



Clinical trial results:

An open-label, multi-centre, randomised controlled trial evaluating the effects of short-course rifapentine-based regimens and additional adherence support on LTBI treatment adherence and completion among adults in the UK

Summary

EudraCT number	2020-004444-29
Trial protocol	GB
Global end of trial date	18 December 2025

Results information

Result version number	v1 (current)
This version publication date	11 April 2026
First version publication date	11 April 2026

Trial information

Trial identification

Sponsor protocol code	RID-TB:Treat
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Additional study identifiers

ISRCTN number	ISRCTN18128181
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	90 High Holborn, London, United Kingdom, WC1V 6LJ
Public contact	Clinical Trials Manager, University College London, +44 2076704619, mrcctu.rid-tb@ucl.ac.uk
Scientific contact	Clinical Trials Manager, University College London, 7957778874 2076704619, mrcctu.rid-tb@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	18 December 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2025
Global end of trial reached?	Yes
Global end of trial date	18 December 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of a 28-dose daily and a 12-dose weekly rifapentine-based regimen compared to the standard 3 month daily rifampicin-based regimen on adherence of treatment for latent TB infection (LTBI).

Adults aged 16-65 years eligible for TB preventive treatment were randomised 2:1:2:2 to:

- 3 months of daily isoniazid plus rifampicin with routine adherence support (3HR, Arm 1)
- 3HR with additional adherence support (3HR+AS, Arm 2)
- weekly isoniazid plus rifapentine for 3 months with AS (3HP+AS, Arm 3)
- daily isoniazid plus rifapentine for 4 weeks (1HP, Arm 4).

Additional adherence support included electronic pill box reminders with supportive text messages.

Protection of trial subjects:

The study engaged new entrants to the UK and contacts of people with active TB who subsequently received a positive LTBI test. This population is potentially marginalised, vulnerable or hard-to-engage in care. Engagement were carried out in such a way that stigma would be minimised, and participants were not disadvantaged in any way. Our PPI partner, TB Alert, has a long history working with the populations that we recruited from, and provided advice for our patient-facing interactions.

Background therapy:

Pyridoxine

Evidence for comparator: -

Actual start date of recruitment	28 June 2023
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: 400
Worldwide total number of subjects	400
EEA total number of subjects	0

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)	399
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants recruited from 13 UK sites between 28 June 2023 and 30 June 2025.

Pre-assignment

Screening details:

LTBI diagnosis defined on the basis of all of the following:

(a) a positive result on an Interferon Gamma Release Assay (IGRA), Tuberculin Skin Test (TST) or C-Tb skin test and

(b) Active TB ruled out by attending clinicians

Eligible for LTBI treatment at TB clinics and national LTBI screening services based on NICE guidelines

Pre-assignment period milestones

Number of subjects started	400
Number of subjects completed	400

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Arm 1: 3HR
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Arm description:

Arm 1 - Standard of Care

Arm type	Active comparator
Investigational medicinal product name	Rifampicin and Isoniazid
Investigational medicinal product code	3HR
Other name	Rifnah
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rifampicin and isoniazid (e.g. Rifinah® 150/100 mg or 300/150 mg. Sanofi Aventis. Fixed dose oral tablet)

<50Kg 3 x Isoniazid/Rifampicin (e.g. fixed dose combination (150/100))

>= 50Kg 2 x Isoniazid / Rifampicin (e.g fixed dose combination (300/150))

Should be taken on an empty stomach (at least 30 minutes before food or 2 hours after food)

Arm title	Arm 2: 3HR + AS
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Arm description:

3HR + additional adherence support

Arm type	Experimental
Investigational medicinal product name	Rifampicin and Isoniazid
Investigational medicinal product code	3HR
Other name	Rifnah
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rifampicin and isoniazid (e.g. Rifinah® 150/100 mg or 300/150 mg. Sanofi Aventis. Fixed dose oral tablet)

<50Kg 3 x Isoniazid/Rifampicin (e.g. fixed dose combination (150/100))
 >= 50Kg 2 x Isoniazid / Rifampicin (e.g fixed dose combination (300/150))
 Should be taken on an empty stomach (at least 30 minutes before food or 2 hours after food)

Arm title	Arm 3: 3HP + AS
Arm description: 3HP + additional adherence support	
Arm type	Experimental
Investigational medicinal product name	Rifapentine + Isoniazid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rifapentine + Isoniazid once weekly for 12 doses (3 months)
 30 to < 32Kg Rifapentine 600 mg _ Isoniazid 15mg / Kg
 23 to < 50Kg Rifapentine 750 mg + Isoniazid 15 mg / kg
 >= 50 kg Rifapentine 900 mg + Isoniazid 15 mg / kg (900 mg maximum)
 Should be taken within one hour after a meal. The maximum recommended dose is 900 mg once weekly for 12 weeks and the maximum dose of isoniazid (15mg / Kg) is 900 mg

Arm title	Arm 4: 1 HP
Arm description: 1 HP	
Arm type	Experimental
Investigational medicinal product name	Rifapentine + isoniazid
Investigational medicinal product code	1HP
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rifapentine plus isoniazid once daily for 28 doses (one month)
 30 to <35 KG Rifapentine 300 mg + 300 mg isoniazid
 35 to < 45 KG Rifapentine 450 mg + 300 mg isoniazid
 >= 45 KG Rifapentine 600 mg + 300 mg isoniazid
 Should be taken within one hour after a meal

Number of subjects in period 1	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS
Started	116	59	113
Completed	87	45	94
Not completed	29	14	19
Other	1	1	-
Participant refused to continue follow-up	14	3	9
Lost to follow-up	14	8	9
Late screening failure	-	2	1

Number of subjects in period 1	Arm 4: 1 HP
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Started	112
Completed	89
Not completed	23
Other	3
Participant refused to continue follow-up	8
Lost to follow-up	11
Late screening failure	1

Baseline characteristics

Reporting groups

Reporting group title	Arm 1: 3HR
Reporting group description: Arm 1 - Standard of Care	
Reporting group title	Arm 2: 3HR + AS
Reporting group description: 3HR + additional adherence support	
Reporting group title	Arm 3: 3HP + AS
Reporting group description: 3HP + additional adherence support	
Reporting group title	Arm 4: 1 HP
Reporting group description: 1 HP	

Reporting group values	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS
Number of subjects	116	59	113
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	116	59	112
From 65-84 years	0	0	1
85 years and over	0	0	0
Age continuous Units: years			
median	33	33	32
inter-quartile range (Q1-Q3)	28 to 39	28 to 36	27 to 38
Gender categorical Units: Subjects			
Female	58	27	59
Male	58	32	54
TB Risk Group Units: Subjects			
High TB burden country	58	29	56
Close contact	12	6	12
Other	46	24	45
BCG vaccination status Units: Subjects			
Vaccinated	77	47	82
Unvaccinated	13	4	11
Unknown	26	8	20

Smoking status			
Units: Subjects			
Current smoker	15	6	10
Ex-smoker	10	9	16
Never smoked	84	40	82
Unknown	7	4	5
Prefer not to say	0	0	0
Weekly alcohol intake			
Units: Subjects			
No alcohol intake	74	37	73
0-4 units	28	8	21
5-9 units	3	4	3
10-14 units	2	2	5
15-20 units	1	2	3
Over 20 units	0	0	0
Unknown	8	6	8
Prefer not to say	0	0	0

Reporting group values	Arm 4: 1 HP	Total	
Number of subjects	112	400	
Age categorical			
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)	112	399	
From 65-84 years	0	1	
85 years and over	0	0	
Age continuous			
Units: years			
median	33		
inter-quartile range (Q1-Q3)	27 to 41	-	
Gender categorical			
Units: Subjects			
Female	48	192	
Male	64	208	
TB Risk Group			
Units: Subjects			
High TB burden country	55	198	
Close contact	12	42	
Other	45	160	
BCG vaccination status			
Units: Subjects			
Vaccinated	78	284	
Unvaccinated	10	38	
Unknown	24	78	
Smoking status			

Units: Subjects			
Current smoker	9	40	
Ex-smoker	9	44	
Never smoked	88	294	
Unknown	5	21	
Prefer not to say	1	1	
Weekly alcohol intake			
Units: Subjects			
No alcohol intake	78	262	
0-4 units	14	71	
5-9 units	7	17	
10-14 units	2	11	
15-20 units	1	7	
Over 20 units	1	1	
Unknown	8	30	
Prefer not to say	1	1	

End points

End points reporting groups

Reporting group title	Arm 1: 3HR
Reporting group description: Arm 1 - Standard of Care	
Reporting group title	Arm 2: 3HR + AS
Reporting group description: 3HR + additional adherence support	
Reporting group title	Arm 3: 3HP + AS
Reporting group description: 3HP + additional adherence support	
Reporting group title	Arm 4: 1 HP
Reporting group description: 1 HP	
Subject analysis set title	Modified intention-to-treat
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The modified intention-to-treat (mITT) population excludes 5 participants, 1 who was randomised to Arm 1 but prescribed 1HP (Arm 4 IMP) in error and 4 who were late screening failures.	
Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol
Subject analysis set description: Excludes 37 participants from the modified intention-to-treat population who did not have any drug intakes recorded by the Wisepill box.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description: Includes all randomised participants except for 19 participants who did not have study drug dispensed. One participant originally randomised to Arm 1 was prescribed 1HP in error and was analysed under Arm 4.	

Primary: Adequate treatment, defined as taking ≥ 90 % of allocated doses

End point title	Adequate treatment, defined as taking ≥ 90 % of allocated doses
End point description: In the primary analyses, adherence is measured using the Wisepill electronic pillboxes. The allowable time-frames for completing treatment are: For 3HP and 3HR- the original 12 weeks treatment period plus 4 weeks extension For 1HP- the original 4 weeks treatment period plus 2 weeks extension	
End point type	Primary
End point timeframe: The allowable time-frame for achieving adequate treatment is considered from the date the study medication was first dispensed, and is defined according to the treatment regimen.	

End point values	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS	Arm 4: 1 HP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100 ^[1]	52 ^[2]	108 ^[3]	97 ^[4]
Units: Subjects	43	25	73	53

Notes:

[1] - 100 complete cases.

[2] - 52 complete cases

[3] - 108 complete cases

[4] - 97 complete cases

Statistical analyses

Statistical analysis title	Co-primary analysis Arm 4 vs Arm 1 (mITT)
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Statistical analysis description:

The primary analyses included all of the mITT population, with imputation methods accounting for missing data.

For EudrACT reporting of number of counts, this was based on complete cases only.

Comparison groups	Arm 1: 3HR v Arm 4: 1 HP
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055 ^[5]
Method	Modified Poisson regression
Parameter estimate	Risk ratio (RR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.73

Notes:

[5] - Modified Poisson regression was used to estimate the risk ratio. BootMI procedure was used to account for missing Wisepill data. An ANOVA model was then fitted to the BxM point estimates to derive the standard error and p-value.

Statistical analysis title	Co-primary analysis Arm 3 vs Arm 1 (mITT)
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Statistical analysis description:

The primary analyses included all of the mITT population, with imputation methods accounting for missing data.

For EudrACT reporting of number of counts, this was based on complete cases only.

Comparison groups	Arm 1: 3HR v Arm 3: 3HP + AS
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[6]
Method	Modified Poisson regression
Parameter estimate	Risk ratio (RR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	1.99

Notes:

[6] - Modified Poisson regression was used to estimate the risk ratio. BootMI procedure was used to account for missing Wisepill data. An ANOVA model was then fitted to the BxM point estimates to derive the standard error and p-value.

Secondary: Proportion (%) of allocated doses missed as measured using Wisepill box

End point title	Proportion (%) of allocated doses missed as measured using Wisepill box
End point description:	
End point type	Secondary
End point timeframe:	
As defined for the primary outcome.	

End point values	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS	Arm 4: 1 HP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	115	57	112	111
Units: Proportion of allocated doses missed				
median (inter-quartile range (Q1-Q3))	13.8 (1.1 to 51.8)	9.9 (0.1 to 58.3)	0.1 (0.0 to 37.7)	3.1 (0.0 to 27.6)

Statistical analyses

Statistical analysis title	Comparing Arm 3 vs Arm 1
Statistical analysis description:	
Based on mITT population, with imputing methods accounting for missing Wisepill data. The absolute difference in the median proportion of doses missed between the arms was estimated.	
Comparison groups	Arm 1: 3HR v Arm 3: 3HP + AS
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 ^[7]
Method	Quantile regression
Parameter estimate	Median difference (final values)
Point estimate	-13.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.1
upper limit	-5.5

Notes:

[7] - BootMI procedure used to account for missing data and estimate the standard error and corresponding p-value.

Statistical analysis title	Comparing Arm 4 vs Arm 1
Comparison groups	Arm 1: 3HR v Arm 4: 1 HP

Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.046 ^[8]
Method	Quantile regression
Parameter estimate	Median difference (final values)
Point estimate	-10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.2
upper limit	-0.2

Notes:

[8] - BootMI procedure used to account for missing data and estimate the standard error and corresponding p-value.

Secondary: Taking at least 90% of doses over treatment period, measured using pill counts

End point title	Taking at least 90% of doses over treatment period, measured using pill counts
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End point description:

End point type	Secondary
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End point timeframe:

Same as that defined for the primary outcome.

End point values	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS	Arm 4: 1 HP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84 ^[9]	41 ^[10]	88 ^[11]	80 ^[12]
Units: subjects	75	39	77	72

Notes:

[9] - 115 in modified intention to treat population

31 participants with missing pill count data

[10] - 57 in modified intention to treat population

16 participants with missing pill count data

[11] - 112 in modified intention to treat population

24 participants with missing pill count data

[12] - 111 in modified intention to treat population

31 participants with missing pill count data

Statistical analyses

Statistical analysis title	Comparing Arm 4 vs Arm 1
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Statistical analysis description:

The original analysis included the overall mITT population accounting for missing data.

For EudrACT reporting of number of participants achieving the endpoint, this was based on complete case analysis.

Comparison groups	Arm 1: 3HR v Arm 4: 1 HP
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Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.102
Method	Modified Poisson regression
Parameter estimate	Risk ratio (RR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.22

Statistical analysis title	Comparing Arm 3 vs Arm 1
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Statistical analysis description:

The original analysis included the overall mITT population accounting for missing data.
For EudrACT reporting of number of participants achieving the endpoint, this was based on complete case analysis.

Comparison groups	Arm 1: 3HR v Arm 3: 3HP + AS
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.989
Method	Modified Poisson regression
Parameter estimate	Risk ratio (RR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.14

Secondary: Early study treatment discontinuation for any reason

End point title	Early study treatment discontinuation for any reason
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End point description:

Early discontinuation of treatment as reported by site staff.

End point type	Secondary
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End point timeframe:

Same as that for the primary outcome.

End point values	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS	Arm 4: 1 HP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	115	57	112	111
Units: subjects	20	7	17	15

Statistical analyses

Statistical analysis title	Comparing Arm 3 vs Arm 1
Statistical analysis description: Based on mITT population.	
Comparison groups	Arm 1: 3HR v Arm 3: 3HP + AS
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.646
Method	Modified Poisson regression
Parameter estimate	Risk ratio (RR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.58

Statistical analysis title	Comparing Arm 4 vs Arm 1
Statistical analysis description: Based on mITT population.	
Comparison groups	Arm 1: 3HR v Arm 4: 1 HP
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Modified Poisson regression
Parameter estimate	Risk ratio (RR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.43

Secondary: Permanently stopping study treatment due to drug-related adverse event

End point title	Permanently stopping study treatment due to drug-related
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End point description:

End point type Secondary

End point timeframe:

As defined for the primary outcome.

End point values	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS	Arm 4: 1 HP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	56	106	108
Units: subjects	4	2	1	4

End point values	Safety population			
Subject group type	Subject analysis set			
Number of subjects analysed	381			
Units: subjects	11			

Statistical analyses

Statistical analysis title	Comparing Arm 3 vs Arm 1
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Statistical analysis description:

Based on safety population.

Comparison groups	Arm 1: 3HR v Arm 3: 3HP + AS
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.37
Method	Fisher exact
Parameter estimate	Not estimated due to sparse data

Statistical analysis title	Comparing Arm 4 vs Arm 1
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Statistical analysis description:

Based on safety population.

Comparison groups	Arm 1: 3HR v Arm 3: 3HP + AS
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Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact
Parameter estimate	No presented due to sparse data

Secondary: Grade >= 3 adverse events up to 20 weeks

End point title	Grade >= 3 adverse events up to 20 weeks
End point description:	
End point type	Secondary
End point timeframe:	
Up to 20 weeks from randomisation date	

End point values	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS	Arm 4: 1 HP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	56	106	108
Units: subjects	1	0	3	3

Statistical analyses

Statistical analysis title	Comparing Arm 4 vs Arm 1
Statistical analysis description:	
Based on safety population.	
Comparison groups	Arm 1: 3HR v Arm 4: 1 HP
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.353
Method	Fisher exact

Statistical analysis title	Comparing Arm 3 vs Arm 1
Statistical analysis description:	
Based on safety population.	
Comparison groups	Arm 3: 3HP + AS v Arm 1: 3HR

Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.618
Method	Fisher exact

Secondary: Development of active TB

End point title	Development of active TB
End point description:	
End point type	Secondary
End point timeframe:	
Up to 12 months from randomisation.	

End point values	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS	Arm 4: 1 HP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	56	106	108
Units: subjects	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date medication first dispensed up to 20 weeks from date of randomisation.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Arm 1: 3HR
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Reporting group description:

3HR

Reporting group title	Arm 2: 3HR + AS
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Reporting group description:

3HR + Additional Adherence Support

Reporting group title	Arm 3: 3HP + AS
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Reporting group description:

3HP + Additional Adherence Support

Reporting group title	Arm 4: 1HP
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Reporting group description:

1HP

Serious adverse events	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	2 / 106 (1.89%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Ovarian abscess			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm 4: 1HP		
Total subjects affected by serious			

adverse events			
subjects affected / exposed	0 / 108 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Reproductive system and breast disorders			
Ovarian abscess			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm 1: 3HR	Arm 2: 3HR + AS	Arm 3: 3HP + AS
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 111 (46.85%)	24 / 56 (42.86%)	53 / 106 (50.00%)
General disorders and administration site conditions			
Hunger			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	2 / 111 (1.80%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	2	1	0
Asthenia			
subjects affected / exposed	2 / 111 (1.80%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	3	1	0

Chest discomfort			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	3 / 111 (2.70%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	3	0	1
Pain			
subjects affected / exposed	0 / 111 (0.00%)	2 / 56 (3.57%)	2 / 106 (1.89%)
occurrences (all)	0	4	2
Night sweats			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	8 / 111 (7.21%)	1 / 56 (1.79%)	11 / 106 (10.38%)
occurrences (all)	8	1	11
Decreased appetite			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	4 / 106 (3.77%)
occurrences (all)	1	0	4
Pyrexia			
subjects affected / exposed	3 / 111 (2.70%)	2 / 56 (3.57%)	5 / 106 (4.72%)
occurrences (all)	3	2	5
Immune system disorders			
Psoriasis			
subjects affected / exposed	2 / 111 (1.80%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	2	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Ovarian abscess			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	0
Menstruation delayed			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain			
subjects affected / exposed	0 / 111 (0.00%)	2 / 56 (3.57%)	0 / 106 (0.00%)
occurrences (all)	0	2	0
Dyspnoea			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	2 / 106 (1.89%)
occurrences (all)	1	0	2
Productive cough			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 111 (0.00%)	2 / 56 (3.57%)	1 / 106 (0.94%)
occurrences (all)	0	2	1
Cough			
subjects affected / exposed	1 / 111 (0.90%)	4 / 56 (7.14%)	2 / 106 (1.89%)
occurrences (all)	1	4	2
Pleuritic pain			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Seasonal allergy			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 111 (0.00%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Sinus pain			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	0
Insomnia			

subjects affected / exposed	1 / 111 (0.90%)	1 / 56 (1.79%)	3 / 106 (2.83%)
occurrences (all)	1	1	3
Agitation			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Product issues			
Device colour issue			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 111 (0.00%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Chest X-ray abnormal			
subjects affected / exposed	2 / 111 (1.80%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	2	0	0
Liver function test increased			
subjects affected / exposed	6 / 111 (5.41%)	1 / 56 (1.79%)	1 / 106 (0.94%)
occurrences (all)	9	1	1
Neutrophil count decreased			
subjects affected / exposed	2 / 111 (1.80%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	2	0	0
Weight decreased			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
White blood cell count decreased			

subjects affected / exposed occurrences (all)	2 / 111 (1.80%) 2	0 / 56 (0.00%) 0	0 / 106 (0.00%) 0
Injury, poisoning and procedural complications Accident at work subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0	0 / 56 (0.00%) 0	1 / 106 (0.94%) 1
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0	0 / 56 (0.00%) 0	1 / 106 (0.94%) 1
Palpitations subjects affected / exposed occurrences (all)	2 / 111 (1.80%) 2	0 / 56 (0.00%) 0	1 / 106 (0.94%) 1
Nervous system disorders Headache subjects affected / exposed occurrences (all)	9 / 111 (8.11%) 10	4 / 56 (7.14%) 5	12 / 106 (11.32%) 13
Bradykinesia subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0	0 / 56 (0.00%) 0	0 / 106 (0.00%) 0
Burning feet syndrome subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0	1 / 56 (1.79%) 1	0 / 106 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	4 / 111 (3.60%) 4	0 / 56 (0.00%) 0	3 / 106 (2.83%) 3
Memory impairment subjects affected / exposed occurrences (all)	1 / 111 (0.90%) 1	0 / 56 (0.00%) 0	0 / 106 (0.00%) 0
Migraine subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0	0 / 56 (0.00%) 0	1 / 106 (0.94%) 1
Tinnitus subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0	0 / 56 (0.00%) 0	0 / 106 (0.00%) 0
Vision blurred			

subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Bradyphrenia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	7 / 111 (6.31%)	4 / 56 (7.14%)	7 / 106 (6.60%)
occurrences (all)	7	4	7
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 111 (0.00%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Scleral discolouration			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 111 (0.90%)	1 / 56 (1.79%)	1 / 106 (0.94%)
occurrences (all)	1	1	1
Faeces discoloured			
subjects affected / exposed	0 / 111 (0.00%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Abdominal pain lower			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			

subjects affected / exposed	0 / 111 (0.00%)	1 / 56 (1.79%)	1 / 106 (0.94%)
occurrences (all)	0	1	1
Abdominal pain			
subjects affected / exposed	3 / 111 (2.70%)	1 / 56 (1.79%)	2 / 106 (1.89%)
occurrences (all)	4	1	2
Diarrhoea			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	2 / 106 (1.89%)
occurrences (all)	1	0	2
Constipation			
subjects affected / exposed	3 / 111 (2.70%)	1 / 56 (1.79%)	1 / 106 (0.94%)
occurrences (all)	3	1	1
Tongue dry			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	10 / 111 (9.01%)	4 / 56 (7.14%)	14 / 106 (13.21%)
occurrences (all)	11	4	20
Haematochezia			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 111 (1.80%)	0 / 56 (0.00%)	6 / 106 (5.66%)
occurrences (all)	2	0	6
Tooth fracture			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			

Blister			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	5 / 111 (4.50%)	2 / 56 (3.57%)	3 / 106 (2.83%)
occurrences (all)	5	2	7
Lip oedema			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	2 / 111 (1.80%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	2	0	1
Acne			
subjects affected / exposed	0 / 111 (0.00%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Pruritus genital			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	4 / 111 (3.60%)	3 / 56 (5.36%)	4 / 106 (3.77%)
occurrences (all)	4	3	4
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	2 / 106 (1.89%)
occurrences (all)	0	0	2
Chromaturia			

subjects affected / exposed	14 / 111 (12.61%)	6 / 56 (10.71%)	13 / 106 (12.26%)
occurrences (all)	14	6	49
Proteinuria			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	2 / 106 (1.89%)
occurrences (all)	1	0	2
Muscular weakness			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	2 / 111 (1.80%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	2	0	1
Arthritis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Neuromuscular pain			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	1	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	2 / 106 (1.89%)
occurrences (all)	0	0	2
Enterobiasis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Anal abscess			

subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 111 (1.80%)	1 / 56 (1.79%)	5 / 106 (4.72%)
occurrences (all)	3	1	5
Eye infection			
subjects affected / exposed	1 / 111 (0.90%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	0 / 111 (0.00%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Genital candidiasis			
subjects affected / exposed	0 / 111 (0.00%)	1 / 56 (1.79%)	0 / 106 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	2 / 111 (1.80%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	2	0	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	1 / 106 (0.94%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	0 / 111 (0.00%)	0 / 56 (0.00%)	0 / 106 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Arm 4: 1HP		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 108 (46.30%)		
General disorders and administration site conditions			

Hunger			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Chest discomfort			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Decreased appetite			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		

Immune system disorders			
Psoriasis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Dermatitis allergic			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Ovarian abscess			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Menstruation delayed			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Chest pain			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Pleuritic pain			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		

Seasonal allergy subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Wheezing subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Sinus pain subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Psychiatric disorders Suicidal ideation subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 3		
Agitation subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Depression subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Anxiety subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Product issues Device colour issue subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Investigations Liver function test abnormal subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
C-reactive protein increased subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Chest X-ray abnormal			

subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Liver function test increased subjects affected / exposed occurrences (all)	11 / 108 (10.19%) 15		
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Weight decreased subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Injury, poisoning and procedural complications Accident at work subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Palpitations subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	16 / 108 (14.81%) 17		
Bradykinesia subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Burning feet syndrome subjects affected / exposed occurrences (all)	0 / 108 (0.00%) 0		
Dizziness			

subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Memory impairment			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Tinnitus			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Bradyphrenia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Neuropathy peripheral			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Scleral discolouration			

subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Faeces discoloured			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Abdominal pain lower			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Tongue dry			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	14 / 108 (12.96%)		
occurrences (all)	14		
Haematochezia			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		

Dysgeusia			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	4 / 108 (3.70%)		
occurrences (all)	4		
Tooth fracture			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Lip oedema			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Swelling face			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Acne			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Pruritus genital			

subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	7 / 108 (6.48%)		
occurrences (all)	7		
Renal and urinary disorders			
Bladder irritation			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Chromaturia			
subjects affected / exposed	14 / 108 (12.96%)		
occurrences (all)	16		
Proteinuria			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Arthritis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Neck pain			

subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Neuromuscular pain			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Enterobiasis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Anal abscess			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Eye infection			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Fungal infection			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Genital candidiasis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Lower respiratory tract infection			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		

Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 March 2021	Clarified exclusion criteria, included maximum recommended dosing, and clarified procedures for assessing safety.
25 April 2022	Removal of arm 6 (i.e. 1HP additional adherence support arm), clarification of an inclusion criteria point. Study sample size, randomisation allocation ratio, estimands, analysis plan updated. Addition of a new questionnaire and fidelity checklist.
30 July 2022	Updates to the assessment table, visit window periods, and Patient Information Sheet (v3.0) to reflect the study design change previously submitted. Addition of a health economics questionnaire. Rifapentine labels and Isoniazid SmPC submitted.
10 October 2022	Remove the 3HP with routine adherence support arm, lower the sample size, adjust the randomisation ratio, adjusting the adherence intervention, simplifying the inclusion and exclusion criteria, and update study hypotheses, primary and secondary objectives. Include single dose regimens with active substance, Rifampicin and Isoniazid, and leave Rifinah as the fixed dose regimen example. Update to the Patient Information Sheet (v4.0) to reflect the study design change.
08 April 2024	Standard of care arms (rifampicin plus isoniazid) can be taken for 84 doses (3 month long cycles of 28 doses) as per standard of care local practice, as well as 90 doses (3 months) as originally stated in the protocol. Update to primary outcome treatment completion timeframe. Clarification of tests needing repeating should they be too old at treatment start.
03 April 2025	Removal of a secondary outcome and rephrasing of a secondary outcome. Addition of optional questionnaire for migrant sensitivity analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported