Clinical trial results:
A Randomized, Double-blind, Multi-center, Multi-national Trial to Evaluate the Efficacy, Safety, and Immunogenicity of SAIT101 Versus Rituximab as a First-line Immunotherapy Treatment in Patients with Low Tumor Burden Follicular Lymphoma

Summary

EudraCT number	2016-001966-27
Trial protocol	HU ES GB CZ BG FR LV HR
Global end of trial date	10 January 2020

Results information

Result version number	v1 (current)
This version publication date	29 August 2020
First version publication date	29 August 2020

Trial information

Trial identification

Sponsor protocol code	AGB002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02809053
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Archigen Biotech Ltd
Sponsor organisation address	1 Francis Crick Avenue, Cambridge, United Kingdom, CB2 0QH
Public contact	Medical Director , Archigen Biotech Ltd, +44 20 3749 5000, info@archigenbio.com
Scientific contact	Medical Director , Archigen Biotech Ltd, +44 20 3749 5000, info@archigenbio.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	09 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 July 2019
Global end of trial reached?	Yes
Global end of trial date	10 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of SAIT101 with rituximab (MabThera®) when administered as a first-line immunotherapy in patients with low tumor burden follicular lymphoma (LTBFL).

Protection of trial subjects:

This study was performed in compliance with International Council for Harmonisation Good Clinical Practices (GCP), including the archiving of essential documents as well as the ethical principles of the Declaration of Helsinki. The study protocol, all study protocol amendments, written study subject information, informed consent form (ICF), Investigator's Brochure and any other relevant documents were reviewed and approved by an independent ethics committee (IEC) or institutional review board (IRB) at each study center.

Background therapy:

No additional background cancer therapies were allowed in the study including other experimental drug, or a concomitant chemotherapy, anticancer hormonal therapy, radiotherapy, or immunotherapy.

The use of concomitant therapy, including prescription and non-prescription drugs, non-drug therapy, dietary supplements, and herbal prescriptions, were permitted as appropriate to treat AEs or comorbid conditions.

Evidence for comparator:

This study was designed to compare the efficacy, pharmacokinetic (PK), pharmacodynamics (PD), safety, and immunogenicity of SAIT101 with rituximab (MabThera®). SAIT101 is being developed as a proposed biosimilar to rituximab.

Actual start date of recruitment	18 January 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	56 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Croatia: 2
Country: Number of subjects enrolled	Czech Republic: 50
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	United States: 5

Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Turkey: 18
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	South Africa: 8
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Chile: 3
Country: Number of subjects enrolled	Ukraine: 13
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Serbia: 4
Country: Number of subjects enrolled	Panama: 1
Country: Number of subjects enrolled	India: 32
Country: Number of subjects enrolled	Georgia: 4
Country: Number of subjects enrolled	Guatemala: 5
Country: Number of subjects enrolled	Belarus: 15
Country: Number of subjects enrolled	Egypt: 15
Country: Number of subjects enrolled	Philippines: 2
Worldwide total number of subjects	315
EEA total number of subjects	154

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	172
From 65 to 84 years	143
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One hundred and one study centres in 29 countries participated in the study. The first participant was enrolled into the study on the 18 January 2017 and the last participant completed week 28 (primary analysis cut-off) on the 17 July 2019.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	315
Number of subjects completed	315

Period 1

Period 1 title	Period A (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	SAIT101

Arm description:

SAIT101: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3 and 4.

Arm type	Active comparator
Investigational medicinal product name	SAIT101
Investigational medicinal product code	SAIT101
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

SAIT101: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3 and 4.

Arm title	MabThera

Arm description:

MabThera: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3, and 4.

Arm type	Active comparator
Investigational medicinal product name	MabThera
Investigational medicinal product code	
Other name	Rituximab
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

MabThera: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3, and 4.

Number of subjects in period 1	SAIT101	MabThera
Started	157	158
Completed	150	152
Not completed	7	6
Consent withdrawn by subject	2	3
Disease progression	2	1
Lost to follow-up	3	1
Death	-	1

Baseline characteristics

Reporting groups	
Reporting group title	SAIT101
Reporting group description:	
SAIT101: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3 and 4.	
Reporting group title	MabThera
Reporting group description:	
MabThera: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3, and 4.	

Reporting group values	SAIT101	MabThera	Total
Number of subjects	157	158	315
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	57.8	58.4	
standard deviation	± 12.38	± 12.78	-
Gender categorical Units: Subjects			
Female	86	88	174
Male	71	70	141
Ethnicity Units: Subjects			
Hispanic or Latino	11	7	18
Not Hispanic or Latino	136	139	275
Unknown or Not Reported	10	12	22
Females of childbearing potential			
Men and women of childbearing potential used highly effective methods of contraception during the course of the treatment period and for at least 12 months after the last infusion of study treatment. A man or woman was of childbearing potential if, in the opinion of the Investigator, he or she was biologically capable of having children and was sexually active.			
Units: Subjects			
Yes	24	20	44
No	133	138	271
Eastern Co-operative Oncology Group (ECOG) performance status			
Measure Description: The ECOG score is used in the evaluation of cancer patients and can help with prognosis and management of the malignant condition because performance status is highly correlated			

with survival. A higher ECOG rating score generally equates to a worst outcome. ECOG scores 0 and 1 are defined as: - ECOG Score 0: Asymptomatic (Fully active, able to carry on all pre-disease activities without restriction); - ECOG Score 1: Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature			
Units: Subjects			
ECOG Score 0	132	118	250
ECOG Score 1	25	40	65
Antidrug Antibody (ADA) Status at Baseline Units: Subjects			
Postive	3	2	5
Negative	138	148	286
Not available	16	8	24
Ann Arbor Staging			
Ann Arbor staging is the staging system for lymphomas, both in Hodgkin's lymphoma and non-Hodgkin lymphoma. Stage I indicates that the cancer is located in a single region. Stage II indicates that the cancer is located in two separate regions, an affected lymph node or lymphatic organ and a second affected area. Stage III indicates that the cancer has spread to both sides of the diaphragm. Stage IV indicates diffuse or disseminated involvement of one or more extralymphatic organs.			
Units: Subjects			
Stage I	1	0	1
Stage II	39	37	76
Stage III	72	69	141
Stage IV	45	52	97
Type of Ann Arbor Staging			
Ann Arbor staging is the staging system for lymphomas, both in Hodgkin's lymphoma (formerly designated Hodgkin's disease) and non-Hodgkin lymphoma (abbreviated NHL). It was initially developed for Hodgkin's, but has some use in NHL. It has roughly the same function as TNM staging in solid tumors Ann Arbor Clinical Stage (CS) as obtained by doctor's examination and tests, An Arbor Pathological Stage (PS) as obtained by exploratory laparotomy with splenectomy.			
Units: Subjects			
Clinical Stage	144	140	284
Pathological Stage	13	18	31
Risk Groups According to Follicular Lymphoma International Prognostic Index (FLIP-2) Score			
Follicular Lymphoma International Prognostic Index (FLIPI) score of 0 to 1 is considered "low risk" with a 10 year overall survival of 70%. A score of 2 is considered "intermediate risk" with a 10 year overall survival of 50%. Finally, a score of ≥ 3 is considered "high risk" with a 10 year overall survival of 35%			
Units: Subjects			
Low Risk (0 to 1 risk factors)	102	103	205
Intermediate Risk (2 risk factors)	40	41	81
High Risk (Greater than or equal to 3 risk factor	15	14	29
Race Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	31	30	61
Black or African American	1	1	2
Native Hawaiian or other Pacific Islander	0	0	0
White	115	111	226
Unknown	2	4	6
Not reported	7	11	18

Height			
Units: Cm			
arithmetic mean	165.96	165.71	
standard deviation	± 9.436	± 10.650	-
Weight			
Weight at baseline			
Units: Kg			
arithmetic mean	73.80	73.54	
standard deviation	± 15.107	± 16.602	-
Body Mass Index			
Units: Kg/m^2			
arithmetic mean	26.76	26.22	
standard deviation	± 4.857	± 4.967	-
Body Surface Area			
Units: m^2			
arithmetic mean	1.812	1.807	
standard deviation	± 0.2032	± 0.2332	-
Disease duration			
Disease duration was derived from initial disease diagnosis date to the date of informed consent. Note that initial disease diagnosis can be confirmed by biopsy after informed consent.			
Units: Years			
arithmetic mean	0.937	0.934	
standard deviation	± 2.1528	± 2.5793	-

Subject analysis sets

Subject analysis set title	Full Anaysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS consisted of all RAN subjects in accordance with the intended treatment group, regardless of the treatment actually received. However, subjects who did not qualify for randomization and were inadvertently randomized into the study were excluded from the FAS, provided these subjects did not receive study treatment. The FAS was considered as the primary analysis set for the primary efficacy endpoint and 1 of the analysis sets for other efficacy endpoints.
The FAS for exploratory analysis (FASEXP) consisted of all FAS subjects who had their tumors assessment measured by PET CT scan.

Subject analysis set title	Pharmacokinetic Analysis Set (PKS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Pharmacokinetic Analysis Set (PKS) included all subjects who received at least 1 dose of study treatment, had at least 1 measured drug serum concentration at a scheduled time point postdose, and had no major protocol deviations or violations thought to significantly affect the PK of the drug. Subjects in the PKS were analyzed according to the treatment received.

Subject analysis set title	Pharmacodynamic Analysis Set (PDS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Pharmacodynamic Analysis Set (PDS) included all subjects who received at least 1 dose of study treatment, had at least 1 measured PD variable (CD19+ B-cell count) at a scheduled time point postdose, and had no major protocol deviations or violations thought to significantly affect the PD of the drug. Subjects in the PDS were analyzed according to the treatment received.

Subject analysis set title	Safety Anaysis Set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set (SAF) consisted of all randomised subjects who received at least 1 dose of study treatment. Subjects were analyzed according to the treatment received. The SAF was to be used as the basis for all safety analyses up to week 52.
If there was any doubt whether a subject was treated or not, they were assumed treated for the purposes of analysis.

Reporting group values	Full Anaysis Set (FAS)	Pharmacokinetic Analysis Set (PKS)	Pharmacodynamic Analysis Set (PDS)
Number of subjects	315	148	148
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	58.1		
standard deviation	± 12.57	±	±
Gender categorical Units: Subjects			
Female	174		
Male	141		
Ethnicity Units: Subjects			
Hispanic or Latino	18		
Not Hispanic or Latino	275		
Unknown or Not Reported	22		
Females of childbearing potential			
Men and women of childbearing potential used highly effective methods of contraception during the course of the treatment period and for at least 12 months after the last infusion of study treatment. A man or woman was of childbearing potential if, in the opinion of the Investigator, he or she was biologically capable of having children and was sexually active.			
Units: Subjects			
Yes	44		
No			
Eastern Co-operative Oncology Group (ECOG) performance status			
Measure Description: The ECOG score is used in the evaluation of cancer patients and can help with prognosis and management of the malignant condition because performance status is highly correlated with survival. A higher ECOG rating score generally equates to a worst outcome. ECOG scores 0 and 1 are defined as: - ECOG Score 0: Asymptomatic (Fully active, able to carry on all pre-disease activities without restriction); - ECOG Score 1: Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature			
Units: Subjects			

ECOG Score 0	250		
ECOG Score 1	65		
Antidrug Antibody (ADA) Status at Baseline Units: Subjects			
Postive	5		
Negative	286		
Not available	24		
Ann Arbor Staging			
Ann Arbor staging is the staging system for lymphomas, both in Hodgkin's lymphoma and non-Hodgkin lymphoma. Stage I indicates that the cancer is located in a single region. Stage II indicates that the cancer is located in two separate regions, an affected lymph node or lymphatic organ and a second affected area. Stage III indicates that the cancer has spread to both sides of the diaphragm. Stage IV indicates diffuse or disseminated involvement of one or more extralymphatic organs.			
Units: Subjects			
Stage I	1		
Stage II	76		
Stage III	141		
Stage IV	30		
Type of Ann Arbor Staging			
Ann Arbor staging is the staging system for lymphomas, both in Hodgkin's lymphoma (formerly designated Hodgkin's disease) and non-Hodgkin lymphoma (abbreviated NHL). It was initially developed for Hodgkin's, but has some use in NHL. It has roughly the same function as TNM staging in solid tumors Ann Arbor Clinical Stage (CS) as obtained by doctor's examination and tests, An Arbor Pathological Stage (PS) as obtained by exploratory laparotomy with splenectomy.			
Units: Subjects			
Clinical Stage	284		
Pathological Stage	31		
Risk Groups According to Follicular Lymphoma International Prognostic Index (FLIP-2) Score			
Follicular Lymphoma International Prognostic Index (FLIPI) score of 0 to 1 is considered "low risk" with a 10 year overall survival of 70%. A score of 2 is considered "intermediate risk" with a 10 year overall survival of 50%. Finally, a score of ≥ 3 is considered "high risk" with a 10 year overall survival of 35%			
Units: Subjects			
Low Risk (0 to 1 risk factors)	205		
Intermediate Risk (2 risk factors)	81		
High Risk (Greater than or equal to 3 risk factor	29		
Race Units: Subjects			
American Indian or Alaska Native			
Asian			
Black or African American			
Native Hawaiian or other Pacific Islander			
White			
Unknown			
Not reported			
Height Units: Cm			
arithmetic mean	165.84		
standard deviation	± 10.048	±	±
Weight			

Weight at baseline			
Units: Kg			
arithmetic mean	73.67		
standard deviation	± 15.850	±	±
Body Mass Index			
Units: Kg/m^2			
arithmetic mean	26.71		
standard deviation	± 4.905	±	±
Body Surface Area			
Units: m^2			
arithmetic mean	1.810		
standard deviation	± 0.2184	±	±
Disease duration			
Disease duration was derived from initial disease diagnosis date to the date of informed consent. Note that initial disease diagnosis can be confirmed by biopsy after informed consent.			
Units: Years			
arithmetic mean	0.935		
standard deviation	± 2.3626	±	±

Reporting group values	Safety Anaysis Set (SAF)		
Number of subjects	315		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±		
Gender categorical			
Units: Subjects			
Female			
Male			
Ethnicity			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			
Females of childbearing potential			
Men and women of childbearing potential used highly effective methods of contraception during the course of the treatment period and for at least 12 months after the last infusion of study treatment. A man or woman was of childbearing potential if, in the opinion of the Investigator, he or she was biologically capable of having children and was sexually active.			

Units: Subjects			
Yes No			
Eastern Co-operative Oncology Group (ECOG) performance status			
Measure Description: The ECOG score is used in the evaluation of cancer patients and can help with prognosis and management of the malignant condition because performance status is highly correlated with survival. A higher ECOG rating score generally equates to a worst outcome. ECOG scores 0 and 1 are defined as: - ECOG Score 0: Asymptomatic (Fully active, able to carry on all pre-disease activities without restriction); - ECOG Score 1: Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature			
Units: Subjects			
ECOG Score 0 ECOG Score 1			
Antidrug Antibody (ADA) Status at Baseline Units: Subjects			
Postive Negative Not available			
Ann Arbor Staging			
Ann Arbor staging is the staging system for lymphomas, both in Hodgkin's lymphoma and non-Hodgkin lymphoma. Stage I indicates that the cancer is located in a single region. Stage II indicates that the cancer is located in two separate regions, an affected lymph node or lymphatic organ and a second affected area. Stage III indicates that the cancer has spread to both sides of the diaphragm. Stage IV indicates diffuse or disseminated involvement of one or more extralymphatic organs.			
Units: Subjects			
Stage I Stage II Stage III Stage IV			
Type of Ann Arbor Staging			
Ann Arbor staging is the staging system for lymphomas, both in Hodgkin's lymphoma (formerly designated Hodgkin's disease) and non-Hodgkin lymphoma (abbreviated NHL). It was initially developed for Hodgkin's, but has some use in NHL. It has roughly the same function as TNM staging in solid tumors Ann Arbor Clinical Stage (CS) as obtained by doctor's examination and tests, An Arbor Pathological Stage (PS) as obtained by exploratory laparotomy with splenectomy.			
Units: Subjects			
Clinical Stage Pathological Stage			
Risk Groups According to Follicular Lymphoma International Prognostic Index (FLIP-2) Score			
Follicular Lymphoma International Prognostic Index (FLIPI) score of 0 to 1 is considered "low risk" with a 10 year overall survival of 70%. A score of 2 is considered "intermediate risk" with a 10 year overall survival of 50%. Finally, a score of ≥ 3 is considered "high risk" with a 10 year overall survival of 35%			
Units: Subjects			
Low Risk (0 to 1 risk factors) Intermediate Risk (2 risk factors) High Risk (Greater than or equal to 3 risk factor			
Race Units: Subjects			
American Indian or Alaska Native			

Asian Black or African American Native Hawaiian or other Pacific Islander White Unknown Not reported			
Height Units: Cm arithmetic mean standard deviation	±		
Weight			
Weight at baseline			
Units: Kg arithmetic mean standard deviation	±		
Body Mass Index Units: Kg/m^2 arithmetic mean standard deviation	±		
Body Surface Area Units: m^2 arithmetic mean standard deviation	±		
Disease duration			
Disease duration was derived from initial disease diagnosis date to the date of informed consent. Note that initial disease diagnosis can be confirmed by biopsy after informed consent.			
Units: Years arithmetic mean standard deviation	±		

End points

End points reporting groups

Reporting group title	SAIT101

Reporting group description:

SAIT101: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3 and 4.

Reporting group title	MabThera

Reporting group description:

MabThera: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3, and 4.

Subject analysis set title	Full Anaysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS consisted of all RAN subjects in accordance with the intended treatment group, regardless of the treatment actually received. However, subjects who did not qualify for randomization and were inadvertently randomized into the study were excluded from the FAS, provided these subjects did not receive study treatment. The FAS was considered as the primary analysis set for the primary efficacy endpoint and 1 of the analysis sets for other efficacy endpoints.
The FAS for exploratory analysis (FASEXP) consisted of all FAS subjects who had their tumors assessment measured by PET CT scan.

Subject analysis set title	Pharmacokinetic Analysis Set (PKS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Pharmacokinetic Analysis Set (PKS) included all subjects who received at least 1 dose of study treatment, had at least 1 measured drug serum concentration at a scheduled time point postdose, and had no major protocol deviations or violations thought to significantly affect the PK of the drug. Subjects in the PKS were analyzed according to the treatment received.

Subject analysis set title	Pharmacodynamic Analysis Set (PDS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Pharmacodynamic Analysis Set (PDS) included all subjects who received at least 1 dose of study treatment, had at least 1 measured PD variable (CD19+ B-cell count) at a scheduled time point postdose, and had no major protocol deviations or violations thought to significantly affect the PD of the drug. Subjects in the PDS were analyzed according to the treatment received.

Subject analysis set title	Safety Anaysis Set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Analysis Set (SAF) consisted of all randomised subjects who received at least 1 dose of study treatment. Subjects were analyzed according to the treatment received. The SAF was to be used as the basis for all safety analyses up to week 52.
If there was any doubt whether a subject was treated or not, they were assumed treated for the purposes of analysis.

Primary: Overall Response Rate (ORR) at Week 28

End point title	Overall Response Rate (ORR) at Week 28

End point description:

Overall Response Rate (ORR) (Complete Response [CR] + Partial Response [PR]) at Week 28, as defined by International Working Group (IWG) criteria 2007. Tumour assessments were assessed by central imaging review per International Working Group (IWG) Criteria 2007. The 95% CI for overall response rate (ORR) was calculated using the Exact method and combined using the Rubin's rule when multiple imputation was applicable.

End point type	Primary

End point timeframe:

Baseline (Day 0) to Week 28

End point values	SAIT101	MabThera	Full Anaysis Set (FAS)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	157	158	157	
Units: Percentage of subjects				
number (confidence interval 95%)				
Overall Response Rate	66.3 (58.64 to 73.87)	70.6 (63.21 to 77.97)	66.3 (58.64 to 73.87)	

Attachments (see zip file)	Plot for Overall Tumor Assessment /AGB002 ORR.PNG

Statistical analyses

Statistical analysis title	Adjusted Difference Rate (%) in ORR

Statistical analysis description:

The 95%CI (confidence interval) for the difference in the overall response rate (ORR) was calculated using the Newcombe-Wilson method based on CMH (Cochran-Mantel-Haenszel) weight with stratification factor FLIPI-2 (low, intermediate and high risk).

Comparison groups	MabThera v SAIT101
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Adjusted Difference Rate (%)
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.8
upper limit	6.35
Variability estimate	Standard error of the mean
Dispersion value	5.4

Primary: Truncated Area Under the Concentration-time Curve (AUC) Over the First and Fourth Dosing Intervals (AUC0 168,w1, AUC0-168,w4)

End point title	Truncated Area Under the Concentration-time Curve (AUC) Over the First and Fourth Dosing Intervals (AUC0 168,w1, AUC0-168,w4)

End point description:

Pharmacokinetic endpoint: truncated area under the concentration-time curve (AUC) over the first (Day 1) and fourth (Day 22) dosing intervals (AUC0 168,w1, AUC0-168,w4).

End point type	Primary

End point timeframe:

Baseline (Day 0) to dosing on Week 1 and Week 4

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	72		
Units: H*µg/ml				
geometric mean (geometric coefficient of variation)				
AUC0-168, week 1	20140 (± 18.7)	19860 (± 18.3)		
AUC0-168, week 4	41290 (± 19)	42600 (± 19.4)		

Statistical analyses

Statistical analysis title	Geometric least square (GLS) Mean Ratio

Statistical analysis description:

Statistical Comparison: geometric least square (GLS) Mean Ratio (90% Confidence Interval (CI)) (%) of SAIT101 versus MabThera Area Under the Concentration time Curve Day 0 to Week 1 (AUC0-168,w1) (h×µg/mL). The statistical comparison of the loge-transformed primary parameters between treatments is based on an analysis of variance model with fixed effect for treatment

Comparison groups	MabThera v SAIT101
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	Mean difference (final values)
Point estimate	101.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	95.86
upper limit	107.24

Notes:

[1] - Standard acceptance limits for bioequivalence (80.00% to 125.00%). Comparison: SAIT101 versus MabThera. Equivalence was demonstrated for SAIT101 and MabThera with exposure pharmacokinetic parameter AUC0-168,w1 within the standard acceptance limits for bioequivalence (80.00% to 125.00%).

Secondary: Overall Response Rate (ORR) at Week 12

End point title	Overall Response Rate (ORR) at Week 12

End point description:

Overall Response Rate (ORR) = Complete Response (CR) + Partial Response (PR). Tumour assessments were assessed by central imaging review per the International Working Group (IWG) Criteria 2007. The 95% CI for overall response rate (ORR) was calculated using the Exact method and combined using the Rubin's rule when multiple imputation was applicable.

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Week 12

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	158		
Units: Percentage of subjects				
number (confidence interval 95%)				
ORR at Week 12	59.6 (51.16 to 67.62)	70.0 (61.99 to 77.20)		

Attachments (see zip file)	Plot for Overall Tumor Assessment and ORR/AGB002 ORR w12.

Statistical analyses

Statistical analysis title	Adjusted Difference Rate of ORR at Week 12

Statistical analysis description:

The 95%CI (confidence interval) for the difference in the overall response rate (ORR) was calculated using the Newcombe-Wilson method based on CMH (Cochran-Mantel-Haenszel) weight with stratification factor FLIPI-2 (low, intermediate and high risk).

Comparison groups	SAIT101 v MabThera
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Adjusted Difference Rate
Point estimate	-10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.92
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	5.42

Notes:

[2] - Comparison: SAIT101 versus MabThera

Secondary: Complete Response (CR) at Weeks 12 and 2

End point title	Complete Response (CR) at Weeks 12 and 2

End point description:

Efficacy Endpoint: Complete Response (CR) at Weeks 12 and 28. Tumour assessments were assessed by central imaging review per International Working Group (IWG) Criteria 2007.

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Week 12 and Week 28

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145	148		
Units: Number of subjects				
CR at Week 12	39	37		
CR at Week 28	51	50		

Statistical analyses

No statistical analyses for this end point

Secondary: Partial Response (PR) at Weeks 12 and 28

End point title	Partial Response (PR) at Weeks 12 and 28

End point description:

Efficacy Endpoint: Partial Response (PR) at Weeks 12 and 28. Tumour assessments were assessed by central imaging review per International Working Group (IWG) Criteria 2007.

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Week 12 and Week 28.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145	148		
Units: Number of subjects				
PR at Week 12	48	68		
PR at Week 28	47	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Stable Disease (SD) at Weeks 12 and 28

End point title	Stable Disease (SD) at Weeks 12 and 28

End point description:

Efficacy endpoint: number of participants with Stable Disease (SD) at Weeks 12 and 28. Tumour assessments were assessed by central imaging review per International Working Group (IWG) Criteria 2007.

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Week 12 and Week 28

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145	148		
Units: Number of subjects				
SD at Week 12	50	39		
SD at Week 28	22	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Progressive Disease (PD) at 12 and 28 Weeks

End point title	Progressive Disease (PD) at 12 and 28 Weeks

End point description:

Efficacy endpoint: number of participants with Progressive Disease (PD) at 12 and 28 Weeks. Tumour assessments were assessed by central imaging review per International Working Group (IWG) Criteria 2007.

End point type	Secondary

End point timeframe:

Baseline (Week 0)to Week 12 and Week 28.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145	148		
Units: Number of subjects				
PD at Week 12	4	1		
PD at Week 28	20	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Event (TTE)

End point title	Time to Event (TTE)

End point description:

Efficacy Endpoint. Time to Event (TTE) is defined as the time of randomisation to the date when an event occurred for a maximum follow-up period of 32 weeks from baseline; an event is disease progression, death due to any cause, or the start of new treatment for follicular lymphoma, whichever comes first.

End point type	Secondary

End point timeframe:

Baseline (Day 0) to time of event or up to a maximum of 32 weeks, whichever is sooner

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	158		
Units: Months				
arithmetic mean (standard deviation)				
Time to event	23.50 (± 7.500)	24.08 (± 6.767)		

Attachments (see zip file)	Kaplan Meier Plot for Time to Event Full Analysis/AGB002 TTE.

Statistical analyses

Statistical analysis title	Time to Event (TTE) Hazard Ratio (HR)

Statistical analysis description:

Time to Event (TTE) Hazard Ratio (HR) of SAIT101:MabThera. The TTE is defined as the time from the date of randomization to the date when an event occurs; an event is disease progression as assessed by Investigator, death due to any cause, or the start of new treatment, whichever comes first.

Comparison groups	SAIT101 v MabThera
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.724
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.853
upper limit	3.482

Notes:

[3] - The estimated Hazard Ratio with 95% CI was obtained from Cox regression model; however, stratification factors, ie, FLIPI-2 (low, intermediate and high risk), were only taken into account if FLIPI-2 score=all.

Secondary: Maximum Concentration (Cmax) After the First Dose and the Fourth Dose (Cmax,w1, Cmax,w4)

End point title	Maximum Concentration (Cmax) After the First Dose and the Fourth Dose (Cmax,w1, Cmax,w4)

End point description:

Pharmacokinetic endpoint: maximum plasma concentration (Cmax, µg/ml) after the first dose (Week 1) and the fourth dose (week 4) (Cmax,w1, Cmax,w4).

End point type	Secondary

End point timeframe:

Baseline (Day 0) to dosing on Week 1 and Week 4

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	72		
Units: µg/m				
geometric mean (geometric coefficient of variation)				
Cmax Week 1	199.3 (± 22.1)	200.6 (± 27.5)		
Cmax Week 4	333.6 (± 22.8)	336.2 (± 20.2)		

Statistical analyses

Statistical analysis title	Cmax GLS Mean Ratio at Week 1

Statistical analysis description:

Statistical Comparison: geometric least square (GLS) Mean Ratio (90% CI) (%) of SAIT101 versus MabThera maximum plasma concentration at Week 1 (Cmax,w1) (h×µg/mL). The statistical comparison of the loge-transformed primary parameters between treatments is based on an analysis of variance model with fixed effect for treatment.

Comparison groups	SAIT101 v MabThera
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	equivalence[4]
Parameter estimate	GLS Mean Difference
Point estimate	99.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	90.85
upper limit	104.4

Notes:

[4] - Standard acceptance limits for bioequivalence (80.00% to 125.00%). Comparison: SAIT101 versus MabThera. Pharmacokinetic equivalence was demonstrated for SAIT101 and MabThera with Cmax,w1 exposure within the standard acceptance limits for bioequivalence (80.00% to 125.00%).

Statistical analysis title	Cmax GLS Mean Ratio at Week 4

Statistical analysis description:

Statistical Comparison: geometric least square (GLS) Mean Ratio (90% CI) (%) of SAIT101 versus MabThera maximum plasma concentration at Week 4 (Cmax,w1) (hg/mL). The statistical comparison of the loge-transformed primary parameters between treatments is based on an analysis of variance model with fixed effect for treatment

Comparison groups	SAIT101 v MabThera
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	equivalence[5]
Parameter estimate	GLS Mean Difference
Point estimate	99.2

Confidence interval	
level	90 %
sides	2-sided
lower limit	92.96
upper limit	105.92

Notes:

[5] - Standard acceptance limits for bioequivalence (80.00% to 125.00%). Comparison: SAIT101 versus MabThera. Pharmacokinetic equivalence was demonstrated for SAIT101 and MabThera with exposure PK parameter Cmax,w4 within the standard acceptance limits for bioequivalence (80.00% to 125.00%).

Secondary: Accumulation Ratio for AUC0-168 Obtained From the Fourth Dose Versus the First Dose (RAUC).

End point title	Accumulation Ratio for AUC0-168 Obtained From the Fourth Dose Versus the First Dose (RAUC).

End point description:

Pharmacokinetic endpoint: accumulation ratio for the Area Under the Concentration Time Cure 0 to 168 hours (AUC0-168) obtained from the fourth dose (Week 4) versus the first dose (Week 1) (RAUC). Accumulation ratio, calculated for AUC0-168 as (AUC0 168,w4/AUC0 168,w1).

End point type	Secondary

End point timeframe:

Baseline (Day 0) to dosing on Week 1 and Week 4

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	72		
Units: µg/m				
geometric mean (geometric coefficient of variation)				
RAUC	2.075 (± 17.2)	2.137 (± 21.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Ratio for the Maximum Plasma Concentration (Cmax) From the Fourth Dose Versus the First Dose (RCmax)

End point title	Accumulation Ratio for the Maximum Plasma Concentration (Cmax) From the Fourth Dose Versus the First Dose (RCmax)

End point description:

Pharmacokinetic endpoint: accumulation ratio for maximum plasma (Cmax) ratio from the fourth dose on Week 4 versus the first dose of treatment on Week 1 (RCmax). Accumulation ratio, calculated for Cmax as (Cmax,w4/Cmax,w1).

End point type	Secondary

End point timeframe:

Baseline (Day 0) to dosing on Week 1 and Week 4.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	72		
Units: µg/ml				
geometric mean (geometric coefficient of variation)				
RCmax	1.706 (± 23.2)	1.671 (± 31.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentrations on Days 1, 8, 15, 22, and 29 (Ctrough).

End point title	Trough Concentrations on Days 1, 8, 15, 22, and 29 (Ctrough).

End point description:

Pharmacokinetic endpoint: trough plasma concentration (Ctrough) during the dosing phase on Days 1, 8, 15, 22, and 29. Concentrations at predose on Days 8, 15, and 22 (µg/mL) and the time equivalent to the predose on Day 29, obtained directly from the observed concentration versus time data.

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Days 1, 8, 15, 22 and 29.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	72		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Ctrough Day 8	60.60 (± 45.5)	61.00 (± 43.4)		
Ctrough Day 15	108.1 (± 26.0)	107.3 (± 32.0)		
Ctrough Day 22	143.0 (± 23.8)	143.3 (± 30.0)		
Ctrough Day 29	181.7 (± 22.1)	190.4 (± 26.1)		

Statistical analyses

Statistical analysis title	Ctrough GLS mean ratio

Statistical analysis description:

Statistical Comparison: geometric least square (GLS) Mean Ratio (90% CI) (%) of SAIT101 versus MabThera trough plasma concentration at the end of the dosing period (Day 29) (Ctrough,d29) (µg/mL) . The statistical comparison of the log-transformed primary parameters between treatments is based on an analysis of variance model with fixed effect for treatment

Comparison groups	SAIT101 v MabThera

Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	equivalence[6]
Parameter estimate	GLS mean ratio
Point estimate	95.45
Confidence interval	
level	90 %
sides	2-sided
lower limit	88.85
upper limit	102.55

Notes:

[6] - Standard acceptance limits for bioequivalence (80.00% to 125.00%). Comparison: SAIT101 versus MabThera. Pharmacokinetic equivalence was demonstrated for SAIT101 and MabThera with exposure PK parameter Ctrough,d29 within the standard acceptance limits for bioequivalence (80.00% to 125.00%).

Secondary: Observed Change From Baseline and Percent Change From Baseline CD19+ B-Lymphocyte Cluster of Differentiation 19 (CD-19+ B-Cell) Counts up to Week 28

End point title	Observed Change From Baseline and Percent Change From Baseline CD19+ B-Lymphocyte Cluster of Differentiation 19 (CD-19+ B-Cell) Counts up to Week 28

End point description:

Pharmacodynamic Endpoint: Arithmetic mean observed change from baseline and percent change from baseline of B-lymphocyte antigen cluster of differentiation 19 (CD-19+ B-cell) counts (cells/μL) up to Week 28 by treatment.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Weeks 1, 2, 3, 4, 5, 12, 20 and 28.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	72		
Units: cells/μL				
arithmetic mean (standard deviation)				
Week 1 Mean Change from Baseline	-128.0 (± 115.71)	-141.6 (± 120.90)		
Week 1 % Change from Baseline	-89.02 (± 26.324)	-95.58 (± 8.294)		
Week 2 Mean Change from Baseline	-144.1 (± 123.34)	-146.8 (± 138.76)		
Week 2 % Change from Baseline	-100.00 (± 0.000)	-100.00 (± 0.000)		
Week 3 Mean Change from Baseline	-142.8 (± 122.63)	-157.4 (± 102.03)		
Week 3 % Change from Baseline	-100.00 (± 0.000)	-100.00 (± 0.000)		
Week 4 Mean Change from Baseline	-141.5 (± 122.92)	-141.2 (± 102.03)		
Week 4 % Change from Baseline	-100.00 (± 0.000)	-100.00 (± 0.000)		
Week 5 Mean Change from Baseline	-140.0 (± 120.74)	-158.5 (± 134.27)		

Week 5 % Change from Baseline	-100.00 (± 0.000)	-100.00 (± 0.000)		
Week 12 Mean Change from Baseline	-144.2 (± 122.09)	-160.1 (± 134.09)		
Week 12 % Change from Baseline	-100.00 (± 0.000)	-100.00 (± 0.000)		
Week 20 Mean Change from Baseline	-140.8 (± 117.98)	-159.5 (± 135.63)		
Week 20 % Change from Baseline	-100.00 (± 0.000)	-100.00 (± 0.000)		
Week 28 Mean Change from Baseline	-136.6 (± 122.80)	-142.2 (± 134.79)		
Week 28 % Change from Baseline	-97.42 (± 12.749)	-96.78 (± 13.476)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve Change From Baseline B-lymphocyte CD19 (CD19+ B-cell) Count Time Curve (AUEC) Over the Dosing Interval

End point title	Area Under the Curve Change From Baseline B-lymphocyte CD19 (CD19+ B-cell) Count Time Curve (AUEC) Over the Dosing Interval

End point description:

Pharmacodynamic Endpoint: Area under the change from baseline CD19+ B-cell count time curve (AUEC) over the first dosing interval on week 1 from time 0 to the time prior to the second dose (AUEC0 168,w1), AUEC over the second dosing interval on week 2 from time 0 to the time prior to the third dose (AUEC0-168,w2), AUEC over the third dosing interval on week 3 from time 0 to the time prior to the fourth dose (AUEC0-168,w3), AUEC over the fourth dosing interval on week 4 from time 0 to 168 hours post dose (AUEC0-168,w4), AUEC from time 0 on week 1 to the time point on week 12 (AUEC0-w12), AUEC from time 0 on week 1 to the time point on week 28 (AUEC0 w28) for the change from baseline CD19+ B-cell count data

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Week 1, 2, 3, 4 12 and 28.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	72		
Units: cellsxday/µL				
arithmetic mean (standard deviation)				
AUEC0-168,w1 (cellsxday/µL)	-946.0 (± 830.29)	-1000 (± 891.82)		
AUEC0-168,w2 (cellsxday/µL)	-987.2 (± 997.57)	-1104 (± 947.68)		
AUEC0-168,w3 (cellsxday/µL)	-944.8 (± 910.79)	-1073 (± 930.95)		
AUEC0-168,w4 (cellsxday/µL)	-956.3 (± 728.52)	-1196 (± 1153.7)		
AUEC0-w12 (cellsxday/µL)	-11330 (± 9854.1)	-12280 (± 10185)		

AUEC0-w28 (cellsxday/µL)	-26370 (± 22794)	-28860 (± 25439)		

Statistical analyses

No statistical analyses for this end point

Secondary: Normalized Area Under the Curve Change From Baseline B-lymphocyte CD19 (CD19+ B-cell) Count Time Curve (AUEC) Over the Dosing Interval

End point title	Normalized Area Under the Curve Change From Baseline B-lymphocyte CD19 (CD19+ B-cell) Count Time Curve (AUEC) Over the Dosing Interval

End point description:

Pharmacodynamic Endpoint: Area under the change from baseline CD19+ B-cell count time curve (AUEC) over the first dosing interval on week 1 from time 0 to the time prior to the second dose (AUEC0 168,w1), AUEC over the second dosing interval on week 2 from time 0 to the time prior to the third dose (AUEC0-168,w2), AUEC over the third dosing interval on week 3 from time 0 to the time prior to the fourth dose (AUEC0-168,w3), AUEC over the fourth dosing interval on week 4 from time 0 to 168 hours post dose (AUEC0-168,w4), AUEC from time 0 on week 1 to the time point on week 12 (AUEC0-w12), AUEC from time 0 on week 1 to the time point on week 28 (AUEC0 w28) for the change from baseline CD19+ B-cell count data. The time-normalized AUEC parameters presented were calculated by dividing the respective AUEC by the time interval used to calculate the AUEC.

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Week 1, 2, 3, 4 12 and 28.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	72		
Units: cells/µL				
arithmetic mean (standard deviation)				
AUEC0-168,w1, normalized cells	-135.0 (± 118.88)	-142.1 (± 125.23)		
AUEC0-168,w2, normalized cells	-137.1 (± 123.43)	-155.1 (± 133.38)		
AUEC0-168,w3, normalized cells	-137.1 (± 123.43)	-155.1 (± 133.38)		
AUEC0-168,w4, normalized cells	-138.7 (± 121.62)	-159.2 (± 136.55)		
AUEC0-w12, normalized cells	-143.0 (± 121.38)	-158.7 (± 133.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Antidrug Antibodies (ADA) & Neutralising Antibody (NAb)

by Visit

End point title	Incidence of Antidrug Antibodies (ADA) & Neutralising Antibody (NAb) by Visit

End point description:

Immunogenicity endpoint: incidence of antidrug antibodies (ADA) and Neutralising Antibody (NAb). Immunogenicity sampling was performed pre-dose at Day 1, weeks 2, 3 and 4 and at any time during the visits at weeks 5, 12, 20 and 28

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 to Weeks 5, 12, 20 and 28.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	156		
Units: Number of subjects				
Week 1 (Baseline) ADA negative	138	148		
Week 1 (Baseline) ADA positive	3	2		
Week 1 (Baseline) NAb negative	3	2		
Week 1 (Baseline) NAb positive	0	0		
Week 2 ADA negative	143	152		
Week 2 ADA positive	1	0		
Week 2 NAb negative	1	0		
Week 2 NAb positive	0	0		
Week 3 ADA negative	138	149		
Week 3 ADA positive	5	0		
Week 3 NAb negative	2	0		
Week 3 NAb positive	0	0		
Week 4 ADA negative	145	149		
Week 4 ADA positive	2	0		
Week 4 NAb negative	2	0		
Week 4 NAb positive	0	0		
Week 5 ADA negative	139	145		
Week 5 ADA positive	2	0		
Week 5 NAb negative	2	0		
Week 5 NAb positive	0	0		
Week 12 ADA negative	137	144		
Week 12 ADA positive	3	0		
Week 12 NAb negative	3	0		
Week 12 NAb positive	3	0		
Week 20 ADA negative	131	144		
Week 20 ADA positive	7	4		
Week 20 NAb negative	7	4		
Week 20 NAb positive	7	0		
Week 28 ADA negative	126	129		
Week 28 ADA positive	10	16		
Week 29 NAb negative	9	16		
Week 29 NAb positive	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Change From Baseline for Immunoglobulins G and M by Scheduled Time

End point title	Observed Change From Baseline for Immunoglobulins G and M by Scheduled Time

End point description:

Exploratory pharmacodynamic endpoint: Mean (SD) Change from Baseline of Immunoglobulin (IgG) and immunoglobulin M (IgM) (mg/dL) by Scheduled Time for Each Treatment (Safety Analysis Set). Samples for IgG and IgM assessment were collected at Baseline and Weeks 1, 2, 3, 4, 5, 12, 20 and 28.

End point type	Secondary

End point timeframe:

Baseline to Weeks 1, 2, 3, 4, 5, 12, 20 and 28.

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	158		
Units: Mg/dL				
arithmetic mean (standard deviation)				
IgG Week 2	-0.21 (± 132.687)	-14.79 (± 132.64)		
IgG Week 3	-17.08 (± 157.848)	-30.04 (± 124.814)		
IgG Week 4	-36.31 (± 132.326)	-34.64 (± 156.790)		
IgG Week 5	-34.62 (± 162.748)	-38.21 (± 170.758)		
IgG Week 12	-28.15 (± 159.898)	-2.30 (± 202.017)		
IgG Week 20	-26.86 (± 189.937)	-22.40 (± 173.420)		
IgG Week 28	-19.33 (± 200.69)	8.70 (± 238.309)		
IgM Week 2	0.34 (± 18.018)	4.60 (± 28.273)		
IgM Week 3	0.87 (± 25.092)	2.12 (± 32.569)		
IgM Week 4	0.64 (± 31.836)	0.03 (± 30.009)		
IgM Week 5	-1.91 (± 29.521)	-2.02 (± 21.771)		
IgM Week 12	8.02 (± 37.876)	9.12 (± 21.671)		
IgM Week 20	-12.94 (± 46.966)	-14.35 (± 26.012)		

IgM Week 28	-22.08 (± 29.200)	-20.85 (± 37.475)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Exploratory Analyses of Tumor Response and Time to Event

End point title	Exploratory Analyses of Tumor Response and Time to Event

End point description:

Exploratory Efficacy Endpoint: Analyses of Tumor Response and Time to Event, as Determined by the Combined International Working Group (IWG) Criteria 2014, Lugano Classification and IWG Criteria 2007 (Central Assessment) (Full Analysis Set)

End point type	Other pre-specified

End point timeframe:

Baseline (Day 0) to Week 28

End point values	SAIT101	MabThera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	158		
Units: Number of subjects				
Complete Response (CR)	53	50		
Partial Response (PR)	47	55		
Stable Disease (SD)	21	25		
Progressive Disease (PD)	19	11		
Unknown (UKN)	1	2		
No Evidence of Disease (NED)	4	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the participant signed the Informed Consent Form (ICF), but prior to the initiation of study drug, only Serious Adverse Events (SAEs) caused by a protocol mandated procedure should be reported.

Adverse event reporting additional description:

All AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) v22.1. If an AE changed from non-SAE to be an SAE, it was treated as a new event and was counted as 2 events in the AE summary. A treatment-emergent AE (TEAE) was defined as any AE with an onset date on or after the date of the first dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	SAIT101

Reporting group description:

SAIT101: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3 and 4.

Reporting group title	MabThera

Reporting group description:

MabThera: Dose of 375 mg/m2 body surface area (BSA) intravenous on Weeks 1, 2, 3, and 4.

Serious adverse events	SAIT101	MabThera	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 157 (1.91%)	4 / 158 (2.53%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 157 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 157 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Paraesthesia			

subjects affected / exposed	1 / 157 (0.64%)	0 / 158 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 157 (0.64%)	0 / 158 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden cardiac death			
subjects affected / exposed	0 / 157 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 157 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cystitis klebsiella			
subjects affected / exposed	1 / 157 (0.64%)	0 / 158 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	0 / 157 (0.00%)	1 / 158 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	SAIT101	MabThera	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 157 (54.14%)	80 / 158 (50.63%)	

Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	3 / 157 (1.91%) 4	4 / 158 (2.53%) 4	
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	18 / 157 (11.46%) 27	26 / 158 (16.46%) 30	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	4 / 157 (2.55%) 5	3 / 158 (1.90%) 3	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	9 / 157 (5.73%) 10	2 / 158 (1.27%) 5	
Paraesthesia subjects affected / exposed occurrences (all)	4 / 157 (2.55%) 6	0 / 158 (0.00%) 0	
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	7 / 157 (4.46%) 7	1 / 158 (0.63%) 1	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	4 / 157 (2.55%) 4	4 / 158 (2.53%) 4	
Fatigue subjects affected / exposed occurrences (all)	6 / 157 (3.82%) 6	7 / 158 (4.43%) 11	
Pyrexia subjects affected / exposed occurrences (all)	4 / 157 (2.55%) 4	2 / 158 (1.27%) 2	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	2 / 157 (1.27%) 2	4 / 158 (2.53%) 4	

Abdominal pain upper subjects affected / exposed occurrences (all)	4 / 157 (2.55%) 4	3 / 158 (1.90%) 3	
Diarrhoea subjects affected / exposed occurrences (all)	5 / 157 (3.18%) 5	5 / 158 (3.16%) 5	
Nausea subjects affected / exposed occurrences (all)	6 / 157 (3.82%) 7	4 / 158 (2.53%) 4	
Vomiting subjects affected / exposed occurrences (all)	1 / 157 (0.64%) 1	4 / 158 (2.53%) 5	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	4 / 157 (2.55%) 4	3 / 158 (1.90%) 3	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	4 / 157 (2.55%) 4	8 / 158 (5.06%) 8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 October 2016	Amendment 01 dated 07 October 2016 implemented the following changes: • Revised the criteria of secondary efficacy endpoints; ORR at week 12 was added. • Revised text describing interim analysis. • Revised text for AESI criteria. • Added text in discontinuation of study treatment criteria. • The schedule of assessment table was updated with a few clarifications with regards to bone marrow biopsy, CT scan, possible items for unscheduled visit added. • Footnotes to the schedule of assessment table were updated for diagnostic biopsies, bone marrow biopsy, and PK sampling. • Revisions were made in the inclusion and exclusion criteria text for clarity about archival tissue, lymphoma, and TB. • Criteria for withdrawal from the study were clarified. • Updated the text on unblinding for interim analysis. • Clarified the vital sign parameter for body temperature. • Serious adverse event criteria for infant death was updated. • Updated text for recording, reporting, and follow-up of AEs. • Definition of PPS was updated. • Text was updated for efficacy analyses. • Text was updated for DSMB review.
27 June 2017	Amendment 02 dated 27 June 2017 implemented the following changes: • Updated the number of Investigators and centers. • Safety and immunogenicity data were added for appropriate interpretation of PK/PD data in interim analysis in PK/PD subpopulation. • Updated the PD endpoint for B-cell recovery. • Time restriction was deleted from premedication criteria. • Summary of study design was updated. • Modified schedule of assessments including footnotes. • Revisions were made in inclusion and exclusion criteria text for clarity. • Re-screening criteria was updated. • Added text for definition of subjects lost to follow-up. • Added text for BSA criteria in treatment administration. • Text was updated for formulation and packaging. • Text for administration of study treatment was updated. • Clarifications were made for anaphylactic reactions. • Text for infusion related reactions was updated. • Clarifications were made for follow-up of AEs. • Appendix 10 was updated time for PK/PD sampling.
03 November 2017	Amendment 03 dated 03 November 2017 implemented the following changes: • Study design was updated with addition of efficacy in interim analysis. • The PD and safety endpoint were modified. • Immunogenicity assessment criteria were updated. • The sample size for PK/PD endpoint was re-estimated and subject numbers were updated for PK/PD assessments. • Treatment for subjects with progressive disease was added. • Infusion related reactions were clarified further. • The PDS were re-defined. • Interim analysis population was updated. • Reference list was updated

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported