Clinical trial results:
A prospective, multicenter, randomized, open-label trial to assess the safety, tolerability and efficacy of dual therapy with boosted Darunavir + Dolutegravir when switching from standard of care ART in HIV-patients with sustained virological Suppression (DUALIS-Study)

Summary

EudraCT number	2015-000360-34
Trial protocol	DE
Global end of trial date	15 June 2018

Results information

Result version number	v1 (current)
This version publication date	29 July 2020
First version publication date	29 July 2020
Summary attachment (see zip file)	CSR_DUALIS (CSR_Dua_20200518_AM-V1_final_clean.pdf)

Trial information

Trial identification

Sponsor protocol code	DUA-1463-SPI-0320-I

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02486133
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität München, Fakultät für Medizin
Sponsor organisation address	Ismaninger Str. 22, Munich, Germany, 81675
Public contact	PD Dr. Christoph Spinner, Klinikum rechts der Isar der TU München, Klinik für Innere Medizin II , Technische Universität München, Fakultät für Medizin, 49 89 4140 2251, christoph.spinner@tum.de
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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	11 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2018
Global end of trial reached?	Yes
Global end of trial date	15 June 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The clinical trial investigates whether a switch strategy of dual therapy with DRV/r + DTG is non-inferior with respect to HIV RNA < 50 cps/ml (ITTe analysis, FDA snapshot analysis (missing, switch or discontinuation of investigational study drugs for any reason = failure; change of NRTI backbone combination will not be classified as failure for primary endpoint analysis)) to a continuous standard of care therapy with DRV/r in combination with 2 NRTIs (ABC/3TC, F/TDF or F/TAF) over 48 weeks in HIV patients, who are on at least 24 weeks prior to randomisation of a stable and fully suppressive ART, consisting of 2 NRTI (ABC/3TC, F/TDF or F/TAF) in combination with DRV/r for a period of at least 28 days prior to randomisation (HIV RNA < 50 cps/ml and within a period of 24 weeks prior to randomisation with one accepted blip of HIV- RNA < 200 cps/ml).

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance the ethical principles of Good Clinical Practice (GCP).
Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision.
The study was regularly monitored by the Sponsor and all investigators connected to the study were GCP trained.

Background therapy:

Standard of care.

Evidence for comparator:

Modern combination antiretroviral therapy (cART) leads to well-controlled HIV infection with a potentially normal life expectancy [1]. Nucleosidic reverse transcriptase inhibitors (NRTIs) play a major role as “ART backbone” and are essential antiretroviral agents according to current European and WHO HIV treatment guidelines. Alternative NRTI free (so called "nuke sparing") therapy options have been evaluated in different studies but were associated with less virologic therapeutic success and higher rates of therapy induced resistance compared to standard regimens in ART naïve patients. This is particularly true for patients with a high baseline viral load.
As an alternative to NRTI-based therapy options, Ritonavir-boosted protease inhibitor (PI/r)-based nuke-sparing dual therapies have been studied widely, mostly in combination with the integrase inhibitor (INI) Raltegravir (RAL).
The HIV protease inhibitor Darunavir (DRV) and the novel INI Dolutegravir (DTG) are both very potent anchor drugs with a high barrier to resistance. Due to a favourable side-effect profile, a once-daily (QD) formulation and its virological potency, DRV is currently one of the most frequently used PIs in Europe and the USA. In addition, the new, once-daily administrable integrase inhibitor DTG showed an excecellent tolerability profile as well as a high resistance barrier.
The nuke-free combination of DTG (50 mg) with the Ritonavir (/r)- or Cobicistat-boosted protease inhibitor DRV (800 mg) may offer a favorable safety and efficacy profile with the advantage of QD-dosing.

Actual start date of recruitment	31 July 2015
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	Germany: 269
Worldwide total number of subjects	269
EEA total number of subjects	269

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)	261
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pre-screening processes were in place. Between 31.07.2015 and 01.06.2018 all patients were randomised.

Pre-assignment

Screening details:

Requirements for inclusion:
HIV- infection within a period of at least 24 weeks suppressive ART prior to randomization, with one accepted blip of HIV- RNA < 200 cps/ml and well-tolerated antiretroviral therapy: consisting of 2 NRTI (ABC/3TC, F/TDF or F/TAF) in combination with DRV/r for a period of at least 28 days Prior to randomization.

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: DRV QD + 2 NRTIs

Arm description:

Control arm:
DRV 800 mg tablets (Prezista®), oral, once daily and
RTV 100 mg tablets (Norvir®), oral, once daily in combination with
Tenofovir disoproxil / emtricitabine 245/200 mg (Truvada®), oral, once daily
or
DRV 800 mg tablets (Prezista®), oral, once daily and RTV 100 mg tablets (Norvir®), oral, once daily in combination with
Abacavir / Lamivudine 600/300 mg (Kivexa®), oral, once daily
or in combination with
Tenofovir alafenamid / emtricitabine 10/200 mg (Descovy®); oral; once daily;
Duration: 48 weeks

Arm type	Active comparator
Investigational medicinal product name	Darunavir
Investigational medicinal product code	J05AE10
Other name	Prezista, SUB25394, 206361-99-1, DARUNAVIR monoethanolat
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

800 mg per day

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	J05AE03
Other name	155213-67-5, SUB10342MIG
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg milligram(s) per day

Investigational medicinal product name	Tenofovir disoproxil / emtricitabine
Investigational medicinal product code	J05AR03
Other name	Truvada
Pharmaceutical forms	Film-coated tablet

Routes of administration	Other use

Dosage and administration details:

200/250 mg milligram(s) per day

Investigational medicinal product name	Abacavir / Lamivudine
Investigational medicinal product code	J05AR02
Other name	Kivexa, EU/1/04/298/001
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

600/300 mg milligram(s) per day

Investigational medicinal product name	Tenofovir alafenamid / emtricitabine
Investigational medicinal product code	J05AR17
Other name	Descovy
Pharmaceutical forms	Film-coated tablet
Routes of administration	Other use

Dosage and administration details:

10/200 mg milligram(s) per day

Arm title	Interventional arm: DRV QD + DTG

Arm description:

DRV 800 mg tablets (Prezista®), oral, once daily and RTV 100 mg tablets (Norvir®), oral, once daily and DTG 50 mg tablets (Tivicay®), oral, once daily.
Duration of intervention per patient 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Darunavir
Investigational medicinal product code	J05AE10
Other name	Prezista, SUB25394, 206361-99-1, DARUNAVIR monoethanolat
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

800 mg per day

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	J05AE03
Other name	155213-67-5, SUB10342MIG
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg milligram(s) per day

Investigational medicinal product name	Dolutegravir
Investigational medicinal product code	J05AX12
Other name	Tivicay, EU/1/13/892/001
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg milligram(s) per day

Number of subjects in period 1	Control Arm: DRV QD + 2 NRTIs	Interventional arm: DRV QD + DTG
Started	135	134
Completed	122	119
Not completed	13	15
Consent withdrawn by subject	4	4
Adverse event, non-fatal	1	6
No exposure to study drug	3	3
Lost to follow-up	5	2

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	269	269	
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			
Age at start of study			
Units: years			
median	48		
full range (min-max)	21 to 73	-	
Gender categorical Units: Subjects			
Female	27	27	
Male	242	242	

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT analysis set consists of all trial subjects enrolled into the trial and randomized with at least a baseline visit and at least one dose of study drug.

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol (PP) population consists of all trial subjects who were treated according to protocol. Patients with major protocol violations have been excluded from the PP analysis due to decision at data review meeting.

Subject analysis set title	SA
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consists of all trial subjects who received at least one dose of IMP.

Reporting group values	ITT	PP	SA
Number of subjects	263	241	266
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Age at start of study			
Units: years median full range (min-max)		48 21 to 71	48 21 to 73
Gender categorical Units: Subjects			
Female	26	23	27
Male	237	218	239

End points

End points reporting groups

Reporting group title	Control Arm: DRV QD + 2 NRTIs

Reporting group description:

Control arm:
DRV 800 mg tablets (Prezista®), oral, once daily and
RTV 100 mg tablets (Norvir®), oral, once daily in combination with
Tenofovir disoproxil / emtricitabine 245/200 mg (Truvada®), oral, once daily
or
DRV 800 mg tablets (Prezista®), oral, once daily and RTV 100 mg tablets (Norvir®), oral, once daily in combination with
Abacavir / Lamivudine 600/300 mg (Kivexa®), oral, once daily
or in combination with
Tenofovir alafenamid / emtricitabine 10/200 mg (Descovy®); oral; once daily;
Duration: 48 weeks

Reporting group title	Interventional arm: DRV QD + DTG

Reporting group description:

DRV 800 mg tablets (Prezista®), oral, once daily and RTV 100 mg tablets (Norvir®), oral, once daily and DTG 50 mg tablets (Tivicay®), oral, once daily.
Duration of intervention per patient 48 weeks.

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT analysis set consists of all trial subjects enrolled into the trial and randomized with at least a baseline visit and at least one dose of study drug.

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol (PP) population consists of all trial subjects who were treated according to protocol. Patients with major protocol violations have been excluded from the PP analysis due to decision at data review meeting.

Subject analysis set title	SA
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consists of all trial subjects who received at least one dose of IMP.

Primary: Number of patients with HIV RNA < 50 cps/ml at week 48 (ITT)

End point title	Number of patients with HIV RNA < 50 cps/ml at week 48 (ITT)

End point description:

End point type	Primary

End point timeframe:

HIV RNA counts collected at visit Week 48.

End point values	Control Arm: DRV QD + 2 NRTIs	Interventional arm: DRV QD + DTG	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	132[1]	131[2]	263	
Units: Patients				
HIV RNA < 50 cps/ml	116	113	229	
HIV RNA >= 50 cps/ml	16	18	34	

Notes:

[1] - The primary endpoint is analyzed on the ITT set.

[2] - The primary endpoint is analyzed on the ITT set.

Statistical analyses

Statistical analysis title	Response rate CI

Statistical analysis description:

Mean difference (proportion(2DR) - proportion(3DR)) with 95.48%CI (based on the adjusted alpha-level accounting for the interim analysis at week 24).

Comparison groups	Control Arm: DRV QD + 2 NRTIs v Interventional arm: DRV QD + DTG v ITT
Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Mean difference (final values)
Point estimate	-0.0162
Confidence interval	
level	95.48 %
sides	2-sided
lower limit	-0.0991
upper limit	0.0667

Notes:

[3] - The non-inferiority margin is 10%.

Secondary: Number of patients with HIV RNA < 50 cps/ml at week 48 (PP)

End point title	Number of patients with HIV RNA < 50 cps/ml at week 48 (PP)

End point description:

End point type	Secondary

End point timeframe:

HIV RNA counts collected at visit Week 48.

End point values	Control Arm: DRV QD + 2 NRTIs	Interventional arm: DRV QD + DTG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119[4]	122[5]		
Units: Patients				
HIV RNA <50 cps/ml	113	116		
HIV RNA >= 50 cps/ml	6	6		

Notes:
[4] - This endpoint was evaluated on the PP set.
[5] - This endpoint was evaluated on the PP set.

Statistical analyses

Statistical analysis title	Response rate CI on PP
Statistical analysis description: Confidence interval for the difference in response rate in the PP analysis set	
Comparison groups	Control Arm: DRV QD + 2 NRTIs v Interventional arm: DRV QD + DTG
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.0068
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.046
upper limit	0.0597

Secondary: Number of patients with HIV RNA < 50 cps/ml at week 24 (ITT)

End point title	Number of patients with HIV RNA < 50 cps/ml at week 24 (ITT)
End point description:	
End point type	Secondary
End point timeframe: Week 24	

End point values	Control Arm: DRV QD + 2 NRTIs	Interventional arm: DRV QD + DTG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	134		
Units: Patients				
HIV RNA < 50 cps/ml	117	116		
HIV RNA >= 50 cps/ml	18	18		

Statistical analyses

Statistical analysis title	Difference in response
Comparison groups	Control Arm: DRV QD + 2 NRTIs v Interventional arm: DRV QD + DTG
Number of subjects included in analysis	269
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0537
upper limit	0.0976

Secondary: Number of patients with HIV RNA < 50 cps/ml at week 24 (PP)

End point title	Number of patients with HIV RNA < 50 cps/ml at week 24 (PP)

End point description:

End point type	Secondary

End point timeframe:

Week 24

End point values	Control Arm: DRV QD + 2 NRTIs	Interventional arm: DRV QD + DTG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119[6]	122[7]		
Units: Patients				
HIV RNA < 50 cps/ml	115	112		
HIV RNA >= 50 cps/ml	4	10		

Notes:

[6] - This endpoint was evaluated on the PP set.

[7] - This endpoint was evaluated on the PP set.

Statistical analyses

Statistical analysis title	Difference in response
Comparison groups	Control Arm: DRV QD + 2 NRTIs v Interventional arm: DRV QD + DTG
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.0331

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0221
upper limit	0.0882

Secondary: Immunological response at week 24 (ITT)

End point title	Immunological response at week 24 (ITT)

End point description:

Change in absolute CD4 cell count from baseline.

End point type	Secondary

End point timeframe:

From Baseline to Week 24

End point values	Control Arm: DRV QD + 2 NRTIs	Interventional arm: DRV QD + DTG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	134		
Units: CD4 cells				
arithmetic mean (standard deviation)	25.2 (± 172.8)	-9.8 (± 137.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In this trial, the period of observation starts after first intake of IMP and ends 4 weeks after last vist.

Adverse event reporting additional description:

Pre-existing diseases (before administration of the IMP) are not documented as adverse events but as concomitant diseases. New diseases and pre-existing diseases that worsen during the trial are documented as AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Control Arm: DRV QD + 2 NRTIs

Reporting group description:

Control arm:
DRV 800 mg tablets (Prezista®), oral, once daily and
RTV 100 mg tablets (Norvir®), oral, once daily in combination with
Tenofovir disoproxil / emtricitabine 245/200 mg (Truvada®), oral, once daily
or
DRV 800 mg tablets (Prezista®), oral, once daily and RTV 100 mg tablets (Norvir®), oral, once daily in combination with
Abacavir / Lamivudine 600/300 mg (Kivexa®), oral, once daily
or in combination with
Tenofovir alafenamid / emtricitabine 10/200 mg (Descovy®); oral; once daily;
Duration: 48 weeks

Reporting group title	Interventional arm: DRV QD + DTG

Reporting group description:

DRV 800 mg tablets (Prezista®), oral, once daily and RTV 100 mg tablets (Norvir®), oral, once daily and DTG 50 mg tablets (Tivicay®), oral, once daily.
Duration of intervention per patient 48 weeks.

Serious adverse events	Control Arm: DRV QD + 2 NRTIs	Interventional arm: DRV QD + DTG	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 133 (5.26%)	7 / 133 (5.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			

subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Papilloma excision			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (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	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paresthesia			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenectomy			

subjects affected / exposed	0 / 133 (0.00%)	2 / 133 (1.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
in-stent arterial stenosis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anorectal disorder			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemorrhoids			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
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			
Bursitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc displacement			

subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal abscess			

subjects affected / exposed	0 / 133 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 133 (0.75%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Control Arm: DRV QD + 2 NRTIs	Interventional arm: DRV QD + DTG	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 133 (60.15%)	82 / 133 (61.65%)	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 133 (5.26%)	4 / 133 (3.01%)	
occurrences (all)	8	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 133 (5.26%)	0 / 133 (0.00%)	
occurrences (all)	8	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 133 (7.52%)	12 / 133 (9.02%)	
occurrences (all)	14	13	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 133 (0.00%)	6 / 133 (4.51%)	
occurrences (all)	0	6	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 133 (3.76%)	8 / 133 (6.02%)	
occurrences (all)	5	8	
Infections and infestations			

Bronchitis			
subjects affected / exposed	4 / 133 (3.01%)	10 / 133 (7.52%)	
occurrences (all)	4	11	
Nasopharyngitis			
subjects affected / exposed	34 / 133 (25.56%)	36 / 133 (27.07%)	
occurrences (all)	46	50	
Gastroenteritis			
subjects affected / exposed	7 / 133 (5.26%)	3 / 133 (2.26%)	
occurrences (all)	8	4	
Syphilis			
subjects affected / exposed	6 / 133 (4.51%)	3 / 133 (2.26%)	
occurrences (all)	6	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2016	Reduction of number of visits, reduction of laboratory parameters, change of inclusion and exclusion criteria: additional IMP Descovy (Emtricitabine/Tenefovir AF) accepted and reduction of required pre-ART period, extension of study period. Further study sites have been submitted and approved.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Premature termination: 15.06.2018 due to lack of recruitment.
Planned: 320 patients (160 patients in interventional (dual) arm and 160 patients in control arm) - In toal N=269 patients were enrolled in the study.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28859438