 65% in the sample size calculation.

The hypotheses are as follows:

- Experimental treatment will be considered ineffective if the MRD negativity in BM after the 4 cycles or at treatment discontinuation (at a molecular level) proportion is ≤ 55% (P_0)
- Experimental treatment will be considered effective if the MRD negativity in BM after the 4 cycles or at treatment discontinuation (at a molecular level) proportion ≥ 70% (P_1)
- α risk of 0.05 and β of 0.20
- one-sided test

Patients will be considered as MRD positive if the patient has no MRD assessment due to whatever the reason.

Sample Size:

A total of 70 evaluable patients will be required for this study. Assuming that some included patients will not receive the treatment or will not be informative for MRD in bone marrow and/or blood at baseline, enrollement will be done until 70 patients are evaluable. For this purpose, about 83 patients should be enrolling (15% drop-out).

Sample size calculation was performed using an exact single-stage phase II design with East 5.4 (A'Hern RP. Sample size tables for exact single-stage phase II designs. Stat Med. 2001. 20(6):859-66).

4.2 Primary criterion analysis

This analysis will be performed once all patients included in efficacy set (70 patients) have completed the 4 cycles of treatment or treatment discontinued prior to cycle 4 and will consist of analyzing:

- Primary criterion : MRD negativity in BM rate after the 4 cycles or at treatment discontinuation of GA-DHAP
- Treatment exposure
- Stem cell collection failure
- Secondary safety endpoints

Among the 70 evaluable patients, if 46 patients or more have a MRD negativity after the 4 cycles or at treatment discontinuation the treatment will be considered as sufficiently effective and further investigations (another trial) will have to be foreseen.

4.3 Final analysis

This analysis will be performed when all included patients will undergo the end of treatment visit (at end of maintenance "on demand" period or at treatment discontinuation) and will consist of the whole statistical analyses.
At this time all secondary and exploratory endpoints will be analyzed.

4.4 Analysis Sets

4.4.1 Included Set (IS)

The included set will include all included patients having signed the informed consent.

4.4.2 Efficacy Set (ES)

The Efficacy set will include all patients having signed the informed consent, received at least one dose of the IMP study drug (Obinutuzumab) and with an informative MRD in BM and/or blood at baseline.

4.4.3 Modified Efficacy Set (mES)

The modified Efficacy Set will include all patients having signed the informed consent, received at least one dose of the IMP study drug (Obinutuzumab), with an informative MRD in BM and/or blood at baseline and an informative MRD in BM after the 4 cycles of GA-DHAP or at treatment discontinuation.

4.4.4 Safety Set (SS)

The Safety set will include all patients having signed the informed consent and received at least one dose of the IMP study drug (Obinutuzumab).

4.5 General statistical approach

4.5.1 Statistical analysis

Continuous data will be summarized in tables displaying number of observations, mean, standard deviation, median, range; quartiles will also be presented when considered relevant.

Categorical data will be expressed as frequencies and percentages (of non-missing data).

Response rates (according to Cheson 1999 or MRD) will be expressed with 90% confidence limits (to be consistent with one sided 5% level of significance) according to Pearson-Clopper method. The number and percent of patients falling into each category of response will be provided.

Time to event will be performed using Kaplan-Meier method. Survival probabilities, median survival and quartiles will be estimated with their 95% CI. Survival curves will be provided. A dedicated analysis on survival (PFS/OS) will be performed in order to determined baseline prognostic factors. The implemented method will take into account the specificities of on-demand treatment during the second maintenance period.

4.5.2 Statistical methods

Unless otherwise noted, statistical tests will be two-sided and performed using a 5% level of significance.

The Kaplan Meier method[1,3], also known as the "product-limit method", is a non-paramatric method for estimating the probability of survival at any given point in time. The kaplan-meier method handles both censored and uncensored data.

The log-rank test[1] is a non-parametric test for comparing the survival distributions of two or more groups. This test is computed using the expected and observed number of events in each group.

Cox proportional-hazard model[1,2,3] is a semi-parametric model used for testing differences in survival times of two or more groups of interest, while allowing to adjust for covariates of interest.

Chi-square test[1] is used to test equality of proportions between two or more populations and is computed by comparing the observed and expected counts when the null hypothesis is true.

The Wilcoxon rank-sum test[1], also called Mann–Whitney *U* test, is a non-paramatric test used to compare disrtibutions from two independent groups and assess whether one has systematically larger values than the other.

The independent samples T-Test[3] is a parametric test used to compare the means of a normally distributed variable for two independent groups.

Logistic regression[1,3] is a regression model in which the outcome is a categorical variable. The log odds of the outcome are modeled as a linear combination of the predictor variables.

4.5.3 Statistical Approach for control of Alpha

No adjustment for multiple comparisons will be made.

4.6 Handling of missing or off-schedule data

No imputation of values for missing data will be performed.

4.7 Software

All outputs will be produced using SAS version 9.4 or higher and AdClin version 3.5.0 or higher.

5 STATISTICAL OUTPUTS

5.1 Study summary

5.1.1 Overall description

Table 4.7-1 Global recruitment status

	All patients N=XX
Included Set	
No	XX (XX.X%)
Yes	XX (XX.X%)

Table 4.7-2 Number of patients by center – Included Set

	Included Set N=XX
Center Name	
Center X	XX (XX.X%)
Center X	XX (XX.X%)
…	XX (XX.X%)

Table 4.7-3 Number of patients at each timepoint – Included Set

	Included Set N=XX
Baseline	
Evaluation at baseline	XX (XX.X%)
Induction	
Cycle 1	XX (XX.X%)
Cycle 2	XX (XX.X%)
Cycle 3	XX (XX.X%)
Cycle 4	XX (XX.X%)
Evaluation after induction	XX (XX.X%)
ASCT	
ASCT	XX (XX.X%)
Evaluation after ASCT	XX (XX.X%)
Maintenance	
V1	XX (XX.X%)
…	XX (XX.X%)
V19	XX (XX.X%)
Evaluation after 3 years of maintenance	XX (XX.X%)
Maintenance on-demand	
On-demand visit 1	XX (XX.X%)
…	XX (XX.X%)
On-demand visit 36	XX (XX.X%)
End of treatment	
Evaluation at the end of treatment	XX (XX.X%)

Table 4.7-4 Number of patients by follow-up interval – Included Set

	Included Set N=XX
Follow-up visits performed	
FU n°1	XX (XX.X%)
FU n°2	XX (XX.X%)
…	XX (XX.X%)

5.1.2 Study dates

Table 4.7-1 Date of inclusion – Included Set

	Included Set N=XX
Inclusion date	
Date of first inclusion	XX/XX/XXXX
Date of last inclusion	XX/XX/XXXX

Table 4.7-2 Date of last visit* last patient – Included Set

	Included Set N=XX
Date of last visit* of last patient	XX/XX/XXXX

* Last visit includes visits performed during follow-up period

Table 5.1.2-3 Study duration* – Included Set

	Included Set N=XX
Study duration* (months)	
N	XX
Mean (SD)	XX.X (XX.X)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

* Study duration is calculated from date of inclusion until date of last contact (including FU).

5.1.3 Follow-up duration

Figure 4.5.3-1 Follow up throughout the study(1) – Included set

(1) Reverse Kaplan-Meier regression model on OS

Table 4.5.3-1 Follow up throughout the study(1) – Survival summary – Included set

	N	Median	95% CI lower	95% CI Upper	Min	Max
Follow up duration (months)	XX	XX	XX	XX	XX	XX

(1) Reverse Kaplan-Meier regression model on OS.

5.2 Study patients

5.2.1 Disposition of patients

Figure 4.7-1 Disposition of patients

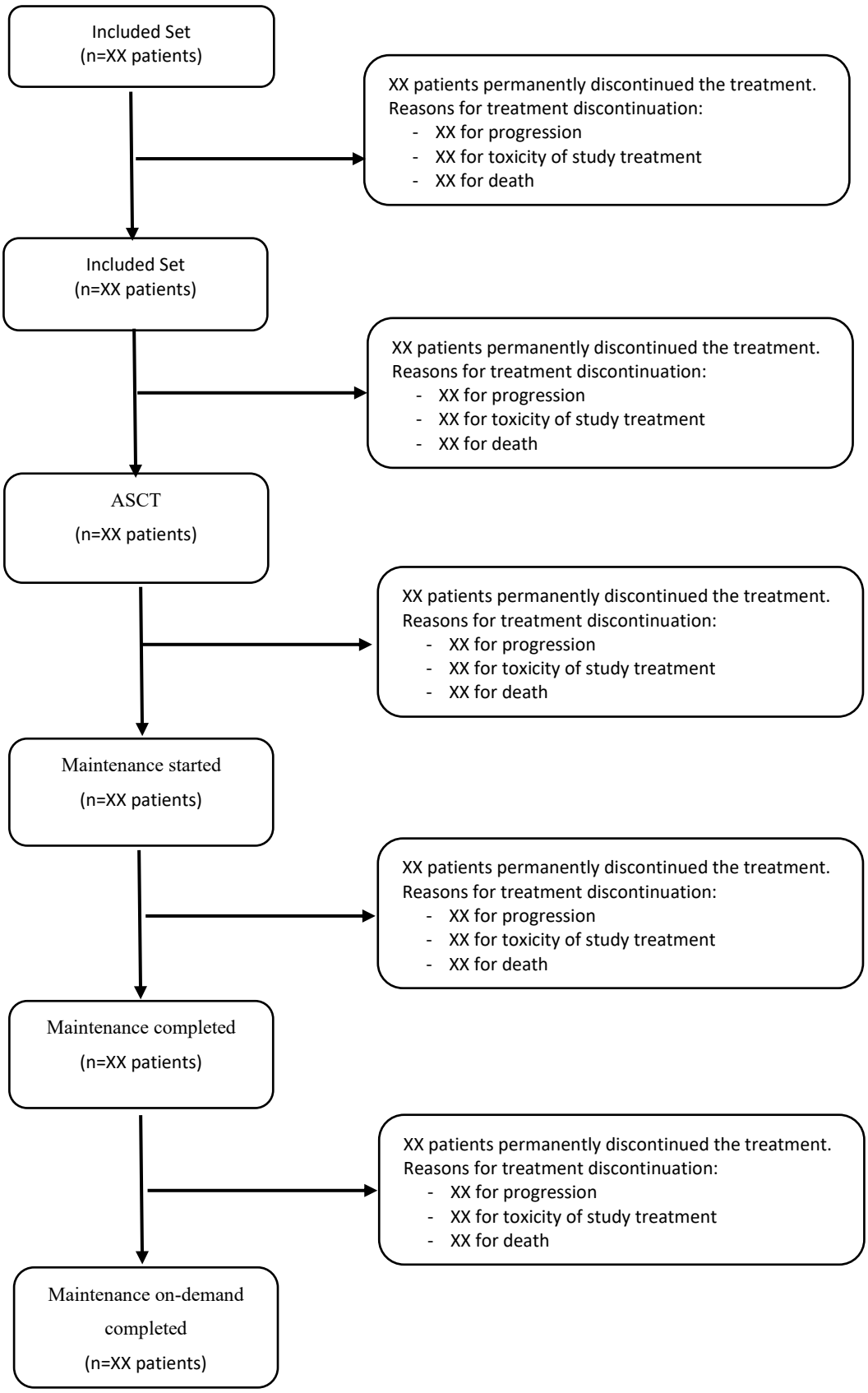


Table 4.7-1 Premature treatment discontinuation – Included Set

	Included Set N=XX
Premature treatment discontinuation	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, reason	
Progressive Disease	XX (XX.X%)
Adverse Event	XX (XX.X%)
Death	XX (XX.X%)
Withdrawal by subject	XX (XX.X%)
Protocol deviation	XX (XX.X%)
Other	XX (XX.X%)
Lack of efficacy	XX (XX.X%)
Non-compliance with study drug	XX (XX.X%)
Physician decision	XX (XX.X%)
If yes, period	
Before treatment	XX (XX.X%)
Induction	XX (XX.X%)
ASCT	XX (XX.X%)
Maintenance	XX (XX.X%)
Follow-Up	XX (XX.X%)
If yes, time since inclusion (months)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

Listing 4.7-1 Premature treatment discontinuation – Included Set (XX patients)

Patient identification number	Date of inclusion	Premature treatment discontinuation				
		Y/N	Date	Period	Reason	Description (eventually)
XXXXX	XX/XX/XXXX	XX	XX/XX/XXXX	XX	XXX	XXX

Listing 4.7-2 Premature treatment discontinuation due to AEs – Included Set (XX patients)

Patient identification number	Date of inclusion	Treatment discontinuation				Adverse event	
		Y/N	Date	Period	Reason	Description	Action taken on GA101
XXXXX	XX/XX/XXXX	XX	XX/XX/XXXX	XX	Adverse Event	XX	XX

Filter: Reason for treatment discontinuation = adverse event

5.2.2 Analysis sets

The included set will include all included patients having signed the informed consent.

The Safety set will include all patients having signed the informed consent and received at least one dose of the IMP study drug (Obinutuzumab).

The Efficacy set will include all patients having signed the informed consent, received at least one dose of the IMP study drug (Obinutuzumab) and with an informative MRD in BM and/or blood at baseline.

The modified Efficacy Set will include all patients having signed the informed consent, received at least one dose of the IMP study drug (Obinutuzumab), with an informative MRD in BM and/or blood at baseline and an informative MRD in BM after the 4 cycles of GA-DHAP or at treatment discontinuation.

Table 5.2.2-1 Analysis Sets – Included Set

	Included Set N=XX
Safety Set	
No	XX (XX.X%)
Yes	XX (XX.X%)
Efficacy Set	
No	XX (XX.X%)
Yes	XX (XX.X%)
Modified Efficacy Set	
No	XX (XX.X%)
Yes	XX (XX.X%)

Listing 5.2.2-1 Patients excluded from Safety Set (XX patients)

Patient identification number	Safety Set	Inclusion date	Received at least one dose of GA101	Number of cycles received
XXXXX	No	XX/XX/XXXX	XX	XX

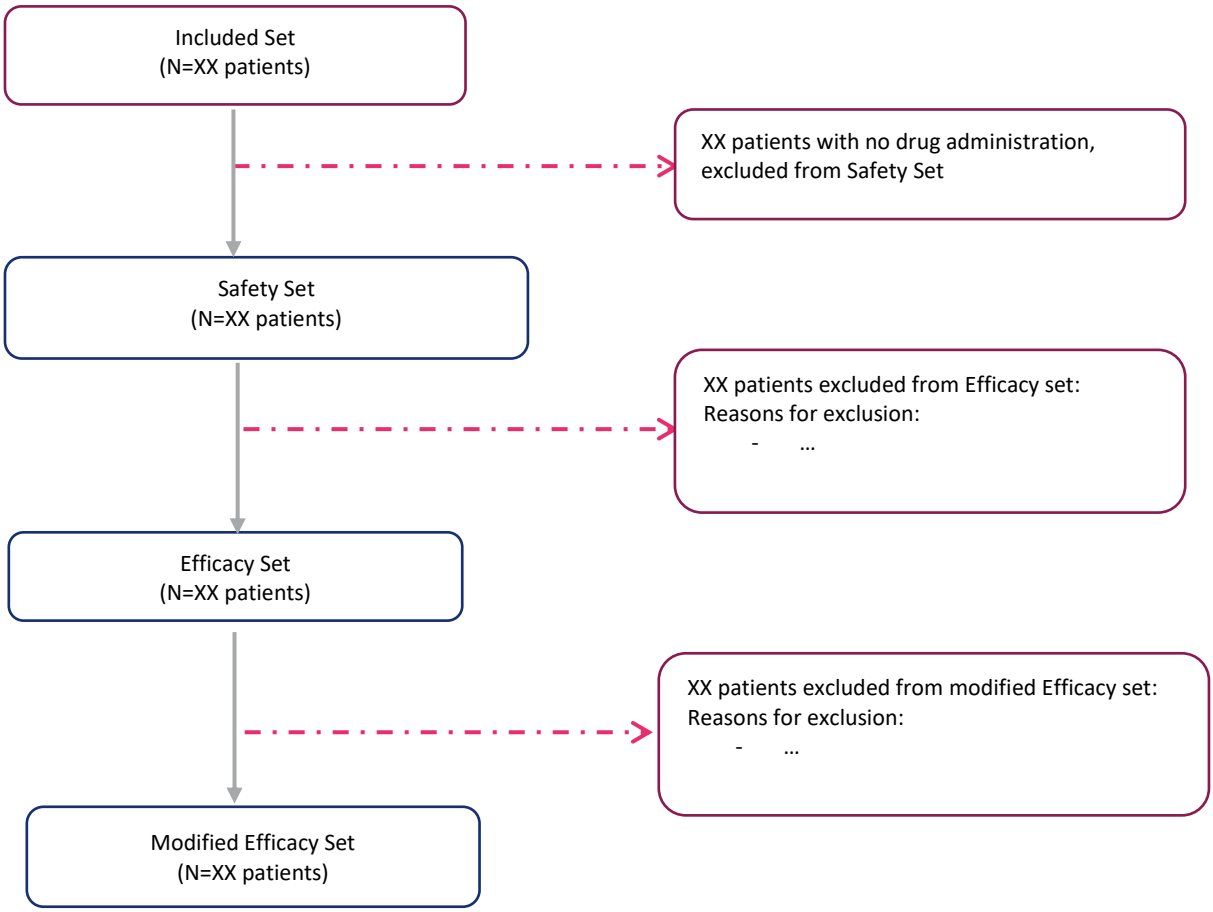
Listing 5.2.2-2 Patients excluded from Efficacy Set (XX patients)

Patient identification number	Efficacy Set	Inclusion date	Received at least one cycle of GA-DHAP	Premature withdrawal	MRD in BM at baseline	MRD in blood at baseline	Number of cycles received
XXXXX	No	XX/XX/XXXX	XX	XX	XX	XX	XX

Listing 5.2.2-3 Patients excluded from Modified Efficacy Set (XX patients)

Patient identification number	Modified Efficacy Set	Inclusion date	Received at least one cycle of GA-DHAP	Premature withdrawal	MRD in BM at baseline	MRD in blood at baseline	MRD in BM after 4 cycles	Number of cycles received
XXXXX	No	XX/XX/XXXX	XX	XX	XX	XX	XX	XX

Figure 5.2.2-1 Analysis Sets



5.3 Inclusion / Exclusion criteria

Table 4.5.3-2 Patients with at least one criterion not fulfilled – Included Set

	Included Set N=XX
Patients with at least one criterion not fulfilled	
No	XX (XX.X%)
Yes	XX (XX.X%)
Patients with at least one inclusion criterion not fulfilled	
No	XX (XX.X%)
Yes	XX (XX.X%)
Patients with at least one exclusion criterion not fulfilled	
No	XX (XX.X%)
Yes	XX (XX.X%)

Table 4.5.3-3 Inclusion Criteria – Included Set

	Included Set N=XX	
	Yes	No
Inclusion Criteria 1	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 2	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 3	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 4	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 5	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 6	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 7	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 8	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 9	XX (XX.X%)	XX (XX.X%)
Inclusion Criteria 10	XX (XX.X%)	XX (XX.X%)

Table 4.5.3-4 Exclusion Criteria – Included Set

	Included Set N=XX		
	Yes	No	NA
Exclusion Criteria 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 5	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 6	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 7	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 8	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 9	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 10	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 11	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 12	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 13	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 14	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 15	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 16	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Exclusion Criteria 17	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Listing 4.5.3-1 Patients with inclusion and or exclusion criterion not fulfilled – Included Set (XX patients)

Patient identification number	Age (years)	Sex	Inclusion date	Date of signature of consent	Criterion not fulfilled		
					Number	Definition	Value of criterion
XXXXX	XX	X	XX/XX/XXXX	XX/XX/XXXX	XX	XX	X

5.4 Protocol deviations

Table 4.7-5 Major protocol deviations – Included Set

	Included Set N=XX
Patients with at least one major protocol deviation	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, type of major protocol deviation	
Treatment received before the signature of informed consent	XX (XX.X%)
Non respect of inclusion criteria	XX (XX.X%)
Non respect of exclusion criteria	XX (XX.X%)
Diagnosis not validated with ANAPATH reviewed	XX (XX.X%)
No BM aspirate done for MRD analysis after induction or PWD	XX (XX.X%)
No BM aspirate done for MRD analysis after 3 year maintenance or PWD	XX (XX.X%)
MRD assessment not done during maintenance-on-demand	XX (XX.X%)
Positive MRD during maintenance-on-demand but no GA101 afterward	XX (XX.X%)

5.5 Demographic and other baseline characteristics

Table 4.7-6 Summary of main baseline characteristics – Included Set

	Included Set N=XX
Sex	
Male	XX (XX.X)
Female	XX (XX.X)
Age at inclusion (years)	
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
Ann Arbor stage	
II	XX (XX.X)
III	XX (XX.X)
IV	XX (XX.X)
Bio-MIPI	
Low risk	XX (XX.X%)
Intermediate risk	XX (XX.X%)
High risk	XX (XX.X%)
Performance status (ECOG)	
0	XX (XX.X)
1	XX (XX.X)
2	XX (XX.X)
3	XX (XX.X)
4	XX (XX.X)
Bulky Disease (cm)	
>= 5	XX (XX.X)
< 5	XX (XX.X)
Bone Marrow involvement (biospy or aspirate)	
Involved	XX (XX.X)
Not Involved	XX (XX.X)
Not Evaluable	XX (XX.X)
B symptoms	
No	XX (XX.X)
Yes	XX (XX.X)
Ki67 (%)	
>= 30%	XX (XX.X)
Median	XX.X
Min ; Max	XX ; XX
Blastoid variant	
No	XX (XX.X)
Yes	XX (XX.X)

5.5.1 Diagnosis

Table 4.7.1-1 Diagnosis at baseline – Included Set

	Included Set N=XX
Time between diagnosis and inclusion (months)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
Pathological diagnosis	
Mantle Cell Lymphoma	XX (XX.X%)
Other histology non authorized	XX (XX.X%)
If Other, specify	
XXX	XX (XX.X%)
XXX	XX (XX.X%)
Pathological report	
No	XX (XX.X%)
Yes	XX (XX.X%)
Diagnosis (local)	
XXX	XX (XX.X%)
XXX	XX (XX.X%)
Diagnosis according to the central review	
XXX	XX (XX.X%)
XXX	XX (XX.X%)
Blastoid variant	
No	XX (XX.X%)
Yes	XX (XX.X%)
Ki67 (%)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

5.5.2 Nodal involvement

Table 4.7.2-1 Nodal involvement at baseline – Included Set

	Included Set N=XX
Patients with at least one nodal involvement	
No	XX (XX.X%)
Yes	XX (XX.X%)

Table 4.7.2-2 Description of nodal involvement at baseline – Included Set

	Included Set N=XX
Cervical Right	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Cervical Left	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Supraclavicular Right	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Supraclavicular Left	
Normal	XX (XX.X%)
Involved	XX (XX.X%)

Not evaluated	XX (XX.X%)
Axillary Right	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Axillary Left	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Epitrochlear Right	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Epitrochlear Left	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Mediastinal	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Retroperitoneal	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Mesenteric	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Iliac right	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Iliac left	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Inguinal right	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Inguinal left	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not evaluated	XX (XX.X%)
Other nodal involvement	
No	XX (XX.X%)
Yes	XX (XX.X%)

Listing 4.7.2-2 Other nodal involvement at baseline – Included Set (XX patients)

Patient identification number	Inclusion date	Other nodal involvement	
		Number	Site
XXXXX	XX/XX/XXXX	XX	XXXX

5.5.3 Extra-nodal involvement

Table 4.7.3-1 Extra-nodal involvement at baseline – Included Set

	Included Set N=XX
Patients with at least one extra-nodal involvement	
No	XX (XX.X%)
Yes	XX (XX.X%)

Table 4.7.3-2 Description of extra-nodal involvement at baseline – Included Set

	Included Set N=XX
Spleen	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Liver	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Pancreas	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Pleura	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Lung	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Ascites	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Pericardium	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Breast	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Gonadal	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Kidney	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Adrenal	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Thyroid	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Skin	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Soft Tissues	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)

Bone	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Blood	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Tonsil	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Cavum	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Parotid	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Orbit	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Sinus	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Meningeal	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Other CNS	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Stomach	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Duodenum	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Small intestine	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Ileo-caecal junction	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Colon	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Rectum	
Normal	XX (XX.X%)
Involved	XX (XX.X%)
Not Evaluated	XX (XX.X%)
Other extra-nodal involvement	
No	XX (XX.X%)
Yes	XX (XX.X%)

Listing 4.7.3-1 Other extra-nodal involvement at baseline – Included Set (XX patients)

Patient identification number	Inclusion date	Other extra-nodal involvement	
		Number	Site
XXXXX	XX/XX/XXXX	XX	XXXX

5.5.4 Bone Marrow

Table 4.7.4-1 Description of BM involvement at baseline – Included Set

	Included Set N=XX
Bone Marrow Biopsy	
Not Involved	XX (XX.X%)
Involved	XX (XX.X%)
Unspecified	XX (XX.X%)
Bone Marrow Aspirate	
Not Involved	XX (XX.X%)
Involved	XX (XX.X%)
Unspecified	XX (XX.X%)

5.5.5 Staging

Table 4.7.5-1 Staging at baseline – Included Set

	Included Set N=XX
Performance status (ECOG)	
0	XX (XX.X%)
1	XX (XX.X%)
2	XX (XX.X%)
3	XX (XX.X%)
4	XX (XX.X%)
Ann Arbor stage	
I	XX (XX.X%)
II	XX (XX.X%)
III	XX (XX.X%)
IV	XX (XX.X%)
B symptoms	
No	XX (XX.X%)
Yes	XX (XX.X%)
MIPI risk group	
Low risk	XX (XX.X%)
Intermediate risk	XX (XX.X%)
High risk	XX (XX.X%)
MIPIb risk group	
Low risk	XX (XX.X%)
Intermediate risk	XX (XX.X%)
High risk	XX (XX.X%)

5.5.6 MRD

Table 4.7.6-7 Informative MRD at baseline – Included Set

	Included Set N=XX
Patients suitable for MRD monitoring	
No	XX (XX.X%)
Yes	XX (XX.X%)
Baseline ddPCR Interpretation on PB	
No	XX (XX.X%)
Yes	XX (XX.X%)
Baseline ddPCR Interpretation on BM	
No	XX (XX.X%)
Yes	XX (XX.X%)

5.6 Evaluation during study

5.6.1 Clinical examination

Table 5.6-1 Clinical examination during treatment – Safety Set

	After Induction N=XX	After ASCT N=XX	After 3 years of maintenance N=XX	End of Treatment N=XX
Performance status (ECOG)				
0	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
2	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
3	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
4	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Result of Clinical Exam				
Normal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Abnormal	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Not done	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

5.6.2 Tumor assessment

Table 5.6-2 Bone marrow results during treatment – Safety Set

	After Induction N=XX	After ASCT N=XX	After 3 years of maintenance N=XX	End of Treatment N=XX
Bone Marrow biopsy				
Not done	XX (XX.X%)	XX (XX.X%)	NA	XX (XX.X%)
Done	XX (XX.X%)	XX (XX.X%)		XX (XX.X%)
If done, results :				
Not involved	XX (XX.X%)	XX (XX.X%)		XX (XX.X%)
Involved	XX (XX.X%)	XX (XX.X%)		XX (XX.X%)
Unspecified	XX (XX.X%)	XX (XX.X%)		XX (XX.X%)
Bone Marrow aspirate				
Not done	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Done	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If done, results :				
Not involved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Involved	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Unspecified	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Listing 5.6-3 Abnormal CT scan during maintenance – Included Set (XX patients)

Patient identification number	Inclusion date	CT scan		
		Period	Result	Abnormality
XXXXX	XX/XX/XXXX	XX	Abnormal	XX

5.6.3 MRD results

Table 5.6.3-1 MRD results according to ddPCR during maintenance – Efficacy Set

	During maintenance					
	After 6M N=XX	After 12M N=XX	After 18M N=XX	After 24M N=XX	After 30M N=XX	After 36M N=XX
MRD results on PB						
Negative	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Positive	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Table 5.6.3-2 MRD results according to ddPCR during maintenance on demand – Efficacy Set

	During maintenance						
	After 6M N=XX	After 12M N=XX	After 18M N=XX	After 24M N=XX	After 30M N=XX	After 36M N=XX	EoT N=XX
MRD results on PB							
Negative	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Positive	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

5.7 Efficacy Analysis

5.7.1 Primary efficacy analysis

5.7.1.1 Main analysis

Table 5.7.1.1-1 MRD results on BM after induction or at treatment discontinuation – Efficacy Set

	ddPCR N=XX	Q-PCR N=XX
MRD after induction		
Negative	XX (XX.XX%)	XX (XX.XX%)
Positive	XX (XX.XX%)	XX (XX.XX%)
Positive < 10E-04	XX (XX.XX%)	XX (XX.XX%)
Missing	XX (XX.XX%)	XX (XX.XX%)
MRD negativity rate*		
Negative	XX (XX.XX%)	XX (XX.XX%)
IC 95%	[XX.XX% - XX.X%]	[XX.XX% - XX.X%]

* Patients without MRD assessment are considered as Positive MRD

Listing 5.7.1-1 Patients with missing MRD results on BM after induction or at treatment discontinuation – Efficacy Set (XX patients)

Patient identification number	Inclusion date	Last period	Patient suitable for MRD monitoring	MRD after Induction	
				Interpretation on PB	Interpretation on BM
XXXXX	XX/XX/XX	XX	XX	XX	XX

5.7.1.2 Sensitivity analysis

Table 5.7.1.21-2 MRD results on BM after induction or at treatment discontinuation – modified Efficacy Set

	ddPCR N=XX	Q-PCR N=XX
MRD after induction		
Negative	XX (XX.XX%)	XX (XX.XX%)
Positive	XX (XX.XX%)	XX (XX.XX%)
Positive < 10E-04	XX (XX.XX%)	XX (XX.XX%)
MRD negativity rate		
Negative	XX (XX.XX%)	XX (XX.XX%)
IC 95%	[XX.XX% - XX.X%]	[XX.XX% - XX.X%]

5.7.2 Progression-Free Surival (PFS)

5.7.2.1 Efficacy Set

Table 5.7.2.1-1 Events according to PFS definition* – Efficacy Set

	Efficacy Set N=XX
Events for PFS	
No event	XX (XX.X%)
Death without progression	XX (XX.X%)
Progression/relapse	XX (XX.X%)

* Response assessment by the investigator

Figure 5.7-1 PFS since inclusion – Efficacy Set

Table 5.7-2 PFS since inclusion – Survival Summary – Efficacy Set

	N	Median	95% Confidence Limits		Min	Max
			Lower	Upper		
PFS (months)	XX	XX.X	XX.X	XX.X	XX.X	XX.X

Table 5.7-3 PFS since inclusion – Survival Estimates – Efficacy Set

Time Point (months)	PFS(%)	95% Confidence Limits		Patients at risk
		Lower	Upper	
0	XX.X	XX.X	XX.X	XX
6	XX.X	XX.X	XX.X	XX
12	XX.X	XX.X	XX.X	XX
…	XX.X	XX.X	XX.X	XX

5.7.2.2 Safety Set

Table 5.7-4 Events for PFS definition* – Safety Set

	Safety Set N=XX
Events for PFS	
No event	XX (XX.X%)
Death without progression	XX (XX.X%)
Progression/relapse	XX (XX.X%)

* Response assessment by the investigator

Figure 5.7-2 PFS since inclusion – Safety Set

Table 5.7-5 PFS since inclusion – Survival Summary – Safety Set

	N	Median	95% Confidence Limits		Min	Max
			Lower	Upper		
PFS (months)	XX	XX.X	XX.X	XX.X	XX.X	XX.X

Table 5.7-6 PFS since inclusion – Survival Estimates – Safety Set

Time Point (months)	PFS(%)	95% Confidence Limits		Patients at risk
		Lower	Upper	
0	XX.X	XX.X	XX.X	XX
6	XX.X	XX.X	XX.X	XX
12	XX.X	XX.X	XX.X	XX
…	XX.X	XX.X	XX.X	XX

5.7.3 Overall Surival (OS)

5.7.3.1 Efficacy Set

Figure 5.72-2 Overall Survival – Efficacy Set

Table 5.72-4 Overall Survival – Survival Summary – Efficacy Set

	N	Median	95% Confidence Limits		Min	Max
			Lower	Upper		
OS (months)	XX	XX.X	XX.X	XX.X	XX.X	XX.X

Table 5.72-5 Overall Survival – Survival Estimates – Efficacy Set

Time Point (months)	OS(%)	95% Confidence Limits		Patients at risk
		Lower	Upper	
0	XX.X	XX.X	XX.X	XX
6	XX.X	XX.X	XX.X	XX
12	XX.X	XX.X	XX.X	XX
…	XX.X	XX.X	XX.X	XX

5.7.3.2 Safety Set

Figure 5.72-2 Overall Survival – Safety Set

Table 5.72-4 Overall Survival – Survival Summary – Safety Set

	N	Median	95% Confidence Limits		Min	Max
			Lower	Upper		
OS (months)	XX	XX.X	XX.X	XX.X	XX.X	XX.X

Table 5.72-5 Overall Survival – Survival Estimates – Safety Set

Time Point (months)	OS(%)	95% Confidence Limits		Patients at risk
		Lower	Upper	
0	XX.X	XX.X	XX.X	XX
6	XX.X	XX.X	XX.X	XX
12	XX.X	XX.X	XX.X	XX
…	XX.X	XX.X	XX.X	XX

5.7.4 Response rate

Table 5.7-6 Response according to Cheson 99 – Efficacy Set

	Evaluation after 3 years of maintenance N=XX	End of treatment N=XX
Response (Cheson 99)		
Complete Metabolic Response	XX (XX.X%)	XX (XX.X%)
Partial Metabolic Response	XX (XX.X%)	XX (XX.X%)
No Metabolic Response	XX (XX.X%)	XX (XX.X%)
Progressive Metabolic Disease	XX (XX.X%)	XX (XX.X%)
Not Evaluated	XX (XX.X%)	XX (XX.X%)
Overall Response Rate (ORR)		
Patients with ORR	XX (XX.X%)	XX (XX.X%)
IC 95%	[XX.X% - XX.X%]	[XX.X% - XX.X%]
Overall Response Rate* (ORR)		
Patients with ORR	XX (XX.X%)	XX (XX.X%)
IC 95%	[XX.X% - XX.X%]	[XX.X% - XX.X%]

* Patients who relapsed or died during treatment phase are considered as non-responders even if they were repsonders before withdrawal.

Table 5.7-2 Response according to Cheson 99 – Safety Set

	Evaluation after 3 years of maintenance N=XX	End of treatment N=XX
Response (Cheson 99)		
Complete Metabolic Response	XX (XX.X%)	XX (XX.X%)
Partial Metabolic Response	XX (XX.X%)	XX (XX.X%)
No Metabolic Response	XX (XX.X%)	XX (XX.X%)
Progressive Metabolic Disease	XX (XX.X%)	XX (XX.X%)
Not Evaluated	XX (XX.X%)	XX (XX.X%)
Overall Response Rate (ORR)		
Patients with ORR	XX (XX.X%)	XX (XX.X%)
IC 95%	[XX.X% - XX.X%]	[XX.X% - XX.X%]
Overall Response Rate* (ORR)		
Patients with ORR	XX (XX.X%)	XX (XX.X%)
IC 95%	[XX.X% - XX.X%]	[XX.X% - XX.X%]

* Patients who relapsed or died during treatment phase are considered as non-responders even if they were repsonders before withdrawal.

5.7.5 PET results

Table 5.7-7 PET scan result – Efficacy Set

	After Induction N=XX	After ASCT N=XX	After 3 years of maintenance N=XX	End of Treatment N=XX
PET scan				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If done, hypermetabolic lesion				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If yes, SUV Max tumoral				
N	XX	XX	XX	XX
Missing	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX
If yes, localisation				
XXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Table 5.7-2 PET scan result – Safety Set

	After Induction N=XX	After ASCT N=XX	After 3 years of maintenance N=XX	End of Treatment N=XX
PET scan				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If done, hypermetabolic lesion				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If yes, SUV Max tumoral				
N	XX	XX	XX	XX
Missing	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX
If yes, localisation				
XXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
XXX	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

5.7.6 MRD results

Table 5.7.6-1 MRD results according to ddPCR on BM – Efficacy Set

	After 36M of maintenance N=XX	After 36M of maintenance on-demand N=XX	End of treatment N=XX
MRD results on BM			
Negative	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Positive	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Missing	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

5.7.7 Duration of MRD negativity

Table 5.7.7 Events since first MRD negativity – Efficacy Set

	Efficacy Set N=XX
Patients with MRD negativity	**XX**
If yes, time to first negative MRD	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
Event according to MRD negativity duration	
No	XX (XX.X%)
Yes	XX (XX.X%)

Duration of MRD negativity is defined as the time from the date of attainment the first negative MRD to the date of positive MRD.
For patients achieving a negative MRD but who have not positive MRD or not MRD assessment at the time of analysis, duration of MRD negativity will be censored on the date of last MRD assessment.

Figure 5.7.7 Duration of MRD negativity – Efficacy Set
Table 5.7.7 Duration of MRD negativity – Efficacy Set – Survival Estimates

5.7.8 Stem cell collection failure

Table 5.7.3.2-1 Description of stem cell collection failure – Safety Set

	Safety Set N=XX
Leukapheresis	
Done	XX (XX.X%)
Not Done	XX (XX.X%)
If not done, specify the reason:	
Progression	XX (XX.X%)
Collection failure	XX (XX.X%)
Toxicity	XX (XX.X%)
Other	XX
If collection failure, specify:	
Sepsis	XX (XX.X%)
Not enough cells	XX (XX.X%)
Logistical problem	XX (XX.X%)
Other cause	XX
If done, Total collected cells CD34+	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

5.8 Progression / Relapse

Table 5.88-1 Summary of progression/relapse – Safety Set

	Safety Set N=XX
Patients who progressed/relapsed	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, time since inclusion (months)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

Table 5.88-2 Involvement at progression/relapse – Safety Set

	Safety Set N=XX
Progression/Relapse	XX
Initial Involvement	
No	XX (XX.X%)
Yes	XX (XX.X%)
New Involvement	
No	XX (XX.X%)
Yes	XX (XX.X%)
Nodal Involvement	
No	XX (XX.X%)
Yes	XX (XX.X%)
Extra-nodal Involvement	
No	XX (XX.X%)
Yes	XX (XX.X%)

Table 5.88-3 Treatment for progression/relapse – Safety Set

	Safety Set N=XX
Progression/relapse	XX
Progression/relapse treatment	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Monoclonal antibody	
No	XX (XX.X%)
Yes	XX (XX.X%)
Other immunotherapy	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Ibrutinib	
Yes	XX (XX.X%)
No	XX (XX.X%)
Chemotherapy	
No	XX (XX.X%)
Yes	XX (XX.X%)
Radiotherapy	
No	XX (XX.X%)
Yes	XX (XX.X%)
Autologous transplant	
No	XX (XX.X%)
Yes	XX (XX.X%)
Allogenic transplant	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, allograft transplant	
Yes	XX (XX.X%)
No	XX (XX.X%)
IMiD	
No	XX (XX.X%)
Yes	XX (XX.X%)

Epigenetic modifiers agents	
No	XX (XX.X%)
Yes	XX (XX.X%)
Kinase inhibitor	
No	XX (XX.X%)
Yes	XX (XX.X%)
Other anti-cancer therapy	
No	XX (XX.X%)
Yes	XX (XX.X%)

Listing 5.88-1 Patients who received chemotherapy for progression/relapse – Safety Set (XX patients)

Patient identification number	Inclusion date	Date of progression	Treatment for progression		
			Chemotherapy	Date	Description
XXXXX	XX/XX/XX	XX/XX/XXXX	Yes	XX/XX/XXXX	XXX

Same listing for other treatment received by at least 1 patient (no listing will be provided if empty) :

- Radiotherapy
- Monoclonal Antibody
- …

Table 5.88-4 Response according to Cheson 99 after treatment for progression/relapse – Safety Set

	Safety Set N=XX
Progression/relapse	XX
Response	
Complete response	XX (XX.X%)
Unconfirmed complete response	XX (XX.X%)
Partial response	XX (XX.X%)
Stable disease	XX (XX.X%)
Progressive disease	XX (XX.X%)
Not evaluated	XX (XX.X%)

5.9 Extent of exposure

5.9.1 Cycles

Table 5.9-1 Cycles perfomed – Safety set

	Safety set N=XX
Cycle performed	
Cycle 1	XX (XX.X%)
Cycle 2	XX (XX.X%)
Cycle 3	XX (XX.X%)
Cycle 4	XX (XX.X%)

Table 5.9-2 Number of cycles perfomed – Safety set

	Safety set N=XX
Number of cycles performed	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

Table 5.99.1-3 Treatment intake duration – Safety set

	Safety set N=XX
Treatment intake duration (months)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

Treatment intake duration is defined as the time between the 1st intake of any induction drugs and the last intake of any induction drugs.

5.9.2 Dose

Table 5.9-3 GA101 administration by cycle during induction period – Safety set

	Cycle 1			Cycle 2	Cycle 3	Cycle 4
	Day 1 N=XX	Day 8 N=XX	Day 15 N=XX	Day 1 N=XX	Day 1 N=XX	Day 1 N=XX
Total dose taken (mg/m²)						
N	XX	XX	XX	XX	XX	XX
Missing	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
PPD (%)						
N	XX	XX	XX	XX	XX	XX
Missing	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
PPD (%)						
< 75%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
[75% - 90%]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
[90% - 110%]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
[110% - 125%]	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
>= 125%	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Expected dose per cycle for GA101 : 1000mg D1 + 1000mg D8 + 1000mg D15 of cycle 1.
Total dose is the sum of dose administered during one day of a cycle.
PPD = (Total dose taken/total dose expected)/100

Table 5.9-2 GA101 administration during induction period – Safety set

	Safety set N=XX
Total dose taken (mg/m²)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
PPD (%)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
PPD (%)	
< 75%	XX (XX.X%)
[75% - 90%]	XX (XX.X%)
[90% - 110%]	XX (XX.X%)
[110% - 125%]	XX (XX.X%)
>= 125%	XX (XX.X%)

Expected total dose during induction for GA101 : 6000mg.
Total dose is the sum of dose administered during induction.
PPD = (Total dose taken/total dose expected)/100

Table 5.9-3 GA101 administration during ASCT – Safety set

	Safety set N=XX
Total dose taken (mg/m²)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
PPD (%)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
PPD (%)	
< 75%	XX (XX.X%)
[75% - 90%]	XX (XX.X%)
[90% - 110%]	XX (XX.X%)
[110% - 125%]	XX (XX.X%)
>= 125%	XX (XX.X%)

Expected total dose during asct for GA101 : 1000mg.
Total dose is the sum of dose administered during asct.
PPD = (Total dose taken/total dose expected)/100

Table 5.9-4 GA101 administration during maintenance – Safety set

	Safety set N=XX
Total dose taken (mg/m²)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
PPD (%)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
PPD (%)	
< 75%	XX (XX.X%)
[75% - 90%]	XX (XX.X%)
[90% - 110%]	XX (XX.X%)
[110% - 125%]	XX (XX.X%)
>= 125%	XX (XX.X%)

Expected total dose during maintenance for GA101 : 1000mg every 2 months.
Total dose is the sum of dose administered during maintenance.
PPD = (Total dose taken/total dose expected)/100

Table 5.9-5 GA101 administration during maintenance on-demand – Safety set

	Safety set N=XX
Total dose taken (mg/m²)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
PPD (%)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
PPD (%)	
< 75%	XX (XX.X%)
[75% - 90%]	XX (XX.X%)
[90% - 110%]	XX (XX.X%)
[110% - 125%]	XX (XX.X%)
>= 125%	XX (XX.X%)

Expected total dose during maintenance for GA101 if positive MRD : 3000mg for the 1st month and then 1000mg every month.
Total dose is the sum of dose administered during maintenance on-demand.
PPD = (Total dose taken/total dose expected)/100

Table 5.9-6 Patients with at least one dose interruption of GA101 – Safety set

	Safety set N=XX
Patients with at least one dose interruption of GA101	
No	XX (XX.X%)
Yes	XX (XX.X%)

Listing 5.9-1 Patients with at least one dose interruption of GA101 – Safety set (XX patients)

Patient identification number	Inclusion date	Number of cycles received	Adverse Event					
			Period	Descritption	Highest grade	Relationship with GA101	Action taken on GA101	Outcome
XXXXX	XX/XX/XXXX	XX	XX	XX	X	XX	XX	XX

Filter: Action taken on GA101 = Drug interrupted

5.10 Safety analysis

5.10.1 Adverse Events

Table 5.101-1 Summary of AEs – Safety set

	Induction N=XX	ASCT N=XX	Maintenance N=XX	Total N=XX
Patients with at least one AE				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If yes, number of Aes by patients				
N	XX	XX	XX	XX
Missing	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Patient with at least one AE of grade >= 3				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Patient with at least one fatal AE				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Patient with at least one AE leading to treatment discontinuation				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Patient with at least one AESI*				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

* AESI = Tumor Lysis Syndrom and IRR grade 4 occuring during or within 24 hours after the GA101 infusion.

Table 5.101-2 Summary of related AEs – Safety set

	Induction N=XX	ASCT N=XX	Maintenance N=XX	Total N=XX
Patients with at least one related AE				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If yes, number of related Aes by patients				
N	XX	XX	XX	XX
Missing	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Patient with at least one related AE of grade >= 3				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Patient with at least one fatal related AE				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Patient with at least one related AE leading to treatment discontinuation				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Patient with at least one related AESI*				
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

* AESI = Tumor Lysis Syndrom and IRR grade 4 occuring during or within 24 hours after the GA101 infusion.

Table 5.101-3 AEs by SOC and PT – Safety set

	Safety set N=XX
AEs	**XX (XX.X%)**
SOC 1	**XX (XX.X%)**
PT 1	XX (XX.X%)
PT …	XX (XX.X%)
SOC …	**XX (XX.X%)**
PT 1	XX (XX.X%)
PT …	XX (XX.X%)

Table 5.101-4 Description of AEs by SOC/PT and by highest intensity – Safety set

System Organ Class	Grade 3 N=XX		Grade 4 N=XX		Grade 5 N=XX	
Preferred Term	Patients	Events	Patients	Events	Patients	Events
AEs	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
SOC 1	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
PT 1	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PT …	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
SOC …	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PT 1	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**	**XX (XX.X%)**
PT …	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)

Table 5.101-5 Characteristics of AEs – Safety set

	Safety set N=XX
Onset period	
Before pr-phase	XX (XX.X%)
Pre-phase	XX (XX.X%)
Induction	XX (XX.X%)
ASCT	XX (XX.X%)
Maintenance	XX (XX.X%)
Maintenance on-demand	XX (XX.X%)
Follow-up	XX (XX.X%)
Highest intensity	
1	XX (XX.X%)
2	XX (XX.X%)
3	XX (XX.X%)
4	XX (XX.X%)
5	XX (XX.X%)
Relationship with GA101	
Unrelated	XX (XX.X%)
Related	XX (XX.X%)
Not applicable	XX (XX.X%)
Relationship with DHAP	
Unrelated	XX (XX.X%)
Related	XX (XX.X%)
Not applicable	XX (XX.X%)
Relationship with ASCT	
Unrelated	XX (XX.X%)
Related	XX (XX.X%)
Not applicable	XX (XX.X%)
Serious AE	
No	XX (XX.X%)
Yes	XX (XX.X%)
AESI*	
No	XX (XX.X%)
Yes	XX (XX.X%)
Outcome	
Not recovered/Not resolved	XX (XX.X%)
Recovered/Resolved	XX (XX.X%)
Recovered/Resolved with sequelae	XX (XX.X%)
Recovering/Resolving	XX (XX.X%)
Fatal	XX (XX.X%)

* AESI = Tumor Lysis Syndrom and IRR grade 4 occuring during or within 24 hours after the GA101 infusion.

Listing 5.10.1-1 Patients with fatal AEs – Safety set (XX AEs reported by XX patients)

Patient identification number	Inclusion date	Number of cycles received	Adverse Event								
			Number	Description	Onset date	Event period	Date when AE became serious	Highest intensity	GA101		Outcome
									Relationship	Action taken	
XXXXX	XX/XX/XXXX	X	Yes	XXXXX	XX/XX/XXXX	XX	XX/XX/XXXX	X	X	XX	XXX

Listing 5.10.1-2 Patients with AEs leading to treatment discontinuation – Safety set (XX AEs reported by XX patients)

Patient identification number	Inclusion date	Number of cycles received	Adverse Event								
			Number	Description	Onset date	Event period	Date when AE became serious	Highest intensity	GA101		Outcome
									Relationship	Action taken	
XXXXX	XX/XX/XXXX	X	Yes	XXXXX	XX/XX/XXXX	XX	XX/XX/XXXX	X	X	XX	XXX

Listing 5.10.1-3 Patients with AESI* – Safety set (XX AEs reported by XX patients)

Patient identification number	Inclusion date	Number of cycles received	Adverse Event								
			Number	Description	Onset date	Event period	Date when AE became serious	Highest intensity	GA101		Outcome
									Relationship	Action taken	
XXXXX	XX/XX/XXXX	X	Yes	XXXXX	XX/XX/XXXX	XX	XX/XX/XXXX	X	X	XX	XXX

* AESI = Tumor Lysis Syndrom and IRR grade 4 occuring during or within 24 hours after the GA101 infusion

5.10.2 Serious Adverse Events

Table 5.102-2 Summary of SAEs – Safety set

	Safety set N=XX
Patients with at least one SAE	
No	XX (XX.X%)
Yes	XX (XX.X%)
Patient with at least one related SAE	
No	XX (XX.X%)
Yes	XX (XX.X%)
Patient with at least one SAE of grade >= 3	
No	XX (XX.X%)
Yes	XX (XX.X%)

Table 5.102-3 SAEs by SOC and PT – Safety set

	Safety set N=XX
AEs	**XX (XX.X%)**
SOC 1	**XX (XX.X%)**
PT 1	XX (XX.X%)
PT …	XX (XX.X%)
SOC …	**XX (XX.X%)**
PT 1	XX (XX.X%)
PT …	XX (XX.X%)

Table 5.102-3 Related SAEs by SOC and PT – Safety set

	Safety set N=XX
Related SAEs	**XX (XX.X%)**
SOC 1	**XX (XX.X%)**
PT 1	XX (XX.X%)
PT …	XX (XX.X%)
SOC …	**XX (XX.X%)**
PT 1	XX (XX.X%)
PT …	XX (XX.X%)

Table 5.102-4 Characteristics of SAEs – Safety set

	Safety set N=XX
Onset period	
Pre-phase	XX (XX.X%)
Induction	XX (XX.X%)
ASCT	XX (XX.X%)
Maintenance	XX (XX.X%)
Maintenance on-demand	XX (XX.X%)
Follow-up	XX (XX.X%)
Highest intensity	
1	XX (XX.X%)
2	XX (XX.X%)
3	XX (XX.X%)
4	XX (XX.X%)
5	XX (XX.X%)
Relationship with GA101	
Unrelated	XX (XX.X%)
Related	XX (XX.X%)
Not applicable	XX (XX.X%)
Relationship with DHAP	
Unrelated	XX (XX.X%)
Related	XX (XX.X%)
Not applicable	XX (XX.X%)
Relationship with ASCT	
Unrelated	XX (XX.X%)
Related	XX (XX.X%)
Not applicable	XX (XX.X%)
Serious AE	
No	XX (XX.X%)
Yes	XX (XX.X%)
AESI*	
No	XX (XX.X%)
Yes	XX (XX.X%)
Outcome	
Not recovered/Not resolved	XX (XX.X%)
Recovered/Resolved	XX (XX.X%)
Recovered/Resolved with sequelae	XX (XX.X%)
Recovering/Resolving	XX (XX.X%)
Fatal	XX (XX.X%)

* AESI = Tumor Lysis Syndrom and IRR grade 4 occuring during or within 24 hours after the GA101 infusion

Listing 5.10.2-2 Patients with SAEs – Safety set (XX SAEs reported by XX patients)

Patient identification number	Inclusion date	Number of cycles received	Adverse Event								
			Number	Description	Onset date	Event period	Date when AE became serious	Highest intensity	GA101		Outcome
									Relationship	Action taken	
XXXXX	XX/XX/XXXX	X	Yes	XXXXX	XX/XX/XXXX	XX	XX/XX/XXXX	X	X	XX	XXX

5.10.3 Other Primay Malignancy (OPM)

Table 5.10.4 OPM – Safety set

	Safety set N=XX
Patients with at least one OPM	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, number of OPMs by patient	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
If yes, time to onset of 1st OPM since inclusion (months)	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

Table 5.10-5 OPM by SOC and PT – Safety set

	Safety set N=XX	
	Patients	Events
OPM	**XX (XX.X%)**	**XX**
SOC 1	**XX (XX.X%)**	**XX**
PT 1	XX (XX.X%)	XX
PT …	XX (XX.X%)	XX
SOC …	**XX (XX.X%)**	**XX**
PT 1	XX (XX.X%)	XX
PT …	XX (XX.X%)	XX

Listing 5.10-1 OPM – Safety set (XX patients)

Patient identification number	Inclusion date	OPM			Death			Study duration (months)
		Date	Time since inclusion (months)	Description	Y/N	Cause	Other concurrent illness description	
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX	XXX	XX	XXX	XXX	XXX

Listing 5.10-2 Narratives of OPMs – Safety set (XX patients)

Patient identification number	Inclusion date	OPM		
		Date	Description	Narrative
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX	XX

5.10.4 Deaths

Table 5.10-6 Deaths – Safety set

	Safety set N=XX
Death	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, cause of death	
Lymphoma	XX (XX.X%)
Toxicity of study treatment (including related cancer)	XX (XX.X%)
Concurrent illness	XX (XX.X%)
Toxicity of additional treatment	XX (XX.X%)
Other cause	XX (XX.X%)
Unknown	XX (XX.X%)
If yes, phase of death	
Induction phase	XX (XX.X%)
ASCT	XX (XX.X%)
Maintenance phase	XX (XX.X%)
Follow-Up	XX (XX.X%)
Disease status at death	
Complete response	XX (XX.X%)
Unconfirmed Complete response	XX (XX.X%)
Partial response	XX (XX.X%)
Stable disease	XX (XX.X%)
Progressive disease	XX (XX.X%)
Not evaluated	XX (XX.X%)

Listing 5.10.4-3 Deaths – Safety set (XX patients)

Patient identification number	Inclusion date	Number of cycles received	Study duration (months)	Death				
				Date	Cause	Specification of concurrent illness	Specification of other concurrent illness	Specification of other reason
XXXXX	XX/XX/XXXX	X	XX.X	XX/XX/XXXX	XXXXX	XXXXX	XXXXX	XXXXX

Listing 5.10.4-4 Narratives of fatal SAE – Safety set (XX patients)

Patient identification number	Inclusion date	OPM		
		Date	Description	Narrative
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX	XX

5.10.5 Clinical Laboratory

Table 5.10-7 Hematology from baseline to End of Treatment – Safety set

	Baseline N=XX	End of induction N=XX	ASCT N=XX	After 3y of maintenance N=XX	EoT N=XX
Hematology done					
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If yes,					
Hemoglobin (g/dL)					
N	XX	XX	XX	XX	XX
Missing	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Leukocytes (g/L)					
N	XX	XX	XX	XX	XX
Missing	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Neutrophils (g/L)					
N	XX	XX	XX	XX	XX
Missing	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Lymphocytes (g/L)					
N	XX	XX	XX	XX	XX
Missing	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Presence of lymphoma cells (g/L)					
N	XX	XX	XX	XX	XX
Missing	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Platelets (g/L)					
N	XX	XX	XX	XX	XX
Missing	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX	XX ; XX	XX ; XX

Table 5.10-2 Biochemistry from baseline to ASCT – Safety set

	Baseline N=XX	End of induction N=XX	ASCT N=XX
Biochemistry done			
No	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
Yes	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
If yes,			
AST (IU/L)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
ALT (IU/L)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Total bilirubin (µmol/L)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Serum creatinine (µmol/L)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Creatinine clearance			
Cockcroft-Gault formula (µmol/L)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
MDRD formula (µmol/L)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
CKD-EPI formula (µmol/L)			
N	XX	XX	XX
Missing	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X	XX.X
Q1 ; Q3	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX
Min ; Max	XX ; XX	XX ; XX	XX ; XX

5.11 Concomitant treatments

5.11.1 Concomitant treatments at inclusion

Table 5.11-1 Concomitant treatments before baseline* – Included Set

	Included Set N=XX
Patients with at least one concomitant treatment	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, number of concomitant treatment per patient	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
Patients with at least one concomitant treatment due to lymphoma	
No	XX (XX.X%)
Yes	XX (XX.X%)

* Concomitant treatment started before C1D1 and ended before C1D1.

Listing 5.11-1 Concomitant treatments before baseline* – Included Set (XX patients)

Patient identification number	Inclusion date	C1D1	Concomitant treatment					
			Start date	Number	Drug Name (INN)	Indication	End date	Ongoing
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX	XXX	XX	XX/XX/XXXX	X

* Concomitant treatment started before C1D1 and ended before C1D1.

Table 5.11-2 Concomitant treatments at baseline* – Included Set

	Included Set N=XX
Patients with at least one concomitant treatment	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, number of concomitant treatment per patient	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
Patients with at least one concomitant treatment due to lymphoma	
No	XX (XX.X%)
Yes	XX (XX.X%)

* Concomitant treatment started before C1D1 and ended during treatment or still on going.

Listing 5.11-2 Concomitant treatments at baseline* – Included Set (XX patients)

Patient identification number	Inclusion date	C1D1	Concomitant treatment					
			Start date	Number	Drug Name (INN)	Indication	End date	Ongoing
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX	XXX	XX	XX/XX/XXXX	X

* Concomitant treatment started before C1D1 and ended during treatment or still on going.

5.11.2 Concomitant treatments during treatment period

Table 5.112-2 Concomitant treatments during treatment* – Included Set

	Included Set N=XX
Patients with at least one concomitant treatment	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, number of concomitant treatment per patient	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX
Patients with at least one concomitant treatment due to lymphoma	
No	XX (XX.X%)
Yes	XX (XX.X%)

* Concomitant treatment started after C1D1 or with missing starting dates but still on going.

Listing 5.112-2 Concomitant treatments during treatment* – Included Set (XX patients)

Patient identification number	Inclusion date	C1D1	Concomitant treatment					
			Start date	Number	Drug Name (INN)	Indication	End date	Ongoing
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX	XXX	XX	XX/XX/XXXX	X

* Concomitant treatment started after C1D1 or with missing starting dates but still on going.

5.12 Non study treatments out of progression

Table 5.122-1 Non study treatment treatment out of progression – Safety Set

	Safety Set N=XX
Non study treatment out of progression	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Monoclonal antibody	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Other immunotherapy	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Chemotherapy	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Radiotherapy	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Autologous transplant	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Allogenic transplant	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, IMiD	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Epigenetic modifiers agents	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Kinase inhibitors	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, Other anti-cancer therapy	
No	XX (XX.X%)
Yes	XX (XX.X%)

Listing 5.122-1 Patients who received monoclonal antibody as non study treatment treatment out of progression – Safety Set (XX patients)

Patient identification number	Inclusion date	Permanent treatment discontinuation		Non study treatment treatment out of progression		
		Date	Reason	Monoclonal antibody	Date	Drug name
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX	Yes	XX/XX/XXXX	XXX

Listing 5.122-2 Patients who received other immunotherapy as non study treatment treatment out of progression – Safety Set (XX patients)

Patient identification number	Inclusion date	Permanent treatment discontinuation		Non study treatment treatment out of progression		
		Date	Reason	Other immunotherapy	Date	Drug name
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX	Yes	XX/XX/XXXX	XXX

Listing 5.122-3 Patients who received chemotherapy as non study treatment treatment out of progression – Safety Set (XX patients)

Patient identification number	Inclusion date	Permanent treatment discontinuation		Non study treatment treatment out of progression		
		Date	Reason	Chemotherapy	Date	Drug name
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX	Yes	XX/XX/XXXX	XXX

Listing 5.122-4 Patients who received autologous transplant as non study treatment treatment out of progression – Safety Set (XX patients)

Patient identification number	Inclusion date	Permanent treatment discontinuation		Non study treatment treatment out of progression			
		Date	Reason	Autologous transplant	Date of transplant	Type of autologous transplant intensive chemotherapy with HSCT	Date of autologous transplant intensive chemotherapy
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX	Yes	XX/XX/XXXX	XXX	XX/XX/XXXX

Listing 5.122-5 Patients who received allogenic transplant as non study treatment treatment out of progression – Safety Set (XX patients)

Patient identification number	Inclusion date	Permanent treatment discontinuation		Non study treatment treatment out of progression			
		Date	Reason	Allogenic transplant	Date of transplant	Type of allogenic transplant intensive chemotherapy with HSCT	Date of allogenic transplant intensive chemotherapy
XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX	Yes	XX/XX/XXXX	XXX	XX/XX/XXXX

Same listing for (no listing if empty) :

- Kinase
- ImiD
- …

6 REFERENCES

1. Regression Methods in Biostatistics; Linear, Logistic, Survival, and Repeated Measures Models – Eric Vittinghoff, David V. Glidden, Stephen C. Shiboski, Charles E. McCulloch - Statistics for Biology and Heath – Springer

2. Modeling Survival Data; Extending the Cox model - Terrry M. Therneau, Patricia M. Grambsch - Statistics for Biology and Heath – Springer

3. Méthodes biostatistiques appliquées à la recherche clinique en cancérologie – Andrew Kramar et Simone Mathoulin-Pélissier – L'innovation thérapeutique en cancérologie – John Libbey Eurotext

7 APPENDICES

7.1 Demographic and other baseline characteristics

Table 5.12-1 Clinical examination at baseline - Included Set

	Included Set N=XX
Clinical examination at baseline	
Normal	XX (XX.X%)
Abnormal	XX (XX.X%)
Not done	XX (XX.X%)
If Abnormal, specify	
Due to active lymphoma	XX (XX.X%)
XXXXX	XX (XX.X%)
Due to study treatment	XX (XX.X%)
XXXXX	XX (XX.X%)
Due to other reason	XX (XX.X%)
XXXXX	XX (XX.X%)

Listing 5.12-1 Patients with abnormal electrocardiogram at baseline – Included Set (XX patients)

Patient identification number	Inclusion date	Electrocardiogram		
		Date	Result	If abnormal, specify
XXXXX	XX/XX/XX	XX/XX/XX	Abnormal	XXXXX

Listing 5.12-2 Patients with other important exams performed at baseline – Included Set (XX patients)

Patient identification number	Inclusion date	Other important exams		
		Number	Description	Date
XXXXX	XX/XX/XX	1	XXXXX	XX/XX/XX
		2	XXXXX	XX/XX/XX

Table 5.12-2 Prior cancer history at baseline – Included Set

	Included Set N=XX
Patients with prior cancer history	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, number of cancer per patient	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

Listing 5.12-3 Prior cancer history at baseline – Included Set (XX patients)

Patient identification number	Inclusion date	Prior cancer history			
		Number	Type of prior cancer	Start date	End date
XXXXX	XX/XX/XX	XX	XXXXX	XX/XXXX	XX/XXXX

Table 5.12-3 Relevant medical history at baseline – Included Set

	Included Set N=XX
Patients with relevant medical history	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, number of disease per patient	
N	XX
Missing	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Q1 ; Q3	XX ; XX
Min ; Max	XX ; XX

Listing 5.12-4 Relevant medical history at baseline – Included Set (XX patients)

Patient identification number	Inclusion date	Relevant medical history			
		Number	Type of disease	Start date	Persisting
XXXXX	XX/XX/XX	XX	XXXXX	XX/XXXX	XX

Table 5.12-4 Serology at baseline – Included Set

	Included Set N=XX
HIV serology	
Negative	XX (XX.X%)
Positive	XX (XX.X%)
Not Done	XX (XX.X%)
HCV serology	
Negative	XX (XX.X%)
Positive	XX (XX.X%)
Not Done	XX (XX.X%)
HBV serology (HBs Ag)	
Negative	XX (XX.X%)
Positive	XX (XX.X%)
Not Done	XX (XX.X%)
HBV serology (anti HBs)	
Negative	XX (XX.X%)
Positive	XX (XX.X%)
Not Done	XX (XX.X%)
HBV serology (anti HBc)	
Negative	XX (XX.X%)
Positive	XX (XX.X%)
Not Done	XX (XX.X%)
HBV vaccination	
No	XX (XX.X%)
Yes	XX (XX.X%)
Unknown	XX (XX.X%)
Result of PCR for viral DNA of BV	
Negative	XX (XX.X%)
Positive	XX (XX.X%)
Not Done	XX (XX.X%)

Table 5.12-5 Female childbearing status - Included Set

	Included Set N=XX
Is female of childbearing potential	
No	XX (XX.X%)
Yes	XX (XX.X%)
If yes, result of pregancy test	
Negative	XX (XX.X%)
Positive	XX (XX.X%)
Not Done	XX (XX.X%)

7.2 Evaluation during study

Listing 5.12-1 Patients with abnormal clinical exam during treatment – Safety Set (XX patients)

Patient identification number	Inclusion date	Clinical exam						
		Period	Date	Result	Due to Lymphoma	Due to study treatment	Due to other reason(s)	Specify
XXXXX	XX/XX/XX	XX	XX/XX/XXXX	Abnormal	XX	XX	XX	XX

7.3 Appendix A: Calculation of total dose and PPD

Percentage of Planned Dose is defined as follow:

$$PPD = \frac{\text{Total dose taken in mg/m}^2}{\text{Total dose expected in mg/m}^2} \times 100$$

Table 7.6-1 Calculation of total dose taken and expected

	Total dose taken	Total dose expected
Cycle i	Sum of doses administered during Cycle i	Sum of doses expected during Cycle i
Cycle i - Cycle j	Sum of doses administered from Cycle i to Cycle j	Sum of doses expected from Cycle i to Cycle j when administered

Table 7.6-2 Expected dose for cycle 1 according to the protocol

Chemotherapy regimen	**Dose**	**D1**	**D2**	**D3**	**D4**	**D8**	**D15**
Dexamethasone	40mg	X	X	X	X		
GA-101 IV	1000mg	X				X	X
Aracytine IV (every 12 hours)	2 g/m^2	X X					
Cisplatinum* IV	100 mg/m^2	X					

Table 7.6-3 Expected dose for cycle 2 to 4 according to the protocol

Chemotherapy regimen	**Dose**	**D1**	**D2**	**D3**	**D4**
Dexamethasone	40mg	X	X	X	X
GA-101 IV	1000mg	X			
Aracytine IV (every 12 hours)	2 g/m^2	X X			
Cisplatinum* IV	100 mg/m^2	X			

7.4 Appendix B: MCL International Prognostic Index (MIPI) and combined biological Index (MIPIb)

Source: Hoster E et al. A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma. Blood 2008; 111:558-565. Erratum in: Blood 2008;111(12):5761.

MIPI Score = 0.03535 x age (years)

+ 0.6978 (if ECOG PS > 1, otherwise 0)

+ 1.367 x $\log_{10}$(LDH/ULN)

+ 0.9393 x $\log_{10}$(WBC count per 10^{-6} L)

$MIPI_b$ Score = 0.03535 x age (years)

+ 0.6978 (if ECOG PS > 1, otherwise 0)

+ 1.367 x $\log_{10}$(LDH/ULN)

+ 0.9393 x $\log_{10}$(WBC count per 10^{-6} L)

+ 0.02142 x Ki67 (%)

ECOG: ECOG performance status, LDH: lactate dehydrogenase, $\log_{10}$: logarithm with respect to base 10, ULN: upper limit of the normal range, LDH/ULN: LDH divided by ULN, WBC: white blood cell, Ki67: cell proliferation.

Risk groups are defined by:

MIPI risk group	**MIPI score**	**$MIPI_b$ score**
Low risk	< 5.7	< 5.7
Intermediate risk	≥ 5.7 and < 6.2	≥ 5.7 and < 6.5
High risk	≥ 6.2	≥ 6.5

7.5 Appendix C: Response Criteria for Lymphoma – Lugano Classification

Bruce D. Cheson, Richard I. Fisher, Sally F. Barrington, Franco Cavalli, Lawrence H. Schwartz, Emanuele Zucca, and T. Andrew Lister. *J Clin Oncol 2014;32(27):3059-68.*

Revised Criteria for Response Assessment		
Response and Site	**PET-CT–Based Response**	**CT-Based Response**
Complete	**Complete metabolic response**	**Complete radiologic response (all of the following)**
Lymph nodes and extralymphatic sites	Score 1, 2, or 3_ with or without a residual mass on 5 Point Scale† It is recognized that in Waldeyer's ring or extranodal sites with high physiologic uptake or with activation within spleen or marrow (eg, with chemotherapy or myeloid colony-stimulating factors), uptake may be greater than normal mediastinum and/or liver. In this circumstance, complete metabolic response may be inferred if uptake at sites of initial involvement is no greater than surrounding normal tissue even if the tissue has high physiologic uptake	Target nodes/nodal masses must regress to ≤ 1.5 cm in LD No extralymphatic sites of disease
Nonmeasured lesion	Not applicable	Not applicable
Organ enlargement	Not applicable	Regress to normal
New lesions	None	None
Bone marrow	No evidence of FDG-avid disease in marrow	Normal by morphology; if indeterminate, IHC negative

Partial	**Partial metabolic response**	**Partial remission (all of the following)**
Lymph nodes and extralymphatic sites	Score 4 or 5† with reduced uptake compared with baseline and residual mass(es) of any size At interim, these findings suggest responding disease At end of treatment, these findings indicate residual disease	≥ 50% decrease in SPD of up to 6 target measurable nodes and extranodal sites When a lesion is too small to measure on CT, assign 5 mm x 5 mm as the default value When no longer visible, 0 x 0 mm For a node > 5 mm x 5 mm, but smaller than normal, use actual measurement for calculation
Nonmeasured lesion	Not applicable	Absent/normal, regressed, but no increase
Organ enlargement	Not applicable	Spleen must have regressed by > 50% in length beyond normal
New lesions	None	None
Bone marrow	Residual uptake higher than uptake in normal marrow but reduced compared with baseline (diffuse uptake compatible with reactive changes from chemotherapy allowed). If there are persistent focal changes in the marrow in the context of a nodal response, consideration should be given to further evaluation with MRI or biopsy or an interval scan	Not Applicable
No Response or stable disease	**No metabolic response**	**Stable Disease**
Target nodes/nodal masses, extranodal lesions	Score 4 or 5 with no significant change in FDG uptake from baseline at interim or end of treatment	< 50% decrease from baseline in SPD of up to 6 dominant, measurable nodes and extranodal sites; no criteria for progressive disease are met
Nonmeasured lesion	Not applicable	No increase consistent with progressionNo increase consistent with progression
Organ enlargement	Not applicable	None
New lesions	None	None
Bone marrow	No change from baseline	Not applicable
Progressive disease	**Progressive Metabolic Response**	**Progressive disease requires at least 1 of the following:**
Individual target nodes/nodal masses	Score 4 or 5 with an increase in intensity of uptake from baseline and/or	PPD progression
Extranodal lesions	New FDG-avid foci consistent with lymphoma at interim or end-of-treatment assessment	An individual node/lesion must be abnormal with: LDi > 1.5 cm and Increase by ≥ 50% from PPD nadir and An increase in LDi or SDi from nadir

		0.5 cm for lesions ≤ 2 cm 1.0 cm for lesions > 2 cm In the setting of splenomegaly, the splenic length must increase by > 50% of the extent of its prior increase beyond baseline (eg, a 15-cm spleen must increase to > 16 cm). If no prior splenomegaly, must increase by at least 2 cm from baseline New or recurrent splenomegaly
Nonmeasured lesion	None	New or clear progression of preexisting nonmeasured lesions
New lesions	New FDG-avid foci consistent with lymphoma rather than another etiology (eg, infection, inflammation). If uncertain regarding etiology of new lesions, biopsy or interval scan may be considered	Regrowth of previously resolved lesions A new node > 1.5 cm in any axis A new extranodal site >1.0 cm in any axis; if < 1.0 cm in any axis, its presence must be unequivocal and must be attributable to lymphoma
Bone Marrow	New or recurrent FDG-avid foci	Assessable disease of any size unequivocally attributable to lymphoma New or recurrent involvement