



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 Analysis 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 (FAEXP) 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 Analysis 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 Analysis 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 | | | |
| <p>Ann Arbor staging is the staging system for lymphomas, both in Hodgkin's lymphoma and non-Hodgkin lymphoma.</p> <p>Stage I indicates that the cancer is located in a single region.</p> <p>Stage II indicates that the cancer is located in two separate regions, an affected lymph node or lymphatic organ and a second affected area.</p> <p>Stage III indicates that the cancer has spread to both sides of the diaphragm.</p> <p>Stage IV indicates diffuse or disseminated involvement of one or more extralymphatic organs.</p> | | | |
| Units: Subjects | | | |
| Stage I | 1 | | |
| Stage II | 76 | | |
| Stage III | 141 | | |
| Stage IV | 30 | | |
| Type of Ann Arbor Staging | | | |
| <p>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</p> <p>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.</p> | | | |
| Units: Subjects | | | |
| Clinical Stage | 284 | | |
| Pathological Stage | 31 | | |
| Risk Groups According to Follicular Lymphoma International Prognostic Index (FLIP-2) Score | | | |
| <p>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%</p> | | | |
| 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 | \pm | \pm |
| 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 Analysis 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 | | | |
| <p>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:</p> <ul style="list-style-type: none"> - 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 | | | |
| Positive | | | |
| Negative | | | |
| Not available | | | |
| Ann Arbor Staging | | | |
| <p>Ann Arbor staging is the staging system for lymphomas, both in Hodgkin's lymphoma and non-Hodgkin lymphoma.</p> <p>Stage I indicates that the cancer is located in a single region.</p> <p>Stage II indicates that the cancer is located in two separate regions, an affected lymph node or lymphatic organ and a second affected area.</p> <p>Stage III indicates that the cancer has spread to both sides of the diaphragm.</p> <p>Stage IV indicates diffuse or disseminated involvement of one or more extralymphatic organs.</p> | | | |
| Units: Subjects | | | |
| Stage I | | | |
| Stage II | | | |
| Stage III | | | |
| Stage IV | | | |
| Type of Ann Arbor Staging | | | |
| <p>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</p> <p>Ann Arbor Clinical Stage (CS) as obtained by doctor's examination and tests, Ann Arbor Pathological Stage (PS) as obtained by exploratory laparotomy with splenectomy.</p> | | | |
| Units: Subjects | | | |
| Clinical Stage | | | |
| Pathological Stage | | | |
| Risk Groups According to Follicular Lymphoma International Prognostic Index (FLIP-2) Score | | | |
| <p>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%</p> | | | |
| 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 Analysis 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 (FAEXP) 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 Analysis 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 Analysis 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 (\pm 7.500) | 24.08 (\pm 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, μ g/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 (C _{max,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 C_{max,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 (C _{max,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 C_{max,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 Curve 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 (C_{max}) From the Fourth Dose Versus the First Dose (RC_{max})

| | |
|-----------------|---|
| End point title | Accumulation Ratio for the Maximum Plasma Concentration (C _{max}) From the Fourth Dose Versus the First Dose (RC _{max}) |
|-----------------|---|

End point description:

Pharmacokinetic endpoint: accumulation ratio for maximum plasma (C_{max}) ratio from the fourth dose on Week 4 versus the first dose of treatment on Week 1 (RC_{max}). Accumulation ratio, calculated for C_{max} as (C_{max,w4}/C_{max,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 (Ctough).

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

End point description:

Pharmacokinetic endpoint: trough plasma concentration (Ctough) during the dosing phase on Days 1, 8, 15, 22, and 29. Concentrations at predose on Days 8, 15, and 22 (◆g/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) | | | | |
| Ctough Day 8 | 60.60 (± 45.5) | 61.00 (± 43.4) | | |
| Ctough Day 15 | 108.1 (± 26.0) | 107.3 (± 32.0) | | |
| Ctough Day 22 | 143.0 (± 23.8) | 143.3 (± 30.0) | | |
| Ctough Day 29 | 181.7 (± 22.1) | 190.4 (± 26.1) | | |

Statistical analyses

| | |
|----------------------------|-----------------------|
| Statistical analysis title | Ctough 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) (Ctough,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 C_{trough},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/ μ L) | -26370 (\pm 22794) | -28860 (\pm 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/ μ L | | | | |
| arithmetic mean (standard deviation) | | | | |
| AUEC0-168,w1, normalized cells | -135.0 (\pm 118.88) | -142.1 (\pm 125.23) | | |
| AUEC0-168,w2, normalized cells | -137.1 (\pm 123.43) | -155.1 (\pm 133.38) | | |
| AUEC0-168,w3, normalized cells | -137.1 (\pm 123.43) | -155.1 (\pm 133.38) | | |
| AUEC0-168,w4, normalized cells | -138.7 (\pm 121.62) | -159.2 (\pm 136.55) | | |
| AUEC0-w12, normalized cells | -143.0 (\pm 121.38) | -158.7 (\pm 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) Paraesthesia subjects affected / exposed occurrences (all) | 9 / 157 (5.73%) 10 4 / 157 (2.55%) 6 | 2 / 158 (1.27%) 5 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) Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 4 / 157 (2.55%) 4 6 / 157 (3.82%) 6 4 / 157 (2.55%) 4 | 4 / 158 (2.53%) 4 7 / 158 (4.43%) 11 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 | <p>Amendment 01 dated 07 October 2016 implemented the following changes:</p> <ul style="list-style-type: none">• 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 | <p>Amendment 02 dated 27 June 2017 implemented the following changes:</p> <ul style="list-style-type: none">• 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 | <p>Amendment 03 dated 03 November 2017 implemented the following changes:</p> <ul style="list-style-type: none">• 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