SHINE Supplementary tables and figures and list of names

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S1: Additional baseline information of children in SHINE

Table S1: Additional baseline characteristics, baseline clinical presentation and AFB smear and culture of children in SHINE

		16 weeks (N=602)	24 weeks (N=602)	Total (N=1204)
Age group N (%)	≤10 years	521 (87)	516 (86)	1037 (86)
	>10 years	81 (13)	86 (14)	167 (14)
Weight-for-height Z score (WHZ)[+]	N	475	476	951
	Median	-0.28	-0.22	-0.24
	IQR	(-1.16, 0.56)	(-1.10, 0.56)	(-1.11, 0.56)
	Min, Max	(-4.34, 4.38)	(-5.09, 6.94)	(-5.09, 6.94)
Weight-for-age Z score (WAZ)[++]	N	602	602	1204
	Median	-1.20	-1.12	-1.15
	IQR	(-2.12,-0.29)	(-2.10, -0.37)	(-2.11,-0.34)
	Min, Max	(-6.71, 2.76)	(-6.30, 3.01)	(-6.71, 3.01)
Height-for-age Z score (HAZ) [++]	N	602	602	1204
	Median	-1.51	-1.39	-1.42
	IQR	(-2.33,-0.61)	(-2.33, -0.59)	(-2.33,-0.60)
	Min, Max	(-6.09, 3.27)	(-13.37, 5.12)	(-13.37, 5.12)
N with smear performed		**602**	**601**	**1203**
No AFB seen on respiratory samples		602 (100)	600 (<100)	1202 (<100)
'Scanty' on respiratory samples		0	1 (<1)*	1 (<1)*
N with Xpert MTB/RIF performed		**601**	**601**	**1202**
N with MTB detected		45 (7)	40 (7)	85 (7)
N with culture performed[θ]		**602**	**602**	**1204**
Culture positive for MTB		**71 (12)**	**75 (12)**	**146 (12)**
Negative		484 (80)	493 (82)	977 (81)
Positive for NTM		33 (5)	27 (4)	60 (5)
Contaminated		14 (2)	7 (1)	21 (2)
Total Number of Respiratory Samples**		**1222**	**1215**	**2437**
Number of Respiratory Samples with MTB detected		**34**	**32**	**66**
Of those with MTB detected, GeneXpert semi-quantitative result:	High	0	0	0
	Medium	0	0	0
	Low	6	5	11
	Very low	26	25	51

Data presented as number of participants (%), unless otherwise stated. IQR=interquartile range [+]Weight-for-height Z score is defined for children up to age 10 only. We present a combined variable for weight-for-height 65-120 cm & weight-for-length 45-110 cm from WHO Child Growth Charts and WHO Reference 2007 Charts.[++]Weight-for Age and Height-for Age Z-Scores use UK WHO Term Growth Reference for all term births (gestation 37-42 weeks). Microbiological results on more than one sample per participant are combined.

AFB=acid-fast bacilli, NTM=non-tuberculous mycobacteria; LJ=Lowenstein Jensen solid culture medium, MGIT =Mycobacteria growth indicator tube liquid culture system. **All respiratory samples are Gastric Aspirate, Gastric Washing, Induced Sputum, Expectorated Sputum*Late screen failure. [θ]Culture definitions: *Positive for MTB (from MGIT or LJ)* include participants with at least 1 positive result for MTB from either MGIT or LJ sample. *Positive for NTM* include participants with positive result for NTM and negative result for MTB. *Contaminated* include participants with all culture results reported as contaminated and not positive for MTB or NTM. *Negative* include participants with a negative result for MTB and who were not positive for NTM (could include participants with sample that was contaminated or had technical problem if at least 1 result was negative for MTB). Microbiological confirmation was from respiratory samples (gastric aspirate/washing, induced or expectorated sputum) and fine needle aspiration of enlarged lymph nodes and was defined as positive for *M. tuberculosis* by culture or Xpert MTB/RIF assay. [¥]Participants did not have a cough for more than 2 weeks or peripheral lymph node(s) suggestive of TB.

S2: Study disposition, participant flow and participant retention

Table S2i: Study disposition and participant flow

	16 weeks	24 weeks	Total
Randomised	**602**	**602**	**1204**
Number of children who did not reach Week 8	**8**	**10**	**18**
Death	4	5	9
Lost to Follow-up	2	2	4
Withdrawals	2	3	5
Number of children who reached Week 8 but not 16	**4**	**3**	**7**
Death	1	1	2
Lost to Follow-up	1	1	2
Withdrawals	2	1	3
Number of children who reached Week 16 but not 24	**2**	**4**	**6**
Death	2	3	5
Lost to Follow-up	0	1	1
Withdrawals	0	0	0
Number of children who reached Week 24 but not 72	**13**	**15**	**28**
Death	5	9	14
Lost to Follow-up	8	6	14
Withdrawals	0	0	0
Number of children who reached Week 72	**575**	**569**	**1144**
Death	0	1	1
Lost to Follow-up	0	0	0
Withdrawals	0	0	0

All randomised children had a date of first dose. Numbers are based on Final Visit form

Table S2ii: Retention based on attendance

	16 weeks	24 weeks	Total
Randomised	**602**	**602**	**1204**
Week 2 Expected	600	598	1198
Week 2 Attended	590 (98)	591 (99)	1181 (99)
Week 4 Expected	597	596	1193
Week 4 Attended	591 (99)	587 (98)	1178 (99)
Week 8 Expected	595	593	1188
Week 8 Attended	587 (99)	584 (98)	1171 (99)
Week 12 Expected	593	592	1185
Week 12 Attended	584 (98)	582 (98)	1166 (98)
Week 16 Expected	592	592	1184
Week 16 Attended	578 (98)	572 (97)	1150 (97)
Week 20 Expected	591	590	1181
Week 20 Attended	553 (94)	573 (97)	1126 (95)
Week 24 Expected	591	589	1180
Week 24 Attended	550 (93)	565 (96)	1115 (94)
Week 28 Expected	589	587	1176
Week 28 Attended	554 (94)	559 (95)	1113 (95)
Week 36 Expected	587	584	1171
Week 36 Attended	551 (94)	549 (94)	1100 (94)
Week 48 Expected	587	581	1168
Week 48 Attended	546 (93)	525 (90)	1071 (92)
Week 60 Expected	586	581	1167
Week 60 Attended	531 (91)	519 (89)	1050 (90)
Week 72 Expected	586	579	1165
Week 72 Attended	560 (96)	550 (95)	1110 (95)

Data presented as number of participants (%), unless otherwise stated. Attendance is based on the Nurse case report form (CRF) entered on the study database for each visit. Expected visits are calculated using the number of nurse forms expected to be on the database (from date of randomisation to upper date of each visit window). Children would be deemed “not expected” after either death or formal withdrawal from the trial. Percentage attendance by visit is calculated as a proportion of expected visits.

S3: Safety endpoint results

Table S3i: Primary safety endpoint, on-treatment grade 3 or higher adverse events up to 30 days after last dose – event type

	16 weeks	24 weeks	Total
Randomised	**602**	**602**	**1204**
No. of Grade 3, 4 or 5 adverse events	**49**	**66**	**115**
Anaemia	0	5 (8)	5 (4)
Bacteraemia, septicaemia	2 (4)	1 (2)	3 (3)
Diarrhoea	5 (10)	2 (3)	7(6)
Epilepsy, seizures, febrile convulsions	3 (6)	3 (5)	6 (5)
Liver	4 (8)	7 (11)	11 (10)
Malaria	2 (4)	1(2)	3 (3)
Neutropenia	2 (4)	2 (3)	4(3)
Other*	15 (31)	15 (23)	30 (26)
Pneumonia/Chest infections/Lower respiratory tract infection	11 (22)	18 (27)	29 (25)
Rash, hypersensitivity reaction	2 (4)	1 (2)	3 (3)
Severe malnutrition	1 (2)	4 (6)	5 (4)
Trauma/accidental injury	0	1 (2)	1 (1)
Upper respiratory tract infection	2 (4)	3 (5)	5 (4)
Urinary tract infection	0	3 (5)	3 (3)

Data presented as number of participants (%), unless otherwise stated. * “Other” events included: asthma, chicken pox, tumours, abnormal lab values, athletes foot, dental abscess, measles, cataract

Table S3ii: Serious adverse events

Randomised	**4 Month** **602**	**6 Month** **602**	**Total** **1204**
No. of SAEs	**88**	**104**	**192**
Patients with at least one SAE	**75 (12)**	**75 (12)**	**150 (12)**
Before 16 weeks			
No. of SAEs	35	50	85
Patients with at least one SAE	33	40	73
After 16 weeks			
No. of SAEs	53	54	107
Patients with at least one SAE	47	44	91

Patients can appear in both before and after 16 week breakdown

Table 3iii: Additional information on Primary safety endpoint events* serious adverse events (SAEs), deaths and Suspected bacterial infections requiring hospitalisation

Randomised	16 weeks (N=602)	24 weeks (N=602)	Total (N=1204)
Participants with at least one DAIDS grade 3, 4 or 5 adverse event ¤	**47 (8)**	**48 (8)**	**95 (8)**
Participants with grade 5 adverse event (Death)	8	9	17
Participants with grade 4 adverse event	7	12	19
Participants with grade 3 adverse event	32	27	59
Participants with at least one grade 3, 4 or 5 adverse events occurring b*efore 16 weeks*	33 (5)	40 (7)	73 (6)
Participants with grade 5 adverse event (Death) before *16 weeks*	6	9	15
Participants with grade 4 adverse event before *16 weeks*	6	10	16
Participants with grade 3 adverse event before *16 weeks*	21	21	42
Participants with at least one grade 3, 4 or 5 adverse event occurring after week 16	14 (2)	12 (2)	26 (2)
Participants with grade 5 adverse event (Death)	2	0	2
Participants with grade 4 adverse event	1	2	3
Participants with grade 3 adverse event	11	10	21
Events described as bacterial infections requiring hospitalisation before week 16	14	15	29
Participants with at least episode of bacterial infection requiring hospitalisation before week 16	13	13	26
Events described as bacterial infections requiring hospitalisation after week 16	26	25	51

Participants with at least one episode of bacterial infection requiring hospitalisation after week 16	26	19	45

Data presented as number of events or number of participants with at least one event (%) as indicated. DAIDS = Division of AIDS table for grading the severity of adult and paediatric adverse events; SAE=serious adverse event, defined using International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) definitions as adverse event resulting in death, is life-threatening, requires hospitalisation or prolongs existing hospitalisation, results in persistent or significant disability or incapacity, consists of a congenital anomaly or birth defect, or considered to be another important medical condition.

* Primary safety endpoint events include on-treatment grade 3 or higher adverse events up to 30 days after the last dose of study drugs.

¤ Participants can appear in both before and after 16 week breakdown.

¥ Adverse drug reactions were defined as being possibly, probably or definitely related to the trial drugs. Further information on these can be found in the listing in the supplementary material and include event type and information on treatment discontinuation. Data presented as number of events or number of participants with at least one event (%) as indicated. *Participants can appear in both before and after 16 week breakdown

S4: Adverse Drug Reactions

Table S4: Listing of Adverse Drug Reactions*

#	Rand. Date	Treatment	Date of Onset	Date of Resolution	Summarised Name of Event	Drug	Causality	Action Taken on Form	Highest Event Grade	Time to event (days)
1[1]	07-Dec-17	24 weeks	10-Dec-17	02-Jan-18	Vomiting, Raised ALT, Raised AST	H, E	Definitely	Reduction	3	4
						Z, R	Definitely	Interrupted[1]		
2	18-Aug-17	24 weeks	22-Aug-17	25-Sep-17	Raised ALT, Raised AST	R	Possibly	Interrupted	4	5
3	01-Jan-18	24 weeks	13-Jan-18	01-Feb-18	Raised ALT	H, R, Z	Possibly	Interrupted	3	13
4	14-Jun-17	16 weeks	28-Jun-17	13-Jul-17	Acute hepatitis	R	Possibly	Reduction	4	15
						H, Z	Possibly	Interrupted		
5	19-Jan-18	24 weeks	02-Feb-18	09-Feb-18	Raised ALT	H, R, Z	Probably	Interrupted	3	15
6	11-Jul-18	16 weeks	03-Aug-18	10-Aug-18	Rash (urticaria)	H, R, Z, E	Possibly	Interrupted[1]	3	24
7	02-Jun-17	24 weeks	25-Jun-17	11-Jul-17	Hypersensitivity reaction	H, R, Z	Possibly	Interrupted	3	24
8	08-Mar-17	24 weeks	04-Apr-17	20-Apr-17	Raised ALT	H, R, Z	Probably	None	3	28
9	25-Aug-16	16 weeks	21-Sep-16	11-Oct-16	Raised creatinine	H, R	Possibly	None	4	28
10[2,3]	03-Feb-17	24 weeks	03-Mar-17	11-Apr-17	Raised ALT, Raised AST	H, R, Z	Possibly	Stopped[2,3]	4	29

#	Rand. Date	Treatment	Date of Onset	Date of Resolution	Summarised Name of Event	Drug	Causality	Action Taken on Form	Highest Event Grade	Time to event (days)
11[3]	19-Jul-18	24 weeks	18-Aug-18	03-Sep-18	Acute hepatitis	H, R, Z	Probably	Interrupted[3]	4	31
12	17-Oct-17	24 weeks	20-Nov-17	27-Nov-17	Sickle cell crisis	H, R, Z, E	Possibly	None	4	35
13[2,3]	12-Apr-18	24 weeks	25-May-18	19-Jul-18	Acute hepatitis	H, R, Z	Possibly	Stopped[2,3]	4	44
14	13-Jun-17	16 weeks	08-Aug-17	28-Aug-17	Colour vision disturbance	E	Definitely	None¥	2	57
15	24-Aug-17	16 weeks	14-Nov-17	21-Nov-17	Anaemia with no clinical symptoms	R	Possibly	None	1	83
16	20-Jun-17	16 weeks	10-Oct-17	07-Nov-17	Raised ALT	H, R	Probably	None	4	113
17	08-06-17	24 weeks	24-Nov-17	21-Dec-17	Raised ALT	H, R	Probably	None	4	170

* Events occurring on treatment or within 30 days of the last dose of study drugs. Adverse drug reactions were defined as being possibly, probably or definitely related to the trial drugs. [1] Reported as interrupted but subsequently stopped according to other data sources; [2] reported as stopped but subsequently restarted according to TB treatment log; [3] treatment restarted without PZA. ¥ No action taken as the event occurred at day 57 at the end of treatment

S5: Deaths

Table S5: Listing of all deaths

#	Randomisation Date	Treatment	HIV status/age/country	Primary cause of Death (local)	ERC Adjudicated Primary Cause of Death	Related to TB (ERC)	Related to Drug (Investigator)	Days to death
1	02-Jun-17	16 weeks	Negative/6 months/ Uganda	Pneumonia no organism identified	Pneumonia no organism identified	Possibly	Unrelated	12
2	18-Aug-16	24 weeks	Negative/11 years/ South Africa	Bronchospasm/Asthma	Bronchospasm/Asthma	Possibly	Unrelated	14
3	21-Feb-17	24 weeks	Positive/1 year/Uganda	Congestive cardiac failure	Anaemia with clinical symptoms	Unrelated/ Unlikely	Possibly	19
4	15-Aug-16	16 weeks	Positive/5 months/ Zambia	Severe malnutrition	Pneumonia - other bacterial	Definitely/ Probably	Unrelated	22
5	19-May-17	16 weeks	Negative/1 year/Uganda	Pneumonia no organism identified	Death, cause unknown	Unknown	Unrelated	23
6	19-May-17	24 weeks	Positive/4 months/Zambia	Unknown	Death, cause unknown	Unrelated/ Unlikely	Unlikely	25
7	07-Jun-18	24 weeks	Negative/8 months/Uganda	Unknown	Traumatic	Unrelated/ Unlikely	Unrelated	54
8	13-Jan-17	24 weeks	Negative/6 months/Uganda	Unknown	Death, cause unknown	Unknown	Unlikely	55
9	01-Dec-16	16 weeks	Negative/10 months/Uganda	Unknown	Death, cause unknown	Unknown	Unlikely	55
10	23-Feb-17	24 weeks	Positive/4 months/Zambia	Severe malnutrition	Chronic diarrhoea not investigated	Possibly	Unlikely	65

#	Randomisation Date	Treatment	HIV status/age/country	Primary cause of Death (local)	ERC Adjudicated Primary Cause of Death	Related to TB (ERC)	Related to Drug (Investigator)	Days to death
11	20-Feb-17	16 weeks	Positive/4 months/Zambia	Septicaemia with organism (unspecified)	Presumed septicaemia/bacteremia - no organism	Possibly	Unlikely	87
12	03-Mar-17	16 weeks	Negative/5 years/Uganda	Unknown	Epilepsy, fits, convulsions	Possibly	Unrelated	124
13	24-Aug-17	16 weeks	Positive/1 years/Zambia	Congestive cardiac failure	Pneumonia - other bacterial	Unrelated/ Unlikely	Unrelated	130
14	14-Nov-16	24 weeks	Positive/6 months/Zambia	Pneumonia no organism identified	Pneumonia no organism identified	Possibly	Unlikely	140
15	20-Nov-17	24 weeks	Negative/8 months/Uganda	Traumatic	Traumatic	Unrelated/ Unlikely	Unrelated	152
16	20-Dec-17	24 weeks	Positive/1 years/Zambia	Severe malnutrition	Severe malnutrition	Unrelated/ Unlikely	Possibly	162
17	03-Feb-17	24 weeks	Positive/1 years/Uganda	Unknown	Death, cause unknown	Unknown	Unrelated	186
18	09-Jul-18	16 weeks	Negative/2 years/Uganda	Acute respiratory failure	Other Solid tumour	Unrelated/ Unlikely	Unrelated	198
19	02-Jun-17	24 weeks	Negative/7 years/Uganda	Hypotension/shock/toxic shock	Congestive cardiac failure	Possibly	Unrelated	203
20	09-Nov-16	16 weeks	Positive/9 months/Zambia	Acute diarrhoea not investigated	Acute diarrhoea not investigated	Unrelated/ Unlikely	Unrelated	214
21	05-Apr-17	24 weeks	Negative/1 years/Uganda	Hypotension/shock/toxic shock	Pneumonia no organism identified	Possibly	Unrelated	227

#	Randomisation Date	Treatment	HIV status/age/country	Primary cause of Death (local)	ERC Adjudicated Primary Cause of Death	Related to TB (ERC)	Related to Drug (Investigator)	Days to death
22	16-Nov-17	16 weeks	Negative/7 months/Zambia	Unknown	Death, cause unknown	Unrelated/ Unlikely	Unlikely	229
23	19-May-17	24 weeks	Negative/1 years/Uganda	Hypotension/shock/toxic shock	Hypotension/shock/toxic shock	Unrelated/ Unlikely	Unrelated	241
24	18-Jul-16	24 weeks	Positive/3 months/Zambia	Unknown	Acute respiratory failure	Possibly	Unrelated	257
25	30-Aug-17	16 weeks	Negative/6 months/Zambia	Unknown	Epilepsy, fits, convulsions	Possibly	Unrelated	268
26	24-May-17	24 weeks	Negative/2 months/Uganda	Disseminate Intravascular coagulopathy (DIC)	Presumed septicaemia/bacteremia - no organism	Unrelated/ Unlikely	Unrelated	309
27	03-May-18	24 weeks	Negative/2 years/Zambia	Unknown	MISSING	MISSING	Unrelated	318
28	09-Oct-17	24 weeks	Positive/1 years/Zambia	Unknown	Tuberculosis - pulmonary - smear negative or not done	Definitely/ Probably	Unlikely	335
29	12-Jul-18	16 weeks	Negative/9 months/Uganda	Hypotension/shock/toxic shock	Hypotension/shock/toxic shock	Unrelated/ Unlikely	Unrelated	408
30	14-Mar-17	24 weeks	Positive/1 years/Uganda	Acute respiratory failure	Pneumonia no organism identified	Possibly	Unrelated	468
31	20-Apr-18	24 weeks	Negative/10 years/Uganda	Traumatic	Traumatic	Unrelated/ Unlikely	Unrelated	514

S6: Unfavourable outcomes in mITT

Table S6: Listing of all unfavourable outcomes in mITT

#	Randomisation Date	Treatment	HIV status/age/country	Age	Site country	mITT unfavourable reason	Days to event
1	28-Jun-17	16 weeks	Negative	1 year	Pune	Official treatment extension	112
2	05-Oct-17	16 weeks	Positive	4 years	Zambia	Official treatment extension	113
3	23-Mar-18	16 weeks	Negative	3 years	Pune	Event after week 16: TB event	117
4	03-Mar-17	16 weeks	Negative	5 years	Uganda	Event after week 16: Death	124
5	24-Aug-17	16 weeks	Positive	1 year	Zambia	Event after week 16: Death	130
6	14-Nov-16	24 weeks	Positive	6 months	Zambia	Event after week 16: Death	140
7	18-Jul-18	24 weeks	Negative	4 years	Uganda	Event after wk16: LTFU and not completed treatment	143
8	20-Nov-17	24 weeks	Negative	8 months	Uganda	Event after week 16: Death	152
9	20-Dec-17	24 weeks	Positive	1 years	Zambia	Event after week 16: Death	162
10	05-Sep-17	16 weeks	Positive	11 years	Zambia	Event after week 16: TB event	171
11	03-Feb-17	24 weeks	Positive	1 year	Uganda	Event after week 16: Death	186
12	09-Jul-18	16 weeks	Negative	2 years	Uganda	Event after week 16: Death	198
13	02-Jun-17	24 weeks	Negative	7 years	Uganda	Event after week 16: Death	203
14	03-Apr-17	16 weeks	Negative	1 year	Zambia	Event after week 16: TB event	204
15	23-Dec-16	16 weeks	Negative	1 year	Uganda	Official treatment restart	209

#	Randomisation Date	Treatment	HIV status/age/country	Age	Site country	mITT unfavourable reason	Days to event
16	09-Nov-16	16 weeks	Positive	9 months	Zambia	Event after week 16: Death	214
17	27-Jun-18	24 weeks	Negative	6 months	Uganda	Official treatment restart	219
18	09-Oct-17	24 weeks	Positive	1 year	Zambia	Event after week 16: TB event	221
19	05-Apr-17	24 weeks	Negative	1 year	Uganda	Event after week 16: Death	227
20	16-Nov-17	16 weeks	Negative	7 months	Zambia	Event after week 16: Death	229
21	22-May-18	24 weeks	Negative	13 years	Chennai	Event after week 16: TB event	232
22	19-May-17	24 weeks	Negative	1 year	Uganda	Event after week 16: Death	241
23	18-Jul-16	24 weeks	Positive	3 months	Zambia	Event after week 16: Death	257
24	30-Aug-17	16 weeks	Negative	6 months	Zambia	Event after week 16: Death	268
25	15-May-18	24 weeks	Negative	1	South Africa	Event after week 16: TB event	274
26	24-May-17	24 weeks	Negative	2 months	Uganda	Event after week 16: Death	309
27	14-Jun-18	16 weeks	Negative	2 years	South Africa	Event after week 16: TB event	318
28	03-May-18	24 weeks	Negative	2 years	Zambia	Event after week 16: Death	318
29	17-Jul-18	16 weeks	Negative	0	South Africa	Event after week 16: TB event	329
30	14-Dec-16	24 weeks	Negative	1 year	South Africa	Event after week 16: TB event	377
31	12-Jul-18	16 weeks	Negative	9 months	Uganda	Event after week 16: Death	408
32	11-Dec-17	16 weeks	Negative	3 months	Zambia	Event after week 16: TB event	421

#	Randomisation Date	Treatment	HIV status/age/country	Age	Site country	mITT unfavourable reason	Days to event
33	14-Mar-17	24 weeks	Positive	1 year	Uganda	Event after week 16: Death	468
34	20-Apr-18	24 weeks	Negative	10 years	Uganda	Event after week 16: Death	514

S7: Cost-effectiveness results

The SHINE health economics analysis investigated the value of the shortened regimen in terms of healthcare cost savings and health outcomes (measured by quality-adjusted life years). Regression analysis was used to control for chance differences in demographic characteristics and symptom severity between the children in each treatment arm.

At 72 weeks, children treated for 16 weeks had similar health outcomes (QALYs were improved by 0.003 (95% CI -0.009 to 0.0144)) and reduced healthcare costs by $17.34 (95% CI $3.77 to $30.91, 2019 USD) compared with those treated in the 24-week arm.

These results indicate that for every 1000 children treated with the shortened regimen, cost savings of up to $17,000 could be achieved. These could in turn be used to improve the implementation of the shortened regimen, such as the provision of diagnostics to identify children with mild TB.

Table S7i: Cost-effectiveness results

	Post 4-month costs only			All costs included (scenario analysis)		
Predicted outcomes	**mITT (base case)**	**ITT**	**Per protocol**	**mITT (base case)**	**ITT**	**Per protocol**
Costs – 24 weeks	138.97 (5.35)	137.64 (5.68)	137.79 (5.15)	396.14 (7.66)	393.81 (7.87)	395.13 (7.58)
Costs – 16 weeks	121.63 (4.82)	122.85 (5.3)	120 (4.74)	395.85 (7.74)	395.3 (7.78)	393.97 (7.36)
Life years – 24 weeks	1.126 (0.004)	1.117 (0.006)	1.126 (0.004)	1.358 (0.004)	1.347 (0.006)	1.357 (0.004)
Life years – 16 weeks	1.132 (0.004)	1.123 (0.006)	1.124 (0.004)	1.353 (0.004)	1.342 (0.006)	1.353 (0.004)
QALYs – 24 weeks	1.124 (0.004)	1.115 (0.006)	1.132 (0.004)	1.364 (0.004)	1.354 (0.006)	1.364 (0.004)
QALYs – 16 weeks	1.127 (0.004)	1.118 (0.006)	1.126 (0.004)	1.356 (0.004)	1.347 (0.006)	1.356 (0.004)
Incremental outcomes						
Costs	-17.34 (6.92)	-14.79 (7.13)	-17.8 (6.87)	-0.3 (10.68)	1.49 (10.78)	-1.16 (10.5)
Life years	0.006 (0.006)	0.006 (0.008)	0.006 (0.006)	0.006 (0.006)	0.007 (0.009)	0.007 (0.006)
QALYs	0.003 (0.006)	0.004 (0.008)	0.003 (0.006)	0.003 (0.006)	0.004 (0.009)	0.003 (0.006)
Cost-effectiveness outcomes						
Cost-per-QALY	Dominant	Dominant	Dominant	Dominant	342	Dominant

QALYs = Quality-adjusted life years; mITT = modified intention to treat; ITT = intention to treat. Standard errors in parentheses. Dominant cost-per-QALY indicates the intervention improves QALYs and reduces healthcare costs.

Table S7ii: Unit cost estimates

Healthcare resource	Country	Unit cost ($US)	Source
Health service use			
Clinic visit	South Africa Uganda Zambia India	13.70 2.54 4.34 3.78	WHO Choice (1) – Cost per outpatient visit Health Centre (No Beds)
Hospital outpatient visit	South Africa Uganda Zambia India	19.27 3.58 6.09 5.33	WHO Choice (1) – Cost per outpatient visit Primary Hospital
Hospital bed day	South Africa Uganda Zambia India	99.39 9.36 15.98 17.98	WHO Choice (1) – Cost per bed day Primary Hospital
Diagnostics			
Tuberculin skin test	All countries	4.47	Kim et al. (2018) (2)
IGRA blood test	South Africa Uganda, Zambia, India	67.51 38.95	Kim et al. (2018) (2) Little et al. (2015) (3)
Chest x-ray	South Africa Uganda, Zambia India	23.02 7.32 3.07	Kim et al. (2018) (2) Vassall et al. (2011) (4) Pande et al. (2015) (5)
GeneXpert / GeneXpert Ultra	South Africa Uganda, Zambia, India	22.86 24.68	Sinanovic et al. (2015) (6) Khaparde et al. (2017) (7)
Genotype MTBDRplus	All countries	27.46	Cunnama et al. (2016) (8)
Liquid culture	All countries	11.52	Shah et al. (2013) (9)
Löwenstein–Jensen medium	All countries	24.30	Chihota et al. (2010) (10)
Drug susceptibility test	South Africa Uganda, Zambia, India	33.95 27.71	Cunnama et al. (2016) (8) Khaparde et al. (2017) (7)
Rapid HIV test	South Africa Uganda Zambia India	7.95 5.08 4.48 8.20	Pooran et al. (2013) (11) Asiimwe et al. (2017) (12) Mwenge et al. (2017) (13) Kundu et al. (2015) (14)
Biochemistry	South Africa Uganda, Zambia	39.16 13.53	Pooran et al. (2013) (11) Kundu et al. (2015) (14)
Haematology	South Africa Uganda, Zambia India	10.41 9.54 10.38	Philips et al. (2020) (15) Barnabas et al. (2020) (16) Venkatesh et al. (2013) (17)
Viral load test	All countries	22	Philips et al. (2020) (15)
Medication (price per tab)			
Isoniazid 50mg, Rifampicin 75mg, Pyrazinamide 150mg	All countries	0.04	Stop TB Partnership Medicines Catalog (2020) (18)
Ethambutol 100mg	All countries	0.23	Stop TB Partnership Medicines Catalog (2020) (18)

Healthcare resource	Country	Unit cost ($US)	Source
Isoniazid 50mg, Rifampicin 75mg	All countries	0.04	Stop TB Partnership Medicines Catalog (2020) (18)
Isoniazid 75mg, Rifampicin 150mg, Pyrazinamide 400mg, Ethambutol 275mg	All countries	0.08	Stop TB Partnership Medicines Catalog (2020) (18)
Isoniazid 75mg, Rifampicin 150mg	All countries	0.04	Stop TB Partnership Medicines Catalog (2020) (18)
Pyrazinamide 150mg	All countries	0.09	Stop TB Partnership Medicines Catalog (2020) (18)
Rifampicin 150mg	All countries	0.06	Stop TB Partnership Medicines Catalog (2020) (18)
Levofloxacin~~axin~~ 150mg	All countries	0.13	Stop TB Partnership Medicines Catalog (2020) (18)
Terizidone 250mg	All countries	1.75	Stop TB Partnership Medicines Catalog (2020) (18)

All estimates inflated from base year to 2019 USD.

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S8: Primary endpoint stratified by microbiological confirmation

Table S8i: Microbiologically confirmed

	4 Month	6 Month	Total
Randomised	**602**	**602**	**1204**
Total in Analysis	**85**	**80**	**165**
Unassessable	7	6	13
Favourable	**76 (89)**	**74 (92)**	**103 (90)**
Unfavourable	**2 (2)**	**0 (0)**	**2 (1)**
Total Assessable	**78**	**74**	**152**
Difference from control in unfavourable rate (Unadjusted)	- 0.9%		
95% confidence interval (Unadjusted)	(-3.4 to 1.6)		

Table S8ii: Not microbiologically confirmed

	4 Month	6 Month	Total
Randomised	**602**	**602**	**1204**
Total in Analysis	**517**	**522**	**1039**
Unassessable	23	23	46
Favourable	**480 (92)**	**481 (92)**	**1008 (98)**
Unfavourable	**14 (3)**	**18 (4)**	**32 (3)**
Total Assessable	**494**	**499**	**993**
Difference from control in unfavourable rate (Unadjusted)	-0.7%		
95% confidence interval (Unadjusted)	(-3.0 to 1.4)		

S9: Primary endpoint results by PP and ITT

Table 9i Primary efficacy analysis results (PP)

	16 weeks	24 weeks	Total
Randomised	**602**	**602**	**1204**
Unassessable	39	44	83
Favourable	**549 (98)**	**541 (97)**	**1090 (97)**
Unfavourable	**14 (2)**	**17 (3)**	**31 (3)**
Total included in analysis (Assessable)	**563**	**558**	**1121**
Difference from control in unfavourable rate (CMH weights, Adjusted)	-0.6%		
95% confidence interval (Adjusted ł)	(-2.4 to **1.3**)		
Difference from control in unfavourable rate (Unadjusted)	-0.6%		
95% confidence interval (Unadjusted)	(-2.5 to **1.4**)		

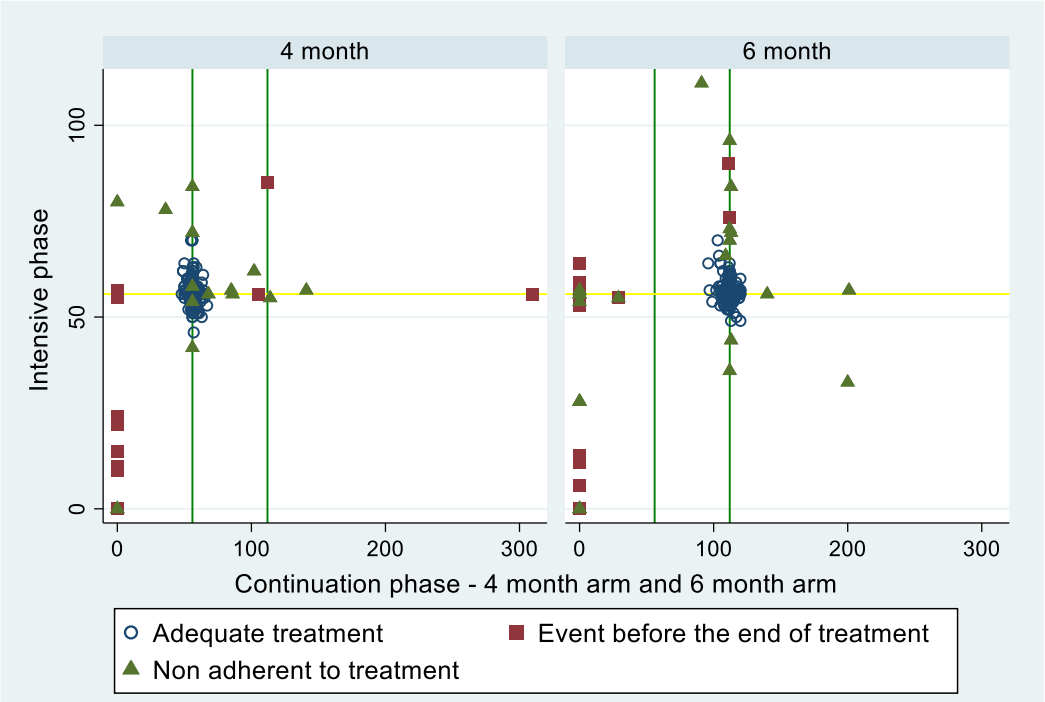
Data presented as number of participants (%), unless otherwise stated. CMH: Cochran–Mantel–Haenszel. *Unadjusted is displayed in figure 2; ł Adjusted for centre, age (over/under 3 years), HIV status and ethambutol use.

Table 9ii Primary efficacy analysis results (ITT)

	16 weeks	24 weeks	Total
Randomised	**602**	**602**	**1204**
Unassessable	0	0	0
Favourable	**558 (93)**	**558 (93)**	**1116 (93)**
Unfavourable	**44 (7)**	**44 (7)**	**88 (7)**
Total (Included in analysis) Assessable	**602**	**602**	**1204**
Difference from control in unfavourable rate (Unadjusted)*	0%		
95% confidence interval (Unadjusted)	(-2.9 to **2.9**)		

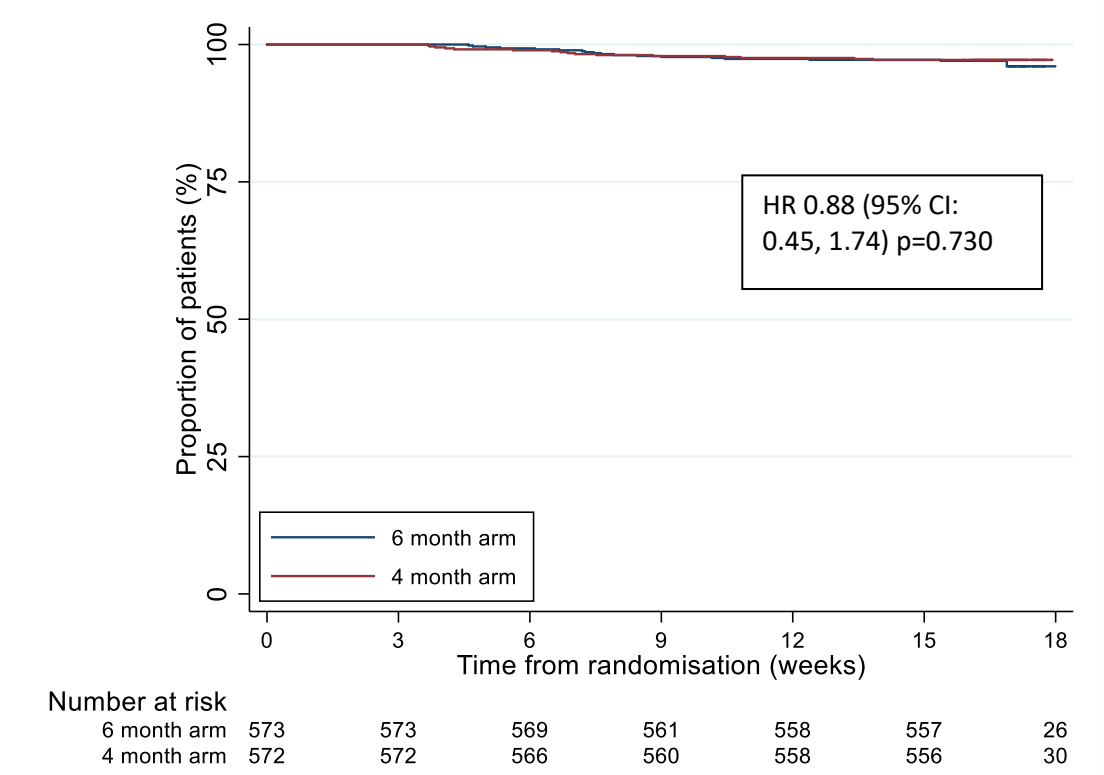
Data presented as number of participants (%), unless otherwise stated. CMH: Cochran–Mantel–Haenszel.

Figure S1: Adherence - the number of daily doses taken in each phase for all children



Y-axis is number of daily doses taken during intensive phase; x-axis is total number of daily doses taken during continuation phase. Green vertical lines indicate 16 weeks and 24 weeks of daily doses respectively. The yellow horizontal lines indicate 8 weeks of the intensive phase of treatment (56 days). The left panel represents drug intake in the 16-week arm, the right panel – drug intake in the 24-week arm. The figure demonstrates that the majority of children were adherent to the allocated duration of treatment.

Figure S2: Time to unfavourable outcome (mITT)



Number at risk

6 month arm	573	573	569	561	558	557	26
4 month arm	572	572	566	560	558	556	30

Figure S3: Time to death (ITT)

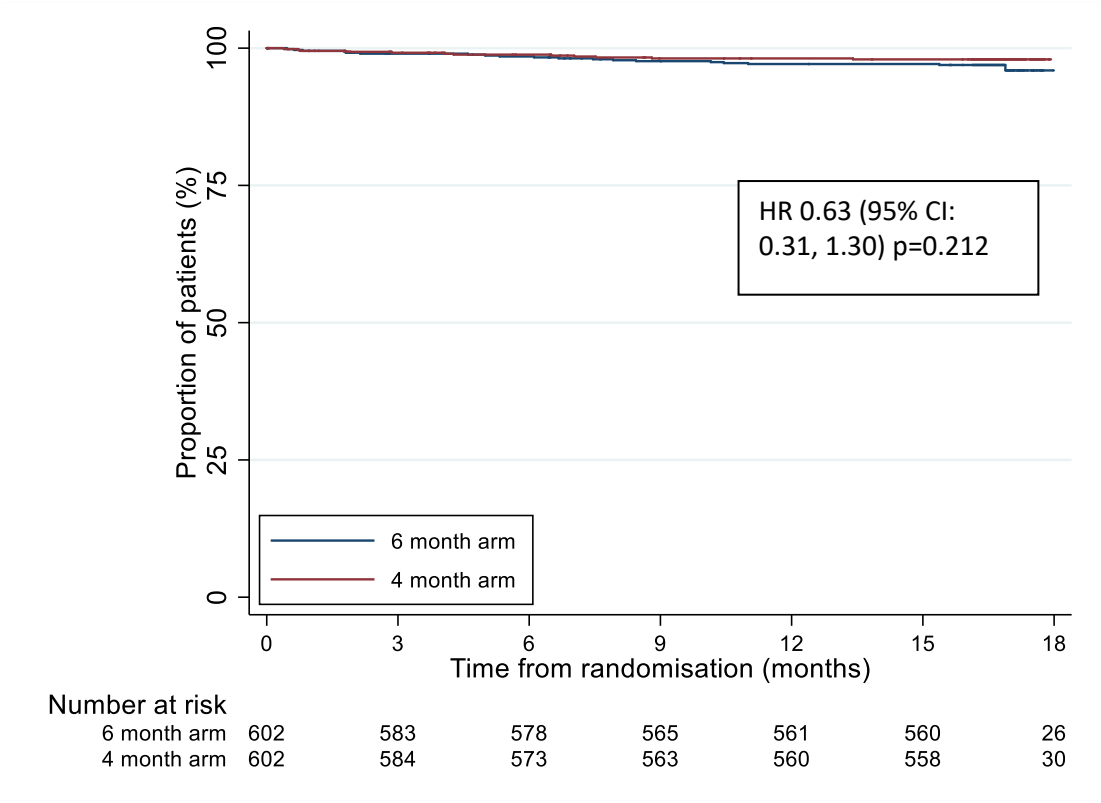


Figure S4: Subgroup Analyses of Primary Efficacy Endpoint

"Lymph node TB" was defined as: Mixed TB (cough OR abnormal CXR) AND abnormal peripheral lymph node OR Lymph node presentation (no cough, but abnormal peripheral lymph node). "Not lymph node TB" was defined as: Respiratory presentation (cough OR abnormal CXR) OR Other presentation (no cough AND NO abnormal peripheral lymph node)