Clinical trial results:
Optimal management of rheumatoid arthritis patients who require biologic therapy (ORBIT study)

Summary

EudraCT number	2009-011268-13
Trial protocol	GB
Global end of trial date	05 May 2015

Results information

Result version number	v1 (current)
This version publication date	04 April 2019
First version publication date	04 April 2019

Trial information

Trial identification

Sponsor protocol code	RN08RH469

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01021735
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Greater Glasgow and Clyde
Sponsor organisation address	West Glasgow Ambulatory Care Hospital, Dalnair Street, Glasgow, United Kingdom, G3 8SW
Public contact	Jurgen Van Melckebeke, NHS Greater Glasgow and Clyde , 0044 141 201 9313, Jurgen.van-melckebeke@ggc.scot.nhs.uk
Scientific contact	Duncan Porter, NHS Greater Glasgow and Clyde , 0044 141 452 6176, duncan.porter@ggc.scot.nhs.uk

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	05 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2015
Global end of trial reached?	Yes
Global end of trial date	05 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To identify whether rituximab therapy or anti-TNF therapy is more effective in improving the clinical symptoms, signs, physical function and health-related quality of life of patients with active rheumatoid arthritis.

Protection of trial subjects:

As part of the study patients required to attend additional hospital visits and investigations which could be above those considered to be standard care.. The visit schedule and the number and type of investigations were fully explained to patient verbally and in writing via the patient information sheet to ensure patients were fully aware what was entailed in the trial prior to them consenting to the study.

The patient information sheet also full explained the design of the study (open label, randomized controlled trial) that half of patient would receive study treatment (Rituximab) with the other half receiving TNF inhibitor therapy.

The side effects of TNF Inhibitor therapy were explained in patient information sheets, as where the expected side effects for the investigational medicinal product (Rituximab). All patients were closely monitored throughou the course of the study for adverse events and were advised to report adverse events to their study team as they arose.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 April 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 295
Worldwide total number of subjects	295
EEA total number of subjects	295

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	228
From 65 to 84 years	67
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study opened to recruitment on 05/04/2010 and closed to recruitment on 18/11/2013. This study was opened to recruitment in the United Kingdom.

Pre-assignment

Screening details:

The screening period for the study was up to 28 days prior to randomisation. Prior to screening investigations commencing patient must have provided informed consent to participate in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Control

Arm description:

Control - TNF Inhibitor

Arm type	Control

No investigational medicinal product assigned in this arm

Arm title	Experimental

Arm description:

Experimental (Rituximab)

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

Dosage and administration details:

1000 mg by intravenous infusion followed by a second 1000 mg intravenous infusion 2 weeks later. Above course can be repeated after a minimum of 20 weeks depending on response – max 3 courses in 12 months

Number of subjects in period 1	Control	Experimental
Started	151	144
Completed	135	134
Not completed	16	10
Adverse event, serious fatal	1	1
Consent withdrawn by subject	4	4
Physician decision	2	1

non compliance	1	-
illness	-	1
Adverse event, non-fatal	2	2
Concomitant illness	2	-
Lost to follow-up	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Control
Reporting group description: Control - TNF Inhibitor	
Reporting group title	Experimental
Reporting group description: Experimental (Rituximab)	

Reporting group values	Control	Experimental	Total
Number of subjects	151	144	295
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	115	113	228
From 65-84 years	36	31	67
85 years and over	0	0	0
Age continuous Units: years			
median	57	58.7	
inter-quartile range (Q1-Q3)	49.5 to 64.5	50.1 to 64.4	-
Gender categorical Units: Subjects			
Female	109	104	213
Male	42	40	82

End points

End points reporting groups	
Reporting group title	Control
Reporting group description: Control - TNF Inhibitor	
Reporting group title	Experimental
Reporting group description: Experimental (Rituximab)	

Primary: Mean change in DAS 28 between 0 and 12 months	
End point title	Mean change in DAS 28 between 0 and 12 months
End point description:	
End point type	Primary
End point timeframe: mean change in DAS 28 between 0 and 12 months.	

End point values	Control	Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	144		
Units: 295				
median (confidence interval 80%)	12.71 (12.6 to 12.8)	12.63 (12.55 to 12.73)		

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description: The analysis of the primary outcome was carried out on the Per Protocol (PP) population. The primary outcome measure was the mean change in DAS28 between 0 and 12 months.	
Comparison groups	Control v Experimental
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.192
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.513
upper limit	0.13

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events were followed until resolution or for at least 30 days after discontinuation of study medication, whichever came first.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	Control

Reporting group description:

Control - TNF Inhibitor

Reporting group title	Experimental

Reporting group description:

Experimental (Rituximab)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Not collected for this study.

Serious adverse events	Control	Experimental	
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 151 (21.19%)	37 / 144 (25.69%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
endometrial cancer			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abdominal hernia repair			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hip arthroplasty			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	1 / 151 (0.66%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shoulder arthroplasty			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fusion surgery			
subjects affected / exposed	1 / 151 (0.66%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal laminectomy			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 151 (1.32%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi organ failure			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	2 / 151 (1.32%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Immunoglobulins decreased			
subjects affected / exposed	1 / 151 (0.66%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigation / Loss of Consciousness			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain assessment			

subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	2 / 151 (1.32%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 151 (0.66%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 151 (0.00%)	2 / 144 (1.39%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Uveitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 151 (0.66%)	2 / 144 (1.39%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic polyp			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cutaneous vasculitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 151 (0.66%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	1 / 151 (0.66%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Labyrinthitis			
subjects affected / exposed	1 / 151 (0.66%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 151 (1.99%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyelonephritis			
subjects affected / exposed	1 / 151 (0.66%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 151 (1.32%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Urinary tract infection			
subjects affected / exposed	2 / 151 (1.32%)	3 / 144 (2.08%)	
occurrences causally related to treatment / all	2 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral tonsillitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 144 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 151 (0.00%)	1 / 144 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Control	Experimental	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 151 (0.00%)	0 / 144 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2010	1. Collection of blood for Bio-bank at three and six months The protocol (Study Flow chart) was amended to reflect blood sampling for the bio-bank at 3 and 6 months. 2. Patient Information Sheet was amended to reflect the changes to the blood sampling component.
08 February 2010	Amendment to Patient Information Sheet – has been amended on at the request of the Sponsor to include more detailed information about the risk of developing the very rare condition, Progressive Multifocal Leukoencephalopathy. Following documents were enclosed with the amendment: • Final ORBIT Patient Information Sheet V2, 16/12/2009 with changes highlighted • Final ORBIT Patient Information Sheet V3, 6/01/2010
19 March 2010	Amendment to study requirement – collection of additional 30mls of blood at baseline, 3 and 6 months for epigenetic analyses in 50 patients. The protocol was changed on Page 15 to reflect this. The PIS was amended on page 3 to reflect the above. Following documents were enclosed with the amendment: • Protocol V2.1 dated 03/02/2010 with changes highlighted • PIS V3.2 dated 11/02/2010 with changes highlighted
20 July 2010	Removal of existing sites: • Perth Royal Infirmary • Victoria Infirmary Glasgow • Dumfries & Galloway Royal Infirmary Additional site added: • University of Newcastle Change of PI at existing sites: • Aberdeen • Ayr Hospital
10 February 2011	1. Temporary halt. A temporary halt to the study was needed to allow the Sponsor to review the merit of the study following a substantial update of the Rituximab SmPC; as a result of EMA not granting approval. As a result a change to the Patient Information Sheet was also required. The temporary halt was submitted to both Ethics and MHRA. 2. Change to PIS V.3.5. The following was included into new PIS V3.5: "Are there any risks involved in taking part? In Europe, the European Medicines Agency (EMA) is responsible for assessing the risks and benefits of drugs. At the moment, it has decided that in routine clinical practice, patients with rheumatoid arthritis who have failed to respond to second line drugs should be treated with anti-TNF drugs (rather than rituximab). This is because there is uncertainty about whether rituximab is as safe and effective as anti-TNF therapy – in technical terms; the EMA says 'the benefit-risk balance of switching directly to rituximab is at present not settled.' However, the EMA has decided that rituximab is a safe and effective treatment for patients with rheumatoid arthritis who have failed to respond to anti-TNF therapy. No research has been done to directly compare the risks and benefits of rituximab and anti-TNF therapy. It is possible that rituximab is better, as good; or worse than anti-TNF therapy, and this study will help to find this out."
03 March 2011	Uplift of temporary halt

02 August 2011	Addition of sites, the following sites have been added: • Poole Hospital NHS Trust • Ipswich Hospital NHS Trust • Plymouth Hospitals NHS Trust • South Devon Healthcare NHS Foundation Trust • West Suffolk Hospitals NHS Trust • University Hospitals Coventry and Warwickshire NHS Trust • Royal Devon and Exeter NHS Trust • Betsi Cadwaladr University Health Board • Royal Cornwall Hospitals Trust • South London Healthcare NHS Trust • Barking, Havering & Redbridge University Hospitals NHS Trust, Queens Hospital and King George Hospital • University Hospital of Wales. • Basildon and Thurrock University Hospital NHS Trust • West Herts Hospital NHS Trust • The Countess of Chester Hospital NHS Foundation Trust Protocol – clarification and minor amendments. New protocol – Protocol V2.2 dated 25/04/2011 Change of Sponsorship – Addition of University as co-sponsor.
16 August 2011	Amendment to Patient Information Sheet: (PIS V4.0 dated 22/06/2012). Included: "As with all therapies for arthritis, very serious side effects can occur rarely with either anti-TNF or Rituximab. For instance, some patients treated with Rituximab have developed allergic reactions, which rarely have proved have proved fatal. Similarly, some patients treated with anti-TNF therapy have developed severe infections that rarely have proved fatal."
26 September 2011	Change of co-sponsorship agreement: the University of Glasgow will now act as co-Sponsor for the above study.
22 May 2013	1. Addition of sites: • Salisbury NHS Foundation Trust • The Royal Wolverhampton Hospitals NHS Trust • University Hospitals Leicester • Oxford University Hospitals NHS Trust • Southend University Hospitals NHS Foundation Trust • Trafford Healthcare NHS Trust • University Hospitals of Morecambe Bay NHS Foundation Trust • Mid Staffordshire NHS Foundation Trust • The Pennine Acute Hospitals NHS Trust • Kettering General Hospital NHS Foundation Trust • Hairmyres Hospital – NHS Lanarkshire Change of PI: • Change of PI at Countess of Chester Hospital NHS Foundation Trust. • Change of PI at Raigmore Hospital , Inverness. • Change PI Hertfordshire. 2. Change to protocol: • point of clarification. New protocol Version 2.3 -01/10/2012 Exclusion criterion: "Current inflammatory joint disease or autoimmune disease other then RA", changed to "Current inflammatory joint disease or autoimmune rheumatic disease other then RA" • Use of blood urine samples for future use 3. Change to Reference Safety Information
10 June 2013	Extension request to the study.
06 June 2014	Update to Reference Safety Information

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 January 2011	A temporary halt to the study was needed to allow the Sponsor to review the merit of the study following a substantial update of the Rituximab SmPC; as a result of EMA not granting approval.	27 January 2011

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27197690