Clinical trial results:
The HALT-LTBI study: Phase IV, multi-site, unblinded, randomised trial of prophylactic daily rifampicin/isoniazid vs. weekly rifapentine/isoniazid for latent tuberculosis infection (LTBI)

Summary

EudraCT number	2013-000750-21
Trial protocol	GB
Global end of trial date	17 May 2017

Results information

Result version number	v1 (current)
This version publication date	12 April 2019
First version publication date	12 April 2019
Summary attachment (see zip file)	MHRA Final Study Report (HALT LTBI End of Study Summary for MHRA.docx)

Trial information

Trial identification

Sponsor protocol code	12/0426

Additional study identifiers

ISRCTN number	ISRCTN04379941
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCL
Sponsor organisation address	Joint Research Office, Gower Street , London , United Kingdom, WC1E 6BT
Public contact	Ibrahim Abubakar, University College London, +44 02076790954, i.abubakar@ucl.ac.uk
Scientific contact	Ibrahim Abubakar, University College London, +44 02076790954, i.abubakar@ucl.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	01 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 May 2017
Global end of trial reached?	Yes
Global end of trial date	17 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess completion rates of two different LTBI treatment regimens (daily rifampicin/isoniazid, the current UK standard treatment, vs weekly rifapentine/isoniazid).

The objective of the pilot phase would be to assess feasibility and safety.

Protection of trial subjects:

Insurance in Place

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	52
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruited individuals were randomised to receive either a daily combination of rifampicin/isoniazid ('standard' practice) for 90 days (three months) versus a weekly combination of rifapentine/isoniazid ('experimental' practice), for 12 weeks. Safety and feasibility was assessed with 52 patients.

Pre-assignment

Screening details:

The probability of being screened encompasses the probability of being offered screening (e.g. via primary care) and of accepting the offer. The number of simulations was N = 1000 which captured both the individual level variation and the uncertainty in the costs and utilities.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental Treatment Arm

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Rifampicin/Isoniazid daily
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 kg or less above 50 kg
3 x Rifinah® 150/100 2 x Rifinah® 300/150
All patients will receive Pyridoxine 10 mg or 25 mg* with their dose (once daily for 90 days)

Investigational medicinal product name	Rifampicin/Isoniazid Weekly
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

< 50 kg ≥ 50 kg
5 x Priftin® 150 mg
(Rifapentine 750 mg)
+
Isoniazid 15 mg/kg
300 mg and or 150 mg oral tablets will be used, therefore:
45-50 kg = 750 mg isoniazid
6 x Priftin® 150 mg
(Rifapentine 900 mg)
+
Isoniazid 15 mg/kg
300 mg and or 150 mg oral tablets will be used, therefore:
50-55 kg = 750 mg isoniazid
Above 55 – 60 kg = 900 mg isoniazid
>60 kg = 900 mg isoniazid
All patients will receive Pyridoxine 10 mg or 25 mg with their dose (once weekly for 12 weeks)*

Arm title	Standard Treatment Arm
Arm description: -	
Arm type	Standard Care
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Experimental Treatment Arm	Standard Treatment Arm
Started	27	25
Completed	27	25

Baseline characteristics

End points

End points reporting groups

Reporting group title	Experimental Treatment Arm
Reporting group description: -	
Reporting group title	Standard Treatment Arm
Reporting group description: -	
Subject analysis set title	Primary Outcome
Subject analysis set type	Full analysis

Subject analysis set description:

LTBI successfully led to the recruitment of 52 participants to explore the feasibility of a full trial. Factors to improve study enrolment were identified including appropriate inclusion criteria. There was no difference in the adverse effect profile between the two arms. Economic modelling suggests that the 12 dose rifapentine based regimen may be cost-effective if it achieves the same level of effectiveness as observed in this pilot study.

Primary: Analysis

End point title	Analysis[1]

End point description:

End point type	Primary

End point timeframe:

Safety and feasibility was assessed with 52 patients. Multivariable logistic regression of the likelihood of completion of treatment and presence of adverse effects was undertaken. Likert scale-derived data from MARS-5 on treatment completion was analysed

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: Please refer to Final Study report for full analysis.

End point values	Experimental Treatment Arm	Standard Treatment Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	25		
Units: 52	27	25		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

To assess frequency of adverse events (AE) when individuals are treated for LTBI.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

Reporting groups

Reporting group title	Randomised Group

Reporting group description: -

Serious adverse events	Randomised Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Randomised Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Please refer to report in attached which details the breakdown of 122 AEs that occurred on this trial.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported