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Subcutaneous Alemtuzumab (CAMPATH®, MabCampath®) in Relapsed/Refractory B-Cell Chronic Lymphocytic Leukemia

This study has been completed.

Sponsor:	Genzyme, a Sanofi Company
Collaborators:	Bayer Healthcare Pharmaceuticals, Inc./Bayer Schering Pharma
Information provided by (Responsible Party):	Sanofi (Genzyme, a Sanofi Company)
ClinicalTrials.gov Identifier:	NCT00328198

Purpose

This is a Phase II, open-label, prospective, multicenter study to evaluate the efficacy and safety of subcutaneously administered alemtuzumab (CAMPATH, MabCampath) as therapy for patients with relapsed or refractory B-CLL who have been previously treated.

Condition	Intervention	Phase
B-Cell Chronic Lymphocytic Leukemia (B-CLL)	Biological/Vaccine: Alemtuzumab	Phase 2

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: A Phase II Trial to Evaluate the Efficacy and Safety of Subcutaneously Administered Alemtuzumab (CAMPATH®, MabCampath®) in Patients With Previously Treated B-Cell Chronic Lymphocytic Leukemia

Further study details as provided by Sanofi (Genzyme, a Sanofi Company):

Primary Outcome Measure:

- Number of Participants With Best Disease Response as Determined by the Independent Response Review Panel (IRRP) [Time Frame: up to 44 weeks] [Designated as safety issue: No]
  Participants were evaluated by the IRRP according to National Cancer Institute (NCI) 1996 response criteria. The best response observed during the study is summarized. Response categories include Complete Response (CR) with normal physical exam, marrow cells and blood values, Partial Response (PR) with a >= 50% decrease from baseline in lymphocytes, lymphadenopathy and liver or spleen exam, Stable Disease (SD) without significant progression from baseline, or Progressive Disease (PD) with increased size/number of nodes, size of liver or spleen, increase in lymphocytes, aggressive histology.
- Percentage of Participants Who Had an Overall Response (OR) as Determined by the Independent Response Review Panel (IRRP) [Time Frame: up to 44 weeks] [Designated as safety issue: No]
  Participants were evaluated by the IRRP according to National Cancer Institute (NCI) 1996 response criteria. The percentage of participants whose best response observed during the study was either a Complete Response (CR) or a Partial Response (PR). Overall Response (OR) = CR + PR. A Complete Response (CR) exhibits a normal physical exam, marrow cells and blood values. A Partial Response (PR) has a >= 50% decrease from baseline in lymphocytes, lymphadenopathy and liver or spleen exam.

Secondary Outcome Measures:

- Kaplan-Meier Estimates of Progression Free Survival as Determined by the Independent Response Review Panel (IRRP) [Time Frame: up to 5 years] [Designated as safety issue: No]
  Progression-free survival was defined as the number of days from the date of first treatment to the date of first objective documentation of progressive disease (PD) as determined by the IRRP, or death due to any cause. Results are expressed in months. Progressive Disease (PD) was defined as an increase in size/number of nodes, size of liver or spleen, increase in lymphocytes, or aggressive histology.
- Kaplan-Meier Estimates of Duration of Response as Determined by the Independent Response Review Panel (IRRP) [Time Frame: up to 5 years] [Designated as safety issue: No]
  Duration of response was analyzed for participants who achieved a complete response (CR) or partial response (PR) and was defined as the number of days from the first date of documented response to the date of progressive disease (PD) as determined by IRRP or death due to any cause. Results are stated in months. Progressive Disease (PD) was defined as an increase in size/number of nodes, size of liver or spleen, increase in lymphocytes, or aggressive histology.
- Kaplan-Meier Estimates of Overall Survival [Time Frame: up to 5 years] [Designated as safety issue: No]
  Overall survival was defined as the time in days from the date of first treatment to the date of death due to any cause for all participants. Results are stated in months.
- Participants With a Minimal Residual Disease (MRD) Status of Negative [Time Frame: 44 weeks] [Designated as safety issue: No]
  MRD negativity represents a very positive response outcome. MRD negativity in this report was defined by the absence of tumor cells in bone marrow, using 4-color flow cytometry. All patients are evaluated for treatment response based on National Cancer Institute Working Group (NCIWG) criteria. Of patients who have achieved a clinical complete response (CR) or partial response (PR) that met National Cancer Institute Working Group (NCIWG) criteria of CR except blood recovery, a bone marrow sample was taken for flow cytometry measure of MRD negativity.
- Participants With Treatment-Emergent Adverse Events (TEAE) [Time Frame: up to 18 weeks of treatment plus 45 days] [Designated as safety issue: Yes]
  Number of participants with treatment-emergent adverse events (TEAEs). AEs were graded by the investigator using the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 and were assessed for relatedness to study treatment (5 point scale from 'not related' to 'definitely related') and severity (5 point scale with grade 5 being most severe). Categories reported include participant counts for treatment-emergent AEs, injection site reactions, AEs for infections, serious AEs, AEs causing discontinuation of study drug(s), deaths and severity.

Enrollment: 86
Study Start Date: May 2006
Primary Completion Date: August 2011
Study Completion Date: August 2011

Arms	Assigned Interventions
Experimental: Dose escalation Alemtuzumab is administered using escalating doses and alternating injection sites. The dose is escalated as tolerated using 3mg, 10mg, and 30mg administered subcutaneously (SC) (if tolerated).	Biological/Vaccine: Alemtuzumab Alemtuzumab is administered using escalating doses and alternating injection sites. The dose is escalated as tolerated using 3mg, 10mg, and 30mg administered subcutaneously (SC) (if tolerated). When escalation to 30 mg is tolerated, all subsequent doses are administered at 30 mg SC 3 times per week at alternating injection sites for up to 18 weeks. Part 1 of the study: The first 20 patients will be randomized to either Arm 1 (dose escalation) or Arm 2 (no escalation). Part 1 of the study has been completed; no additional patients will be enrolled in Part 1. An assigned review panel has reviewed the safety data from Part 1 and determined that all patients will be enrolled and treated under a no escalation schedule for Part 2 of the study. Other Names: Campath®, MabCampath®
Experimental: No escalation Alemtuzumab treatment is started immediately at the 30mg dose (with no escalation period), administered subcutaneously at alternating injection sites 3 times per week for up to 18 weeks.	Biological/Vaccine: Alemtuzumab Alemtuzumab treatment is started immediately at the 30mg dose (with no escalation period), administered SC at alternating injection sites 3 times per week for up to 18 weeks. Part 2 of the study: All patients are currently being enrolled under the no escalation schedule for Part 2 of the study. All patients in Part 2 will be treated with 30mg of alemtuzumab (with no escalation period) administered SC (at alternating injection sites) 3 times per week (e.g., Monday, Wednesday, Friday) for up to 18 weeks. Alemtuzumab is to be administered in a supervised medical setting on an outpatient basis for the first three weeks, after which some study centers may allow a home administration option, with one weekly clinic visit. Under the home administration option, alemtuzumab may be administered by the patient or care giver if the patient meets conditions specified in the protocol guidelines for home administration. Other Names: Campath®, MabCampath®

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- A diagnosis of B-cell chronic lymphocytic leukemia (B-CLL); according to the National Cancer Institute Working Group (NCI WG) Criteria.
- World Health Organization (WHO) performance status of 0, 1, or 2.
- Life expectancy ≥ 12 weeks.
- Previous therapy with at least one but no more than 5 regimens (single agent or combination regimen). One therapy regimen is defined as consecutive, contiguous cycles of the same drug(s) with no treatment interruptions lasting > 3 months.
- Patient requires treatment for CLL per the following criteria: -Rai stage III or IV; -Rai stage 0-II with at least one of the following - evidence of progressive marrow failure as manifested by the development of, or worsening of, anemia and/or thrombocytopenia; Massive (i.e. greater than 6 cm below the left costal margin) or progressive splenomegaly; Progressive lymphocytosis with an increase of greater than 50% over a 2-month period or an anticipated doubling time of less than 6 months; Lymphocyte count > 100*10^9/L; B symptoms.
- More than 3 weeks since prior chemotherapy. Patient must have recovered from the acute side effects incurred as a result of previous therapy.
- More than 3 weeks since using investigational agents. Patient must have recovered from the acute side effects incurred as a result of previous therapy.
- Serum creatinine and conjugated (direct) bilirubin less than or equal to 2 times the institutional upper limit of normal (ULN) unless secondary to direct infiltration of the liver with CLL.
- Female patients with childbearing potential must have a negative pregnancy test (serum or urine) within 2 weeks of first dose of study drug(s). All patients must agree to use an effective contraceptive method while on study treatment, if appropriate, and for a minimum of 6 months following study therapy.
- Signed, written informed consent (in the US, includes The Health Insurance Portability and Accountability Act of 1996 (HIPAA) authorization)

Exclusion Criteria:

- Positive Coombs test and evidence of active hemolysis.
- Platelet count less than 50*10^9/L without splenomegaly.
- History of anaphylaxis following exposure to rat or mouse derived CDR-grafted humanized monoclonal antibodies.
- Previously treated with CAMPATH.
- Previous bone marrow transplant.
- Known central nervous system (CNS) involvement with B-CLL
- Active infection, including human immunodeficiency virus (HIV) positive.
- Active second malignancy.
- Recent documented history (within 2 years) of active tuberculosis (TB), current active TB infection, currently receiving anti-tuberculous medication (e.g., INH, rifampin, streptomycin, pyrazinamide, or others).
- Active hepatitis or a history of prior viral hepatitis B or hepatitis C, or positive hepatitis B serologies. Patients with a positive hepatitis B surface antibody (HBsAb) test with a documented history of prior hepatitis B immunization are eligible as long as other criteria are met (i.e. negative tests for: hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb) and hepatitis C virus antibody (HCVAb)).
- Other severe, concurrent diseases (e.g., cardiac or pulmonary disease), mental disorders, or major organ malfunction (liver, kidney) that could interfere with the patient ability to participate in the study.
- Pregnant or nursing women.

- Cytomegalovirus (CMV) positive by polymerase chain reaction (PCR) (above the level of detection). A patient that is PCR positive will require treatment to reduce the viral load to a non-detectable level; but such a patient may be considered for study entry once the infection has been treated.
- Medical condition requiring chronic use of oral corticosteroids at a dose higher than physiologic replacement.

Contacts and Locations

Locations

United States, California

Moores Cancer Center

La Jolla, California, United States, 92093-0820

Wilshire Oncology Medical Group

La Verne, California, United States, 91750

United States, Colorado

University of Colorado Cancer Center at University of Colorado Health Sciences Center

Aurora, Colorado, United States, 80045

Rocky Mountain Cancer Centers

Colorado Springs, Colorado, United States, 80909

United States, Mississippi

North Mississippi Hematology & Oncology Associates, Ltd.

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United States, Ohio

Mid Ohio Oncology Hematology, Inc.

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United States, Texas

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Investigators

Study Director:	Medical Monitor	Genzyme Corporation

More Information

Responsible Party:	Genzyme, a Sanofi Company
Study ID Numbers:	CAM203 2005-005074-69 [EudraCT Number]
Health Authority:	United States: Food and Drug Administration Belgium: The Federal Public Service (FPS) Health, Food Chain Safety and Environment Czech Republic: State Institute for Drug Control France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Serbia and Montenegro: Agency for Drugs and Medicinal Devices United Kingdom: Medicines and Healthcare Products Regulatory Agency

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Study Results

Participant Flow

Pre-Assignment Details	109 patients screened and 86 enrolled and treated.

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Treatment

	Alemtuzumab 30mg
Started	86 [1]
Completed	48 [2]
Not Completed	38
Adverse Event	21
Death	1
Physician Decision	5
Withdrawal by Subject	5
Evidence of disease progression	2
Non-compliance	1
Confirmed complete response, MRD -	3

[1] 16 participants escalated the dose. 70 participants started at the 30 mg target dose.
[2] Depending upon protocol version, completed treatment was either 12 or 18 weeks in duration.

Follow-up

	Alemtuzumab 30mg
Started	78 [1]
Completed	43
Not Completed	35
Lost to Follow-up	4
Death	31

[1] Eight participants did not enter Follow-up

Baseline Characteristics

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Baseline Measures

	Alemtuzumab 30mg
Number of Participants	86
Age, Continuous [units: years] Mean (Standard Deviation)	65.32 (9.035)
Gender, Male/Female [units: participants]	
Female	29
Male	57
Race/Ethnicity, Customized [units: participants]	
American Indian or Alaska Native	0
Asian	1
Native Hawaiian or Other Pacific Islander	0
Black or African American	2
White	82
Other	1
Current Rai Stage [1] [units: participants]	
Rai Stage 0	7
Rai Stage I	10
Rai Stage II	22

	Alemtuzumab 30mg
Rai Stage III	7
Rai Stage IV	40
Current Binet Stage [2] [units: participants]	
Stage A	20
Stage B	22
Stage C	44
World Health Organization (WHO) Performance [3] [units: participants]	
0	55
1	28
2	3

[1] Rai staging is a way to categorize the disease progression of chronic lymphocytic leukemia (CLL); higher stages reflect increasing severity. Data represents the Rai Stage when the participant entered the study.

Rai Stage 0: Lymphocytosis only, Rai Stage I: Lymphocytosis and lymphadenopathy, Rai Stage II: Lymphocytosis and hepatomegaly +/- splenomegaly, Rai Stage III Lymphocytosis with anemia, Rai Stage IV Lymphocytosis with thrombocytopenia

[2] Binet staging is another way to categorize chronic lymphocytic leukemia (CLL). Data represents the Binet Stage when the participant entered the study.

Stage A CLL is characterized by no anemia or thrombocytopenia and fewer than three areas of lymphoid involvement (Rai stages 0, I, and II).

Stage B CLL is characterized by no anemia or thrombocytopenia with three or more areas of lymphoid involvement (Rai stages I and II).

Stage C CLL is characterized by anemia and/or thrombocytopenia regardless of the number of areas of lymphoid enlargement (Rai stages III and IV).

[3] The WHO performance status classification categorises patients as:

0: able to carry out all normal activity without restriction

1. restricted in strenuous activity but ambulatory and able to carry out light work
2. ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With Best Disease Response as Determined by the Independent Response Review Panel (IRRP)
Measure Description	Participants were evaluated by the IRRP according to National Cancer Institute (NCI) 1996 response criteria. The best response observed during the study is summarized. Response categories include Complete Response (CR) with normal physical exam, marrow cells and blood values, Partial Response (PR) with a >= 50% decrease from baseline in lymphocytes, lymphadenopathy and liver or spleen exam, Stable Disease (SD) without significant progression from baseline, or Progressive Disease (PD) with increased size/number of nodes, size of liver or spleen, increase in lymphocytes, aggressive histology.
Time Frame	up to 44 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Measured Values

	Alemtuzumab 30mg
Number of Participants Analyzed	86
Number of Participants With Best Disease Response as Determined by the Independent Response Review Panel (IRRP) [units: participants]	
Overall response (CR+PR)	37
Complete response (CR)	5
Partial response (PR)	32
Stable disease (SD)	24
Progressive disease (PD)	4
Not Evaluable (NE)	21

2. Primary Outcome Measure:

Measure Title	Percentage of Participants Who Had an Overall Response (OR) as Determined by the Independent Response Review Panel (IRRP)
Measure Description	Participants were evaluated by the IRRP according to National Cancer Institute (NCI) 1996 response criteria. The percentage of participants whose best response observed during the study was either a Complete Response (CR) or a Partial Response (PR). Overall Response (OR) = CR + PR. A Complete Response (CR) exhibits a normal physical exam, marrow cells and blood values. A Partial Response (PR) has a >= 50% decrease from baseline in lymphocytes, lymphadenopathy and liver or spleen exam.
Time Frame	up to 44 weeks
Safety Issue?	No

Analysis Population Description

Full analysis set. 95% confidence interval calculated using exact binomial method.

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Measured Values

	Alemtuzumab 30mg
Number of Participants Analyzed	86
Percentage of Participants Who Had an Overall Response (OR) as Determined by the Independent Response Review Panel (IRRP) [units: percentage of participants] Number (95% Confidence Interval)	43.0 (32.4 to 54.2)

3. Secondary Outcome Measure:

Measure Title	Kaplan-Meier Estimates of Progression Free Survival as Determined by the Independent Response Review Panel (IRRP)

Measure Description	Progression-free survival was defined as the number of days from the date of first treatment to the date of first objective documentation of progressive disease (PD) as determined by the IRRP, or death due to any cause. Results are expressed in months. Progressive Disease (PD) was defined as an increase in size/number of nodes, size of liver or spleen, increase in lymphocytes, or aggressive histology.
Time Frame	up to 5 years
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Measured Values

	Alemtuzumab 30mg
Number of Participants Analyzed	86
Kaplan-Meier Estimates of Progression Free Survival as Determined by the Independent Response Review Panel (IRRP) [units: months] Median (95% Confidence Interval)	12.43 (9.934 to 14.375)

4. Secondary Outcome Measure:

Measure Title	Kaplan-Meier Estimates of Duration of Response as Determined by the Independent Response Review Panel (IRRP)
Measure Description	Duration of response was analyzed for participants who achieved a complete response (CR) or partial response (PR) and was defined as the number of days from the first date of documented response to the date of progressive disease (PD) as determined by IRRP or death due to any cause. Results are stated in months. Progressive Disease (PD) was defined as an increase in size/number of nodes, size of liver or spleen, increase in lymphocytes, or aggressive histology.
Time Frame	up to 5 years
Safety Issue?	No

Analysis Population Description
Participants who had a complete response or a partial response

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Measured Values

	Alemtuzumab 30mg
Number of Participants Analyzed	37
Kaplan-Meier Estimates of Duration of Response as Determined by the Independent Response Review Panel (IRRP) [units: months] Median (95% Confidence Interval)	11.09 (9.013 to 14.572)

5. Secondary Outcome Measure:

Measure Title	Kaplan-Meier Estimates of Overall Survival
Measure Description	Overall survival was defined as the time in days from the date of first treatment to the date of death due to any cause for all participants. Results are stated in months.
Time Frame	up to 5 years
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Measured Values

	Alemtuzumab 30mg
Number of Participants Analyzed	86
Kaplan-Meier Estimates of Overall Survival [units: months] Median (95% Confidence Interval)	38.29 (30.099 to NA) [1]

[1] values were not calculable since there were not enough events for the statistical estimation, ie, few participants died

6. Secondary Outcome Measure:

Measure Title	Participants With a Minimal Residual Disease (MRD) Status of Negative
Measure Description	MRD negativity represents a very positive response outcome. MRD negativity in this report was defined by the absence of tumor cells in bone marrow, using 4-color flow cytometry. All patients are evaluated for treatment response based on National Cancer Institute Working Group (NCIWG) criteria. Of patients who have achieved a clinical complete response (CR) or partial response (PR) that met National Cancer Institute Working Group (NCIWG) criteria of CR except blood recovery, a bone marrow sample was taken for flow cytometry measure of MRD negativity.
Time Frame	44 weeks
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Measured Values

	Alemtuzumab 30mg
Number of Participants Analyzed	86
Participants With a Minimal Residual Disease (MRD) Status of Negative [units: participants]	4

7. Secondary Outcome Measure:

Measure Title	Participants With Treatment-Emergent Adverse Events (TEAE)
Measure Description	Number of participants with treatment-emergent adverse events (TEAEs). AEs were graded by the investigator using the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 and were assessed for relatedness to study treatment (5 point scale from 'not related' to 'definitely related') and severity (5 point scale with grade 5 being most severe). Categories reported include participant counts for treatment-emergent AEs, injection site reactions, AEs for infections, serious AEs, AEs causing discontinuation of study drug(s), deaths and severity.
Time Frame	up to 18 weeks of treatment plus 45 days
Safety Issue?	Yes

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Measured Values

	Alemtuzumab 30mg
Number of Participants Analyzed	86
Participants With Treatment-Emergent Adverse Events (TEAE) [units: participants]	
>=1 TEAE	82
>=1 TEAE related to drug	80
>=1 injection site reaction	49
>=1 injection site reaction related to drug	48
>=1 infection	49
>=1 infection related to drug	35
>=1 serious AE	46
>=1 serious AE related to drug	39
Discontinued study drug due to AE	21

	Alemtuzumab 30mg
Discontinued study drug due to related AE	20
Deaths	12
Deaths within 30 days of last dose	3
TEAE with worst severity grade 1	3
TEAE with worst severity grade 2	8
TEAE with worst severity grade 3	18
TEAE with worst severity grade 4	45
TEAE with worst severity grade 5	8

Reported Adverse Events

Time Frame	Treatment-emergent AEs: up to 18 weeks of treatment plus 45 additional days
Additional Description	In the event a single participant has experienced both a serious and a non-serious form of the same adverse event term, the individual has been included in the numerator ("number of affected participants") of both adverse event tables. Events are listed independent of relationship to treatment reported.

Reporting Groups

	Description
Alemtuzumab 30mg	Participants received a target dose of alemtuzumab 30mg by subcutaneous injection three times a week for up to 18 weeks. Some participants started in the Escalation subpopulation and started at a lower dose and escalated from 3mg to 10 mg to the target 30 mg dose in the first 1-2 weeks.

Serious Adverse Events

	Alemtuzumab 30mg
	Affected/At Risk (%)
Total	46/86 (53.49%)
Blood and lymphatic system disorders	
Bone marrow failure [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Febrile neutropenia [A] †	6/86 (6.98%)
Idiopathic thrombocytopenic purpura [A] †	1/86 (1.16%)
Neutropenia [A] †	2/86 (2.33%)
Pancytopenia [A] †	4/86 (4.65%)
Thrombocytopenia [A] †	2/86 (2.33%)
Cardiac disorders	
Angina unstable [A] †	1/86 (1.16%)
Atrial fibrillation [A] †	1/86 (1.16%)
Left ventricular failure [A] †	1/86 (1.16%)
Gastrointestinal disorders	
Gastrointestinal haemorrhage [A] †	2/86 (2.33%)
Large intestine perforation [A] †	1/86 (1.16%)
Peritonitis [A] †	1/86 (1.16%)
Rectal haemorrhage [A] †	1/86 (1.16%)
General disorders	
Asthenia [A] †	1/86 (1.16%)
Chills [A] †	2/86 (2.33%)
Device dislocation [A] †	1/86 (1.16%)
Localised oedema [A] †	1/86 (1.16%)
Oedema peripheral [A] †	1/86 (1.16%)
Pyrexia [A] †	6/86 (6.98%)
Hepatobiliary disorders	
Bile duct obstruction [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Cholangitis acute [A] †	1/86 (1.16%)
Hepatorenal syndrome [A] †	1/86 (1.16%)
Immune system disorders	
Hypersensitivity [A] †	1/86 (1.16%)
Infections and infestations	
Abscess neck [A] †	1/86 (1.16%)
Aspergillosis [A] †	1/86 (1.16%)
Bacteraemia [A] †	1/86 (1.16%)
Bronchitis [A] †	2/86 (2.33%)
Bronchopneumonia [A] †	1/86 (1.16%)
Bronchopulmonary aspergillosis [A] †	3/86 (3.49%)
Cellulitis [A] †	3/86 (3.49%)
Cytomegalovirus infection [A] †	9/86 (10.47%)
Ear infection [A] †	1/86 (1.16%)
Escherichia bacteraemia [A] †	1/86 (1.16%)
Herpes zoster [A] †	1/86 (1.16%)
Infection [A] †	1/86 (1.16%)
Lower respiratory tract infection [A] †	1/86 (1.16%)
Meningitis [A] †	1/86 (1.16%)
Parainfluenzae virus infection [A] †	1/86 (1.16%)
Pneumonia [A] †	5/86 (5.81%)
Pneumonia fungal [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Septic shock [A] †	2/86 (2.33%)
Upper respiratory tract infection [A] †	2/86 (2.33%)
Urinary tract infection [A] †	2/86 (2.33%)
Injury, poisoning and procedural complications	
Fractured ischium [A] †	1/86 (1.16%)
Investigations	
Cytomegalovirus test positive [A] †	2/86 (2.33%)
Liver function test abnormal [A] †	1/86 (1.16%)
Metabolism and nutrition disorders	
Decreased appetite [A] †	1/86 (1.16%)
Diabetes mellitus [A] †	1/86 (1.16%)
Hypercalcaemia [A] †	1/86 (1.16%)
Musculoskeletal and connective tissue disorders	
Muscular weakness [A] †	1/86 (1.16%)
Polymyositis [A] †	1/86 (1.16%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Ear neoplasm [A] †	1/86 (1.16%)
Richter's syndrome [A] †	2/86 (2.33%)
Nervous system disorders	
Cerebrovascular accident [A] †	1/86 (1.16%)
Encephalitis [A] †	1/86 (1.16%)
Headache [A] †	2/86 (2.33%)
Hypoglycaemic coma [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Sciatica [A] †	1/86 (1.16%)
Renal and urinary disorders	
Nephrolithiasis [A] †	1/86 (1.16%)
Renal failure acute [A] †	2/86 (2.33%)
Reproductive system and breast disorders	
Oedema genital [A] †	1/86 (1.16%)
Respiratory, thoracic and mediastinal disorders	
Acute respiratory distress syndrome [A] †	1/86 (1.16%)
Chronic obstructive pulmonary disease [A] †	1/86 (1.16%)
Pleural effusion [A] †	1/86 (1.16%)
Pleurisy [A] †	1/86 (1.16%)
Skin and subcutaneous tissue disorders	
Leukocytoclastic vasculitis [A] †	1/86 (1.16%)
Vascular disorders	
Orthostatic hypotension [A] †	1/86 (1.16%)
Shock haemorrhagic [A] †	1/86 (1.16%)
Venous thrombosis limb [A] †	1/86 (1.16%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (14.0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Alemtuzumab 30mg
	Affected/At Risk (%)
Total	81/86 (94.19%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Blood and lymphatic system disorders	
Anaemia [A] †	28/86 (32.56%)
Anaemia haemolytic autoimmune [A] †	1/86 (1.16%)
Febrile neutropenia [A] †	1/86 (1.16%)
Haemolysis [A] †	2/86 (2.33%)
Idiopathic thrombocytopenic purpura [A] †	1/86 (1.16%)
Leukocytosis [A] †	1/86 (1.16%)
Leukopenia [A] †	27/86 (31.4%)
Lymphopenia [A] †	14/86 (16.28%)
Neutropenia [A] †	43/86 (50%)
Thrombocytopenia [A] †	17/86 (19.77%)
Cardiac disorders	
Angina pectoris [A] †	1/86 (1.16%)
Angina unstable [A] †	1/86 (1.16%)
Atrial flutter [A] †	1/86 (1.16%)
Bradycardia [A] †	1/86 (1.16%)
Palpitations [A] †	3/86 (3.49%)
Sinus tachycardia [A] †	1/86 (1.16%)
Tachycardia [A] †	4/86 (4.65%)
Ear and labyrinth disorders	
Ear pain [A] †	1/86 (1.16%)
Vertigo [A] †	3/86 (3.49%)
Endocrine disorders	

	Alemtuzumab 30mg
	Affected/At Risk (%)
Hypothyroidism [A] †	1/86 (1.16%)
Eye disorders	
Conjunctivitis [A] †	1/86 (1.16%)
Dry eye [A] †	1/86 (1.16%)
Erythema of eyelid [A] †	1/86 (1.16%)
Eye haemorrhage [A] †	1/86 (1.16%)
Eye irritation [A] †	1/86 (1.16%)
Eye pain [A] †	1/86 (1.16%)
Lacrimation increased [A] †	1/86 (1.16%)
Gastrointestinal disorders	
Abdominal distension [A] †	2/86 (2.33%)
Abdominal pain [A] †	7/86 (8.14%)
Abdominal pain upper [A] †	5/86 (5.81%)
Aphthous stomatitis [A] †	1/86 (1.16%)
Ascites [A] †	1/86 (1.16%)
Constipation [A] †	5/86 (5.81%)
Diarrhoea [A] †	15/86 (17.44%)
Dry mouth [A] †	1/86 (1.16%)
Dyspepsia [A] †	2/86 (2.33%)
Epigastric discomfort [A] †	1/86 (1.16%)
Flatulence [A] †	1/86 (1.16%)
Gastritis [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Gastrointestinal disorder [A] †	1/86 (1.16%)
Gastrointestinal haemorrhage [A] †	1/86 (1.16%)
Gastrooesophageal reflux disease [A] †	1/86 (1.16%)
Gingival pain [A] †	1/86 (1.16%)
Haematochezia [A] †	1/86 (1.16%)
Hiatus hernia [A] †	1/86 (1.16%)
Ileus [A] †	1/86 (1.16%)
Inguinal hernia [A] †	1/86 (1.16%)
Melaena [A] †	1/86 (1.16%)
Mouth haemorrhage [A] †	1/86 (1.16%)
Mouth ulceration [A] †	2/86 (2.33%)
Nausea [A] †	17/86 (19.77%)
Odynophagia [A] †	1/86 (1.16%)
Peptic ulcer [A] †	1/86 (1.16%)
Retching [A] †	1/86 (1.16%)
Stomatitis [A] †	3/86 (3.49%)
Tongue coated [A] †	1/86 (1.16%)
Toothache [A] †	2/86 (2.33%)
Vomiting [A] †	14/86 (16.28%)
General disorders	
Asthenia [A] †	6/86 (6.98%)
Axillary pain [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Catheter site haematoma [A] †	1/86 (1.16%)
Chills [A] †	20/86 (23.26%)
Fatigue [A] †	25/86 (29.07%)
Hypothermia [A] †	1/86 (1.16%)
Influenza like illness [A] †	1/86 (1.16%)
Injection site erythema [A] †	29/86 (33.72%)
Injection site haematoma [A] †	1/86 (1.16%)
Injection site pain [A] †	2/86 (2.33%)
Injection site pruritus [A] †	4/86 (4.65%)
Injection site rash [A] †	4/86 (4.65%)
Injection site reaction [A] †	14/86 (16.28%)
Injection site swelling [A] †	1/86 (1.16%)
Malaise [A] †	2/86 (2.33%)
Oedema peripheral [A] †	8/86 (9.3%)
Pain [A] †	6/86 (6.98%)
Pyrexia [A] †	30/86 (34.88%)
Hepatobiliary disorders	
Hepatic function abnormal [A] †	1/86 (1.16%)
Hyperbilirubinaemia [A] †	2/86 (2.33%)
Immune system disorders	
Drug hypersensitivity [A] †	1/86 (1.16%)
Hypersensitivity [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Seasonal allergy [A] †	1/86 (1.16%)
Infections and infestations	
Acute sinusitis [A] †	1/86 (1.16%)
Balanitis candida [A] †	1/86 (1.16%)
Bronchitis [A] †	2/86 (2.33%)
Cellulitis [A] †	1/86 (1.16%)
Clostridial infection [A] †	1/86 (1.16%)
Cytomegalovirus infection [A] †	6/86 (6.98%)
Escherichia urinary tract infection [A] †	1/86 (1.16%)
Eye infection [A] †	1/86 (1.16%)
Folliculitis [A] †	1/86 (1.16%)
Influenza [A] †	1/86 (1.16%)
Lower respiratory tract infection [A] †	2/86 (2.33%)
Nasopharyngitis [A] †	7/86 (8.14%)
Oesophageal candidiasis [A] †	1/86 (1.16%)
Oral candidiasis [A] †	1/86 (1.16%)
Oral fungal infection [A] †	1/86 (1.16%)
Oral herpes [A] †	1/86 (1.16%)
Oropharyngeal candidiasis [A] †	1/86 (1.16%)
Pneumonia [A] †	2/86 (2.33%)
Respiratory tract infection [A] †	4/86 (4.65%)
Rhinitis [A] †	6/86 (6.98%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Sinusitis [A] †	3/86 (3.49%)
Sinusitis aspergillus [A] †	1/86 (1.16%)
Systemic candida [A] †	1/86 (1.16%)
Tinea capitis [A] †	1/86 (1.16%)
Tinea infection [A] †	1/86 (1.16%)
Tracheitis [A] †	1/86 (1.16%)
Upper respiratory tract infection [A] †	5/86 (5.81%)
Urinary tract infection [A] †	4/86 (4.65%)
Injury, poisoning and procedural complications	
Arthropod bite [A] †	1/86 (1.16%)
Contusion [A] †	2/86 (2.33%)
Fall [A] †	1/86 (1.16%)
Fibula fracture [A] †	1/86 (1.16%)
Post procedural complication [A] †	1/86 (1.16%)
Procedural pain [A] †	2/86 (2.33%)
Thermal burn [A] †	1/86 (1.16%)
Investigations	
Alanine aminotransferase increased [A] †	1/86 (1.16%)
Aspartate aminotransferase increased [A] †	1/86 (1.16%)
Beta 2 microglobulin increased [A] †	1/86 (1.16%)
Blood alkaline phosphatase increased [A] †	2/86 (2.33%)
Blood bilirubin increased [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Blood creatinine increased [A] †	2/86 (2.33%)
Blood iron decreased [A] †	1/86 (1.16%)
Blood potassium decreased [A] †	2/86 (2.33%)
Blood pressure increased [A] †	1/86 (1.16%)
Blood urea increased [A] †	1/86 (1.16%)
Body temperature increased [A] †	1/86 (1.16%)
CD4 lymphocytes decreased [A] †	1/86 (1.16%)
Cytomegalovirus test positive [A] †	13/86 (15.12%)
Eosinophil count increased [A] †	1/86 (1.16%)
Gamma-glutamyltransferase increased [A] †	1/86 (1.16%)
International normalised ratio increased [A] †	1/86 (1.16%)
Neutrophil count decreased [A] †	1/86 (1.16%)
Protein total decreased [A] †	2/86 (2.33%)
Serum ferritin increased [A] †	1/86 (1.16%)
Weight decreased [A] †	8/86 (9.3%)
White blood cell count decreased [A] †	1/86 (1.16%)
Metabolism and nutrition disorders	
Decreased appetite [A] †	12/86 (13.95%)
Fluid retention [A] †	2/86 (2.33%)
Hyperglycaemia [A] †	2/86 (2.33%)
Hyperkalaemia [A] †	1/86 (1.16%)
Hyperuricaemia [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Hypoalbuminaemia [A] †	2/86 (2.33%)
Hypocalcaemia [A] †	1/86 (1.16%)
Hypokalaemia [A] †	3/86 (3.49%)
Hyponatraemia [A] †	3/86 (3.49%)
Increased appetite [A] †	1/86 (1.16%)
Malnutrition [A] †	1/86 (1.16%)
Pseudohyperkalaemia [A] †	1/86 (1.16%)
Musculoskeletal and connective tissue disorders	
Arthralgia [A] †	4/86 (4.65%)
Back pain [A] †	5/86 (5.81%)
Bone pain [A] †	1/86 (1.16%)
Joint effusion [A] †	1/86 (1.16%)
Joint swelling [A] †	2/86 (2.33%)
Muscle spasms [A] †	4/86 (4.65%)
Muscular weakness [A] †	2/86 (2.33%)
Musculoskeletal chest pain [A] †	3/86 (3.49%)
Musculoskeletal discomfort [A] †	1/86 (1.16%)
Musculoskeletal pain [A] †	1/86 (1.16%)
Musculoskeletal stiffness [A] †	1/86 (1.16%)
Myalgia [A] †	2/86 (2.33%)
Pain in extremity [A] †	4/86 (4.65%)
Polymyositis [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Spondylitis [A] †	1/86 (1.16%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Fibroma [A] †	1/86 (1.16%)
Melanocytic naevus [A] †	1/86 (1.16%)
Nervous system disorders	
Ageusia [A] †	1/86 (1.16%)
Dizziness [A] †	7/86 (8.14%)
Dysarthria [A] †	1/86 (1.16%)
Dyskinesia [A] †	1/86 (1.16%)
Headache [A] †	16/86 (18.6%)
Hemiparesis [A] †	1/86 (1.16%)
Hypoaesthesia [A] †	1/86 (1.16%)
Lethargy [A] †	4/86 (4.65%)
Migraine [A] †	1/86 (1.16%)
Neuralgia [A] †	1/86 (1.16%)
Paraesthesia [A] †	5/86 (5.81%)
Peripheral sensory neuropathy [A] †	2/86 (2.33%)
Sciatica [A] †	1/86 (1.16%)
Somnolence [A] †	1/86 (1.16%)
Syncope [A] †	1/86 (1.16%)
Tremor [A] †	3/86 (3.49%)
Psychiatric disorders	

	Alemtuzumab 30mg
	Affected/At Risk (%)
Agitation [A] †	2/86 (2.33%)
Anxiety [A] †	4/86 (4.65%)
Confusional state [A] †	2/86 (2.33%)
Depression [A] †	2/86 (2.33%)
Insomnia [A] †	9/86 (10.47%)
Mood altered [A] †	1/86 (1.16%)
Neurosis [A] †	1/86 (1.16%)
Stress [A] †	1/86 (1.16%)
Renal and urinary disorders	
Dysuria [A] †	2/86 (2.33%)
Haematuria [A] †	1/86 (1.16%)
Nocturia [A] †	1/86 (1.16%)
Pollakiuria [A] †	2/86 (2.33%)
Renal failure [A] †	2/86 (2.33%)
Reproductive system and breast disorders	
Balanitis [A] †	1/86 (1.16%)
Breast oedema [A] †	1/86 (1.16%)
Respiratory, thoracic and mediastinal disorders	
Chronic obstructive pulmonary disease [A] †	1/86 (1.16%)
Cough [A] †	14/86 (16.28%)
Dysphonia [A] †	2/86 (2.33%)
Dyspnoea [A] †	14/86 (16.28%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Dyspnoea exertional [A] †	2/86 (2.33%)
Epistaxis [A] †	1/86 (1.16%)
Haemoptysis [A] †	1/86 (1.16%)
Hypoxia [A] †	2/86 (2.33%)
Oropharyngeal pain [A] †	3/86 (3.49%)
Orthopnoea [A] †	1/86 (1.16%)
Pleural effusion [A] †	1/86 (1.16%)
Pleurisy [A] †	1/86 (1.16%)
Productive cough [A] †	2/86 (2.33%)
Pulmonary hypertension [A] †	1/86 (1.16%)
Respiratory disorder [A] †	1/86 (1.16%)
Respiratory failure [A] †	1/86 (1.16%)
Respiratory tract congestion [A] †	1/86 (1.16%)
Rhinorrhoea [A] †	1/86 (1.16%)
Sinusitis noninfective [A] †	1/86 (1.16%)
Tachypnoea [A] †	1/86 (1.16%)
Throat tightness [A] †	1/86 (1.16%)
Tonsillar disorder [A] †	1/86 (1.16%)
Vasomotor rhinitis [A] †	1/86 (1.16%)
Skin and subcutaneous tissue disorders	
Blister [A] †	1/86 (1.16%)
Dermatitis allergic [A] †	1/86 (1.16%)

	Alemtuzumab 30mg
	Affected/At Risk (%)
Dry skin [A] †	3/86 (3.49%)
Ecchymosis [A] †	1/86 (1.16%)
Eczema [A] †	1/86 (1.16%)
Erythema [A] †	9/86 (10.47%)
Hyperhidrosis [A] †	3/86 (3.49%)
Night sweats [A] †	12/86 (13.95%)
Petechiae [A] †	3/86 (3.49%)
Pityriasis rosea [A] †	1/86 (1.16%)
Pruritus [A] †	11/86 (12.79%)
Pruritus generalised [A] †	1/86 (1.16%)
Rash [A] †	8/86 (9.3%)
Rash generalised [A] †	1/86 (1.16%)
Rash maculo-papular [A] †	1/86 (1.16%)
Skin reaction [A] †	2/86 (2.33%)
Urticaria [A] †	3/86 (3.49%)
Vascular disorders	
Haematoma [A] †	1/86 (1.16%)
Hypertension [A] †	4/86 (4.65%)
Hypotension [A] †	6/86 (6.98%)
Orthostatic hypotension [A] †	3/86 (3.49%)
Phlebitis [A] †	1/86 (1.16%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (14.0)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

In multi-site studies, PI can publish after an independent multi-investigator publication (in which the PI can participate) or 18 months after study completion. PI gives Genzyme a draft 60 days before publication. Genzyme can ask that confidential information be removed, and can defer publication another 60 days upon notifying PI that it will file a patent application on inventions contained in the draft.

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