Clinical trial results:
A randomised, prospective study, assessing changes in cerebral function in treatment naive HIV-1 infected subjects commencing either boosted atazanavir with Truvada or boosted darunavir with maraviroc and Kivexa

Summary

EudraCT number	2011-002656-14
Trial protocol	GB
Global end of trial date	20 October 2015

Results information

Result version number	v1 (current)
This version publication date	01 June 2017
First version publication date	01 June 2017

Trial information

Trial identification

Sponsor protocol code	1733

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01367236
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	Room 221, Medical School Building, St Marys Campus, Norfolk Place , London, United Kingdom, W2 1PG
Public contact	Alan Winston, Imperial College London, +44 207886 1603, a.winston@imperial.ac.uk
Scientific contact	Alan Winston, Imperial College London, +44 207886 1603, a.winston@imperial.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	21 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 October 2015
Global end of trial reached?	Yes
Global end of trial date	20 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

When commencing antiretroviral therapy (anti-HIV therapy) for the first time, improvements in the function of the brain are frequently observed. For example memory and concentration may improve. However, whether these improvements may differ between different anti-HIV therapies is largely unknown. The purpose of this study is to compare two different combination anti-HIV therapies over 48 weeks and to assess if differences in improvement in the function of the brain are observed over this period.

Protection of trial subjects:

Ethical approval was gained prior to the trial commencing.
Suitable subjects currently attending one of the trial sites for the management of their HIV care were recruited during routine hospital visits, and hence were under the care of a HIV consultant.
Subjects did not exit their standard care pathway and study participation caused no additional risk.
Each subject signed an Informed Consent Form prior to the conduct of any screening procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2012
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: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	60
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

60 subjects were recruited in total - the first subject was consented on 08/03/2013 and randomised on 26/03/2013; the final subject was consented on 30/10/2014 and randomised on 17/11/2014. All subjects were recruited in the UK at 6 trial sites.

Pre-assignment

Screening details:

Suitable subjects currently attending one of the trial sites for the management of their HIV care will be recruited during routine hospital visits. Each subject must sign an Informed Consent Form prior to the conduct of any screening procedures after having adequate time to read through the PIS. 72 subjects screened in total (12 screen failures).

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	Standard of care – non 'neuroART' arm

Arm description:

Standard HIV antiretroviral therapy treatment

Arm type	Active comparator
Investigational medicinal product name	Atazanavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Atazanavir 300 mg daily

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

Dosage and administration details:

Tenofovir 245 mg daily*
Emtricitabine 200 mg daily*

* as the fixed dose combination Truvada™

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

Dosage and administration details:

Ritonavir 100 mg daily

Arm title	Novel therapeutic approach – 'neuroART' arm

Arm description:

Novel therapeutic approach

Arm type	Experimental
Investigational medicinal product name	Kivexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lamivudine 300 mg daily**
Abacavir 600 mg daily**

** as the fixed dose combination Kivexa ™

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

Dosage and administration details:

Maraviroc 150 mg once daily

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

Dosage and administration details:

Ritonavir 100 mg daily

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

Dosage and administration details:

Darunavir 800 mg daily

Number of subjects in period 1	Standard of care – non 'neuroART' arm	Novel therapeutic approach – 'neuroART' arm
Started	30	30
Completed	27	29
Not completed	3	1
Consent withdrawn by subject	3	-
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Standard of care – non 'neuroART' arm
Reporting group description:	
Standard HIV antiretroviral therapy treatment	
Reporting group title	Novel therapeutic approach – 'neuroART' arm
Reporting group description:	
Novel therapeutic approach	

Reporting group values	Standard of care – non 'neuroART' arm	Novel therapeutic approach – 'neuroART' arm	Total
Number of subjects	30	30	60
Age categorical			
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	31.24	34.84	
inter-quartile range (Q1-Q3)	27.1 to 38	28.19 to 40.57	-
Gender categorical			
Units: Subjects			
Female	1	1	2
Male	29	29	58
Site			
Number of subjects recruited per site			
Units: Subjects			
Brighton	7	7	14
Birmingham	3	3	6
Chelsea & Westminster	2	1	3
King' College	3	4	7
St Thomas	7	8	15
St Mary's	8	7	15
Race			
Units: Subjects			
Black	5	6	11
Mixed	1	1	2
Other	1	1	2
White	23	22	45

Employment Status Units: Subjects			
Employed or self-employed full-time	17	17	34
Employed or self-employed part-time	4	3	7
Full time student/education/training	1	6	7
Unemployed	5	3	8
Unknown	3	1	4
Screening CD4+ lymphocyte count ≤ 350 cells/µL Units: Subjects			
Yes	17	15	32
No	12	12	24
Unknown	1	3	4
Educational status Units: Subjects			
A levels (or equivalent qualifications at age 18)	2	9	11
Finished education with no qualifications	2	0	2
O levels/GCSEs (or equivalent qualifications at 16	7	0	7
Other qualifications	3	5	8
University degree or above	13	15	28
Unknown	3	1	4
Tropism results Units: Subjects			
Dual tropic	0	1	1
Mixed tropic	0	1	1
r5 tropic	21	19	40
x4 tropic	5	4	9
Unknown	4	5	9
HIV-Clade Units: Subjects			
HIV-Clade a	0	1	1
HIV-Clade b	22	23	45
HIV-Clade c	3	1	4
HIV-Clade d	0	1	1
Other	5	3	8
Unknown	0	1	1
Plasma HIV-RNA5			
Viral load value			
Units: Subjects			
Above 500	1	0	1
Between 100k to 499k	5	4	9
Between 51k to 99k	24	26	50
Smoking history Units: Subjects			
The patient is not a current smoker	19	18	37
The patient is a current smoker	11	12	23
Alcohol History Units: Subjects			
The patient currently drinks alcohol	23	21	44

Th patient does not currently drink alcohol	7	9	16
Recreational Drug History Units: Subjects			
The patient does not currently take drugs	21	23	44
The patient currently takes recreational drugs	9	7	16
Medical History Units: Subjects			
Not experienced any past and/or disease or surgery	13	12	25
Experienced any past and/or diseases or surgeries	16	18	34
Unknown	1	0	1
HLA-B5701 Units: Subjects			
HLA-B5701 negative	30	30	60
HLA-B5701 positive	0	0	0
AIDS events Units: Subjects			
Number of subjects with an AIDS Event	2	1	3
Number of subjects without an AIDS Event	28	29	57
Patient Questionnaire – I have trouble remembering things Units: Subjects			
No	23	24	47
Yes	6	6	12
Unknown	1	0	1
Patient Questionnaire – I have trouble concentrating Units: Subjects			
No	26	22	48
Yes	3	8	11
Unknown	1	0	1
Patient Questionnaire – My thinking is clear Units: Subjects			
No	2	3	5
Yes	27	26	53
Unknown	1	1	2
Lawton Instrumental Activities of Daily Living Scale – Ability to use telephone Units: Subjects			
Operates telephone on own initiative	29	30	59
Unknown	1	0	1
Lawton Instrumental Activities of Daily Living Scale – Shopping Units: Subjects			
Takes care of all shopping needs independently	28	30	58
Shops independently for small purchases	1	0	1

Unknown	1	0	1
Lawton Instrumental Activities of Daily Living Scale – Food Preparation Units: Subjects			
Plans, prepares and serves adequate meals independ	29	30	59
Unknown	1	0	1
Lawton Instrumental Activities of Daily Living Scale – Housekeeping Units: Subjects			
Maintains house alone with occasional assistance	28	28	56
Performs light daily tasks such as dishwashing	1	2	3
Unknown	1	0	1
Lawton Instrumental Activities of Daily Living Scale – Laundry Units: Subjects			
Does personal laundry completely	29	30	59
Unknown	1	0	1
Lawton Instrumental Activities of Daily Living Scale – Mode of Transportation Units: Subjects			
Travels independently on public transportation	28	30	58
Travels on public transportation when assisted	1	0	1
Unknown	1	0	1
Lawton Instrumental Activities of Daily Living Scale – Responsibility for own medication Units: Subjects			
Is responsible for taking medication	29	30	59
Unknown	1	0	1
Lawton Instrumental Activities of Daily Living Scale – Ability to handle finances Units: Subjects			
Manages financial matters independently	28	28	56
Manages day to day purchases	1	1	2
Incapable of handling money	0	1	1
Unknown	1	0	1
Framingham Risk Score Units: Subjects			
Over 30%	7	10	17
12%	0	1	1
5%	0	1	1
2%	0	2	2
<1%	2	1	3
Error	20	13	33
1%	1	2	3
CD4+ lymphocyte count (screening)			
At screening			
Units: cells/µL			
median	367.5	410	

inter-quartile range (Q1-Q3)	286 to 576	330 to 541	-
CD4+ lymphocyte count (baseline)			
Units: cells/µL			
median	434	364.5	
inter-quartile range (Q1-Q3)	308 to 540	301 to 509	-
Biochemistry blood test - glucose			
Units: mmol/L			
median	5	5	
inter-quartile range (Q1-Q3)	4 to 5	4 to 5	-
Biochemistry blood test - Amylase			
Units: U/L			
median	67	55	
inter-quartile range (Q1-Q3)	53 to 91	40 to 71	-
Biochemistry blood test - Sodium			
Units: mmol/L			
median	139	140	
inter-quartile range (Q1-Q3)	138 to 140	138 to 140	-
Biochemistry blood test - Potassium			
Units: mmol/L			
median	4	4	
inter-quartile range (Q1-Q3)	4 to 4	4 to 4	-
Biochemistry blood test - Creatinine			
Units: µmol/L			
median	73	81	
inter-quartile range (Q1-Q3)	69 to 85	67 to 85	-
Biochemistry blood test - ALT			
Units: iU/L			
median	23	23	
inter-quartile range (Q1-Q3)	21 to 29	17 to 36	-
Biochemistry blood test - AST			
Units: iU/L			
median	27	27	
inter-quartile range (Q1-Q3)	24 to 42	22 to 33	-
Biochemistry blood test - Alkaline Phosphatase			
Units: iU/L			
median	70	65	
inter-quartile range (Q1-Q3)	61 to 81	58 to 77	-
Biochemistry blood test - Bilirubin			
Units: umol/L			
median	9	8	
inter-quartile range (Q1-Q3)	7 to 11	7 to 10	-
Biochemistry blood test - Protein			
Units: g/L			
median	77	76	
inter-quartile range (Q1-Q3)	72 to 80	74 to 79	-
Fasting lipids blood test - Total Cholesterol			
Units: mmol/L			
median	3.8	4.2	
inter-quartile range (Q1-Q3)	3.4 to 4.3	3.5 to 4.7	-
Fasting lipids blood test - HDL			

Units: mmol/L			
median	1.03	1.1	
inter-quartile range (Q1-Q3)	0.86 to 1.34	0.82 to 1.3	-
Fasting lipids blood test - LDL			
Units: mmol/L			
median	2.31	2.52	
inter-quartile range (Q1-Q3)	1.9 to 2.7	2 to 3	-
Fasting lipids blood test - Triglycerides			
Units: mmol/L			
median	1.3	1.2	
inter-quartile range (Q1-Q3)	1 to 1.45	1 to 1.6	-
Haematology blood test - Hb			
Units: g/dl			
median	14.35	14.3	
inter-quartile range (Q1-Q3)	13.5 to 15.2	13.7 to 15.5	-
Haematology blood test - WBC			
Units: x109/l			
median	5.05	4.9	
inter-quartile range (Q1-Q3)	4.3 to 7.1	4.3 to 5.6	-
Haematology blood test - RBC			
Units: x1012/l			
median	4.92	4.88	
inter-quartile range (Q1-Q3)	4.55 to 5.04	4.53 to 5.19	-
Haematology blood test - Neutrophils			
Units: x109/l			
median	2.45	2.45	
inter-quartile range (Q1-Q3)	1.8 to 3.3	2.1 to 3.1	-
Haematology blood test - Monocytes			
Units: x109/l			
median	0.55	0.5	
inter-quartile range (Q1-Q3)	0.4 to 0.7	0.4 to 0.5	-
Haematology blood test - Platelets			
Units: x109/l			
median	200.5	212	
inter-quartile range (Q1-Q3)	166 to 233	177 to 240	-
Haematology blood test - Eosinophils			
Units: x109/l			
median	0.1	0.14	
inter-quartile range (Q1-Q3)	0.04 to 0.2	0.1 to 0.3	-
Vital signs - height			
Units: cm			
median	178.25	175.25	
inter-quartile range (Q1-Q3)	173 to 181.1	170.1 to 182	-
Vital signs - weight			
Units: kg			
median	75.75	77	
inter-quartile range (Q1-Q3)	65.6 to 84.9	67.6 to 87.8	-
Vital signs - systolic blood pressure			
Units: mmHg			
median	123	126	
inter-quartile range (Q1-Q3)	116 to 133	117 to 132	-
Vital signs - diastolic blood pressure			

Units: mmHg			
median	71	72.5	
inter-quartile range (Q1-Q3)	67 to 81	68 to 77	-
Viral Load			
Units: copies per milliliter of blood			
median	44864	50959	
inter-quartile range (Q1-Q3)	21292 to 70841	26491 to 76141	-

End points

End points reporting groups

Reporting group title	Standard of care – non ‘neuroART’ arm
Reporting group description: Standard HIV antiretroviral therapy treatment	
Reporting group title	Novel therapeutic approach – ‘neuroART’ arm
Reporting group description: Novel therapeutic approach	

Primary: To assess differences in neurocognitive function at week 48 between study treatment arms

End point title	To assess differences in neurocognitive function at week 48 between study treatment arms
End point description: COGSTATE battery comprised of 11 tasks in the form of a computerised assessment.	
End point type	Primary
End point timeframe: 48 weeks	

End point values	Standard of care – non ‘neuroART’ arm	Novel therapeutic approach – ‘neuroART’ arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: neurocognitive score				
arithmetic mean (confidence interval 95%)	0.1596713 (-0.0401165 to 0.3270786)	0.2532748 (0.0525634 to 0.4155249)		

Attachments (see zip file)	CogUK primary analysis graph/CogUK primary analysis graph.

Statistical analyses

Statistical analysis title	generalised linear mixed model
Statistical analysis description: Adjusting valuables: treatment, baseline cognitive score, time, centre, plasma group, time x treatment interaction	
Comparison groups	Standard of care – non ‘neuroART’ arm v Novel therapeutic approach – ‘neuroART’ arm

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437 [1]
Method	Mixed models analysis

Notes:

[1] - Initial status (intercept) for treatment effect, adjusted = -0.00304 (-0.12, 0.11). P-value = 0.96
Rate of change (slope) for treatment at week 48 = 0.09360 (-0.14, 0.33). P-value = 0.437

Adverse events

Adverse events information

Timeframe for reporting adverse events:

An assessment of all Serious Adverse Events (SAEs) and Adverse Events (AEs) that have occurred was undertaken at every patient visit and recorded on the eCRF from randomisation to week 48.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Full analysis set

Reporting group description: -

Serious adverse events	Full analysis set		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 60 (5.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioma			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Full analysis set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 60 (88.33%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Penile neoplasm			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Feeling cold			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Local swelling			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Reproductive system and breast disorders			

Dysmenorrhoea			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Epistaxis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	6		
Rhinitis allergic			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Disorientation			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Euphoric mood			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Mood swings			

subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Investigations			
Weight decreased			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Repetitive strain injury			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Nervous system disorders			
Burning sensation			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	3		
Dysgeusia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	16		
Lethargy			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		

Paraesthesia			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Somnolence			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Ocular icterus			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	10		
Scleral discolouration			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	22 / 60 (36.67%)		
occurrences (all)	25		
Dyspepsia			

subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	3		
Haematochezia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	13		
Oesophageal pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Proctitis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Alopecia			

subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Blister			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Hyperhidrosis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Night sweats			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Rash pruritic			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Yellow skin			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Polyuria			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		

Proteinuria			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Renal mass			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Chlamydial infection			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Conjunctivitis			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Conjunctivitis viral			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Ear infection			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Gastrointestinal infection			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Genital Herpes				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Genital herpes simplex				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Gonorrhoea				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	2			
Herpes simplex				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Herpes virus infection				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	6			
Herpes zoster				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Hordeolum				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	4			
Influenza				
subjects affected / exposed	4 / 60 (6.67%)			
occurrences (all)	4			
Lower respiratory tract infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	4 / 60 (6.67%)			
occurrences (all)	4			
Oral candidiasis				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Oral herpes				

subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Pilonidal cyst			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Proctitis gonococcal			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Syphilis			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Tonsillitis			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Tooth infection			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2011	Minor changes to Patient Information Sheet, Informed Consent Form, GP letter and patient appointment card
05 March 2013	Change in protocol - It is considered that at the screening visit blood tests may be used if estimated within the previous 28 days. This is in line with the routine medical procedures at clinic visits and saves the patient from unnecessary venepuncture.
25 April 2013	Change in inclusion criteria - remove the inclusion criteria relating to CD4 lymphocyte count
07 May 2013	Change in protocol - A new 800mg strength of DARUNAVIR has been authorised. Therefore, for patients randomised to ARM 2 (Novel therapeutic approach – 'neuroART' arm), a single 800mg tablet of Darunavir will be prescribed where possible. This will simplify and reduce the tablet burden and the final doses prescribed will not alter.
29 January 2015	The Principal Investigator at the site in Brighton, Professor Martin Fisher has transferred his duties for the CogUK trial to Dr Amanda Clarke.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported