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12-Dose Once-Weekly Isoniazid and Rifapentine for Treatment of Latent *Mycobacterium tuberculosis* Infection

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Abstract

Latent tuberculosis infection influences a quarter (1.7 billion people) of the world's population and is a critical driver of the broad global burden of active tuberculosis in all settings. When left untreated, 5%–15% of patients with latent tuberculosis infection will eventually advance active tuberculosis, with the pitfall of progression being highest during the first two years following primary infection. The choice between the 12-dose once-weekly regimen and distinctive confirmed latent tuberculosis infection management regimens based on various factors, involving the feasibility of directly observed therapy, resources for medicine procurement and patient monitoring, medical and social situations of the patient that perhaps influences management completion and, preferences of the patient and the prescribing physician. Individuals who wish to avoid pregnancy should know that rifapentine (like distinctive rifamycin) reduces the effectiveness of hormonal contraceptives. These individuals should thought-out using a different, or additional, form of contraception when receiving rifapentine-based tuberculosis preventive therapy. A short-course regimen named 3HP, constituting once-weekly high-dose rifapentine (RPT) plus isoniazid (INH) for a total 12 doses, is recently gaining popularity for latent tuberculosis infection treatment because its completion rate approaches 90% and it is as effective as and less hepatotoxic (0%–1.5% vs 1.2%–5.3%) than 9-month daily INH (9H).

Keywords: Isoniazid; Latent tuberculosis; Rifapentine; Treatment

Introduction

Latent tuberculosis infection (LTBI) is described by an infection with *Mycobacterium tuberculosis* without any diagnosable symptoms, radiological, or microbiological confirmation of active disease [1]. On the other hand, the spectrum of latent tuberculosis infection is active disease, often typically described by reclamation and outgrowth of *Mycobacterium tuberculosis* in culture from the influenced individual [2, 3]. From a public health point of view, tuberculosis is as much a reflection of meager social circumstances as it is a biomedical situation. Those who are poorest are at highest peril of both exposures to *Mycobacterium tuberculosis*, and progression from latent infection to active disease [4]. The WHO estimates that 23% of the world's population has LTBI and is at risk of developing active disease [5]. LTBI treatment has evolved over decades. Currently, novel rifapentine-based regimens have observed efficacy in suppressing tuberculosis disease with much shorter management durations. In addition, these regimens have revealed

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equal or better safety profiles and higher patient compliance [6]. The aim of LTBI management is to decrease the pitfall of reactivation. Management with isoniazid (INH) is the traditional standard and regimens of six and nine months of INH have been recommended. However, the prolonged course of management necessitated with INH has led to advancement of various optional rifamycin-based regimens. The World Health Organization recently recommends the following regimens as alternatives for LTBI treatment: six months of daily INH (INH-6), nine months of daily INH (INH-9), INH and rifapentine once weekly for twelve weeks (INH/RPT-3), three to four months daily INH plus rifampin (INH/RFMP 3–4), and three to four months daily rifampin alone (RFMP 3–4). INH/RPT-3 is a relatively fresh regimen, the simplicity and short duration of which offer considerable appeal. The prevention of TB trial, a wide randomized controlled trial (RCT) of INH/RPT-3, currently reported non-inferiority to the standard LTBI management regimen of INH-9 [7-9]. Management of LTBI in people at more pitfalls for development to active TB is a chief technique for controlling and excluding TB. For individuals with LTBI, isoniazid (INH) treatment for six to twelve months has been observed to decrease the pitfall for development to active TB disease by 60%–90%]10, 11]. However, because of the INH regimen's long management duration, dearth of patient tolerability and pitfall for hepatotoxicity, its effectiveness in suppressing TB disease has been blocked by insufficient acceptance and low management completion rates [12]. Latent tuberculosis infection (LTBI) is an asymptomatic immunological state of heightened subsequent pitfall of active tuberculosis (TB). Approximately $1/_4$ of the global population is estimated to have LTBI [13]. Hence, to achieve the aims of the End TB strategy by 2035, management for LTBI is respected as an irreplaceable constituent of public health policy [14, 15]. A short-course regimen named 3HP, constituting once-weekly high-dose rifapentine (RPT) plus isoniazid (INH) for a total 12 doses, is recently obtaining popularity for LTBI management because its completion rate approaches 90% and it is as effective as and less hepatotoxic (0%–1.5% vs 1.2%–5.3%) than 9-month daily INH (9H). However, approximately half of subjects taking 3HP experience adverse drug reactions; delineated as any unintended, detrimental events attributed to the regular usage of study medications [16, 17]. The choice between the 12-dose once-weekly regimen and distinctive confirmed LTBI management regimens based on various factors, involving the feasibility of DOT, resources for medicine procurement and patient monitoring, medical and social situations of the patient that perhaps influence management completion and, preferences of the patient and the prescribing physician. When choosing a regimen for LTBI, thought-out possible important rifampin-associated medicine interactions involving, but not restrained to hormonal contraceptives, antiretrovirals, and anticoagulants. Usage of a non-hormonal birth-control technique is recommended when rifampin or rifapentine is administered to a sexually active female. Recently, a three month once-weekly regimen with rifapentine plus isoniazid (3HP, both with a maximum dose of 900 mg) is the shortest regimen recommended by the WHO [18, 19]. A current-completed large-scale clinical trial of isoniazid plus rifapentine given weekly for 3 months (the inhibit TB study) resulted the efficacy of this shorter regimen to be non-inferior to isoniazid monotherapy but with much better completion rates [20]. However, in this survey directly-observed therapy (DOT) was used to ameliorate adherence, greatly accelerating the regimen's cost [21, 22]. CDC continues to recommend 3HP for management of LTBI in adults and nowadays recommends usage of 3HP 1) in persons with LTBI aged 2–17 years; 2) in persons with LTBI who have HIV infection, involving acquired immunodeficiency syndrome (AIDS), and are receiving antiretroviral drugs with acceptable drug-drug interactions with rifapentine; and 3) by DOT or self-administered therapy (SAT) in persons aged ≥2 years [23, 24]. The 12-dose regimen is not recommended for: children younger than two years of age; people with HIV/AIDS who are receiving antiretroviral treatment [25]; people who are known or familiarized to have been infected with INH or rifampin (RIF) resistant M. tuberculosis; pregnant women, including adolescents, or women anticipating to become pregnant while taking this regimen. Rifapentine differs structurally from rifampin, having a cyclopentyl ring as a side chain

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instead of a methyl group. This structural change affects the PK of rifapentine significantly. It has highly protein binding (around 99%), and because of that protein binding, a longer elimination half-life analogized to rifampin. Rifapentine was confirmed by the FDA in 1998. Because of its long elimination $t1/_2$, it can be dosed once weekly along with isoniazid (INH) in the management of latent TB. An ultrashort course regimen of four weeks of daily rifapentine plus INH is now being evaluated for management of LTBI [26, 27]. Like distinctive rifamycin, rifapentine also has the implicit to antecedent of adverse events, involving hepatotoxicity [28]. People living with HIV V in areas where malaria or solemn bacterial infections are frequent should take 3HP together with trimethoprim and sulfamethoxazole to prevent severe bacterial infections such as pneumonia or toxoplasmosis.

Pathophysiology

Mechanism of action: Like distinctive rifamycin, rifapentine suppresses bacterial DNA-dependent RNA polymerase. Rifamycin are unique among medicines that function by this mechanism, because the suppression of RNA polymerase will happen even when enzyme exposure to the medicine is very brief in otherwise metabolically dormant organisms; this has implications for the usage of these medicines for treatment of LTBI [29].

Pharmacokinetics: After oral administration, rifapentine is highly absorbed from the GIT, reaching peak serum concentrations in five to six hours. The absolute bioavailability of rifapentine is not known, but the relative bioavailability of 600 mg in patients with TB compared to healthy adults was found to be ~70%. Rifapentine is 97–99% protein bound, mainly to albumin. The volume of distribution of rifapentine in adults ranges from 70.2 ± 9.1 L and 1.4 ± 0.81 L/kg in children [30]. The mean rifapentine elimination $t1/_2$ ranges from 13.2 to 14.1 hours. The active metabolite reaches peak concentration in 14.4–17.8 hours, and the mean elimination $t1/_2$ is 13.3–24.3 hours. The effect of food, however, significantly affects rifapentine's bioavailability, as demonstrated in several studies [31]. Keung demonstrated that fat elevated rifapentine bioavailability by fifty one percent when used as single doses in patients who were infected with HIV [32]. Zvada et al.revealed that meal type impacted absorption; fat rich meals escalated the oral bioavailability of rifapentine by eight six percent, bulk meager-fat meals by thirty three percent, and bulk fat rich meal by forty six percent, and high-fluid, low-fat meal by 49% [33]. The consequences of high-fat food, accelerating the bioavailability of rifapentine, were attested in subsequent studies. This is of course quite distinctive from rifampin, whose bioavailability is highest in a fasting state [34]. Rifapentine is metabolized by arylacetamide deacetylase. The medication is metabolized consummately by the liver and is excreted substantially (70%) in feces. The medicine is metabolized by hydrolysis and deacetylation to 25-O-desacetyl rifapentine, which is microbiologically active, rendering 38% of the drug's overall activity [35]. Clearance of rifapentine increases with increasing duration of drug exposure. In a single-dose pk survey including patients with several levels of hepatic dysfunction, rifapentine was well tolerated, regardless of the aetiology or severity of hepatic dysfunction. Patients with hepatic and/or renal impairment should be monitored closely when receiving rifapentine. Because the medicine and its metabolite are highly protein bound (98%), hemodialysis would not be anticipated to accelerate their elimination [36, 37].

Drug interactions: Isoniazid may interact with foods containing tyramine/histamine (such as cheese, red wine, certain types of fish). This interaction may cause increased blood pressure, flushing of the skin, headache, dizziness, or fast/pounding heartbeat. Individuals who wish to avoid pregnancy should know that rifapentine (like distinctive rifamycin) reduces the effectiveness of hormonal contraceptives. These individuals should thought-out using a distinctive, or additional, form of contraception when receiving rifapentine-based TPT. Rifapentine induces cytochrome P450 enzymes and can also accelerate the metabolism of certain drugs, such as birth control pills and antiretroviral drugs, methadone, warfarin, b-blockers, benzodiazepines, and oral anticoagulants [38, 39]. While daily rifapentine

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decreases the concentrations of moxifloxacin, a medicine metabolized by phase II enzymes, importantly, thrice-weekly rifapentine lowers moxifloxacin exposures solely modestly, and once-weekly rifapentine has a negligible effect on moxifloxacin exposures. Rifapentine decreases the trough concentrations of raltegravir, a medicine metabolized by UGT1A1, by about 41% with daily dosing, but this decrement is not considered to be clinically significant. Interestingly, a survey that evaluated the outcome of rifapentine and rifampin on the concentration of bedaquline revealed that rifapentine 600 mg daily found in 3.96-fold elevate in the clearance of bedaquiline [40].

Safety profile of 3HP in children and young people: 3HP can be used by adolescents and children as young as 2 years of age. The medicine has not yet been surveyed in children under 2 years; however, a study looking at safety and optimal dosing of 3HP in this age group will commenced in 2019. The survey is using a child-friendly formulation of 3HP advanced by Sanofi that dissolves in water and tastes like mango. While waiting for the sequences of this survey, infants and children under 2 years who need TPT can take either 3HR or 6 months of isoniazid (6H). 6H is selected for children with HIV receiving nevirapine, lopinavir-ritonavir, or dolutegravir because it does not necessitate ARV dose adjustments [41, 42].

Safety profile of 3HP in pregnant women: Pregnancy elevates the pitfall of TB infection progressing to active TB disease. Rifapentine is recently not recommended for use in individuals who are pregnant. This is owing to a dearth of data on the safety of giving rifapentine during pregnancy. The WHO recommends that pregnant women with HIV take IPT, although the solely clinical trial of IPT in this population found more adverse pregnancy consequences among women who took IPT during pregnancy analogized with those who did so after delivery. Anyone who takes IPT during pregnancy or in the postpartum period should be closely monitored, particularly since the peril of hepatotoxicity is increased during pregnancy and pursuing birth. Rifampicin is also secure in pregnancy, and certain clinicians select to use rifampicin-based TPT (e.g., 4R). Which TPT regimen to receive, and when to launch management, should be decisions made together by pregnant individuals and their health care givers after openly weighing all the perils and potential merits [43-45].

Safety of 3HP in patients treated for hepatitis C virus: Rifamycin, involving rifapentine, are not preferred to use together with variety of the direct-acting antiretroviral drugs used to manage hepatitis C virus. This is because rifamycin can decline the concentration of hepatitis C medications to subtherapeutic levels [46].

Safety of 3HP in patients living with HIV: Rifapentine is safe to use in patients living with human immunodeficiency virus, but interactions between rifapentine and certain antiretrovirals must be managed. 3HP is safe to use with efavirenz- and raltegravir-based ART. A current study explained the safety and pharmacokinetics of giving 3HP with dolutegravir. Importantly, patients living with human immunodeficiency virus in areas where malaria or severe bacterial infections are common should take 3HP together with cotrimoxazole [47].

Adverse drug reactions: Rifapentine-based tuberculosis preventive therapy is safe and well tolerated. 3HP cause pitfall of hematologic toxicity than isoniazid preventive therapy and 3HP seems to pose least pitfall of hepatotoxicity than isoniazid preventive therapy. Rare adverse events called hypersensitivity reactions which characterized by flu-like symptoms (fever, chills, headaches, dizziness, and fatigue), systemic drug reactions, gastrointestinal problems, skin rash, neutropenia and elevation of liver enzymes, orange-red discoloration of body fluids, hypotension or syncope after taking 3HP [48, 49].

Conclusion

Treatment of LTBI in people at great pitfall for development to active TB is a chief technique for controlling and removing TB. The intention of LTBI management is to decrease the peril of reactivation. The WHO recently recommends the following regimens as alternatives for LTBI management: six months of daily INH (INH-6), nine months of daily INH (INH-9), INH

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and rifapentine once weekly for twelve weeks (INH/RPT-3), 3–4 months daily INH plus rifampin (INH/RFMP 3–4), and 3–4 months daily rifampin alone (RFMP 3–4). Rifapentine induces cytochrome P450 enzymes and can also accelerate the metabolism of certain drugs, such as birth control pills and antiretroviral drugs, methadone, warfarin, b-blockers, benzodiazepines, and oral anticoagulants. Rifapentine-based tuberculosis preventive therapy is secure and well tolerated. 3HP cause pitfall of hematologic toxicity than isoniazid preventive therapy and 3HP seems to pose least pitfall of hepatotoxicity than isoniazid preventive therapy.

Abbreviations

CDC: Communicable disease center; INH: Isoniazid; RPT: Rifapentine; LTBI: Latent TB Infection; M. TB: *Mycobacterium tuberculosis*; IPT: Isoniazid Preventive Therapy; ARVs: Antiretrovirals; MIC: Minimum Inhibitory Concentration; DOT: Directly Observed Therapy; TB: Tuberculosis; INH-RPT: Isoniazid with SAT: Self-administered therapy; Rifapentine; 3HP: Isoniazid and Rifapentine; 3RH: Rifampicin and Isoniazid; RIF: Rifampicin; TPT: Tuberculosis Preventive Therapy.

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References

1. Heyd A, Heffernan C, Storey K, Wild TC, Long R. Treating latent tuberculosis infection (LTBI) with isoniazid and rifapentine (3HP) in an inner-city population with psychosocial barriers to treatment adherence: A qualitative descriptive study. PLOS Global Public Health. 2021 Dec 8;1(12): e0000017.

2. Bereda G. Three Months of Rifapentine Plus Isoniazid to Prevent Human Immuno Deficiency Virus Related Tuberculosis. Journal of HIV & Retro Virus. 2021;7(3):0-.

3. Hibma JE, Radtke KK, Dorman SE, Jindani A, Dooley KE, Weiner M, McIlleron HM, Savic RM. Rifapentine population pharmacokinetics and dosing recommendations for latent tuberculosis infection. American journal of respiratory and critical care medicine. 2020 Sep 15;202(6):866-77.

4. Pease C, Hutton B, Yazdi F, Wolfe D, Hamel C, Quach P, Skidmore B, Moher D, Alvarez GG. Efficacy and completion rates of rifapentine and isoniazid (3HP) compared to other treatment regimens for latent tuberculosis infection: a systematic review with network meta-analyses. BMC Infectious Diseases. 2017 Dec;17(1):1-1.

5. Sterling TR, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, Hackman J, Hamilton CD, Menzies D, Kerrigan A, Weis SE. Three months of rifapentine and isoniazid for latent tuberculosis infection. New England Journal of Medicine. 2011 Dec 8;365(23):2155-66.

6. Njie GJ, Morris SB, Woodruff RY, Moro RN, Vernon AA, Borisov AS. Isoniazid-rifapentine for latent tuberculosis infection: a systematic review and meta-analysis. American journal of preventive medicine. 2018 Aug 1;55(2):244-52.

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Molecular Biology and Drug Design

Review Article Open Access

7. Huang HL, Lee MR, Cheng MH, Lu PL, Huang CK, Sheu CC, Lai PC, Chen TC, Wang JY, Chong IW. Impact of age on outcome of rifapentine-based weekly therapy for latent tuberculosis infection. Clinical Infectious Diseases. 2021 Sep 1;73(5): e1064-71.

8. Houben RM, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. PLoS medicine. 2016 Oct 25;13(10): e1002152.

9. Sun HY, Huang YW, Huang WC, Chang LY, Chan PC, Chuang YC, Ruan SY, Wang JY, Wang JT. Twelve-dose weekly rifapentine plus isoniazid for latent tuberculosis infection: A multicentre randomised controlled trial in Taiwan. Tuberculosis. 2018 Jul 1; 111:121-6.

10. Simkins J, Abbo LM, Camargo JF, Rosa R, Morris MI. Twelve-week rifapentine plus isoniazid versus 9-month isoniazid for the treatment of latent tuberculosis in renal transplant candidates. Transplantation. 2017 Jun 1;101(6):1468-72.

11. Sterling TR, Moro RN, Borisov AS, Phillips E, Shepherd G, Adkinson NF, Weis S, Ho C, Villarino ME. Tuberculosis Trials Consortium Flu-like and other systemic drug reactions among persons receiving weekly rifapentine plus isoniazid or daily isoniazid for treatment of latent tuberculosis infection in the PREVENT Tuberculosis study. Clin Infect Dis. 2015;61(4):527-35.

12. Coleman JJ, Pontefract SK. Adverse drug reactions. Clinical Medicine. 2016 Oct;16(5):481.

13. Gao L, Zhang H, Xin H, Liu J, Pan S, Li X, Guan L, Shen F, Liu Z, Wang D, Guan X. Short-course regimens of rifapentine plus isoniazid to treat latent tuberculosis infection in older Chinese patients: a randomised controlled study. European Respiratory Journal. 2018 Dec 1;52(6).

14. https://clinicaltrials.gov/ct2/show/NCT01404312

15. Holland DP, Sanders GD, Hamilton CD, Stout JE. Potential economic viability of two proposed rifapentine-based regimens for treatment of latent tuberculosis infection. PloS one. 2011 Jul 18;6(7): e22276.

16. Mullie GA, Schwartzman K, Zwerling A, N'Diaye DS. Revisiting annual screening for latent tuberculosis infection in healthcare workers: a cost-effectiveness analysis. BMC medicine. 2017 Dec;15(1):1-5.

17. Borisov AS, Morris SB, Njie GJ, Winston CA, Burton D, Goldberg S, Woodruff RY, Allen L, LoBue P, Vernon A. Update of recommendations for use of once-weekly isoniazid-rifapentine regimen to treat latent Mycobacterium tuberculosis infection. Morbidity and Mortality Weekly Report. 2018 Jun 29;67(25):723.

18. Sandul AL, Nwana N, Holcombe JM, Lobato MN, Marks S, Webb R, Wang SH, Stewart B, Griffin P, Hunt G, Shah N. High rate of treatment completion in program settings with 12-dose weekly isoniazid and rifapentine for latent Mycobacterium tuberculosis infection. Clinical Infectious Diseases. 2017 Oct 1;65(7):1085-93.

19. Alfarisi O, Alghamdi WA, Al-Shaer MH, Dooley KE, Peloquin CA. Rifampin vs. rifapentine: what is the preferred rifamycin for tuberculosis? Expert Review of Clinical Pharmacology. 2017 Oct 3;10(10):1027-36.

20. Jereb JA, Goldberg SV, Powell K, Villarino ME, Lobue P. Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent Mycobacterium tuberculosis infection.

21. Villarino ME, Scott NA, Weis SE, Weiner M, Conde MB, Jones B, Nachman S, Oliveira R, Moro RN, Shang N, Goldberg SV. Treatment for preventing tuberculosis in children and adolescents: a randomized clinical trial of a 3-month, 12-dose regimen of a combination of rifapentine and isoniazid. JAMA pediatrics. 2015 Mar 1;169(3):247-55.

Journal of
Molecular Biology and Drug Design

Review Article Open Access

22. Belknap R, Holland D, Feng PJ, Millet JP, Caylà JA, Martinson NA, Wright A, Chen MP, Moro RN, Scott NA, Arevalo B. Self-administered versus directly observed once-weekly isoniazid and rifapentine treatment of latent tuberculosis infection: a randomized trial. Annals of internal medicine. 2017 Nov 21;167(10):689-97.

23. Denholm JT, McBryde ES, Eisen D, Street A, Matchett E, Chen C, Shultz T, Biggs B, Leder K. SIRCLE: a randomised controlled cost comparison of self-administered short-course isoniazid and rifapentine for cost-effective latent tuberculosis eradication. Internal Medicine Journal. 2017 Dec;47(12):1433-6.

24. M McClintock AH, Eastment M, McKinney CM, Pitney CL, Narita M, Park DR, Dhanireddy S, Molnar A. Treatment completion for latent tuberculosis infection: a retrospective cohort study comparing 9 months of isoniazid, 4 months of rifampin and 3 months of isoniazid and rifapentine. BMC infectious diseases. 2017 Dec;17(1):1-8.

25. Tasillo A, Salomon JA, Trikalinos TA, Horsburgh CR, Marks SM, Linas BP. Cost-effectiveness of testing and treatment for latent tuberculosis infection in residents born outside the United States with and without medical comorbidities in a simulation model. JAMA internal medicine. 2017 Dec 1;177(12):1755-64.

26. Savic RM, Weiner M, MacKenzie WR, Engle M, Whitworth WC, Johnson JL, Nsubuga P, Nahid P, Nguyen NV, Peloquin CA, Dooley KE. Defining the optimal dose of rifapentine for pulmonary tuberculosis: exposure–response relations from two phase II clinical trials. Clinical Pharmacology & Therapeutics. 2017 Aug;102(2):321-31.

27. Swindells S, Ramchandani R, Gupta A, Benson CA, Leon-Cruz J, Mwelase N, Jean Juste MA, Lama JR, Valencia J, Omoz-Oarhe A, Supparatpinyo K. One month of rifapentine plus isoniazid to prevent HIV-related tuberculosis. New England Journal of Medicine. 2019 Mar 14;380(11):1001-11.

28. Sun HY, Huang YW, Huang WC, Chang LY, Chan PC, Chuang YC, Ruan SY, Wang JY, Wang JT. Twelve-dose weekly rifapentine plus isoniazid for latent tuberculosis infection: A multicentre randomised controlled trial in Taiwan. Tuberculosis. 2018 Jul 1; 111:121-6.

29. Centers for Disease Control and Prevention. Latent tuberculosis infection: a guide for primary health care providers. Atlanta: Centers for Disease Control and Prevention. 2013:1-40.

30. https://www.croiconference.org/

31. https://extranet.who.int/pqweb/medicines/dossier-status

32. World Health Organization. Latent TB infection: updated and consolidated guidelines for programmatic management. Geneva, Switzerland: World Health Organization; 2018.

33. Swindells S, Ramchandani R, Gupta A, Benson CA, Leon-Cruz J, Mwelase N, Jean Juste MA, Lama JR, Valencia J, Omoz-Oarhe A, Supparatpinyo K. One month of rifapentine plus isoniazid to prevent HIV-related tuberculosis. New England Journal of Medicine. 2019 Mar 14;380(11):1001-11.

34. Savic RM, Weiner M, MacKenzie WR, Engle M, Whitworth WC, Johnson JL, Nsubuga P, Nahid P, Nguyen NV, Peloquin CA, Dooley KE. Defining the optimal dose of rifapentine for pulmonary tuberculosis: exposure–response relations from two phase II clinical trials. Clinical Pharmacology & Therapeutics. 2017 Aug;102(2):321-31.

35. Francis J, Zvada SP, Denti P, Hatherill M, Charalambous S, Mungofa S, Dawson R, Dorman S, Gupte N, Wiesner L, Jindani A. A population pharmacokinetic analysis shows that arylacetamide deacetylase (AADAC) gene polymorphism and HIV infection affect the exposure of rifapentine. Antimicrobial agents and chemotherapy. 2019 Mar 27;63(4): e01964-18.

Journal of
Molecular Biology and Drug Design

Review Article Open Access

36. Dooley KE, Savic RM, Park JG, Cramer Y, Hafner R, Hogg E, Janik J, Marzinke MA, Patterson K, Benson CA, Hovind L. Novel dosing strategies increase exposures of the potent antituberculosis drug rifapentine but are poorly tolerated in healthy volunteers. Antimicrobial agents and chemotherapy. 2015 Jun 1;59(6):3399-405.

37. Conde MB, Mello FC, Duarte RS, Cavalcante SC, Rolla V, Dalcolmo M, Loredo C, Durovni B, Armstrong DT, Efron A, Barnes GL. A phase 2 randomized trial of a rifapentine plus moxifloxacin-based regimen for treatment of pulmonary tuberculosis. PLoS One. 2016 May 9;11(5): e0154778.

38. Alfarisi O, Alghamdi WA, Al-Shaer MH, Dooley KE, Peloquin CA. Rifampin vs. rifapentine: what is the preferred rifamycin for tuberculosis? Expert Review of Clinical Pharmacology. 2017 Oct 3;10(10):1027-36.

39. Dorman SE, Savic RM, Goldberg S, Stout JE, Schluger N, Muzanyi G, Johnson JL, Nahid P, Hecker EJ, Heilig CM, Bozeman L. Daily rifapentine for treatment of pulmonary tuberculosis. A randomized, dose-ranging trial. American journal of respiratory and critical care medicine. 2015 Feb 1;191(3):333-43.

40. Jeremiah K, Denti P, Chigutsa E, Faurholt-Jepsen D, PrayGod G, Range N, Castel S, Wiesner L, Hagen CM, Christiansen M, Changalucha J. Nutritional supplementation increases rifampin exposure among tuberculosis patients coinfected with HIV. Antimicrobial agents and chemotherapy. 2014 Jun;58(6):3468-74.

41. Gao L, Li X, Liu J, Wang X, Lu W, Bai L, Xin H, Zhang H, Li H, Zhang Z, Ma Y. Incidence of active tuberculosis in individuals with latent tuberculosis infection in rural China: follow-up results of a population-based, multicentre, prospective cohort study. The Lancet Infectious Diseases. 2017 Oct 1;17(10):1053-61.

42. Jiang Q, Lu L, Wu J, Yang C, Prakash R, Zuo T, Liu Q, Hong J, Guo X, Gao Q. Assessment of tuberculosis contact investigation in Shanghai, China: An 8-year cohort study. Tuberculosis. 2018 Jan 1; 108:10-5.

43. LoBue PA, Mermin JH. Latent tuberculosis infection: the final frontier of tuberculosis elimination in the USA. The Lancet Infectious Diseases. 2017 Oct 1;17(10): e327-33.

44. Sun HY, Huang YW, Huang WC, Chang LY, Chan PC, Chuang YC, Ruan SY, Wang JY, Wang JT. Twelve-dose weekly rifapentine plus isoniazid for latent tuberculosis infection: A multicentre randomised controlled trial in Taiwan. Tuberculosis. 2018 Jul 1; 111:121-6.

45. Motta I, Calcagno A, Bonora S. Pharmacokinetics and pharmacogenetics of anti-tubercular drugs: a tool for treatment optimization? Expert opinion on drug metabolism & toxicology. 2018 Jan 2;14(1):59-82.

46. Menzies D, Adjobimey M, Ruslami R, Trajman A, Sow O, Kim H, Obeng Baah J, Marks GB, Long R, Hoeppner V, Elwood K. Four months of rifampin or nine months of isoniazid for latent tuberculosis in adults. New England Journal of Medicine. 2018 Aug 2;379(5):440-53.

47. Jagger A, Reiter-Karam S, Hamada Y et al. National policies on the management of latent tuberculosis infection: review of 98 countries. Bull World Health Organ 2018; 96: 173–84F.

48. Badje A, Moh R, Gabillard D, Guéhi C, Kabran M, Ntakpé JB, Le Carrou J, Kouame GM, Ouattara E, Messou E, Anzian A. Effect of isoniazid preventive therapy on risk of death in west African, HIV-infected adults with high CD4 cell counts: long-term follow-up of the Temprano ANRS 12136 trial. The Lancet global health. 2017 Nov 1;5(11): e1080-9.

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Molecular Biology and Drug Design

Review Article Open Access

49. Sterling TR, Moro RN, Borisov AS, Phillips E, Shepherd G, Adkinson NF, Weis S, Ho C, Villarino ME, Tuberculosis Trials Consortium, Sterling TR. Flu-like and other systemic drug reactions among persons receiving weekly rifapentine plus isoniazid or daily isoniazid for treatment of latent tuberculosis infection in the PREVENT tuberculosis study. Clinical Infectious Diseases. 2015 Aug 15;61(4):527-35.