



Clinical trial results:

A pilot 24-week open-label, randomized, controlled clinical trial to assess the safety, tolerability and efficacy of dual therapy with Raltegravir/Lamivudine combination when replacing standard combination therapy in HIV-infected patients with prolonged virological suppression. RALAM Study

Summary

EudraCT number	2014-003142-27
Trial protocol	ES
Global end of trial date	28 February 2017

Results information

Result version number	v1 (current)
This version publication date	05 April 2025
First version publication date	05 April 2025

Trial information

Trial identification

Sponsor protocol code	RALAM
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02284035
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundació Clinic per a la Recerca Biomédica
Sponsor organisation address	C/ Villarroel, 170, Barcelona, Spain,
Public contact	Judit Pich, CTU Clinic (Clinical Trial Unit), jpich@recerca.clinic.cat
Scientific contact	Dr. Esteban Martínez, Hospital Clínic, estebanm@clinic.cat

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	28 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2017
Global end of trial reached?	Yes
Global end of trial date	28 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy in virological suppression assessed with standard plasma HIV-1 RNA detection (limit of detection 37 copies/mL).

Protection of trial subjects:

Informed consent was obtained from all participants to ensure they understood the study's risks and benefits. A Data and Safety Monitoring Board (DSMB) periodically reviewed the study data for safety and efficacy. Comprehensive clinical assessments and regular laboratory tests were conducted at follow-up visits. Adverse events were monitored and reported promptly. Virological monitoring and treatment adherence assessments were performed to ensure participant well-being.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 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	Spain: 75
Worldwide total number of subjects	75
EEA total number of subjects	75

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)	75
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All trial subjects were recruited at a single site in Spain: Hospital Clínic de Barcelona.

Recruitment period: 01-June-2015 to 01-December-2015

Pre-assignment

Screening details:

Screening visit: Conducted within 2-4 weeks prior to the study start. During this visit, written informed consent was obtained from each patient, and demographic data, medical history, complete physical examination, and laboratory tests (including hematology, biochemistry, and plasma viral load) were performed to confirm eligibility.

Period 1

Period 1 title	Baseline visit (randomization)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 (experimental)

Arm description:

Study group: Raltegravir / 3TC (MK0518B)

Arm type	Experimental
Investigational medicinal product name	MK0518B (Raltegravir/3TC)
Investigational medicinal product code	ATC: J05AR16
Other name	Dutrebis, Lamivudine, Raltegravir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

MK0518B (Raltegravir/3TC): 300/150mg twice daily, administered orally in the 300/150 mg film-coated tablets according to instructions in the prescribing information.

EFFICAC MESURMENTS: Plasma viral load (HIV-RNA) will be mesured at weeks 0, 4, 12 and 24. SAFETY ASSESSMENTS: at ech visit, a physical examination and a blood test will be performed.

Arm title	Group 2 (control)
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Arm description:

Standard combination therapy (to continue current treatment).

Arm type	Active comparator
Investigational medicinal product name	No investigational medicinal product assigned in this arm
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

All drug products included in the antiretroviral regimen will be part of the standard prescription and will be used according to the prescribing information. EFFICAC MESURMENTS: Plasma viral load (HIV-RNA) will be mesured at weeks 0, 4, 12 and 24. SAFETY ASSESSMENTS: at ech visit, a physical examination and a blood test will be performed.

Number of subjects in period 1	Group 1 (experimental)	Group 2 (control)
Started	50	25
Consent withdrawn by subject	49	25
Completed	49	25
Not completed	1	0
Consent withdrawn by subject	1	-

Period 2

Period 2 title	Week 4
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 (experimental)

Arm description:

Study group: Raltegravir / 3TC (MK0518B)

Arm type	Experimental
Investigational medicinal product name	MK0518B (Raltegravir/3TC)
Investigational medicinal product code	ATC: J05AR16
Other name	Dutrebis, Lamivudine, Raltegravir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

MK0518B (Raltegravir/3TC): 300/150mg twice daily, administered orally in the 300/150 mg film-coated tablets according to instructions in the prescribing information.

EFFICAC MESURMENTS: Plasma viral load (HIV-RNA) will be mesured at weeks 0, 4, 12 and 24. SAFETY ASSESSMENTS: at ech visit, a physical examination and a blood test will be performed.

Arm title	Group 2 (control)
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Arm description:

Standard combination therapy (to continue current treatment).

Arm type	Active comparator
Investigational medicinal product name	No investigational medicinal product assigned in this arm
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

All drug products included in the antiretroviral regimen will be part of the standard prescription and will be used according to the prescribing information. EFFICAC MESURMENTS: Plasma viral load (HIV-RNA) will be mesured at weeks 0, 4, 12 and 24. SAFETY ASSESSMENTS: at ech visit, a physical examination and a blood test will be performed.

Number of subjects in period 2	Group 1 (experimental)	Group 2 (control)
Started	49	25
Completed	49	21
Not completed	0	4
Consent withdrawn by subject	-	2
Lost to follow-up	-	1
Lack of efficacy	-	1

Period 3

Period 3 title	Week 12
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 (experimental)

Arm description:

Study group: Raltegravir / 3TC (MK0518B)

Arm type	Experimental
Investigational medicinal product name	MK0518B (Raltegravir/3TC)
Investigational medicinal product code	ATC: J05AR16
Other name	Dutrebis, Lamivudine, Raltegravir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

MK0518B (Raltegravir/3TC): 300/150mg twice daily, administered orally in the 300/150 mg film-coated tablets according to instructions in the prescribing information.

EFFICAC MESURMENTS: Plasma viral load (HIV-RNA) will be mesured at weeks 0, 4, 12 and 24. SAFETY ASSESSMENTS: at ech visit, a physical examination and a blood test will be performed.

Arm title	Group 2 (control)
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Arm description:

Standard combination therapy (to continue current treatment).

Arm type	Active comparator
Investigational medicinal product name	No investigational medicinal product assigned in this arm
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

All drug products included in the antiretroviral regimen will be part of the standard prescription and will be used according to the prescribing information. EFFICAC MESURMENTS: Plasma viral load (HIV-RNA) will be mesured at weeks 0, 4, 12 and 24. SAFETY ASSESSMENTS: at ech visit, a physical examination and a blood test will be performed.

Number of subjects in period 3	Group 1 (experimental)	Group 2 (control)
Started	49	21
Completed	48	20
Not completed	1	1
Pregnancy	1	-
Lost to follow-up	-	1

Period 4

Period 4 title	Week 24
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 (experimental)

Arm description:

Study group: Raltegravir / 3TC (MK0518B)

Arm type	Experimental
Investigational medicinal product name	MK0518B (Raltegravir/3TC)
Investigational medicinal product code	ATC: J05AR16
Other name	Dutrebis, Lamivudine, Raltegravir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

MK0518B (Raltegravir/3TC): 300/150mg twice daily, administered orally in the 300/150 mg film-coated tablets according to instructions in the prescribing information.

EFFICAC MESURMENTS: Plasma viral load (HIV-RNA) will be mesured at weeks 0, 4, 12 and 24. SAFETY ASSESSMENTS: at ech visit, a physical examination and a blood test will be performed.

Arm title	Group 2 (control)
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Arm description:

Standard combination therapy (to continue current treatment).

Arm type	Active comparator
Investigational medicinal product name	No investigational medicinal product assigned in this arm
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

All drug products included in the antiretroviral regimen will be part of the standard prescription and will be used according to the prescribing information. EFFICAC MESURMENTS: Plasma viral load (HIV-RNA)

will be measured at weeks 0, 4, 12 and 24. SAFETY ASSESSMENTS: at each visit, a physical examination and a blood test will be performed.

Number of subjects in period 4	Group 1 (experimental)	Group 2 (control)
Started	48	20
Completed	47	20
Not completed	1	0
Physician decision	1	-

Baseline characteristics

Reporting groups

Reporting group title	Group 1 (experimental)
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Reporting group description:

Study group: Raltegravir / 3TC (MK0518B)

Reporting group title	Group 2 (control)
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Reporting group description:

Standard combination therapy (to continue current treatment).

Reporting group values	Group 1 (experimental)	Group 2 (control)	Total
Number of subjects	50	25	75
Age categorical Units: Subjects			
Adults > 18 years	49	25	74
Not recorded	1	0	1
Age continuous Units: years			
arithmetic mean	50	50	
standard deviation	± 12	± 13	-
Gender categorical Units: Subjects			
Female	12	4	16
Male	37	21	58
Not recorded	1	0	1
Risk group Units: Subjects			
Homosexual	32	17	49
Heterosexual	13	7	20
Other	4	1	5
Not recorded	1	0	1
Race Units: Subjects			
White	46	23	69
Afroamerican	0	1	1
Not recorded	4	1	5
Hispanic ethnicity Units: Subjects			
Yes	35	18	53
No	9	2	11
Not recorded	6	5	11

End points

End points reporting groups

Reporting group title	Group 1 (experimental)
Reporting group description:	
Study group: Raltegravir / 3TC (MK0518B)	
Reporting group title	Group 2 (control)
Reporting group description:	
Standard combination therapy (to continue current treatment).	
Reporting group title	Group 1 (experimental)
Reporting group description:	
Study group: Raltegravir / 3TC (MK0518B)	
Reporting group title	Group 2 (control)
Reporting group description:	
Standard combination therapy (to continue current treatment).	
Reporting group title	Group 1 (experimental)
Reporting group description:	
Study group: Raltegravir / 3TC (MK0518B)	
Reporting group title	Group 2 (control)
Reporting group description:	
Standard combination therapy (to continue current treatment).	
Reporting group title	Group 1 (experimental)
Reporting group description:	
Study group: Raltegravir / 3TC (MK0518B)	
Reporting group title	Group 2 (control)
Reporting group description:	
Standard combination therapy (to continue current treatment).	
Reporting group title	Group 1 (experimental)
Reporting group description:	
Study group: Raltegravir / 3TC (MK0518B)	
Reporting group title	Group 2 (control)
Reporting group description:	
Standard combination therapy (to continue current treatment).	

Primary: Proportion of patients free of therapeutic failure

End point title	Proportion of patients free of therapeutic failure
End point description:	
On treatment population	
End point type	Primary
End point timeframe:	
24 weeks	

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	23		
Units: Subjects				
Yes	47	20		
No	1	3		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Group 1 (experimental) v Group 2 (control)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Newcombe method 10

Secondary: Proportion of patients with viral load below 37 copies/ml at 24 weeks

End point title	Proportion of patients with viral load below 37 copies/ml at 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	25		
Units: Subjects				
Yes	49	24		
No	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in metabolic parameters including fasting plasma lipids (cholesterol total)

End point title	Changes from baseline in metabolic parameters including fasting plasma lipids (cholesterol total)
End point description:	
End point type	Secondary

End point timeframe:

24 weeks

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	25		
Units: mg/dL				
least squares mean (confidence interval 95%)	0.803 (-16.986 to 18.593)	-1.280 (-27.798 to 25.238)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of adverse events in both treatment arms

End point title	Incidence of adverse events in both treatment arms
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End point description:

End point type	Secondary
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End point timeframe:

24 weeks

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	25		
Units: Number of adverse events				
Adverse events	57	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with serious adverse events related to study medication

End point title	Proportion of patients with serious adverse events related to study medication
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End point description:

End point type	Secondary
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End point timeframe:

24 weeks

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	25		
Units: Subjects				
Yes	3	3		
No	46	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in treatment adherence during all the study duration (Morisky-Green test)

End point title	Changes in treatment adherence during all the study duration (Morisky-Green test)
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End point description:

ODDS ratio and 95% confidence interval.

End point type	Secondary
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End point timeframe:

24 weeks

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	24		
Units: Subjects				
number (confidence interval 95%)	1.074 (0.471 to 2.449)	1.074 (0.903 to 12.130)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from metabolic parameters including fasting plasma lipids (LDL) at 24 weeks

End point title	Changes from metabolic parameters including fasting plasma lipids (LDL) at 24 weeks
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End point description:

End point type	Secondary
End point timeframe:	
24 weeks	

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	22		
Units: mg/dl				
least squares mean (confidence interval 95%)	-0.611 (-16.103 to 14.881)	2.222 (-20.663 to 25.108)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in metabolic parameters including fasting plasma lipids (HDL) at 24 weeks

End point title	Changes from baseline in metabolic parameters including fasting plasma lipids (HDL) at 24 weeks
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End point description:

End point type	Secondary
End point timeframe:	
24 weeks	

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	25		
Units: mg/dl				
least squares mean (confidence interval 95%)	1.158 (-4.530 to 6.845)	-0.099 (-8.578 to 8.380)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in metabolic parameters including fasting plasma lipids (triglycerides) at 24 weeks

End point title	Changes from baseline in metabolic parameters including fasting plasma lipids (triglycerides) at 24 weeks
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End point description:

End point type	Secondary
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End point timeframe:

24 weeks

End point values	Group 1 (experimental)	Group 2 (control)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	25		
Units: mg/dl				
least squares mean (confidence interval 95%)	0.992 (0.822 to 1.196)	0.901 (0.681 to 1.191)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported throughout the entire study period, which spanned 24 weeks, with medical visits at weeks 4, 12, and 24.

Assessment type	Systematic
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Dictionary used

Dictionary name	DAIDS
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Dictionary version	1.0
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Reporting groups

Reporting group title	Continue previous treatment
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Reporting group description:

Control group

Reporting group title	RAL/3TC
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Reporting group description:

Experimental group. Raltegravir/ lamivudine.

Serious adverse events	Continue previous treatment	RAL/3TC	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 25 (12.00%)	3 / 49 (6.12%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Elevated LDH, CK, anemia, and thrombocytopenia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	1 / 25 (4.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Scheduled surgery			
subjects affected / exposed	0 / 25 (0.00%)	1 / 49 (2.04%)	
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			
Constitutional syndrome, hilar adenopathy, and anemia study subjects affected / exposed	1 / 25 (4.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Episode of diarrhea subjects affected / exposed	1 / 25 (4.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Febrile syndrome subjects affected / exposed	1 / 25 (4.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	1 / 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	Continue previous treatment	RAL/3TC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 25 (64.00%)	32 / 49 (65.31%)	
Investigations			
Laboratory subjects affected / exposed	5 / 25 (20.00%)	3 / 49 (6.12%)	
occurrences (all)	5	3	
Cardiac disorders			
Cardiovascular subjects affected / exposed	0 / 25 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Nervous system disorders			
Neurologic subjects affected / exposed	4 / 25 (16.00%)	5 / 49 (10.20%)	
occurrences (all)	4	5	
Pregnancy, puerperium and perinatal conditions			

Pregnancy subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 49 (2.04%) 1	
General disorders and administration site conditions Systemic subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	0 / 49 (0.00%) 0	
Eye disorders Ophtalmologic subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	3 / 49 (6.12%) 3	
Gastrointestinal disorders Gastrointestinal subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	16 / 49 (32.65%) 16	
Skin and subcutaneous tissue disorders Dermatologic subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	2 / 49 (4.08%) 2	
Renal and urinary disorders Genitourinary subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 49 (2.04%) 1	
Musculoskeletal and connective tissue disorders Muscular subjects affected / exposed occurrences (all)	5 / 25 (20.00%) 5	14 / 49 (28.57%) 14	
Infections and infestations Infection subjects affected / exposed occurrences (all)	6 / 25 (24.00%) 6	12 / 49 (24.49%) 12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 November 2014	The objective of the amendment was to modify the change in the formulation of the investigational medicinal product. Amend the protocol version: Version 2.0 dated 7 November 2014.

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/31335805>