Clinical trial results:
An open-label, single-arm, multi-center phase 2 trial with ofatumumab in patients with relapsed/progressive Diffuse Large B-Cell Lymphoma (DLBCL) ineligible for transplant or relapsed/progression after autologous transplant

Summary

EudraCT number	2007-004190-26
Trial protocol	BE DK GB FR ES IT
Global end of trial date	18 August 2014

Results information

Result version number	v1 (current)
This version publication date	13 April 2016
First version publication date	07 March 2015

Trial information

Trial identification

Sponsor protocol code	GEN415

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	Final
Date of interim/final analysis	13 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of ofatumumab in patients with relapsed/progressive DLBCL ineligible for transplant or relapsed/progression after autologous transplant

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	60 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	Belgium: 23
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	81
EEA total number of subjects	77

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	31
From 65 to 84 years	49
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This was an open-label, single-arm, multi-center phase II trial. During the treatment phase, participants (par.) received 8 weekly infusions of ofatumumab (first infusion of 300 mg followed by 7 infusions of 1000 mg).

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Ofatumumab

Arm description:

Participants received 8 weekly intravenous (iv) infusions of ofatumumab: first infusion of 300 milligrams (mg), followed by 7 infusions of 1000 mg

Arm type	Experimental
Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Treatment administration: Participants were given ofatumumab by intravenous infusion as follows: First infusion of 300 mg, followed by seven weekly infusions of 1000 mg. Pre-medication with oral paracetamol 1000 mg (or equivalent) and cetirizine 10 mg (or equivalent) before every infusion and glucocorticoid equivalent to 100 mg prednisolone before infusions 1 and 2 was administered 30 minutes to 2 hours prior to treatment with ofatumumab.

Investigational medicinal product name	Paracetamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Pre-medication with oral paracetamol 1000 mg (or equivalent) before every infusion.

Investigational medicinal product name	Cetirizine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pre-medication with oral cetirizine 10 mg (or equivalent) before every infusion.

Investigational medicinal product name	Glucocorticoid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pre-medication with oral glucocorticoid equivalent to 100 mg prednisolone before infusions 1 and 2 was administered 30 minutes to 2 hours prior to treatment with ofatumumab.

Number of subjects in period 1	Ofatumumab
Started	81
Completed	9
Not completed	72
Consent withdrawn by subject	1
Received Alternate Anticancer Therapy	8
Adverse event, non-fatal	6
Death	3
Participant Refusal	1
Took Prohibited Medication	2
Insurance Expired	1
Disease Progression	47
Protocol deviation	3

Baseline characteristics

Reporting groups	
Reporting group title	Ofatumumab
Reporting group description:	
Participants received 8 weekly intravenous (iv) infusions of ofatumumab: first infusion of 300 milligrams (mg), followed by 7 infusions of 1000 mg	

Reporting group values	Ofatumumab	Total	
Number of subjects	81	81	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	64.9		
standard deviation	± 14.51	-	
Gender categorical Units: Subjects			
Female	36	36	
Male	45	45	
Race Units: Subjects			
Asian	2	2	
Hispanic or Latino	2	2	
White	76	76	
Missing	1	1	
Number of Participants with the Indicated Prior Therapy			
Study participants had to have either prior autologous stem cell transplant (ASCT) or had to be ineligible for ASCT to be eligible for inclusion.			
Units: Subjects			
Prior ASCT	25	25	
Ineligible for ASCT	56	56	

End points

End points reporting groups

Reporting group title	Ofatumumab

Reporting group description:

Participants received 8 weekly intravenous (iv) infusions of ofatumumab: first infusion of 300 milligrams (mg), followed by 7 infusions of 1000 mg

Primary: Number of participants with objective response

End point title	Number of participants with objective response[1]

End point description:

Objective response of ofatumumab treatment was assessed according to the "revised response criteria for malignant lymphoma." Participants with objective response were defined as responders with complete remission (CR) or partial remission (PR) of disease. CR is defined as the disappearance of all evidence of disease, and PR is defined as the regression of measurable disease with no new sites of disease. Full Analysis Set (FAS): all participants who were exposed to study drug irrespective of their compliance to the planned course of treatment. Response rate is calculated as the number of responses divided by the number of par. treated, expressed as a percentage. Objective response: Estimated value = 11%, 2-sided 95% CI=5% to 20%. The exact (Clopper-Pearson) method was used to calculate the confidence interval (CI).

End point type	Primary

End point timeframe:

6-month period from start of treatment (up to Week 24)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical information is entered in the endpoint description. The system does not allow statistical data to be entered in the statisticial analysis section for studies with 1 treatment arm.

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	81[2]			
Units: Participants	9			

Notes:

[2] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants classified as responders and non-responders for objective response

End point title	Number of participants classified as responders and non-responders for objective response[3]

End point description:

According to the "revised response criteria for malignant lymphoma," responders included par. with CR and PR, and non-responders included par. with stable disease (SD) and progressive disease (PD). Par. not evaluable (NE) were also considered to be non-responders. PD is defined as any new lesion or an increase by more than or equal to 50% of previously involved sites from baseline. SD is defined as failure to attain CR, PR, or PD. Response rate is calculated as the number of responses divided by the number of par. treated, expressed as a percentage. Responders with CR: Estimated value = 2%, 2-sided 95% CI=0% to 9%. Responders with PR: Estimated value = 9%, 2-sided 95% CI=4% to 17%. Non-responders with SD: Estimated value = 17%, 2-sided 95% CI=10% to 27%. Non-responders with

PD: Estimated value = 42%, 2-sided 95% CI=31% to 53%. Non-responders with NE: Estimated value = 30%, 2-sided 95% CI=20% to 41%. The exact (Clopper-Pearson) method was used to calculate the CI.

End point type	Primary

End point timeframe:

6-month period from start of treatment (up to Week 24)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical information is entered in the endpoint description. The system does not allow statistical data to be entered in the statisticial analysis section for studies with 1 treatment arm.

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	81[4]			
Units: Participants				
Responders with CR	2			
Responders with PR	7			
Non-responders with SD	14			
Non-responders with PD	34			
Non-responders with NE	24			

Notes:

[4] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

The duration of response was defined as the time from the initial response (CR or PR) to the time of relapse, progression, or death. If the participant was lost to follow-up, the endpoint was censored, and the censoring date was the date of the last attended visit at which the endpoint was assessed. The upper limit of the 95% confidence interval could not be determined (not reached) because too few participants experienced the event; therefore, the value of 99999 was entered which represents NA.

End point type	Secondary

End point timeframe:

From date of start of treatment to 2 years or withdrawal

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	9[5]			
Units: Months				
median (confidence interval 95%)	9.5 (5.4 to 99999)			

Notes:

[5] - FAS. Only participants with CR or PR were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

PFS was defined as the time from treatment start until progression or death.

End point type	Secondary

End point timeframe:

From date of start of treatment to 2 years or withdrawal

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	81[6]			
Units: Months				
median (confidence interval 95%)	2.5 (2.3 to 4.9)			

Notes:

[6] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Time to next Diffuse Large B-Cell Lymphoma (DLBCL) therapy

End point title	Time to next Diffuse Large B-Cell Lymphoma (DLBCL) therapy

End point description:

Time to next DLBCL therapy was defined as the time from the first infusion date to the time of the first administration of the next DLBCL treatment other than ofatumumab. If the participants were lost to follow-up, the endpoint was censored, and the censoring date was the date of the last attended visit at which the endpoint was assessed. The median and the upper limit of the 95% confidence interval could not be determined (not reached) because too few participants experienced the event; therefore, the value of 99999 was entered which represents NA.

End point type	Secondary

End point timeframe:

From date of start of treatment to 5 years or withdrawal

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	81[7]			
Units: Months				
median (confidence interval 95%)	99999 (7.4 to 99999)			

Notes:

[7] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival is defined as the time from first infusion to death. Overall survival was a secondary endpoint in the study. However, since many participants withdrew from the study after developing disease progression overall survival could not be reliably estimated.

End point type	Secondary

End point timeframe:

From date of start of treatment to 5 years or withdrawal

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: Months				
median (standard deviation)	()			

Notes:

[8] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive human anti-human antibodies (HAHA) at Screening and at Visits 12, 13, 14, and 18

End point title	Number of participants with positive human anti-human antibodies (HAHA) at Screening and at Visits 12, 13, 14, and 18

End point description:

HAHA are indicators of immune response to ofatumumab. Blood samples were collected from participants at Visits 1, 12, 13, 14, and 18 and analyzed in batches. The number of participants with positive results at each visit is reported.

End point type	Secondary

End point timeframe:

Screening visit (<= 14 days before treatment start), Visit 12 (Month 6), Visit 13 (Month 9), Visit 14 (Month 12), and Visit 18 (Month 24)

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	79[9]			
Units: participants				
Screening, n=79	0			
Visit 12 (Month 6), n=20	0			
Visit 13, (Month 9), n=16	0			
Visit 14 (Month 12), n=16	0			
Visit 18 (Month 24), n=8	0			

Notes:

[9] - FAS. Data are provided for the number of participants attending each visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Median percent change from Baseline in CD45+CD19+ and CD45+CD20+ cells in the peripheral blood at the indicated visits

End point title	Median percent change from Baseline in CD45+CD19+ and CD45+CD20+ cells in the peripheral blood at the indicated visits

End point description:

B cells (CD45+CD19+ and CD45+CD20+) were measured in peripheral blood samples by flow cytometry. Percent change from Baseline = (value at the indicated visits minus the value at Baseline divided by the value at Baseline) * 100.

End point type	Secondary

End point timeframe:

Baseline and Visit 10 (Week 8), Visit 11 (Week 11), Visit 12 (Month 6), Visit 13 (Month 9), Visit 14 (Month 12), Visit 15 (Month 15), Visit 16 (Month 18), Visit 17 (Month 21), Visit 18 (Month 24), Visit 19 (Month 30), Visit 20 (Month 36)

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	42[10]			
Units: percent change in cells				
median (full range (min-max))				
CD45+CD19+, Visit 10 (Week 8), n=42	-100 (-100 to 0)			
CD45+CD19+, Visit 11 (Week 11), n=29	-100 (-100 to 56)			
CD45+CD19+, Visit 12 (Month 6), n=18	-100 (-100 to 0)			
CD45+CD19+, Visit 13 (Month 9), n=15	-100 (-100 to 0)			
CD45+CD19+, Visit 14 (Month 12), n=13	-100 (-100 to 0)			
CD45+CD19+, Visit 15 (Month 15), n=12	-60.7 (-100 to 12)			
CD45+CD19+, Visit 16 (Month 18), n=8	6 (-88 to 179)			
CD45+CD19+, Visit 17 (Month 21), n=8	-6.9 (-58 to 56)			
CD45+CD19+, Visit 18 (Month 24), n=5	-11.1 (-100 to 50)			
CD45+CD19+, Visit 19 (Month 30), n=2	80.8 (12 to 150)			
CD45+CD19+, Visit 20 (Month 36), n=2	68.6 (-36 to 174)			
CD45+CD20+, Visit 10 (Week 8), n=42	-100 (-100 to 0)			

CD45+CD20+, Visit 11 (Week 11), n=29	-100 (-100 to 56)			
CD45+CD20+, Visit 12 (Month 6), n=18	-100 (-100 to 0)			
CD45+CD20+, Visit 13 (Month 9), n=15	-100 (-100 to 0)			
CD45+CD20+, Visit 14 (Month 12), n=13	-100 (-100 to 0)			
CD45+CD20+, Visit 15 (Month 15), n=12	-57.3 (-100 to 0)			
CD45+CD20+, Visit 16 (Month 18), n=8	6 (-88 to 171)			
CD45+CD20+, Visit 17 (Month 21), n=8	-6.9 (-58 to 28)			
CD45+CD20+, Visit 18 (Month 24), n=5	-11.1 (-100 to 50)			
CD45+CD20+, Visit 19 (Month 30), n=2	75.2 (7 to 143)			
CD45+CD20+, Visit 20 (Month 36), n=2	68.6 (-36 to 174)			

Notes:

[10] - FAS. Data are provided for the number of participants attending each visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who experienced at least one adverse event (AE)

End point title	Number of participants who experienced at least one adverse event (AE)

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. The protocol-defined AE reporting period was from the first infusion (Visit 2/Week 0) to Visit 18 (Month 24 of follow-up) or time of withdrawal (treatment and follow-up).

End point type	Secondary

End point timeframe:

From the date of start of treatment to 2 years or withdrawal

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	81[11]			
Units: Participants	78			

Notes:

[11] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Screening in complement (CH50) levels

End point title	Percent change from Screening in complement (CH50) levels

End point description:

CH50 was mistakenly registered as an outcome measure with the protocol record. Samples were not collected, and no analysis will take place. Thus, no data will be reported for this outcome measure.

End point type	Secondary

End point timeframe:

Screening and post-baseline visits (last visit was to occur 24 months post first dose)

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: percent change in complement levels				

Notes:

[12] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(0-inf) and AUC(0-168) for ofatumumab at the eighth infusion

End point title	AUC(0-inf) and AUC(0-168) for ofatumumab at the eighth infusion

End point description:

AUC is defined as the area under the ofatumumab concentration-time curve as a measure of drug exposure. AUC(0-168) is the AUC from the start of infusion to 168 hours after the start of the infusion; AUC(0-inf) is the AUC from the start of infusion extrapolated to infinity. Data are provided for the number of participants attending each visit for whom the parameter value could be calculated. Participants contributing AUC(0-inf) data also contributed AUC(0-168) data.

End point type	Secondary

End point timeframe:

Visit 9 (Week 7; up to 11 months after last dose)

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	46[13]			
Units: micrograms*hour/milliliter (µg.h/mL)				
geometric mean (geometric coefficient of variation)				
AUC(0-inf), n=30 AUC(0-168), n=46	720388 (± 79) 110193 (± 27)			

Notes:

[13] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax and Ctrough for ofatumumab at the first and eighth infusions

End point title	Cmax and Ctrough for ofatumumab at the first and eighth infusions

End point description:

Cmax is defined as the maximum concentration of drug in serum samples. Ctrough is defined as the minimum observed concentration prior to the start of the next dose. No drug is present prior to the first infusion; therefore, there are no Ctrough results for the first dose.

End point type	Secondary

End point timeframe:

Visit 2 (Week 0) and Visit 9 (Week 7)

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	74[14]			
Units: micrograms per milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)				
First infusion Cmax; 300 mg, n=74	109 (± 42)			
Eighth infusion Cmax; 1000 mg, n=48	839 (± 24)			
Eighth infusion Ctrough; 1000 mg, n=48	497 (± 34)			

Notes:

[14] - FAS. Data are provided for the number of participants attending each visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life (T1/2) for ofatumumab at the eigth infusion

End point title	Half-life (T1/2) for ofatumumab at the eigth infusion

End point description:

t1/2 is defined as terminal half-life and is the time required for the amount of drug in the body to decrease by half. Data are provided for the number of participants at each visit for whom the parameter could be calculated.

End point type	Secondary

End point timeframe:

Visit 9 (Week 7; up to 11 months after last dose)

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	30[15]			
Units: Hours				
geometric mean (geometric coefficient of variation)	637 (± 51)			

Notes:
[15] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) of ofatumumab at the eighth infusion

End point title	Clearance (CL) of ofatumumab at the eighth infusion

End point description:

CL is the clearance of drug from serum, which is defined as the volume of serum from which the drug is cleared per unit time. Data are presented for the number of participants at each visit for whom the parameter can be calculated.

End point type	Secondary

End point timeframe:

Visit 9 (Week 7; up to 11 months after last dose)

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	46[16]			
Units: milliliters per hour (mL/h)				
geometric mean (geometric coefficient of variation)	9.1 (± 28)			

Notes:
[16] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of distribution at steady state (Vss) of ofatumumab at the eighth infusion

End point title	Volume of distribution at steady state (Vss) of ofatumumab at the eighth infusion

End point description:

Vss is the volume of distribution at steady state of ofatumumab. Data are presented for the number of participants attending each visit for whom the parameter can be calculated.

End point type	Secondary

End point timeframe:

Visit 9 (Week 7; up to 11 months after the last dose)

End point values	Ofatumumab			
Subject group type	Reporting group			
Number of subjects analysed	30[17]			
Units: liters				
geometric mean (geometric coefficient of variation)	8.3 (± 45)			

Notes:

[17] - FAS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) were reported from first infusion (Week 0) to Month 24 of follow-up (FU)/withdrawal (treatment and FU). Serious AEs were reported through Month 60 (treatment, FU, and extended FU).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Ofatumumab

Reporting group description:

Participants received 8 weekly iv infusions of ofatumumab: first infusion of 300 mg, followed by 7 infusions of 1000 mg

Serious adverse events	Ofatumumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	37 / 81 (45.68%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 5		
Pyrexia			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			

subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Multi-organ failure				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Oedema peripheral				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleuritic pain				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Haemoglobin decreased				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur fracture				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Neurological symptom				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paraparesis				

subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	3 / 81 (3.70%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eyelid ptosis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastritis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis acute			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic function abnormal			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis acute			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Central line infection			

subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Ofatumumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 81 (86.42%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	4 / 81 (4.94%)		
occurrences (all)	5		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 81 (16.05%)		
occurrences (all)	15		
Oedema peripheral			

subjects affected / exposed	13 / 81 (16.05%)		
occurrences (all)	15		
Pyrexia			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	8		
Asthenia			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	7		
Non-cardiac chest pain			
subjects affected / exposed	3 / 81 (3.70%)		
occurrences (all)	9		
Infusion related reaction			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences (all)	3		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	11		
Dyspnoea			
subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	8		
Pharyngolaryngeal pain			
subjects affected / exposed	4 / 81 (4.94%)		
occurrences (all)	5		
Rales			
subjects affected / exposed	4 / 81 (4.94%)		
occurrences (all)	4		
Pleural effusion			
subjects affected / exposed	3 / 81 (3.70%)		
occurrences (all)	3		
Throat irritation			

subjects affected / exposed occurrences (all)	3 / 81 (3.70%) 4		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 4 / 81 (4.94%) 4		
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	 5 / 81 (6.17%) 6		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	 3 / 81 (3.70%) 4		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	 3 / 81 (3.70%) 3		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 5 / 81 (6.17%) 7 4 / 81 (4.94%) 6		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Lymphopenia	 10 / 81 (12.35%) 12 9 / 81 (11.11%) 11 9 / 81 (11.11%) 10		

subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	7		
Thrombocytopenia			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	5		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	4 / 81 (4.94%)		
occurrences (all)	4		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	15 / 81 (18.52%)		
occurrences (all)	15		
Abdominal pain			
subjects affected / exposed	11 / 81 (13.58%)		
occurrences (all)	12		
Constipation			
subjects affected / exposed	11 / 81 (13.58%)		
occurrences (all)	13		
Nausea			
subjects affected / exposed	10 / 81 (12.35%)		
occurrences (all)	12		
Vomiting			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	6		
Abdominal pain upper			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	5		
Stomatitis			
subjects affected / exposed	4 / 81 (4.94%)		
occurrences (all)	4		
Dry mouth			
subjects affected / exposed	3 / 81 (3.70%)		
occurrences (all)	3		
Dyspepsia			

subjects affected / exposed occurrences (all)	3 / 81 (3.70%) 3		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	 7 / 81 (8.64%) 8 6 / 81 (7.41%) 6 4 / 81 (4.94%) 5		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all)	 5 / 81 (6.17%) 5 4 / 81 (4.94%) 4 2 / 81 (2.47%) 2 2 / 81 (2.47%) 2		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Herpes zoster subjects affected / exposed occurrences (all)	 6 / 81 (7.41%) 7 5 / 81 (6.17%) 8 4 / 81 (4.94%) 4		
Metabolism and nutrition disorders			

Anorexia subjects affected / exposed occurrences (all)	8 / 81 (9.88%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2007	Amendment No.: 01 Update the protocol with changes in accordance with the transfer of sponsorship of the trial Gen415 from Genmab A/S to GlaxoSmithKine (GSK)as of 28 April 2008.
18 July 2008	Amendment No.: 02 Clarify and elaborate on inclusion criteria no. 1. In the same connection exclusion criteria 15 and the section on pre-medicaton will be updated due to errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported