Clinical trial results:
Torch: A phase II study to determine the safety and efficacy of the dual mTORC inhibitor AZD2014 and to investigate additional toxicities in combination with rituximab in relapsed refractory DLBCL

Summary

EudraCT number	2014-003588-39
Trial protocol	GB
Global end of trial date	05 February 2019

Results information

Result version number	v1 (current)
This version publication date	14 February 2020
First version publication date	14 February 2020
Summary attachment (see zip file)	TORCH original article Haematological Oncology (TORCH Original Article Hem Onc 2019 R1.pdf)

Trial information

Trial identification

Sponsor protocol code	RG_14-212

Additional study identifiers

ISRCTN number	ISRCTN10760016
ClinicalTrials.gov id (NCT number)	NCT02752204
WHO universal trial number (UTN)	-
Other trial identifiers	CAS number: NH2003

Notes:

Sponsors

Sponsor organisation name	University of Birmingham
Sponsor organisation address	CRCTU, University of Birmingham, Edgbaston, Birmingham, United Kingdom, B15 2TT
Public contact	TORCH Trial Cordinator, CRCTU, 44 1213717863, torch@trials.bham.ac.uk
Scientific contact	TORCH Trial Cordinator, University of Birmingham, 44 1213717863, torch@trials.bham.ac.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 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and activity of AZD2014 as a single agent in the treatment of Diffuse large B-Cell Lymphoma (DLBCL) by measuring the best overall response to the treatment within 6 cycles.

Protection of trial subjects:

Specific dose modifications were recommended to decrease the incidence and relieve the symptoms of:
nausea and vomiting;
stomatitis, oral mucositis, and mouth ulcers;
rash and/or skin toxicity;
hyperglycaemia;
interstitial lung disease;
changes to ECG;
Severe fatigue;
diarrhoea;
and electrolite changes.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

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)	13
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

36 patients were recruited between November 2015 and April 2017. Patients from 13 Haemato-oncology centres (those selected for the LLR Trials Acceleration Programme) in the UK were invited to join the trial.

Pre-assignment

Screening details:

Screening commenced following consent and prior to patient registration in order to confirm eligibility. Screening assessments included: medical history, height, weight, demographic data, blood tests, clinical and cardiac assessments, ECOG performance, assessment of constitutional symptoms, urinalysis, bone marrow biopsy, pregnancy test and PET-CT.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Monotherapy

Arm description:

Vistusertib was administered to 30 patients in an intermittent dosing schedule of 125 mg b.d. for two days per week, for up to six 28-day cycles.

Arm type	Stage 1
Investigational medicinal product name	Vistusertib
Investigational medicinal product code	AZD2014
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

125mg tablet given twice daily. 2 days on, 5 days off for up to 6 cycles.

Arm title	combination (stage 2)

Arm description:

Patients received up to 6 cycles of vistusertib (125mg) BD, 2 days on and 5 days off, in addition to 375mg/m2 rituximab on day 1 of each cycle.

Arm type	Stage 2
Investigational medicinal product name	Vistusertib
Investigational medicinal product code	AZD2014
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

125mg tablet given twice daily. 2 days on, 5 days off for up to 6 cycles.

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	Mabthera, Rixathon, Truxima
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

375mg/m2 administered by intravenous infusion on day 1 of a weekly cycle.

Number of subjects in period 1	Monotherapy	combination (stage 2)
Started	30	6
Completed	4	1
Not completed	26	5
death	2	1
Toxicity	2	-
disease recurrence	22	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial
Reporting group description:	
All patients that entered the trial	

Reporting group values	Overall Trial	Total	
Number of subjects	36	36	
Age categorical			
Ages of all patients who entered the trial			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	13	13	
From 65-84 years	23	23	
85 years and over	0	0	
Age continuous			
Summary of age			
Units: years			
median	68.5		
full range (min-max)	33 to 82	-	
Gender categorical			
Units: Subjects			
Female	21	21	
Male	15	15	
Disease status			
Number of patients with refractory or relapsed lymphoma			
Units: Subjects			
Refractory Lymphoma	17	17	
Relapsed Lymphoma	19	19	
Baseline Haematology - Haemoglobin			
Baseline levels of haemoglobin			
Units: g/L			
arithmetic mean	117.3		
full range (min-max)	86 to 147	-	
HbA1C			
Measurement of glycated haemoglobin			
Units: mmol/mol			
arithmetic mean	37.8		
full range (min-max)	28 to 67	-	
Lymphocytes			
Haematology assessment, number of lymphocytes (x 10^9) per L			

Units: 10^9/L			
arithmetic mean	1.0		
full range (min-max)	0.1 to 2.6	-	
Neutrophils			
Number of neutrophils (x 10^9) per L			
Units: 10^9/L			
arithmetic mean	6.7		
full range (min-max)	1.1 to 16.7	-	
Platelets			
Number of platelets(x 10^9) per L			
Units: 10^9/L			
arithmetic mean	235.1		
full range (min-max)	73 to 417	-	
White blood cell count			
Number of white blood cells (x 10^9) per L			
Units: 10^9/L			
arithmetic mean	8.3		
full range (min-max)	1.7 to 18.4	-	
ALT			
Amount of alanine aminotransferase			
Units: U/L			
arithmetic mean	21.8		
full range (min-max)	10 to 55	-	
Bilirubin			
Amount of bilirubin			
Units: U/L			
arithmetic mean	9.5		
full range (min-max)	3 to 20	-	
Cholesterol			
Amount of cholesterol			
Units: mmol/L			
arithmetic mean	5.1		
full range (min-max)	3.4 to 8.8	-	
Serum Creatine			
Amount of serum creatine			
Units: umol/L			
arithmetic mean	77.9		
full range (min-max)	38 to 169	-	
Glucose			
Baseline blood glucose levels			
Units: mmol/L			
arithmetic mean	5.9		
full range (min-max)	3.7 to 10.9	-	
HDL Cholesterol			
Baseline blood levels of HDL cholesterol			
Units: mmol/L			
arithmetic mean	1.5		
full range (min-max)	0.8 to 5.3	-	
Time from diagnosis			
Time from diagnosis to date of registration to the trial			
Units: days			
median	691		

full range (min-max)	15 to 5670	-	

Subject analysis sets

Subject analysis set title	All patients across trial
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who entered the trial

Reporting group values	All patients across trial		
Number of subjects	36		
Age categorical			
Ages of all patients who entered the trial			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	13		
From 65-84 years	23		
85 years and over	0		
Age continuous			
Summary of age			
Units: years			
median			
full range (min-max)			
Gender categorical			
Units: Subjects			
Female			
Male			
Disease status			
Number of patients with refractory or relapsed lymphoma			
Units: Subjects			
Refractory Lymphoma			
Relapsed Lymphoma			
Baseline Haematology - Haemoglobin			
Baseline levels of haemoglobin			
Units: g/L			
arithmetic mean			
full range (min-max)			
HbA1C			
Measurement of glycated haemoglobin			
Units: mmol/mol			
arithmetic mean			
full range (min-max)			

Lymphocytes			
Haematology assessment, number of lymphocytes (x 10^9) per L			
Units: 10^9/L arithmetic mean full range (min-max)			
Neutrophils			
Number of neutrophils (x 10^9) per L			
Units: 10^9/L arithmetic mean full range (min-max)			
Platelets			
Number of platelets(x 10^9) per L			
Units: 10^9/L arithmetic mean full range (min-max)			
White blood cell count			
Number of white blood cells (x 10^9) per L			
Units: 10^9/L arithmetic mean full range (min-max)			
ALT			
Amount of alanine aminotransferase			
Units: U/L arithmetic mean full range (min-max)			
Bilirubin			
Amount of bilirubin			
Units: U/L arithmetic mean full range (min-max)			
Cholesterol			
Amount of cholesterol			
Units: mmol/L arithmetic mean full range (min-max)			
Serum Creatine			
Amount of serum creatine			
Units: umol/L arithmetic mean full range (min-max)			
Glucose			
Baseline blood glucose levels			
Units: mmol/L arithmetic mean full range (min-max)			
HDL Cholesterol			
Baseline blood levels of HDL cholesterol			
Units: mmol/L arithmetic mean full range (min-max)			
Time from diagnosis			
Time from diagnosis to date of registration to the trial			

Units: days median full range (min-max)			

End points

End points reporting groups

Reporting group title	Monotherapy
Reporting group description:	
Vistusertib was administered to 30 patients in an intermittent dosing schedule of 125 mg b.d. for two days per week, for up to six 28-day cycles.	
Reporting group title	combination (stage 2)
Reporting group description:	
Patients received up to 6 cycles of vistusertib (125mg) BD, 2 days on and 5 days off, in addition to 375mg/m2 rituximab on day 1 of each cycle.	
Subject analysis set title	All patients across trial
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects who entered the trial	

Primary: Best Overall Response during the first 6 cycles of treatment

End point title	Best Overall Response during the first 6 cycles of treatment[1]
End point description:	

End point type	Primary
End point timeframe:	
Best response achieved during the first 6 cycles of treatment	

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: No statistical analysis were conducted in relation to this primary outcome as this is a single arm trial so the interpretation of the primary outcome was made in relation to desirable characteristics defined in the sample size calculation.

End point values	Monotherapy	combination (stage 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	6		
Units: Response				
Partial Response	2	0		
No response / stable disease	6	1		
Progressive disease	13	1		
Discontinued treatment prior to response assesment	0	1		
Discontinued treatment, died prior to assessment	9	2		
Died prior to response assessment	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

Time from date of registration to the date of death from any cause

End point values	Monotherapy	combination (stage 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	6		
Units: months				
median (confidence interval 95%)	6.45 (3.42 to 13.87)	0.94 (0.32 to 9000000000)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival

End point description:

End point type	Secondary

End point timeframe:

Calculated from date of registration until date of disease progression or death from any cause

End point values	Monotherapy	combination (stage 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	6		
Units: months				
median (confidence interval 95%)	1.7 (1.61 to 1.97)	0.79 (0.07 to 900000)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum percentage decrease during the first 6 cycles

End point title	Maximum percentage decrease during the first 6 cycles

End point description:

End point type	Secondary

End point timeframe:

The first 6 treatment cycles

End point values	All patients across trial			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: percentage decrease				
arithmetic mean (full range (min-max))	33.9 (-85.5 to 720)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response Rate Post 6 Cycles

End point title	Best Overall Response Rate Post 6 Cycles

End point description:

End point type	Secondary

End point timeframe:

Best overall response rate post 6 cycles of treatment until the end of the trial

End point values	Monotherapy	combination (stage 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[2]	1[3]		
Units: Response				
Complete Response	1	0		
Partial Response	5	0		
Progressive Disease	2	0		
Response Assessment Not Performed	8	1		

Notes:

[2] - Only 16 of the 30 patients randomized to this group attended follow up visits post 6 cycles

[3] - Only 1 of the 6 patients randomized to this group attended follow up visits post 6 cycles

Statistical analyses

No statistical analyses for this end point

Secondary: Tolerability

End point title	Tolerability

End point description:

Tolerability of AZD2014 both alone and in combination with Rituximab was assessed

using toxicities recorded during trial treatment. The study needed to observe at least 21 tolerable outcomes (i.e at most 9 toxicities that lead to treatment delays or dose modification) during the first 2 cycles to conclude that the treatment was tolerable at the current dose. For the combination therapy at least 4 tolerable outcomes (i.e at most 2 toxicities that lead to treatment delay or dose modification) during the first 2 cycles needed to be observed to conclude the combination therapy was tolerable at the current dose.

End point type	Secondary

End point timeframe:

First 2 cycles of treatment

End point values	Monotherapy	combination (stage 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	6		
Units: Response				
Tolerated	21	5		
Not Tolerated	9	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response[4]

End point description:

End point type	Secondary

End point timeframe:

Duration of response was dened to be the time from rst documented response until relapse/progression, as determined by the Revised Response Criteria, or date of last follow up if relapse/progression free. Patients who die before a relapse/progression

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome was defined to be the time from first documented response until relapse/progression, since responses during this trial were observed only in the monotherapy group with no responses documented within the combination group results are given for only the monotherapy group as per the outcome definition.

End point values	Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	7[5]			
Units: Months				
median (confidence interval 95%)	0 (0 to 0)			

Notes:

[5] - Responses were only observed within 7 of the 30 patients randomized to this group.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the date of commencement of protocol defined treatment until 30 days after administration of the last treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	All patients entered in the trial

Reporting group description:

All patients who entered the trial

Serious adverse events	All patients entered in the trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 36 (47.22%)		
number of deaths (all causes)	32		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	3 / 36 (8.33%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Diarrhea				
subjects affected / exposed	4 / 36 (11.11%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Gastric hemorrhage				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mucositis oral				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders - other				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal disorders				
Pneumonitis				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Lung infection				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	1 / 36 (2.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Urinary tract infection			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations - other			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients entered in the trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 36 (97.22%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Electrocardiogram QT corrected interval prolonged			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	4		
Neutrophil count decreased			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Weight loss			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Vascular disorders			

Hypertension			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Dysgeusia			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
General disorders and administration site conditions			
edema limbs			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	14 / 36 (38.89%)		
occurrences (all)	20		
Fever			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	9		
General disorders and administration site conditions - other			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	7		
Pain			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 36 (19.44%)		
occurrences (all)	9		
Constipation			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	6		
Diarrhoea			
subjects affected / exposed	15 / 36 (41.67%)		
occurrences (all)	21		

Dyspepsia			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	5		
Gastrointestinal disorder			
subjects affected / exposed	7 / 36 (19.44%)		
occurrences (all)	15		
Mucositis oral			
subjects affected / exposed	10 / 36 (27.78%)		
occurrences (all)	14		
Nausea			
subjects affected / exposed	16 / 36 (44.44%)		
occurrences (all)	21		
Vomiting			
subjects affected / exposed	9 / 36 (25.00%)		
occurrences (all)	13		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	4		
Dyspnea			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	7		
Productive cough			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders - other			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders - other			
subjects affected / exposed	6 / 36 (16.67%)		
occurrences (all)	6		

Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Psychiatric disorders - other			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Renal and urinary disorders			
Renal and urinary disorders - other			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Urinary frequency			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorder - other			
subjects affected / exposed	10 / 36 (27.78%)		
occurrences (all)	11		
Infections and infestations			
Infections and infestations - other			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	6		
Skin infection			
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	6		
Dehydration			

subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2015	SA2: Substantial amendment made for ethical approval. This included reduction of patient identifiable data collected from Date of Birth to Year of Birth. Minor clarifications and typographical corrections were made.
18 May 2015	SA 3: Substantial amendment made for MHRA approval. This included an update to exclusion criteria (platelet count). Addition of exclusions for rituximab patients added. Additional advice for toxicities with rituximab added.
06 July 2016	SA 9: Substantial amendment made. This included an update to saliva sample (no longer optional), clarification of screening assessment, and insertion of ISRCTN number. Removal of QT interval prolonging drugs drugs and ECG requirements from the exclusions. Rewording of the eligibility criteria relating to patients with hepatitis infection. Amendment of dose modification information. Reduction of ECG frequency. Updated list of concomitant medications to be avoided.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31385336