Taking Side Effects Seriously- An Interactive and Evidence-Based Webinar Series: Nausea and Vomiting

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POPULATION HEALTH DIVISION
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DISEASE PREVENTION & CONTROL

Conflict of Interest Disclosure Statement

- Neither I, nor my spouse/partner have financial or other relationships with any commercial interest organizations within the past 12 months.

TB Treatment and Drug-Related Adverse Events

- Common, but not frequently discussed or highlighted
- Occur in all ages and with all drugs
- Negatively affect TB treatment including effectiveness, adherence, duration, and confidence in the treatment plan
- Negatively affect patient quality of life, and can lead to loss of work, income and long-term disability

Adverse events lead to increased morbidity and mortality

- If a patient cannot tolerate first line drug(s), clinicians resort to alternative drugs (e.g., fluoroquinolones, linezolid or injectable agents). These drugs can cause more severe adverse events
- Treatment breaks, re-challenges and additional monitoring lead to longer treatment durations and more use of clinical and public health resources.

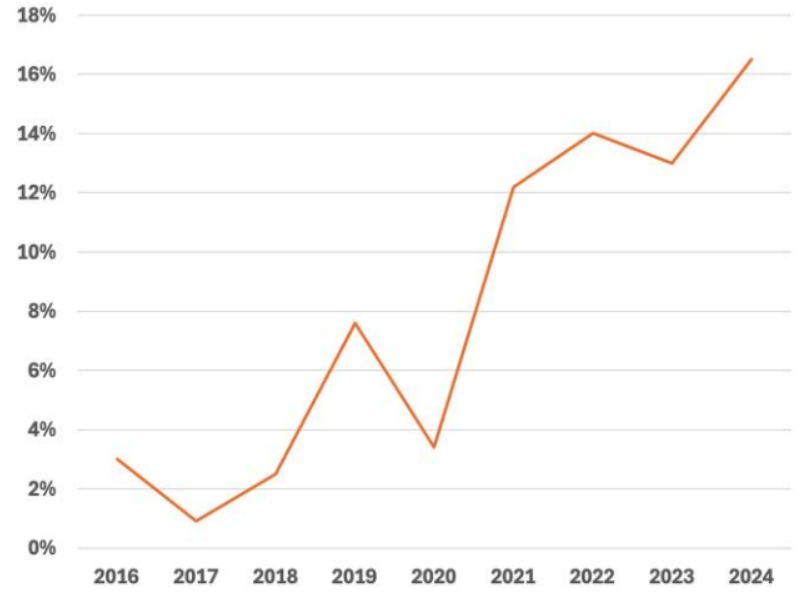


Figure 1. Trend in Linezolid Use for Treatment of Drug-Susceptible Tuberculosis in San Francisco, 2016–2024.

Lack of acknowledgement of impact of adverse events on TB treatment

- There are few clinical trials or guidelines on management of drug-related adverse events.
- Original scoring system comes from cancer clinical trials
  - Adverse events are categorized as grade 1-5, ranging from mild to severe (requires medical intervention, hospitalization, or death).
  - Most clinical trials monitor for grade 3-5 (severe) adverse events.
  - However, milder adverse events (grade 1- 2) cause distress and anxiety for both patient and providers.

Table Common Terminology Criteria for Adverse Events Grade and Clinical Severity[1]

Grade	Clinical severity
1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL
3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL
4	Life-threatening consequences; urgent intervention indicated
5	Death related to adverse event

ADL indicates activities of daily living.

More detail at URL: https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v6.pdf

Risk Factors for TB Drug Adverse Events

- Older age
- Comorbidities: HIV, immunosuppression, diabetes, chronic liver disease
- Pregnancy/post-partum
- ETOH use
- Extrapulmonary site
- Longer treatment duration
- Certain TB drugs in the regimen

Hosford JD et al. Tuberculosis (Edinb). 2015 March ; 95(2): 112–122 , Shu CC et al. Int J Tuberc Lung Dis 2013; 17(7):934–939, Hagiya H et al. Epidemiol Infect. 2018 Nov 9;147:e38. Shi C et al. Medicine (Baltimore). 2024 May 17;103(20):e38273, Choi et al. Pharmacoepidemiol Drug Saf. 2022 Nov;31(11):1153-1163. Nahid et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis. 2016 Oct 1;63(7):e147-e195.

Older age is a strong risk factor

Contributing factors:

- Decreased hepatic function/increased risk of hepatoxicity*
- More co-morbid illnesses
- Polypharmacy and drug-drug interactions with rifamycins
- Decreased renal function--> potentially higher levels of drugs
- Dementia/cognitive decline makes recognition of adverse events challenging
  - Difficulty with following instructions during screening exams (vision, hearing, neurologic)
  - Challenges in identifying/reporting side effects

*Hosford JD et al. Tuberculosis (Edinb). 2015 March ; 95(2): 112–122 , Shu CC et al. Int J Tuberc Lung Dis 2013; 17(7):934–939, Hagiya H et al. Epidemiol Infect. 2018 Nov 9;147:e38.

Tuberculosis in Older Adults: Seattle and King County, Washington

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Background. In the United States, tuberculosis (TB) incidence rates are highest among adults aged ≥65 years. We performed this study to evaluate outcomes of older patients undergoing treatment for TB disease, including the frequency of adverse events related to TB treatment.

Methods. This study evaluated adult patients who were diagnosed with pulmonary TB from 2009 to 2014 in King County, Washington. Patient characteristics, manifestation of TB, and treatment outcomes in different age groups were compared. Frequency and type of adverse events that resulted in treatment interruption were evaluated and patients aged ≥65 years were compared with selected younger patients.

Results. There were 403 patients who met the study criteria, 111 of whom were aged ≥65 years. Older patients were significantly less likely to have cavitation on chest radiographs. Patients aged ≥65 years were less likely to complete TB treatment (76.6% vs 94.9%, $P < .0001$) and were more likely to die during treatment (18.9% vs 2.1%, $P < .0001$). The difference in these outcomes was heightened for those aged ≥75 years compared with those aged <75 years. Those aged ≥75 years were also more likely to have an adverse event attributable to TB medication and were more likely to have an adverse event later in therapy. Regardless of age, pyrazinamide was responsible for the majority of adverse reactions.

Conclusions. Adults aged ≥65 years with pulmonary TB had less-advanced disease but a higher risk of complications during treatment such as death or adverse events. This effect was most pronounced among those aged ≥75 years.

Keywords. tuberculosis; older adults; adverse events.

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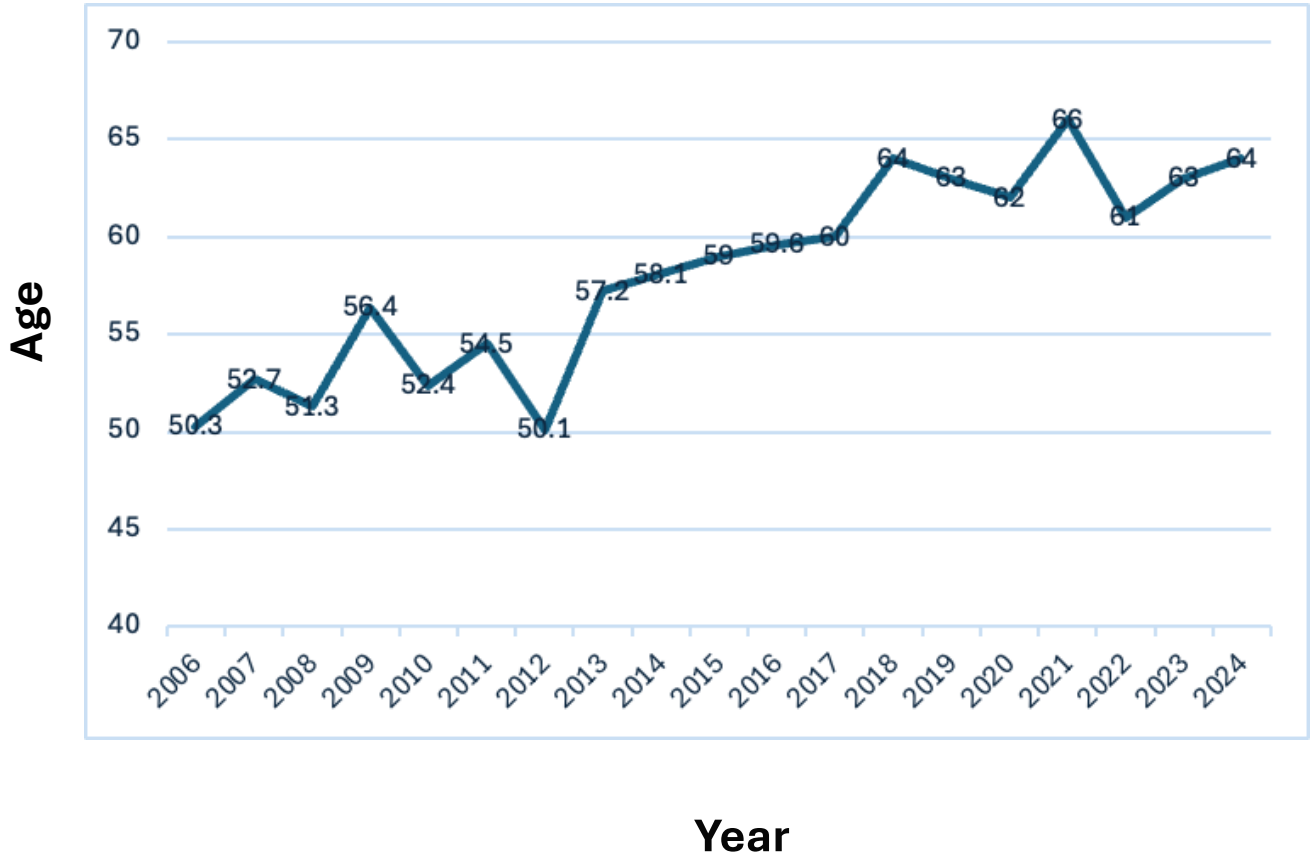
- **Elderly ≥ 65 years more likely to have treatment interruption due to a medication adverse event (32% vs 7%) including liver injury, hypersensitivity, arthralgias/myalgias, and GI intolerance.**
- **PZA accounted for ~50% of adverse events, followed by RIF, INH, EMB.**

2024 SF TB Cases

Total: 92 active cases (incidence 11 per 100,000)

- **Median age: 64 years (range 0-94)**
- Majority patients born in China, Philippines, Central America
- 65 (71%) had ≥ 1 comorbidity
- 42 (46%) residents had ≥ 2 comorbidities.
  - Diabetes mellitus 19 (21%)
  - Immunocompromised status 12 (13%) including HIV 2 (2%)
- ~10% with housing, ETOH and/or substance use challenges

TB case median age, 2008-2024



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Clinical Infectious Diseases

BRIEF REPORT

Adverse Events Associated With Treatment for Pan-Susceptible Tuberculosis in San Francisco

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Of 373 patients treated for drug-susceptible tuberculosis, 35.4% (46.2% aged ≥65 years) developed moderate/severe adverse events that required treatment interruption (34.8%), first-line drug discontinuation (26.2%, primarily pyrazinamide), second-line drug initiation (30.0%), and treatment duration up to 3.8 months longer. More safe and effective options are needed, including for the elderly.

Keywords. tuberculosis; TB; adverse events; elderly.

Current treatment recommendations for drug-susceptible tuberculosis (TB) include daily isoniazid, rifampin, pyrazinamide, and ethambutol (HRZE) [1]. TB treatment can be associated with adverse events (AEs) that require resource-intensive management including frequent clinic visits, symptom assessment, and laboratory monitoring. HRZE intolerance can result in longer treatment duration. For example, if pyrazinamide cannot be taken for the first 8 weeks, current guidelines recommend extending treatment duration to 9 months [1]. Likewise, if rifampin is not included in the regimen, duration can extend up to 18 months [2].

In 2020, patients aged ≥65 years had the highest TB incidence in the United States [3]. Compared with their younger counterparts, older patients may have higher risk of AEs including hepatotoxicity, leading to substantial treatment-related morbidity [4–7]. We reviewed TB cases in San Francisco treated over a 5-year period, including in patients aged ≥65 years, to understand the potential challenges of managing antituberculous drug-associated AEs.

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METHODS

We reviewed medical records of TB cases evaluated at the San Francisco Department of Public Health Tuberculosis Clinic from 1 January 2016 through 31 December 2020. We extracted data including clinical course, treatment regimens, symptoms, and laboratory results, which were used to assess drug-associated AEs. Patients with monoresistance to an anti-tuberculous drug were excluded from the denominator for specific drug-associated AEs. Patients with multidrug resistance or who died during treatment were excluded; deaths due to drug-related AEs were not excluded.

All patients underwent diagnostic evaluation, treatment, and management according to national recommendations [1]. Standard dosing included isoniazid 300 mg daily, rifampin 600 mg daily, and weight-based daily dosing of ethambutol (15–20 mg/kg) and pyrazinamide (20–25 mg/kg) [1]. For patients with creatinine clearance <30 mg/dL, ethambutol and pyrazinamide were dosed 3 times per week [1]. Recommended treatment durations were 6 months for culture-positive pulmonary TB, 9 months for cavitary pulmonary disease or for those with delayed mycobacterial culture conversion, and 9–12 months for spinal disease or TB meningitis [1]. Individual regimens were managed depending on clinician discretion. Treatment variations included withholding pyrazinamide (eg, if the patient had a history of gout), replacing rifampin with rifabutin for patients on concurrent medications with drug–drug interactions (eg, rifampin interaction with coumadin or methadone), or using liver-sparing regimens that excluded isoniazid, pyrazinamide, or a rifamycin (eg, in patients with cirrhosis). When an AE developed, standard practice included stopping all TB drugs and rechallenging 1-by-1 to determine if AE recurrence was associated with a specific drug. AEs were deemed to be treatment-related if they resolved after hold of a specific TB medication and/or recurred after reintroduction. Clinician discretion was also used to assess whether an AE was treatment-related or due to another cause. If first-line TB drugs were permanently discontinued, clinician assessment was used to decide whether to start a second-line agent. Options included drugs commonly recommended for drug-resistant TB, including fluoroquinolones (moxifloxacin 400 mg daily or levofloxacin 750 mg daily), linezolid 600 mg daily, or amikacin dosed at 10 mg/kg intramuscularly or intravenously 5 times weekly. The Common Terminology Criteria for Adverse Events (CTCAE) was used to assess drug-associated AEs, with grades 1, 2, and 3 indicating mild, moderate, and severe AEs, respectively; grade 4 indicating life-threatening consequences; and grade 5 indicating death [8].

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San Francisco 5-year review

N=373 (132 > age 65 years)

- 35% (46% > 65 years) developed moderate/severe adverse events
  - PZA: ~20% (~30% > 65 years)
  - Rifamycin: ~13.5% (~17% > 65 years)
  - INH: ~9% (~12% > 65 years)
- 26-30% required first line drug discontinuation, and started a second line drug (FQ or linezolid)
  - FQs associated with AEs in ~40% in all ages
- Adverse event(s) associated with treatment duration up to 3.8 months longer

Recent "Short Course" TB Regimens (Susceptible and MDR) and Adverse Events



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

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ABSTRACT

BACKGROUND

Rifapentine-based regimens have potent antimycobacterial activity that may allow for a shorter course in patients with drug-susceptible pulmonary tuberculosis.

METHODS

In an open-label, phase 3, randomized, controlled trial involving persons with newly diagnosed pulmonary tuberculosis from 13 countries, we compared two 4-month rifapentine-based regimens with a standard 6-month regimen consisting of rifampin, isoniazid, pyrazinamide, and ethambutol (control) using a noninferiority margin of 6.6 percentage points. In one 4-month regimen, rifampin was replaced with rifapentine; in the other, rifampin was replaced with rifapentine and ethambutol with moxifloxacin. The primary efficacy outcome was survival free of tuberculosis at 12 months.

RESULTS

Among 2516 participants who had undergone randomization, 2343 had a culture positive for *Mycobacterium tuberculosis* that was not resistant to isoniazid, rifampin, or fluoroquinolones (microbiologically eligible population; 768 in the control group, 791 in the rifapentine–moxifloxacin group, and 784 in the rifapentine group), of whom 194 were coinfected with human immunodeficiency virus and 1703 had cavitation on chest radiography. A total of 2234 participants could be assessed for the primary outcome (assessable population; 726 in the control group, 756 in the rifapentine–moxifloxacin group, and 752 in the rifapentine group). Rifapentine with moxifloxacin was noninferior to the control in the microbiologically eligible population (15.5% vs. 14.6% had an unfavorable outcome; difference, 1.0 percentage point; 95% confidence interval [CI], −2.6 to 4.5) and in the assessable population (11.6% vs. 9.6%; difference, 2.0 percentage points; 95% CI, −1.1 to 5.1). Noninferiority was shown in the secondary and sensitivity analyses. Rifapentine without moxifloxacin was not shown to be noninferior to the control in either population (17.7% vs. 14.6% with an unfavorable outcome in the microbiologically eligible population; difference, 3.0 percentage points [95% CI, −0.6 to 6.6]; and 14.2% vs. 9.6% in the assessable population; difference, 4.4 percentage points [95% CI, 1.2 to 7.7]). Adverse events of grade 3 or higher occurred during the on-treatment period in 19.3% of participants in the control group, 18.8% in the rifapentine–moxifloxacin group, and 14.3% in the rifapentine group.

CONCLUSIONS

The efficacy of a 4-month rifapentine-based regimen containing moxifloxacin was noninferior to the standard 6-month regimen in the treatment of tuberculosis. (Funded by the Centers for Disease Control and Prevention and others; Study 31/A5349 ClinicalTrials.gov number, NCT02410772.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Nahid at the UCSF Center for Tuberculosis, University of California, San Francisco, 1001 Potrero Ave. 5K1, San Francisco, CA 94110, or at pnahid@ucsf.edu.

Drs. Dorman, Nahid, and Kurbatova contributed equally to this article.

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Why are shorter regimens desired?

- TB treatment takes too long
- Long duration is associated with non-adherence
- Long duration is associated with more adverse events
- Long duration is more resource-intensive (symptom and laboratory monitoring, clinical visits, Directly Observed Therapy)

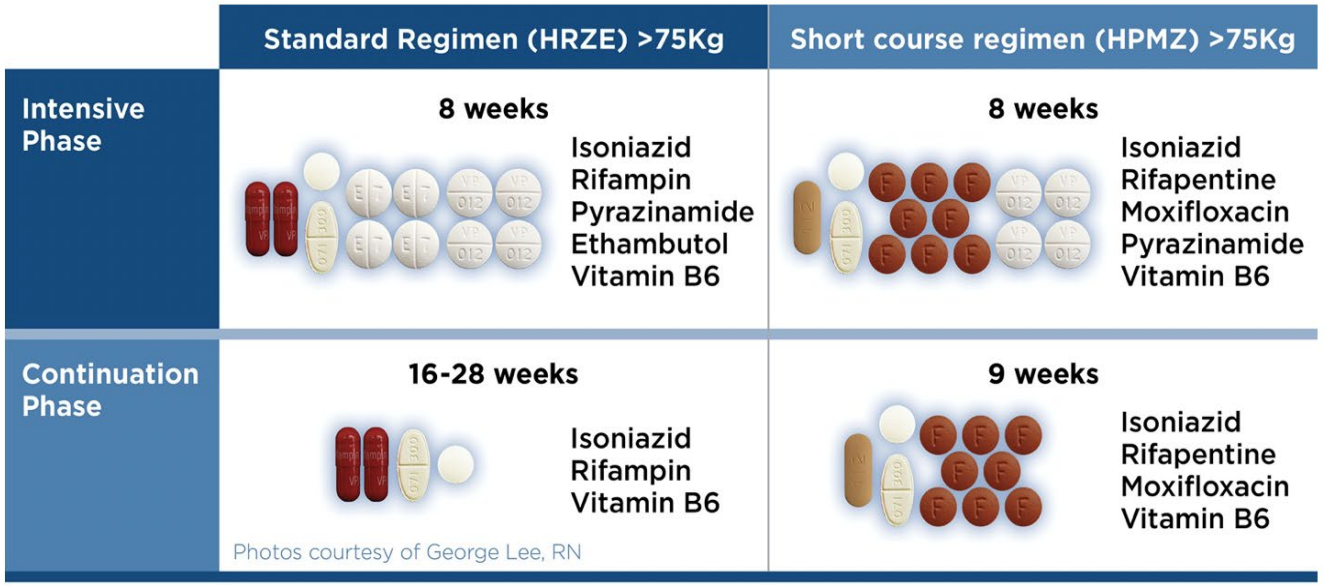
Ideal new regimen

- Potent/bactericidal
- Well-tolerated
- Low pill burden
- Once daily
- Inexpensive
- Already used in other infections with good safety data at established doses

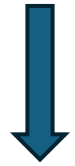
New 4 month TB treatment regimen (HPMZ)

(ATS first-line recommendation for pan-susceptible TB)

Pill burden: HRZE versus HPMZ



- Isoniazid 300 mg daily
- Rifapentine 1200 mg daily
- Moxifloxacin 400 mg daily
- Pyrazinamide (weight based)



- Isoniazid 300 mg daily
- Rifapentine 1200 mg daily
- Moxifloxacin 400 mg daily

RESEARCH SUMMARY

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

Dorman SE et al. DOI: 10.1056/NEJMoa2033400

CLINICAL PROBLEM

The standard treatment of drug-susceptible pulmonary tuberculosis is a 6-month course of a daily rifamycin-based antimicrobial regimen. A more potent regimen with improved rifamycin exposure might shorten treatment duration, potentially improving adherence and reducing adverse effects and costs.

CLINICAL TRIAL

Design: A randomized, open-label, noninferiority trial of two 4-month rifapentine-containing regimens, as compared with a standard 6-month rifampin-containing regimen, for the treatment of drug-susceptible tuberculosis.

Intervention: 2516 participants 12 years of age or older with newly diagnosed tuberculosis were randomly assigned to a 6-month control regimen, a 4-month regimen in which rifampin was replaced with rifapentine (rifapentine group), or a 4-month regimen in which rifampin was replaced with rifapentine and ethambutol with moxifloxacin (rifapentine–moxifloxacin group). The primary efficacy outcome was survival free of tuberculosis at 12 months after randomization, and safety was assessed through day 14 after the last dose of a trial drug.

RESULTS

Efficacy: The rifapentine–moxifloxacin regimen, but not the rifapentine regimen, was shown to be noninferior to the control regimen.

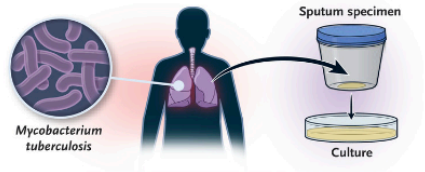
Safety: The percentages of patients who had adverse events of grade 3 or higher or who discontinued the assigned regimen prematurely did not differ significantly between the rifapentine–moxifloxacin group and the control group but were lower in the rifapentine group than in the control group.

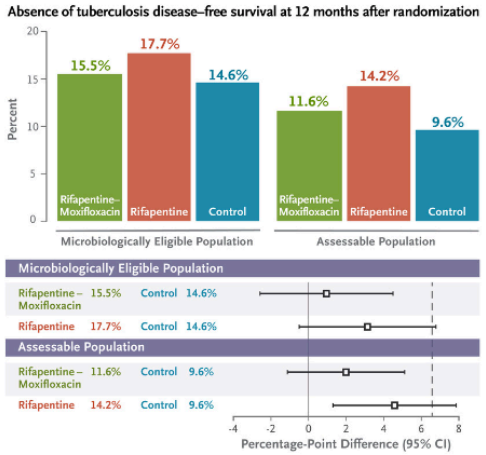
LIMITATIONS AND REMAINING QUESTIONS

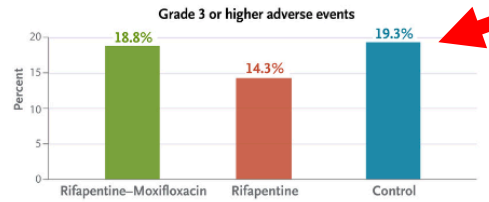
Further study is required to understand the following:

- How the trial regimens perform in HIV-coinfected patients
- Whether the shorter treatment duration offsets the likely higher cost of the rifapentine–moxifloxacin regimen

Links: Full article | NEJM Quick Take | Editorial







CONCLUSIONS

A 4-month regimen containing rifapentine and moxifloxacin was noninferior in efficacy and similar in safety and premature discontinuation to a standard 6-month antimicrobial regimen for the treatment of tuberculosis.

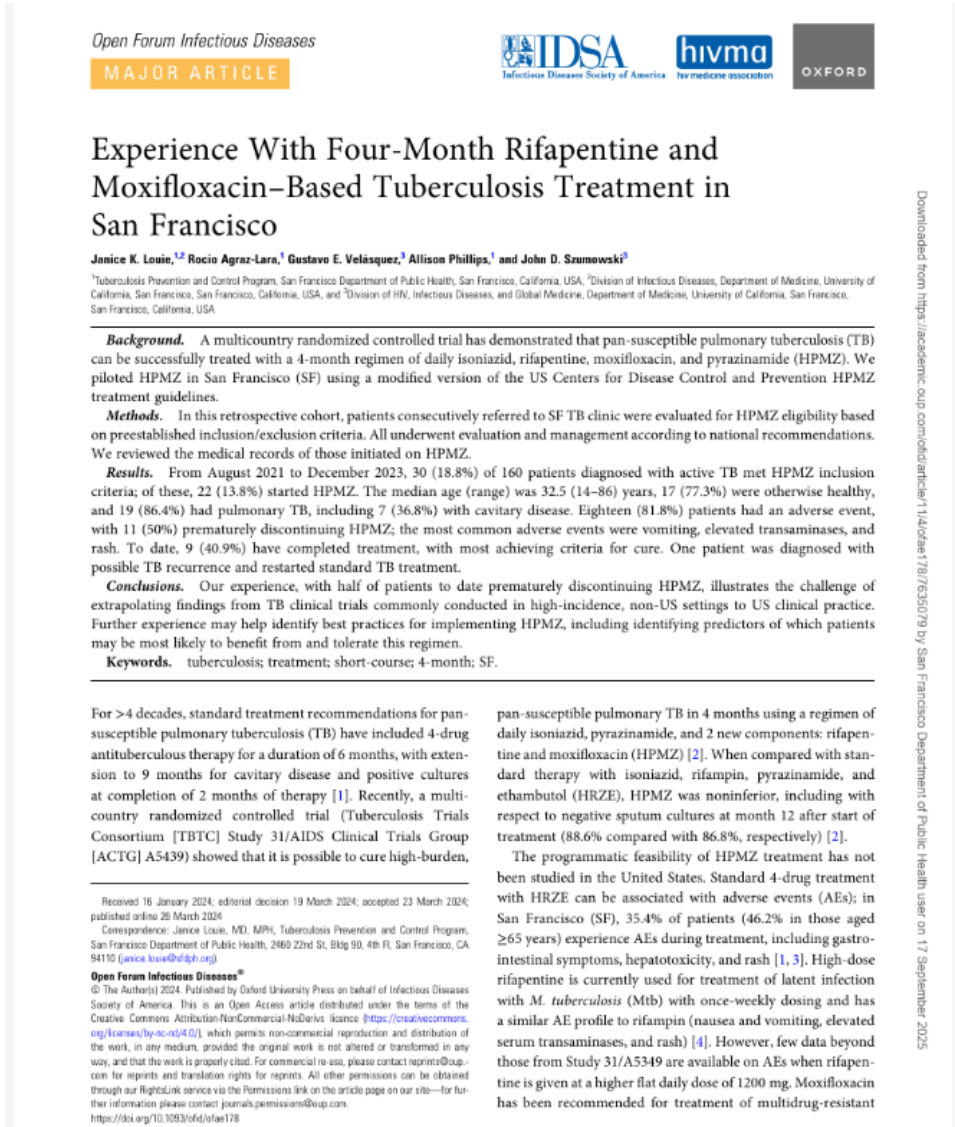
HPMZ 4-month regimen

(1% of participants recruited in US)

Findings:

- Efficacy: HPMZ 4-month regimen non-inferior to 6-9 months of HRZE
- Safety: HPMZ participants- 18.8% had severe adverse events compared to 19.3% for HRZE (?high by US standards)

Dorman et al, Four month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis. N Engl J Med 2021; 384:1705-1718



Open Forum Infectious Diseases

MAJOR ARTICLE

Experience With Four-Month Rifapentine and Moxifloxacin–Based Tuberculosis Treatment in San Francisco

Janice K. Louie,[1,2] Rocio Agraz-Lara,[1] Gustavo E. Velásquez,[3] Allison Phillips,[1] and John D. Szumowski[3]

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Background. A multicountry randomized controlled trial has demonstrated that pan-susceptible pulmonary tuberculosis (TB) can be successfully treated with a 4-month regimen of daily isoniazid, rifapentine, moxifloxacin, and pyrazinamide (HPMZ). We piloted HPMZ in San Francisco (SF) using a modified version of the US Centers for Disease Control and Prevention HPMZ treatment guidelines.

Methods. In this retrospective cohort, patients consecutively referred to SF TB clinic were evaluated for HPMZ eligibility based on preestablished inclusion/exclusion criteria. All underwent evaluation and management according to national recommendations. We reviewed the medical records of those initiated on HPMZ.

Results. From August 2021 to December 2023, 30 (18.8%) of 160 patients diagnosed with active TB met HPMZ inclusion criteria; of these, 22 (13.8%) started HPMZ. The median age (range) was 32.5 (14–86) years, 17 (77.3%) were otherwise healthy, and 19 (86.4%) had pulmonary TB, including 7 (36.8%) with cavitary disease. Eighteen (81.8%) patients had an adverse event, with 11 (50%) prematurely discontinuing HPMZ; the most common adverse events were vomiting, elevated transaminases, and rash. To date, 9 (40.9%) have completed treatment, with most achieving criteria for cure. One patient was diagnosed with possible TB recurrence and restarted standard TB treatment.

Conclusions. Our experience, with half of patients to date prematurely discontinuing HPMZ, illustrates the challenge of extrapolating findings from TB clinical trials commonly conducted in high-incidence, non-US settings to US clinical practice. Further experience may help identify best practices for implementing HPMZ, including identifying predictors of which patients may be most likely to benefit from and tolerate this regimen.

Keywords. tuberculosis; treatment; short-course; 4-month; SF.

For >4 decades, standard treatment recommendations for pan-susceptible pulmonary tuberculosis (TB) have included 4-drug antituberculous therapy for a duration of 6 months, with extension to 9 months for cavitary disease and positive cultures at completion of 2 months of therapy [1]. Recently, a multicountry randomized controlled trial (Tuberculosis Trials Consortium [TBTC] Study 31/AIDS Clinical Trials Group [ACTG] A5439) showed that it is possible to cure high-burden, pan-susceptible pulmonary TB in 4 months using a regimen of daily isoniazid, pyrazinamide, and 2 new components: rifapentine and moxifloxacin (HPMZ) [2]. When compared with standard therapy with isoniazid, rifampin, pyrazinamide, and ethambutol (HRZE), HPMZ was noninferior, including with respect to negative sputum cultures at month 12 after start of treatment (88.6% compared with 86.8%, respectively) [2].

The programmatic feasibility of HPMZ treatment has not been studied in the United States. Standard 4-drug treatment with HRZE can be associated with adverse events (AEs); in San Francisco (SF), 35.4% of patients (46.2% in those aged ≥65 years) experience AEs during treatment, including gastrointestinal symptoms, hepatotoxicity, and rash [1, 3]. High-dose rifapentine is currently used for treatment of latent infection with *M. tuberculosis* (Mtb) with once-weekly dosing and has a similar AE profile to rifampin (nausea and vomiting, elevated serum transaminases, and rash) [4]. However, few data beyond those from Study 31/A5349 are available on AEs when rifapentine is given at a higher flat daily dose of 1200 mg. Moxifloxacin has been recommended for treatment of multidrug-resistant

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- In San Francisco over a 2-year period, of 160 patients treated for active TB, 30 (18.8%) met inclusion criteria for HPMZ
- 22 (13.8%) started HPMZ
  - Median age 32.5 years (range 14-86 years)
  - 78% otherwise healthy
  - 86% with pulmonary TB (seven cavitary)

Louie JK, Agraz-Lara R, Velásquez G, Phillips P, Szumowski JD. Experience With Four-Month Rifapentine and Moxifloxacin–Based Tuberculosis Treatment in San Francisco, *Open Forum Infectious Diseases*, Volume 11, Issue 4, April 2024, ofae178

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Table 2. HPMZ Treatment Outcomes in San Francisco, August 1, 2021–December 31, 2023

	Total
No. patients started on active TB treatment	160
No. patients offered HPMZ based on inclusion/exclusion criteria	30 (18.8)[a]
No. patients started on HPMZ	22 (13.8)[b]
Median age (range), y	32.5 (14–86)
Male	11/22 (50)
Comorbid illness[c]	
Previous healthy	17/22 (77.3)
Diabetes mellitus	3/22 (13.6)
Chronic liver disease	2/22 (9.1)
Alcohol use disorder	2/22 (9.1)
Chronic lung disease	1/22 (4.5)
TB disease site[d,e]	
Pulmonary	19/22 (86.4)
Unilobar disease	10/19 (52.6)
Multilobar/bilateral disease	9/19 (47.4)
Cavitary	7/19 (36.8)
Pleural only	1/22 (4.5)
Lymph node	2/22 (9.1)
Microbiology, pulmonary disease site	
Acid-fast bacilli smear–positive	12/19 (63.2)
Xpert MTB/RIF–positive	13/19 68.4)
Culture-positive	15/19 (78.9)
Adverse events	
Any adverse event	18/22 (81.8)
Mild (CTCAE grade 1)[f]	7/22 (38.9)
Gastrointestinal (nausea and/or vomiting)	4/22 (18.2)
Rash	2/22 (9.0)
Myalgias	1/22 (4.5)
Moderate (CTCAE grade 2)[f]	10/22 (45.5)
Gastrointestinal (nausea and/or vomiting)	5/22 (22.7)
Nausea and/or vomiting with liver function test values >3× upper limit of normal	2/22 (9.1)
Dermatologic	2/22(9.1)
Dizziness, flushing, palpitations, anxiety	1/22 (4.5)
Severe (CTCAE grade 3)[f]	1/22 (4.5)
Syncope, weakness, nausea, electrolyte abnormality	1/22 (4.5)
HPMZ treatment discontinued due to adverse event(s)	11/22 (50.0)
Median time to first adverse event occurrence (range), d	4.3 (1–63)
Median time to HPMZ cessation (range), d	10.5 (3–70)
Cases who completed HPMZ treatment	9/22 (40.9)
Median time to HPMZ treatment completion (range), d	126 (120–198)

Results

- 81.8% had an adverse event
  - Nausea/vomiting: 9/22 (40.9%)
  - Rash: 4/22 (18%)
  - Transaminitis: 2/22 (11%)
- 11 (50%) stopped due to AE
- No known microbiologic failures or relapses

Louie JK, Agraz-Lara R, Velásquez G, Phillips P, Szumowski JD. Experience With Four-Month Rifapentine and Moxifloxacin–Based Tuberculosis Treatment in San Francisco, *Open Forum Infectious Diseases*, Volume 11, Issue 4, April 2024, ofae178

Additional unpublished data (Jan 2024-Dec 2025)

An additional 20 patients started on HPMZ since Jan 2024

- Median age 38.5 (range 14-64 years)
- 55% otherwise healthy
- 13 (65%) with adverse events; seven (54%) with nausea/vomiting, five provided with Zofran daily 30 minutes pre-dose with improvement
- 9 completed HPMZ treatment (50%)

Similar experience in NYC

Challenges to initiate and complete a 4-month rifapentine-moxifloxacin TB treatment regimen

M.E. Galvis[1], G.E. Gao[2], M.M. Salerno[2], M. Whitehead[3], D. Juste[2], C. Buchanan[3], C. Chuck[2], F. Iskhakova[3], M. Macaraig[2], F. Dworkin[3], J. Burzynski[2], D. Nilsen[2]

[1]Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, USA;

[2]Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, Long Island City, NY, USA;

[3]Bureau of Public Health Clinics, New York City Department of Health and Mental Hygiene, Long Island City, NY, USA.

NYC Health Department

April 2022- Dec 2023

- N=617; 46% ineligible
- 36 (5.8%) initiated on HPMZ
- 13 (36%) completed HPMZ treatment
- 23 (64%) discontinued, including 15 (41.7%) due to adverse events
  - 47% with nausea

Galvis ME, Gao GE, Salerno MM, Whitehead M, Juste D, Buchanan C, Chuck C, Iskhakova F, Macaraig M, Dworkin F, Burzynski J, Nilsen D. Challenges to initiate and complete a 4-month rifapentine-moxifloxacin TB treatment regimen. Int J Tuberc Lung Dis. 2025 Jun 27;29(7):318-324.

HPMZ does not meet most criteria for an ideal new regimen

- Potent/bactericidal- yes
- Once daily- yes
- Low pill burden- no (15→ 11 pills)
- Inexpensive- no
- Already used in other infections with good safety data at established doses- no
- Well-tolerated- no
  - **Nausea is the most common adverse event with HPMZ**

GI Side Effects – Patient Perspectives

- “Sometimes on a bad day, I got frustrated because I felt like my medication was not working anyways, so then I did not want the stomach side effects as well if I take it.”
- ”The nausea is worse than actually vomiting.”
- “I literally lost hope … I was throwing up every day multiple times a day, extreme nausea from the moment I wake up…”
- “I’ve been taking Isoniazid for two months now … all of a sudden I’m having stomach pains so bad I want to die.”