Pediatric Four Month Regimen (Shine Trial)

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November 6, 2025

TB Nurse Expert Meeting · November 6-7, 2025 · San Antonio, Texas

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Nurse Expert Meeting 2025
San Antonio, Texas
November 7, 2025

Financial Disclosure

Consultant for Oak Therapeutics NIH SBIR grant

SHINE Trial

Shorter Treatment for Minimal Tuberculosis (TB) in Children

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Shorter Treatment for Nonsevere Tuberculosis in African and Indian Children

A. Turkova, G.H. Wills, E. Wobudeya, C. Chabala, M. Palmer, A. Kinikar, S. Hissar, L. Choo, P. Musoke, V. Mulenga, V. Mave, B. Joseph, K. LeBeau, M.J. Thomason, R.B. Mboizi, M. Kapasa, M.M. van der Zalm, P. Raichur, P.K. Bhavani, H. McIlleron, A.-M. Demers, R. Aarnoutse, J. Love-Koh, J.A. Seddon, S.B. Welch, S.M. Graham, A.C. Hesseling, D.M. Gibb, and A.M. Crook, for the SHINE Trial Team*

Trial Design

- Multicenter, open-label, parallel-group, non-inferiority, randomized controlled, two-arm trial
- Comparing a 4-month vs the standard 6-month regimen
- Used fixed-dose, combination dispersible tablets
  - mg/kg: INH 10 (7-15), rifampin 15 (10-20), EMB 20 (15-25), PZA 35 (30-40)
- Endpoint: favorable outcome; TB-free survival at 72 weeks
- Margin of Inferiority set at 6%

Inclusion Criterion

- Age 0-16 years
- Weight ≥ 3kg.
- Clinician has decided to treat with standard first-line regimen
- Symptomatic but non-severe TB including:
  - extrathoracic lymph node TB; intra-thoracic uncomplicated (hilar) lymph node TB
  - minimal or no parenchymal abnormality on CXR
  - smear negative on gastric aspirate/other respiratory sample

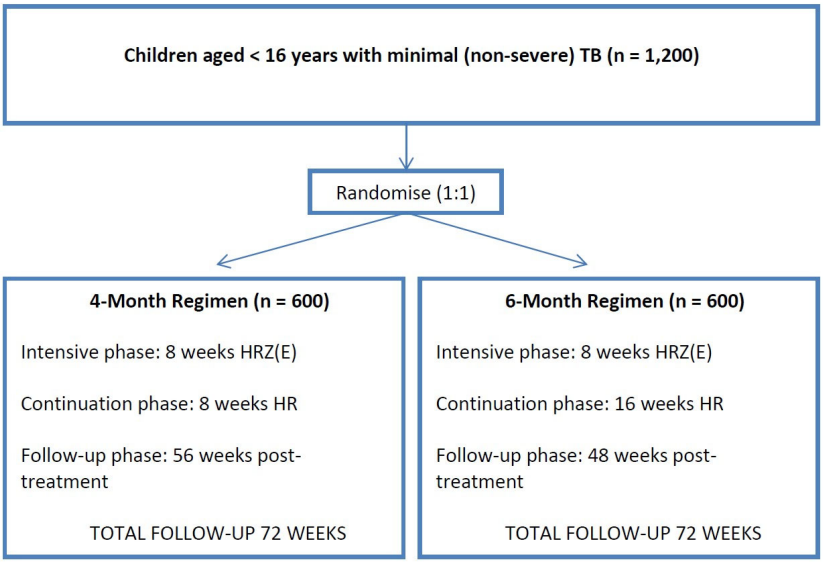
Note: GeneXpert may be positive or negative and a negative GeneXpert can be used as a substitute for a negative smear;
culture of respiratory sample may be positive or negative;
lymph node aspirate may be smear/culture/GeneXpert positive or negative)

- Not treated for previous TB unless successfully treated > 2 years since last completed treatment
- Known (or pending confirmation of) HIV status; HIV-infected or HIV-uninfected
- Willing and likely to adhere to 72 weeks follow up
- Informed written consent from the parent/legal caregiver(s) and assent in children
- Home address accessible for visiting and intending to remain within the recruitment area

Exclusion Criterion

1. Smear-positive respiratory sample TB
   (note: smear-positive peripheral lymph node sample is allowed)
2. Premature (<37 weeks) **and** aged under 3 months
3. Miliary TB, spinal TB, TB meningitis, osteoarticular TB, abdominal TB, congenital TB
4. Pre-existing non-tuberculous disease likely to prejudice the response to, or assessment of, treatment e.g. liver or kidney disease, peripheral neuropathy, cavitation
5. Any known contraindication to taking anti-TB drugs
6. Known contact with drug resistant adult source case (including mono- resistant TB)
7. Known drug resistance in the child
8. Severely sick
9. Pregnancy

Methods



Demographic and Clinical Characteristics of the Participants at Baseline.

Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

Characteristic	4-Month Treatment (N=602)	6-Month Treatment (N=602)	Total (N=1204)
Age			
Median (interquartile range) — yr	3.4 (1.5 to 6.9)	3.5 (1.5 to 7.1)	3.5 (1.5 to 7.0)
Range	2 mo to 15 yr	2 mo to 15 yr	2 mo to 15 yr
Female sex — no. (%)	297 (49)	286 (48)	583 (48)
Site country — no. (%)			
Uganda	188 (31)	188 (31)	376 (31)
Zambia	183 (30)	181 (30)	364 (30)
South Africa	156 (26)	159 (26)	315 (26)
India	75 (12)	74 (12)	149 (12)
HIV-positive status — no. (%)	65 (11)	62 (10)	127 (11)
WHO weight band — no. (%)			
3–3.9 kg	0	3 (<1)	3 (<1)
4–7.9 kg	86 (14)	92 (15)	178 (15)
8–11.9 kg	162 (27)	152 (25)	314 (26)
12–15.9 kg	126 (21)	116 (19)	242 (20)
16–24.9 kg	142 (24)	153 (25)	295 (25)
≥25 kg	86 (14)	86 (14)	172 (14)
Clinical presentation — no. (%)			
Respiratory tuberculosis	398 (66)	406 (67)	804 (67)
Mixed respiratory and peripheral lymph-node tuberculosis	182 (30)	171 (28)	353 (29)
Peripheral lymph-node tuberculosis	19 (3)	21 (3)	40 (3)
Other†	3 (<1)	4 (1)	7 (1)
M. tuberculosis culture and Xpert MTB/RIF testing results — no. (%)‡			
All positive results	85 (14)	80 (13)	165 (14)
Tuberculosis culture–positive only	40 (7)	40 (7)	80 (7)
Xpert MTB/RIF–positive only	14 (2)	5 (1)	19 (2)
Tuberculosis culture–positive and Xpert MTB/RIF–positive	31 (5)	35 (6)	66 (5)

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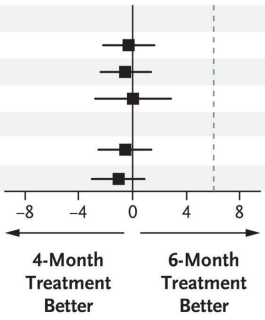
Unadjusted Analysis of the Primary Efficacy and Key Secondary Outcomes in the Trial Populations.

	No. of Patients	4-Month Treatment	6-Month Treatment	Risk Difference (95% CI)
		no. of participants with event/total no. (%)		6% *percentage points*
Primary outcome				
Modified intention-to-treat population	1145	16/572 (3)	18/573 (3)	−0.3 (−2.3 to 1.6)
Per-protocol population	1121	14/563 (2)	17/558 (3)	−0.6 (−2.5 to 1.4)
Intention-to-treat population	1204	44/602 (7)	44/602 (7)	0 (−2.9 to 2.9)
Key secondary outcome				
Modified intention-to-treat population	910	10/450 (2)	13/460 (3)	−0.6 (−2.6 to 1.4)
Per-protocol population	895	8/445 (2)	13/450 (3)	−1.1 (−3.1 to 0.9)



Tedrova A et al. N Engl J Med2022;386:911-922

Primary Efficacy Analysis (Modified Intention-to-Treat Population).

Table 2. Primary Efficacy Analysis (Modified Intention-to-Treat Population).*

Outcome	4-Month Treatment (N=572)	6-Month Treatment (N=573)	Difference (95% CI)	
			Adjusted Analysis†	Unadjusted Analysis
			percentage points	
Unfavorable status — no. (%)	16 (3)	18 (3)	−0.4 (−2.2 to 1.5)	−0.3 (−2.3 to 1.6)
Death from any cause after 4 mo	7 (1)	12 (2)		
Loss to follow-up after 4 mo but during treatment period	0‡	1 (<1)		
Treatment failure				
Tuberculosis recurrence	6 (1)	4 (1)		
Extension of treatment	2 (<1)	0		
Restart of treatment§	1 (<1)	1 (<1)		
Favorable status — no. (%)	556 (97)	555 (97)		

AMERICAN THORACIC SOCIETY DOCUMENTS

Updates on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis
An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline

Jussi J. Saukkonen*, Raquel Duarte*, Sonal S. Munsiff*, Carla A. Winston*, Manoj J. Mammen, Ibrahim Abubakar, Carlos Acuña-Villaorduña, Pennan M. Barry, Mayara L. Bastos, Wendy Carr, Hassan Chami, Lisa L. Chen, Terence Chorba, Charles L. Daley, Anthony J. Garcia-Prats, Kelly Holland, Ioannis Konstantinidis, Marc Lipman, Giovanni Battista Migliori, Farah M. Parvez, Adrienne E. Shapiro, Giovanni Sotgiu, Jeffrey R. Starke, Angela M. Starks, Sanket Thakore, Shu-Hua Wang, Jonathan M. Wortham, and Payam Nahid; on behalf of the American Thoracic Society, U.S. Centers for Disease Control and Prevention, European Respiratory Society, and Infectious Diseases Society of America

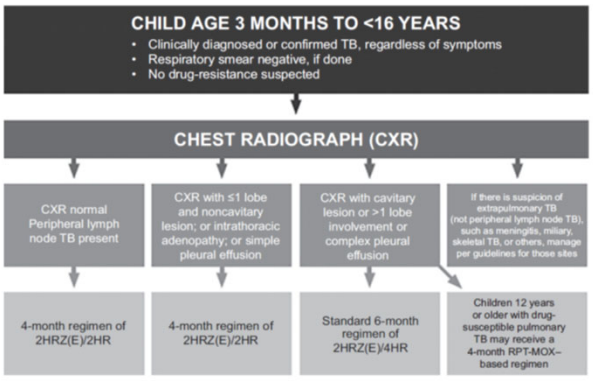


Figure 1. Identifying children eligible for 4-month regimens. Figure developed by the Joint Panel on the basis of data in the SHINE trial and Study 31/A5349 to address eligibility of some children for either the RPT/MOX regimen or the 4-month standard drug regimen. CXR = chest x-ray; HRZE = isoniazid, rifampin, pyrazinamide, ethambutol; RPT-MOX = rifapentine-moxifloxacin.

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Questions?

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Case Study

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City Chest Clinic

Patient on SHINE Regimen 2023

- Age 0-16 yrs
- Weight ≥ 3kg.
- Non-severe TB: extrathoracic lymph node TB; intra-thoracic uncomplicated (hilar) lymph node TB minimal or no parenchymal abnormality on CXR smear negative on gastric aspirate/other respiratory

- 2 y/o
- 1st nurse visit weight was 26 lbs 4 ounces/ >11kgs
- Aysmptomatic, only clinical findings

Patient on SHINE Regimen 2023

- 2 y/o female born in Afghanistan. Arrived to the U.S. in June 2021
- Contact to her older 12 y/o sibling who was diagnosed with pulmonary cavitary TB
- 1st evaluation included:
  - T-spot that resulted positive drawn 08-23-2023
  - chest x-ray on 08-29-2023 that read: Parahilar peribronchial wall thickening without focal consolidation
  - Nurse assessment was negative. No symptoms, no lymphadenopathy.

Patient on SHINE Regimen 2023

- Due to chest x-ray result and close contact, decision was made to hold off on starting TB medication for TBI only, until repeat x-ray
- 2nd x-ray on 9-12-23 read: Parahilar peribronchial wall thickening without focal consolidation.
- No change on x-ray after 15 days to exclude a viral reason for the abnormal reading, decision as made to treat for TB disease.

Patient on SHINE Regimen 2023

- Treatment started on 09-26-2023, with Isoniazid, Rifampin and Pyrazinamide. No Ethambutol since source case pan-sensitive
- Repeat chest x-ray on 12-06-23 read: lungs are clear. No pleural effusion or pneumothorax.
- Weight on 12-06-23 went from 26 lbs 4 oz to 28 lbs
- Pyrazinamide discontinued on 12-12-23 after 40 doses

Patient on SHINE Regimen 2023

- Treatment discontinued on 02-20-2024 after 90 doses of directly observed therapy.
- End of treatment chest x-ray on 02-27-24 read: lungs are clear. No pleural effusion or pneumothorax
- Weight on 02-14-24 went from 26 lbs 4 oz(starting weight) to 29 lbs 2 oz

Patient on SHINE Regimen 2023

- In closure: child, with minimal disease, had excellent tolerability to medication.
- Treated a few weeks over due to city closures, a few "missed" doses
- Appointments were made as close as possible to milestones (2 month x-ray, 4 month x-ray) but sometimes vary due to availability.

Thank you!

- San Antonio Metro Health District/ City Chest Clinic 210-207-8823
- Carol M. Staton, RN