ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/03/2015

ClinicalTrials.gov ID: NCT00430352

Study Identification

Unique Protocol ID:	MO19872
Brief Title:	MAXIMA Study: A Study of Maintenance Therapy With MabThera (Rituximab) in Patients With Non-Hodgkin's Lymphoma.
Official Title:	A Study to Evaluate the Safety of MabThera (Rituximab) Maintenance Therapy in Patients With Follicular Non-Hodgkin's Lymphoma Who Have Responded to Induction Therapy.
Secondary IDs:	

Study Status

Record Verification:	June 2015
Overall Status:	Completed
Study Start:	September 2006
Primary Completion:	May 2011 [Actual]
Study Completion:	May 2011 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: parere 76/06 Board Name: Comitato Etico AO S. Croce e Carle Board Affiliation: unknown Phone: +39 0171 641571 Email: comitato.etico@ospedale.cuneo.it
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Italy: Ministry of Health

Study Description

Brief Summary:	This single arm study will evaluate the safety and efficacy of MabThera maintenance therapy following a MabThera-containing induction regimen in first line or relapsed patients with follicular non-Hodgkin's lymphoma. All patients will receive MabThera 375mg/m2 body surface area, as an intravenous infusion, every 8 weeks. The anticipated time on study treatment is 1-2 years, and the target sample size is 500+ individuals.
Detailed Description:	

Conditions

Conditions:	Non-Hodgkin's Lymphoma
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	545 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: rituximab [MabThera/Rituxan] 375mg/m2 iv every 8 weeks

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, >=18 years of age;
- histologically confirmed grade 1, 2 or 3a follicular non-Hodgkin's lymphoma;
- patients who have received adequate (>=8 cycles) induction therapy with MabThera as first line treatment, or treatment for relapsed disease;
- demonstrated partial or complete response to induction therapy.

Exclusion Criteria:

- stable or progressive disease after most recent induction therapy;
- transformation to high grade lymphoma;
- patients with prior or concomitant malignancies, except non-melanoma skin cancer or adequately treated in situ cancer of the cervix.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Germany
Recklinghausen, Germany, 45657

Finland

Haemeenlinna, Finland, 13530

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Milano, Italy, 20133

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Targu-mures, Romania, 540136

Brazil
Porto Alegre, RS, Brazil, 90610-000

Italy
Bari, Italy, 70124

Spain
Burgos, Burgos, Spain, 09006

Sweden
Uppsala, Sweden, 75185

Italy
Padova, Italy, 35128

Bosnia and Herzegovina
Kasindo, Bosnia and Herzegovina, 71123

Ecuador
Quito, Ecuador, 2569

Russian Federation
Stavropol, Russian Federation, ND

Spain
Castellon, Castellon, Spain, 12004

Germany
Jena, Germany, 07743

Spain
Murcia, Murcia, Spain, 30120

Argentina
Córdoba, Argentina, 5016

Germany
Freiburg, Germany, 79110

Italy
Vicenza, Italy, 36100

Bulgaria
Pleven, Bulgaria, 5800

Russian Federation
Moscow, Russian Federation, 129110

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Zagreb, Croatia, 10000

Sweden
Sundsvall, Sweden, 85186

Russian Federation
Belgorod, Russian Federation, ND

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Holon, Israel, 5810001

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Stuttgart, Germany, 70176

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Pavia, Italy, 27100

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Ramat Gan, Israel, 52662

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Germany
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Spain
Ciudad Real, Ciudad Real, Spain, 13005

Sweden
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Argentina
Corrientes, Argentina, 3400

Italy
Lecce, Italy, 73100

Siena, Italy, 53100

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Salvador, BA, Brazil, 40170-110

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Ankara, Turkey, 06100

Mexico
Puebla, Mexico, 72530

Germany
Mutlangen, Germany, 73557

Mexico
Monterrey, Mexico, 64380

Italy
Torrette Di Ancona, Italy, 60020

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Moscow, Russian Federation, 125101

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Germany
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Romania
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References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Rituximab 375 Milligrams Per Square Meter (mg/m^2)	Participants received rituximab 375 mg/m^2 intravenously (IV) once every 8 weeks for a total 12 infusions until progression, relapse, start of a new treatment, death, or toxicity.

Overall Study

	Rituximab 375 Milligrams Per Square Meter (mg/m^2)
Started	545
Completed	407
Not Completed	138
Disease progression	58
Withdrawal by Subject	11
Adverse Event	16
Death	5
Not specified	48

Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) population: all participants who completed a baseline visit and at least 1 further assessment.

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Baseline Measures

	Rituximab 375 mg/m^2
Number of Participants	545

	Rituximab 375 mg/m^2
Age, Continuous [units: years] Mean (Standard Deviation)	56.3 (11.47)
Gender, Male/Female [units: participants]	
Female	313
Male	232

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With an Adverse Event (AE) - Overall Summary
Measure Description	Data presented include percentage of participants with any AE, any infusion-related AE, any serious adverse event (SAE), any infusion-related SAE (counted separately from SAEs), death, and participants with toxicity as the primary cause for treatment discontinuation.
Time Frame	24 months
Safety Issue?	No

Analysis Population Description

Safety Population: any participant who received at least 1 dose of study treatment.

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	534
Percentage of Participants With an Adverse Event (AE) - Overall Summary [units: percentage of participants]	
Any AE	67.4
Any infusion-related AE	5.8

	Rituximab 375 mg/m^2
Any non-infusion related SAE	20.2
Any infusion-related SAE	0.2
Deaths	7.5
Toxicity as primary cause for discontinuation	3.0

2. Secondary Outcome Measure:

Measure Title	Progression-Free Survival - Percentage of Participants With an Event
Measure Description	PFS was measured from the day of first rituximab maintenance infusion until the date of first documented disease progression or death by any cause. Participants who experienced none of these events at the time of analysis (clinical cutoff) and participants who were lost to follow-up were censored at their last clinical assessment date.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Progression-Free Survival - Percentage of Participants With an Event [units: percentage of participants]	24.0

3. Secondary Outcome Measure:

Measure Title	Progression-Free Survival - Time to Event

Measure Description	PFS was measured from the day of first rituximab maintenance infusion until the date of first documented disease progression or death by any cause. Participants who experienced none of these events at the time of analysis (clinical cutoff) and participants who were lost to follow-up were censored at their last clinical assessment date.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Progression-Free Survival - Time to Event [units: months] Median (95% Confidence Interval)	NA (NA to NA) [1]

[1] Median and 95 percent (%) confidence interval (CI) for PFS could not be estimated due to the large number of censored participants and the short duration of follow-up.

4. Secondary Outcome Measure:

Measure Title	Event-Free Survival (EFS) - Percentage of Participants With an Event
Measure Description	The percentage of participants who experienced PD or death or required a next or new lymphoma treatment over a study period of 2 years with 1 year of follow-up. EFS was measured from the day of first rituximab maintenance infusion until the date of first documented disease progression, death by any cause, or the institution of new anti-lymphoma treatment. Participants who experienced none of these events at the end of the study and participants who were lost to follow-up were censored at their last clinical assessment date.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Event-Free Survival (EFS) - Percentage of Participants With an Event [units: percentage of participants]	24.4

5. Secondary Outcome Measure:

Measure Title	Event-Free Survival (EFS) - Time to Event
Measure Description	EFS was measured from the day of first rituximab maintenance infusion until the date of first documented disease progression, death by any cause, or the institution of new anti-lymphoma treatment. Participants who experienced none of these events at the end of the study and participants who were lost to follow-up were censored at their last clinical assessment date.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Event-Free Survival (EFS) - Time to Event [units: months] Median (95% Confidence Interval)	NA (NA to NA) [1]

[1] Median and 95% CI for EFS could not be estimated due to the large number of censored participants and the short duration of follow-up.

6. Secondary Outcome Measure:

Measure Title	Overall Survival (OS) - Percentage of Participants With an Event
Measure Description	As a measure of overall survival (OS), the percentage of participants who died over the study period of 2 years with 1 year of follow-up. OS was determined from the day of first rituximab maintenance infusion until the date of death irrespective of cause. Participants who had not died at the time of end of the whole study and participants who were lost to follow up were censored at the date of the last contact.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Overall Survival (OS) - Percentage of Participants With an Event [units: percentage of participants]	7.3

7. Secondary Outcome Measure:

Measure Title	Overall Survival (OS) - Time to Event
Measure Description	OS was determined from the day of first rituximab maintenance infusion until the date of death irrespective of cause. Participants who had not died at the time of end of the whole study and participants who were lost to follow up were censored at the date of the last contact.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose

Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Overall Survival (OS) - Time to Event [units: percentage of participants] Median (95% Confidence Interval)	NA (NA to NA) [1]

[1] Median and 95% CI for OS could not be estimated due to the large number of censored participants and the short duration of follow-up.

8. Secondary Outcome Measure:

Measure Title	Time to Next Lymphoma Treatment (NLT) - Percentage of Participants With an Event
Measure Description	As a measure of time to NLT (TNLT), the percentage of participants with new lymphoma treatment over a study period of 2 years with 1 year of follow-up. TNLT was measured from the date of first rituximab maintenance infusion to the date of first documented intake of any new anti-lymphoma treatment (chemotherapy, radiotherapy, immunotherapy, etc). Participants who did not have documentation that an NLT had started and participants who were lost to follow up were censored at their last visit where the assessment for start of any new lymphoma medication was actually made.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Time to Next Lymphoma Treatment (NLT) - Percentage of Participants With an Event [units: percentage of participants]	17.4

9. Secondary Outcome Measure:

Measure Title	Time to NLT - Time to Event
Measure Description	TNLT was measured from the date of first rituximab maintenance infusion to the date of first documented intake of any new anti-lymphoma treatment (chemotherapy, radiotherapy, immunotherapy, etc). Participants who did not have documentation that an NLT had started and participants who were lost to follow up were censored at their last visit where the assessment for start of any new lymphoma medication was actually made.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Time to NLT - Time to Event [units: months] Median (95% Confidence Interval)	NA (NA to NA) [1]

[1] Median and 95% CI for time to NLT could not be estimated due to the large number of censored participants and the short duration of follow-up.

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Response by Best Response to Study Treatment
Measure Description	Percentage of participants with complete response (CR), unconfirmed CR (CRu), no change, or progressive disease (PD). For each participant, the last response to induction therapy immediately prior to study entry was compared to the best response observed during rituximab maintenance therapy. Where possible, assessment of response was based on the International Workshop to Standardize Response Criteria for Non-Hodgkin's Lymphoma (NHL).
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose
Safety Issue?	No

Analysis Population Description

ITT population; only participants who received any study treatment were included in the analysis.

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	545
Percentage of Participants With Response by Best Response to Study Treatment [units: percentage of participants]	
CR/CRu	2.1
No change	87.5
PD	10.5

11. Secondary Outcome Measure:

Measure Title	Percentage of Participants With PR Who Converted to CRu
Measure Description	Percentage of participants with PR or CR(u) conversion while on rituximab maintenance therapy over a study period of 2 years with 1 year of follow-up. For each participant, the last response to induction therapy immediately prior to study entry was compared to the best response observed during rituximab maintenance therapy. Assessment and definition of response was based on the International Workshop to Standardize Response Criteria for NHL.
Time Frame	Baseline, every 8 weeks during treatment, and 3, 6, 9 and 12 months after last dose

Safety Issue?	No

Analysis Population Description

ITT population; only participants with PR to most recent treatment were included in the analysis.

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Measured Values

	Rituximab 375 mg/m^2
Number of Participants Analyzed	161
Percentage of Participants With PR Who Converted to CRu [units: percentage of participants] Number (95% Confidence Interval)	6.2 (3.0 to 11.1)

Reported Adverse Events

Time Frame	AEs were collected at up through 12 months after last dose (1 year follow-up).
Additional Description	AEs were collected at up through 12 months after last dose (1 year follow-up). AEs occuring within 24 hours of infusion were considered infusion-related reactions (IRRs) and were collected and reported as separate events mutually exclusive from all 'other' AEs collected and reported. These events appear in the table labeled as 'IRR'.

Reporting Groups

	Description
Rituximab 375 mg/m^2	Participants received rituximab 375 mg/m^2 IV for up to 12 infusions in total every 8 weeks until progression, relapse, start of a new treatment, death, or toxicity.

Serious Adverse Events

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Total	109/534 (20.41%)
Blood and lymphatic system disorders	
Febrile neutropenia [A] *	3/534 (0.56%)
Idiopathic thrombocytopenic purpura [A] *	1/534 (0.19%)
Neutropenia [A] *	4/534 (0.75%)
Cardiac disorders	
Acute coronary syndrome [A] *	1/534 (0.19%)
Acute myocardial infarction [A] *	1/534 (0.19%)
Angina pectoris [A] *	1/534 (0.19%)
Angina unstable [A] *	1/534 (0.19%)
Arrhythmia [A] *	1/534 (0.19%)
Cardiomyopathy [A] *	1/534 (0.19%)
Cardiopulmonary failure [A] *	1/534 (0.19%)
Coronary artery disease [A] *	2/534 (0.37%)
Left ventricular dysfunction [A] *	1/534 (0.19%)
Myocarditis [A] *	1/534 (0.19%)
Palpitation [A] *	1/534 (0.19%)
Supraventricular tachycardia [A] *	2/534 (0.37%)
Eye disorders	
Cataract [A] *	1/534 (0.19%)
Eye haemorrhage [A] *	1/534 (0.19%)
Glaucoma [A] *	1/534 (0.19%)

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Gastrointestinal disorders	
Abdominal hernia [A] *	1/534 (0.19%)
Abdominal pain [A] *	1/534 (0.19%)
Coeliac disease [A] *	1/534 (0.19%)
Colitis [A] *	1/534 (0.19%)
Diarrhoea [A] *	3/534 (0.56%)
Enterocolitis [A] *	1/534 (0.19%)
Food poisoning [A] *	1/534 (0.19%)
Gastritis [A] *	1/534 (0.19%)
Gastrointestinal haemorrhage [A] *	1/534 (0.19%)
Gastrointestinal obstruction [A] *	1/534 (0.19%)
Oesophageal varices haemorrhage [A] *	1/534 (0.19%)
Oesophagitis [A] *	1/534 (0.19%)
Pancreatitis [A] *	1/534 (0.19%)
Umbilical hernia [A] *	1/534 (0.19%)
Upper gastrointestinal haemorrhage [A] *	1/534 (0.19%)
General disorders	
Chest pain [A] *	2/534 (0.37%)
Fatigue [A] *	1/534 (0.19%)
Pyrexia [A] *	4/534 (0.75%)
Sudden death [A] *	1/534 (0.19%)
Hepatobiliary disorders	

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Biliary colic [A] *	1/534 (0.19%)
Cholangitis [A] *	1/534 (0.19%)
Cholecystitis [A] *	1/534 (0.19%)
Liver disorder [A] *	1/534 (0.19%)
Infections and infestations	
Abdominal abscess [A] *	1/534 (0.19%)
Appendicitis [A] *	3/534 (0.56%)
Arthritis bacterial [A] *	1/534 (0.19%)
Aspergilloma [A] *	1/534 (0.19%)
Bronchiolitis [A] *	1/534 (0.19%)
Bronchitis [A] *	1/534 (0.19%)
Cellulitis [A] *	1/534 (0.19%)
Cerebral aspergillosis [A] *	1/534 (0.19%)
Diverticulitis [A] *	1/534 (0.19%)
Gastroenteritis [A] *	1/534 (0.19%)
Groin abscess [A] *	1/534 (0.19%)
Herpes zoster [A] *	1/534 (0.19%)
Meningitis enteroviral [A] *	1/534 (0.19%)
Otitis media [A] *	1/534 (0.19%)
Pneumocystis jiroveci pneumonia [A] *	1/534 (0.19%)
Pneumonia [A] *	7/534 (1.31%)
Pulmonary tuberculosis [A] *	1/534 (0.19%)

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Respiratory tract infection [A] *	1/534 (0.19%)
Sinusitis [A] *	2/534 (0.37%)
Injury, poisoning and procedural complications	
Ankle fracture [A] *	1/534 (0.19%)
Foot fracture [A] *	1/534 (0.19%)
Humerus fracture [A] *	1/534 (0.19%)
Joint dislocation [A] *	1/534 (0.19%)
Multiple fractures [A] *	1/534 (0.19%)
Road traffic accident [A] *	1/534 (0.19%)
Investigations	
Alanine aminotransferase increased [A] *	1/534 (0.19%)
Aspartate aminotransferase increased [A] *	1/534 (0.19%)
Blood lactate dehydrogenase increased [A] *	1/534 (0.19%)
Metabolism and nutrition disorders	
Diabetes mellitus [A] *	1/534 (0.19%)
Hyperglycaemia [A] *	1/534 (0.19%)
Musculoskeletal and connective tissue disorders	
Back pain [A] *	1/534 (0.19%)
Bursitis [A] *	1/534 (0.19%)
Intervertebral disc protrusion [A] *	1/534 (0.19%)
Musculoskeletal pain [A] *	2/534 (0.37%)
Osteoarthritis [A] *	2/534 (0.37%)
Osteonecrosis [A] *	2/534 (0.37%)

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Acute leukaemia [A] *	2/534 (0.37%)
Basal cell carcinoma [A] *	1/534 (0.19%)
Bowen's disease [A] *	1/534 (0.19%)
Metastatic gastric cancer [A] *	1/534 (0.19%)
Osteosarcoma recurrent [A] *	1/534 (0.19%)
Prostate cancer [A] *	2/534 (0.37%)
Sarcoma [A] *	1/534 (0.19%)
Skin cancer [A] *	1/534 (0.19%)
Uterine leiomyoma [A] *	1/534 (0.19%)
Nervous system disorders	
Cerebral haemorrhage [A] *	3/534 (0.56%)
Cerebral ischaemia [A] *	1/534 (0.19%)
Cerebrovascular accident - IRR [A] *	1/534 (0.19%)
Dizziness [A] *	1/534 (0.19%)
Epilepsy [A] *	1/534 (0.19%)
Ischaemic stroke [A] *	1/534 (0.19%)
Paraplegia [A] *	1/534 (0.19%)
Polyneuropathy [A] *	1/534 (0.19%)
Thalamus haemorrhage [A] *	1/534 (0.19%)
Transient ischaemic attack [A] *	1/534 (0.19%)
Psychiatric disorders	

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Depressed mood [A] *	1/534 (0.19%)
Renal and urinary disorders	
Renal failure [A] *	1/534 (0.19%)
Respiratory, thoracic and mediastinal disorders	
Chronic obstructive pulmonary disease [A] *	1/534 (0.19%)
Dyspnoea [A] *	3/534 (0.56%)
Hypoventilation [A] *	1/534 (0.19%)
Nasal septum deviation [A] *	1/534 (0.19%)
Pleural effusion [A] *	2/534 (0.37%)
Pleurisy [A] *	1/534 (0.19%)
Pneumonia aspiration [A] *	1/534 (0.19%)
Pulmonary congestion [A] *	1/534 (0.19%)
Respiratory failure [A] *	1/534 (0.19%)
Skin and subcutaneous tissue disorders	
Eczema [A] *	1/534 (0.19%)
Erythema [A] *	1/534 (0.19%)
Social circumstances	
Pregnancy of partner [A] *	1/534 (0.19%)
Surgical and medical procedures	
Female sterilisation [A] *	1/534 (0.19%)
Finger amputation [A] *	1/534 (0.19%)
Inguinal hernia repair [A] *	1/534 (0.19%)
Small intestinal resection [A] *	1/534 (0.19%)

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Vascular disorders	
Jugular vein thrombosis [A] *	1/534 (0.19%)
Vascular occlusion [A] *	1/534 (0.19%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (10.1)

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Total	207/534 (38.76%)
Gastrointestinal disorders	
Diarrhoea [A] *	31/534 (5.81%)
General disorders	
Fatigue [A] *	40/534 (7.49%)
Pyrexia [A] *	27/534 (5.06%)
Infections and infestations	
Nasopharyngitis [A] *	38/534 (7.12%)
Investigations	
Blood lactate dehydrogenase increased [A] *	37/534 (6.93%)
Neutrophil count decreased [A] *	29/534 (5.43%)
Musculoskeletal and connective tissue disorders	
Arthralgia [A] *	34/534 (6.37%)
Back pain [A] *	35/534 (6.55%)
Nervous system disorders	

	Rituximab 375 mg/m^2
	Affected/At Risk (%)
Headache [A] *	31/534 (5.81%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] *	50/534 (9.36%)
Vascular disorders	
Hypertension [A] *	32/534 (5.99%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (10.1)

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.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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