

Talaromycosis (Formerly Penicilliosis)

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Epidemiology

Talaromycosis is an invasive fungal infection caused by the thermally dimorphic fungus *Talaromyces marneffe* (formerly *Penicillium marneffe*), which is endemic in Southeast Asia (in northern Thailand, Vietnam, and Myanmar), East Asia (in southern China, Hong Kong, and Taiwan), and South Asia (in northeastern India).¹⁻⁴ *Talaromyces marneffe* was formerly classified under the *Penicillium* subgenus *Biverticillium* based on morphological characteristics. In 2011, the subgenus *Biverticillium* was found to form a monophyletic group with *Talaromyces* that is distinct from *Penicillium*, and was taxonomically unified with the *Talaromyces* genus.⁵ Hence, *Penicillium marneffe* was changed to *Talaromyces marneffe*, and the disease penicilliosis is now called talaromycosis.

The wild bamboo rat is the only known animal reservoir of *T. marneffe*^{6,7}; however, case-control studies suggest that human infection results from inhalation of fungal spores released from a soil-related environmental reservoir (plants and farmed animals) rather than from direct bamboo rat-to-human transmission.^{8,9} Talaromycosis incidence increases 30% to 50% during the rainy months (May–November)^{3,10} because of expansion of the environmental reservoir and increased humidity.¹¹ Reactivation of latent infection has been demonstrated in non-autochthonous cases with a history of remote travel to endemic countries, occurring up to 52 years after exposure.¹²⁻¹⁴ There has been one case of presumed laboratory-acquired talaromycosis. Donor-acquired transmission has been reported in a lung transplant recipient from Belgium.^{15,16}

HIV is a major risk factor for talaromycosis, accounting for approximately 88% of disease in hyperendemic regions.² *T. marneffe* is a major cause of HIV-associated opportunistic infections in these regions, making up 4% to 16% of hospital admissions due to advanced HIV disease,^{2,3,17-19} and is a leading cause of HIV-associated bloodstream infection and HIV-associated deaths in Vietnam and southern China.^{17,20-22} Infection occurs predominantly in individuals^{2,3,23} who have very advanced HIV disease with a CD4 T lymphocyte (CD4) cell count of <100 cells/mm³. Talaromycosis is increasingly diagnosed in immunocompromised individuals, including those with HIV, who are returning travelers or immigrants from the endemic regions.^{12,13,24} People who have a primary immunodeficiency condition (e.g., idiopathic CD4 lymphopenia, anti-interferon-gamma autoantibody-associated immunodeficiency, conditions due to mutations in CYBB or CD40L, or gain-of-function mutation in STAT1/STAT3 pathways) or a secondary immunosuppressive condition (e.g., other autoimmune diseases, solid organ and hematopoietic stem cell transplantations, T lymphocyte-depleting immunosuppressive drugs, and novel anticancer targeted therapies, such as anti-CD20 monoclonal antibodies and kinase inhibitors) are also at risk for talaromycosis.²⁵ It is estimated that worldwide each year approximately 17,300 people with HIV or other immunocompromising conditions are diagnosed with talaromycosis, and approximately 4,900 infection-related deaths occur.²⁶ Talaromycosis-related mortality approaches 30% in people both with and without HIV, despite antifungal therapy.^{2,3,23,27,28}

Clinical Manifestations

Disseminated infection involving multiple organ systems is the most common manifestation of talaromycosis in people with advanced HIV disease. The infection frequently begins as a subacute illness characterized by fever, weight loss, hepatosplenomegaly, lymphadenopathy, and respiratory and gastrointestinal abnormalities.^{3,29} These clinical features are nonspecific and are indistinguishable from those of disseminated tuberculosis, other systemic mycoses, or infections due to intracellular pathogens, such as *Salmonella* species.

Skin lesions are the most specific, albeit late, clinical manifestations of talaromycosis and are present in 40% to 80% of patients.²⁷ Skin lesions are typically central-umbilicated papules that appear first on the face and then spread to the trunk and extremities. Pulmonary symptoms such as cough or shortness of breath occur in approximately 40% of patients. Gastrointestinal symptoms including diarrhea or abdominal pain occur in 30% of patients. Hepatosplenomegaly is common, presenting in up to 60% of patients, and together with intra-abdominal lymphadenopathy causes abdominal distention and pain.^{3,18} A rare complication occurring in about 4% of patients is meningoencephalitis, with a rapid disease course and a high mortality of up to 80%.³⁰ Coinfection with oropharyngeal candidiasis occurs in up to 50% of patients and with tuberculosis in 22% of patients.³

Common laboratory findings associated with talaromycosis include anemia and thrombocytopenia due to bone marrow infiltration. Anemia can be profound and may require multiple red cell transfusions. Elevation of aminotransferases is common, with a serum aspartate aminotransferase over alanine aminotransferase ratio of approximately 2.³

Chest radiographical abnormalities are broad and nonspecific, ranging from diffuse interstitial disease to reticulonodular infiltrates to alveolar infiltrates.^{3,31}

Diagnosis

A diagnosis of talaromycosis should be considered in all people with HIV with a CD4 count of <100 cells/mm³ who have traveled to or have lived in talaromycosis-endemic areas and present with a systemic infection involving the reticuloendothelial system (i.e., lymph nodes, liver, spleen, and bone marrow).

Skin lesions in talaromycosis develop on the face, trunk, and extremities and typically have a central-necrotic appearance. However, skin lesions are a late manifestation of talaromycosis and are absent in up to 60% of patients.^{1,3,32} Diagnostic methods for talaromycosis are still primarily based on conventional microscopy, histology, and culture. Culture results usually return within 4 to 5 days but can take up to 28 days. Diagnostic delay, particularly in patients presenting without fever or skin lesions, is associated with increased mortality.^{2,3,25,33} The development of antigen detection and polymerase chain reaction (PCR)-based assays has offered rapid, sensitive, and specific non-culture-based diagnostics that may substantially change the way talaromycosis is diagnosed and managed (discussed in more detail in the Nucleic Acid Diagnosis and Antigen Diagnosis sub-sections below).³⁴⁻³⁶

Microscopy, Histology, and Culture Are the Gold Standard Diagnostic Methods

Microscopy. A presumptive diagnosis of talaromycosis can be made based on the microscopic examination of Giemsa-, Wright's-, or Grocott-Gomori Methenamine Silver-stained samples of skin

lesion scrapings, lymph node aspirate, bone marrow aspirate, or tissue sections showing round-to-oval extracellular and intramacrophage yeast-like organisms measuring 3 to 6 µm in diameter. Presence of a clear midline septum in a dividing yeast cell distinguishes *T. marneffei* from *Histoplasma*, *Emergomyces*, or *Candida* species.¹ In some patients, the fungus can be identified by microscopic examination of a Wright's-stained peripheral blood smear.³⁷

Histology. A definitive diagnosis of talaromycosis can be made by the histopathologic demonstration of the organism in biopsy specimens. There are three histopathological forms: (1) a granulomatous reaction formed by histiocytes, lymphocytes, epithelioid, and giant cells, which can be seen in reticuloendothelial organs in patients who are HIV-negative or immunocompetent; (2) a suppurative reaction that develops with the joining of multiple abscesses seen in the lung and subcutaneous tissues of immunocompetent patients; and (3) an anergic and necrotizing reaction characterized by focal necrosis surrounded by distended histiocytes containing proliferating fungi seen in the lung, liver, and spleen of immunocompromised patients.³⁸

Culture. Most frequently, a definitive diagnosis of talaromycosis is based on isolation of the organism from cultures of blood and/or other clinical specimens.

Compared to other endemic dimorphic fungi, *T. marneffei* grows more readily in standard BACTEC blood culture media and Sabouraud dextrose agar incubating between 4 and 14 days but can take up to 28 days to grow from selective fungal culture media. At 25°C to 32°C, the fungus grows as a mold producing yellow-green colonies with sulcate folds that produce a red pigment that diffuses into the surrounding media. Microscopically, filamentous hyphae with characteristic spore-bearing structures called conidiophores and conidia can be seen. At 32°C to 37°C, the fungus makes the morphological transition from a mold to a yeast, producing tan-colored colonies without a red diffusible pigment. In laboratory media, only the transitional sausage-shaped cells can be seen microscopically. The round-to-oval yeast cells are only seen in natural tissue.¹

Culture yield is the highest from bone marrow (100%), followed by skin lesions (90%) and blood (50% to 70%).^{3,39} Less commonly, talaromycosis has been diagnosed from sputum, pleural fluid, peritoneal fluid, cerebrospinal fluid, pericardial fluid, stool, and urine.

Nucleic Acid Diagnosis

Molecular diagnostics for talaromycosis have been based on real-time PCR amplification and sequence identification of the 5.8S rRNA and the 18S rRNA genes within the fungal ribosome's internally transcribed spacer regions and the *MP1* gene specific to *T. marneffei*.⁴⁰⁻⁴³ These assays have improving sensitivity (60% to 88%) and high specificity (100%), making them excellent rapid rule in tests for talaromycosis.⁴⁴ At present, these real-time PCR assays are available as in-house assays at selected centers only, and have not been prospectively validated, standardized, or commercially developed for clinical use.

Antigen Diagnosis

Several *T. marneffei*-specific antigen tests are in late-stage clinical validation but are not yet widely available for clinical use. The commercial assay for the detection of *Aspergillus* galactomannan cross-reacts with *T. marneffei* with a sensitivity between 64.5% and 95.8%.^{45,46} However, due to cross-reactivity with other endemic fungi, such as *Histoplasma* and *Blastomyces*, it has not been adopted clinically. A *T. marneffei*-specific cell wall mannoprotein Mp1p enzyme immunoassay has

been shown to be more sensitive than blood culture (86.3% vs. 72.8%) and highly specific (98.1%),⁴⁷ and is available non-commercially in the United States from the laboratory of Dr. Thuy Le at Duke University (1-919-684-0952). Several *T. marneffei*-specific point-of-care antigen assays with promising clinical performance are undergoing late-stage clinical validation, which would offer a tool for early diagnosis near the patient and a screen-and-treat approach that potentially reduces mortality.³⁴⁻³⁶

Antigen Screening in Patients With Advanced HIV Disease

In hyperendemic regions, prevalence of *T. marneffei* antigenemia in people with advanced HIV disease is high and progressively increases with lower CD4 counts. A study in China¹¹ found that prevalence of antigenemia increased from 4.5% to 28.4% as the CD4 count decreased from 200 to 50 cells/mm³ and a study in Vietnam⁴⁸ identified a prevalence of antigenemia of 4.2% in asymptomatic people with CD4 counts <100 cells/mm³. Importantly, antigenemia in asymptomatic patients with a CD4 count <100 cells/mm³ was found to be independently associated with 12-month mortality,⁴⁸ and antigen can be detected weeks to months earlier than culture allows.⁴⁹ Thus, antigen tests have potential utility to detect subclinical infection for pre-emptive antifungal therapy in regions where these tests are available.

Matrix-Assisted Laser Desorption/Ionization–Time of Flight Method

The matrix-assisted laser desorption/ionization–time of flight (MALDI-TOF) mass spectrometry (MS) method has been used for identification of *Talaromyces* to the species level from cultured specimens based on either an in-house database generated from an institution's *T. marneffei* clinical strain collection^{50,51} or from the comprehensive National Institutes of Health Mold Database.^{52,53} MALDI-TOF MS represents a rapid and reliable tool for downstream fungal identification, eliminating the need to demonstrate thermal dimorphism.

Preventing Exposure

Two case-control studies in Thailand and Vietnam demonstrated that people with stage 4 HIV disease, as defined by the World Health Organization, or a CD4 count <100 cells/mm³ who had an occupational exposure to plants and farmed animals had twofold higher odds of infection.^{8,9} The risk was higher in the rainy and humid months between May and November.^{3,10}

Residency or a history of traveling to the highland regions (as short as 3 days) was a risk factor for talaromycosis in people with advanced HIV disease in southern Vietnam.⁸ These data suggest that people with HIV who have a CD4 count <100 cells/mm³ or individuals whose T cell function is suppressed due to a health condition (e.g., primary immune deficiency) or medication (e.g., immunosuppressants or prolonged corticosteroids) should avoid visiting the areas where talaromycosis is hyperendemic, particularly highland regions during the rainy and humid months **(BIII)**.

Preventing Disease

Recommendations for Preventing First Episode of Talaromycosis (Primary Prophylaxis)
<p>Indication for Primary Prophylaxis</p> <p>People with a CD4 count <100 cells/mm³ who are not taking ART or who have treatment failure without access to effective ART options, or people with a CD4 count ≥ 100 cells/mm³ but have a condition that suppresses their T cell function, <i>and</i> who either—</p> <ul style="list-style-type: none">• Reside in the hyperendemic regions in northern Thailand, throughout Vietnam, and southern China (particularly in highland regions during the rainy humid months) (BI) <i>or</i>• Are from countries outside of the hyperendemic region and must travel to the region (BIII). <p>Primary Prophylaxis</p> <p><i>For Individuals Residing in Hyperendemic Areas</i></p> <ul style="list-style-type: none">• Preferred Therapy: Itraconazole 200 mg PO once daily (BI)• Alternative Therapy: Fluconazole 400 mg PO once weekly (BII) <p><i>For Individuals Traveling to Hyperendemic Areas</i></p> <ul style="list-style-type: none">• Primary prophylaxis for travelers should begin 3 days prior to travel to allow serum drug level to reach steady state and may continue for 1 week after travel (BIII).• Preferred Therapy: Begin itraconazole 200 mg PO once daily 3 days before travel and continue for 1 week after leaving the hyperendemic area (BIII).• Alternative Therapy: Begin fluconazole 400 mg PO 3 days before travel, then continue 400 mg PO once weekly while in the area and take final dose after leaving the endemic area (BIII). <p>Indication for Discontinuing Primary Prophylaxis for People Who Reside in Hyperendemic Areas</p> <ul style="list-style-type: none">• CD4 count ≥ 100 cells/mm³ for ≥ 6 months in response to ART (BII) <i>or</i>• Virologic suppression for ≥ 6 months on ART (BIII) <p>Indication for Restarting Primary Prophylaxis</p> <ul style="list-style-type: none">• CD4 count decreases to <100 cells/mm³ (BII) and person still resides in or travels to hyperendemic areas. <p>Pregnancy Considerations</p> <ul style="list-style-type: none">• Given the teratogenic risks of azole antifungals, individuals on primary prophylaxis with itraconazole or fluconazole should postpone pregnancy until their CD4 counts have been restored with ART, such that prophylaxis can be discontinued (BIII). If a woman becomes pregnant while receiving itraconazole or fluconazole prophylaxis, the decision as to whether to continue should be individualized based on current CD4 count, virologic suppression, with shared decision-making between the clinician and patient.

Key: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; PO = orally

Primary prophylaxis has been shown to reduce the incidence of talaromycosis and other invasive fungal infections. A double-blind, placebo-controlled trial in Chiang Mai, Thailand,⁵⁴ demonstrated that oral itraconazole 200 mg daily for primary prophylaxis significantly reduced the occurrence of invasive fungal infections (predominantly cryptococcosis and talaromycosis) in people with HIV with a CD4 count <200 cells/mm³. In a retrospective study in Chiang Mai, fluconazole (400 mg weekly) was shown to be as effective as itraconazole (200 mg daily) for primary prophylaxis.⁵⁵

Indication for Primary Prophylaxis

Primary prophylaxis is only recommended for patients with HIV with CD4 counts <100 cells/mm³ who reside in the hyperendemic regions in northern Thailand, southern China, and northern and southern Vietnam who are unable to have antiretroviral therapy (ART) for whatever reasons or have treatment failure without access to effective antiretroviral options **(BI)**. The drug choices for prophylaxis are oral itraconazole 200 mg once daily **(BI)** or oral fluconazole 400 mg once weekly **(BII)**.

Primary prophylaxis is **not recommended** in people with HIV who are on effective ART with an undetectable viral load and is **not recommended** in geographic areas outside of the mentioned hyperendemic regions **(AIII)**.

For people with HIV from the United States and from other countries outside of the endemic region who are not on effective ART and have a CD4 count <100 cells/mm³ or people with a CD4 count ≥ 100 cells/mm³ but who have a condition that suppresses their T cell function, and who must travel to the hyperendemic areas mentioned, primary prophylaxis with either itraconazole (preferred) or fluconazole should begin 3 days prior to travel to allow serum drug level to reach steady state and may continue for 1 week after travel **(BIII)**.

Discontinuation of Primary Prophylaxis

Primary prophylaxis for talaromycosis can reasonably be discontinued in people with HIV who are on effective ART and have a sustained CD4 count ≥ 100 cells/mm³ for at least 6 months **(BII)**. In areas where viral load monitoring has replaced CD4 count monitoring, primary prophylaxis can reasonably be discontinued in people with HIV who achieve sustained virologic suppression for at least 6 months **(BIII)**.⁵⁴⁻⁵⁶ Once stopped, primary prophylaxis should be restarted in individuals whose CD4 count decreases to <100 cells/mm³ **(BII)** if the person still resides in or travels to hyperendemic areas.

Antigen Screen-and-Treat Strategy for Disease Prevention

In hyperendemic areas, emerging data suggest that *T. marneffei* antigen can be detected weeks to months before culture detection in people with advanced HIV disease^{49,57}; thus providing a window of opportunity for screening preclinical or asymptomatic disease and providing pre-emptive treatment to prevent disease development. Point-of-care antigen detection assays in development may allow for research to determine the benefit of a screen-and-treat approach as more cost-effective strategy for disease prevention.

Treating Disease

Recommendations for Treating Disseminated Talaromycosis Infection
Induction Therapy <i>Preferred Therapy</i> <ul style="list-style-type: none">• Liposomal amphotericin B 3 to 5 mg/kg/day IV for 2 weeks (AIII), followed by consolidation therapy• If liposomal amphotericin B is not available: Amphotericin B deoxycholate 0.7 mg/kg/day IV for 2 weeks (AI), followed by consolidation therapy

Alternative Therapy (if amphotericin B is not available, contraindicated, or not tolerated)

- Voriconazole 6 mg/kg IV every 12 hours on Day 1 (loading dose) and then voriconazole 4 mg/kg IV every 12 hours for 2 weeks (BII), followed by consolidation therapy, or
- Voriconazole 600 mg PO every 12 hours on Day 1 (loading dose) and then voriconazole 400 mg PO every 12 hours for 2 weeks (BII); followed by consolidation therapy

Note: Itraconazole is not recommended as induction therapy for talaromycosis regardless of disease severity (AI).

Consolidation Therapy (after induction therapy)

- Itraconazole* 200 mg PO every 12 hours for 10 weeks (AI), followed by maintenance therapy or secondary prophylaxis, or
- Voriconazole 200 mg PO every 12 hours for 10 weeks (BII), followed by maintenance therapy or secondary prophylaxis

Maintenance Therapy (after consolidation therapy)

- Itraconazole* 200 mg PO daily (AI)

Criteria for Discontinuing Chronic Maintenance Therapy

- CD4 count ≥ 100 cells/mm³ for ≥ 6 months in response to ART (BII), or
- Virologic suppression for ≥ 6 months on ART (BIII)

Criteria for Restarting Chronic Maintenance Therapy

- CD4 count decreases to < 100 cells/mm³ (BIII)

* Itraconazole capsules should be taken after a meal or taken with a cola drink as gastric acidification is required for optimal absorption. Itraconazole solution should be taken on an empty stomach.

Other Considerations

- ART should be initiated as early as one week after the initiation of induction therapy for talaromycosis to improve overall outcomes (AII).
- ART should not be withheld because of concerns for possible development of IRIS (AIII).

Therapeutic Drug Monitoring for Itraconazole and Voriconazole

- Given erratic absorption of itraconazole, extensive interindividual variability due to differences in CYP2C19 alleles associated with voriconazole metabolism, nonlinear PK of voriconazole, and potential for drug interactions with ARV drugs; when available, TDM to guide therapy is recommended. (see the [Drug–Drug Interactions tables](#) in the [Adult and Adolescent Antiretroviral Guidelines](#) for further recommendations).
- Itraconazole and voriconazole concentrations should be monitored beginning 5 days after initiation of therapy, and doses adjusted as needed to obtain serum trough concentrations > 0.5 $\mu\text{g/mL}$ for itraconazole (for a combined level of itraconazole plus its antifungal active metabolite hydroxyitraconazole) and > 1 $\mu\text{g/mL}$ for voriconazole (BIII). Because it is more bioavailable, itraconazole solution is generally preferred over the capsule formulation.

Pregnancy Considerations

- Itraconazole and voriconazole should be avoided during the first trimester of pregnancy unless the benefit is felt to outweigh the risk (BIII).
- Amphotericin B should be used instead of high-dose azoles in the first trimester of pregnancy (BIII).
- After the first trimester, treatment with itraconazole should be considered for consolidation or maintenance therapy (AIII).

- Women on maintenance therapy with itraconazole or other azoles should postpone pregnancy until their CD4 counts have been restored with ART, such that prophylaxis can be discontinued (**BIII**).
- Voriconazole is not recommended for use during pregnancy, especially in the first trimester (**AIII**).

Key: ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte; CYP = cytochrome P450; IRIS = immune reconstitution inflammatory syndrome; IV = intravenous; PK = pharmacokinetic; PO = orally; TDM = therapeutic drug monitoring

Disseminated talaromycosis, its most common manifestation, is fatal if untreated.⁵⁸ With antifungal therapy, case fatality rates range from 10% to 30%.^{2,3,17,27} Therefore, early initiation of antifungal therapy is necessary.

Antifungal therapy for talaromycosis consists of induction, consolidation, and maintenance phases. Treatment recommendations are based on several observational studies in Thailand and China⁵⁹⁻⁶³ and a multicenter randomized controlled trial of Itraconazole Versus Amphotericin B for Penicilliosis (IVAP) in Vietnam.⁶⁴

In an earlier noncomparative prospective study of 74 patients in Thailand, induction therapy with amphotericin B deoxycholate for 2 weeks, followed by consolidation therapy with itraconazole for 10 weeks was shown to be highly effective. Treatment success rate (defined by negative blood culture and resolution of fever and skin lesions at the end of a 12-week treatment course) was 97%.⁵⁹

Voriconazole has been used for induction therapy in case series of patients who could not tolerate amphotericin B. It was shown to have favorable clinical and microbiological outcomes in 8 of 9 (88.9%) patients in Thailand,⁶¹ and in 10 of 14 (71.4%) patients and in 47 of 57 (82.5%) patients in two studies conducted in China.^{60,63}

The IVAP trial randomized 440 patients across five hospitals in Vietnam and demonstrated that induction therapy with amphotericin B was superior to itraconazole with respect to 6-month mortality (absolute risk of death was 11% and 21%, respectively; absolute risk difference, 9.7 percentage points; 95% confidence interval, 2.8 to 16.6; $P = 0.006$). Patients in the amphotericin B arm had significantly lower rates of disease complications, including disease relapse and immune reconstitution inflammatory syndrome (IRIS), and had a fourfold faster rate of blood fungal clearance. The difference in mortality between the arms was not dependent on disease severity (based on positive blood culture, blood fungal count, or requirement for oxygen support at presentation) or by a participant's immune status (CD4 count <50 cells/mm³ or ≥ 50 cells/mm³), ART status, or intravenous (IV) drug use.⁶⁴

The recommended induction therapy for all patients with disseminated disease, regardless of clinical severity, is amphotericin B: preferably liposomal amphotericin B 3 to 5 mg/kg/day IV for 2 weeks where available (**AIII**), or amphotericin B deoxycholate 0.7 mg/kg/day IV for 2 weeks (**AI**).

Induction therapy should be followed by consolidation therapy with oral itraconazole, 200 mg every 12 hours for a subsequent duration of 10 weeks (**AI**).⁶⁴ After this period, maintenance therapy with oral itraconazole 200 mg/day is recommended to prevent recurrence until the CD4 count rises above 100 cells/mm³ for ≥ 6 months (**AI**).⁶⁵

For patients unable to tolerate any form of amphotericin B, induction therapy with IV voriconazole 6 mg/kg every 12 hours on Day 1 (loading dose), then 4 mg/kg every 12 hours (**BII**), or with oral voriconazole 600 mg every 12 hours on Day 1 (loading dose), then 400 mg every 12 hours for 2 weeks is recommended (**BII**).^{60,61} Thereafter, either oral itraconazole (**AI**) or oral voriconazole

(BII) at a dose of 200 mg every 12 hours can be used for consolidation therapy for 10 weeks, followed by itraconazole 200 mg/day for maintenance therapy **(AI)**. The optimal dose of voriconazole for maintenance therapy beyond 12 weeks has not been studied.

Itraconazole is **not recommended** as an induction therapy for talaromycosis, regardless of disease severity **(AI)**.⁶⁴

In Vitro Antifungal Susceptibility Profile of Available Antifungal Drugs

The minimum inhibitory concentrations (MIC) are low for itraconazole (MICs 0.008–0.25 µg/mL), intermediate for amphotericin B (MICs 0.5–1 µg/mL), and high for fluconazole (MICs 0.5–16 µg/mL) across studies. One study correlated MIC data of 30 clinical isolates with patient outcomes and showed poor clinical response in patients treated with fluconazole, consistent with the higher MICs for fluconazole. The MICs are low for flucytosine (MICs 0.06–0.5 µg/ml), voriconazole (MICs 0.016–0.063 µg/mL), and posaconazole (MICs 0.001–0.002 µg/ml), but are high for echinocandins (2–8 µg/mL).^{66–68} These results suggest promising activity of voriconazole, posaconazole, and flucytosine for the treatment of talaromycosis, and suggest that the echinocandins are less effective against *T. marneffe*i. Data are lacking on the frequencies of primary or acquired antifungal resistance on therapy, and clinical cut-off threshold to define resistance has not been defined.

Special Considerations Regarding Antiretroviral Therapy Initiation

In a multicenter randomized controlled trial in China, early initiation of ART (<2 weeks after initiation of talaromycosis treatment, median 11 days, interquartile range [IQR] 7–13) was associated with significantly lower mortality and AIDS-defining events over 48 weeks compared to delayed initiation (2–4 weeks after initiation of talaromycosis treatment, median 21 days, IQR 17–29).⁶⁹ The certainty of evidence was reduced as significantly more patients in the early ART arm were excluded from the final analysis.

In the IVAP trial, the median time to ART initiation in both arms was 3 weeks (range 1–5 weeks). Paradoxical IRIS events occurred in 6.4% in the itraconazole arm and 0% in the amphotericin B arm, suggesting that ART can be safely initiated as early as 1 week after starting effective induction therapy with amphotericin B.⁶⁴

ART should therefore be initiated as early as 1 week after the initiation of induction therapy for talaromycosis to improve outcomes **(AII)**.

Prevention and Management of IRIS

Both unmasking and paradoxical IRIS have been described in patients with talaromycosis after ART is initiated.^{70–72} In the IVAP trial, 188 of 432 (44%) patients had started ART a median of 3 to 4 months before developing talaromycosis, indicating the role of ART in the unmasking of subclinical infection in a significant proportion of patients.⁶⁴ This finding highlights the need to screen for subclinical infection with a sensitive antigen test (where available) and the potential utility of pre-emptive antifungal therapy to prevent disease and unmasking IRIS. In patients starting ART after a diagnosis of talaromycosis, paradoxical IRIS events only occurred in patients treated with itraconazole induction therapy,⁶⁴ demonstrating the role of effective induction therapy with

amphotericin B in the prevention of paradoxical IRIS. ART should not be withheld because of concerns for possible development of IRIS **(AIII)**.

Patients with paradoxical IRIS typically present with inflammatory manifestations that include erythematous or immunological skin lesions such as erythema nodosum, large and painful peripheral lymph nodes, and synovitis of small joints. Most symptoms can be managed by judicious use of nonsteroidal anti-inflammatory drugs. Corticosteroids are reserved for synovitis that interferes with daily function.⁷² Although the IRIS events in the IVAP trial were managed effectively with continuation of ART and antifungal therapy, they were associated with higher morbidity, lower quality of life, increased diagnostic testing, duration of hospitalization, and cost.⁶⁴

Monitoring of Response to Therapy and Adverse Events (Including IRIS)

Adverse Event Monitoring

Patients treated with amphotericin B (or liposomal amphotericin B) should be monitored for infusion-related adverse reactions (fever, rigors, nausea, vomiting), electrolyte disturbances (particularly hypokalemia and hypomagnesemia), nephrotoxicity (rise in creatinine), and anemia. Hydration with 500 mL to 1,000 mL of normal saline and potassium supplementation before each amphotericin B infusion reduces the risk of nephrotoxicity during treatment. Infusion-related adverse reactions can be ameliorated by pre-treatment with acetaminophen and diphenhydramine.⁷³ Patients on azoles should be regularly monitored for liver function test abnormalities, as all have risk of hepatotoxicity. Additionally, individuals on voriconazole should be monitored for vision changes, neurotoxicity, skin rash, photosensitivity, adrenal insufficiency, and periostitis while those on itraconazole should be monitored for peripheral edema, hypertension, hypokalemia, and congestive heart failure.

Drug–Drug Interactions and Therapeutic Drug Monitoring

Itraconazole and voriconazole and antiretroviral (ARV) drugs such as protease inhibitors, some integrase strand transfer inhibitors, and non-nucleoside reverse transcriptase inhibitors can have bidirectional interactions with each other, leading to increased or decreased drug concentrations (see [Drug–Drug Interactions](#) in the [Adult and Adolescent Antiretroviral Guidelines](#)). Close monitoring or use with non-interacting ART regimens (e.g., dolutegravir/tenofovir alafenamide/emtricitabine) is recommended when using these drugs together.

In settings where therapeutic drug monitoring (TDM) is available, serum itraconazole and voriconazole levels should be monitored in all patients starting 5 days after therapy initiation to ensure optimal drug exposure **(BIII)**. For timing to obtain a trough level of each drug, see the [Fungus Education Hub Antifungal Therapeutic Drug Monitoring web page](#). TDM is recommended because itraconazole and voriconazole can interact with some ARV drugs. Absorption of itraconazole is highly dependent on gastric acid pH. Extensive interindividual variability in voriconazole pharmacokinetics is expected due to differences in cytochrome P450 2C19 alleles associated with voriconazole metabolism and nonlinear pharmacokinetics of voriconazole. Optimal target serum concentrations of antifungals for talaromycosis are not well defined.⁷⁴ In line with recommendations for other endemic fungi, target serum trough concentrations for itraconazole should be >0.5 µg/mL (for a combined itraconazole and its antifungal active metabolite hydroxyitraconazole level) and >1 µg/mL for voriconazole **(BIII)**. Because it is more bioavailable, itraconazole solution is generally

preferred over the capsule formulation. For maximal absorption, the itraconazole capsule should be taken with food or a cola drink, and itraconazole liquid should be taken on an empty stomach.

Managing Treatment Failure and Relapse

Talaromycosis treatment failure and disease relapse were associated with ineffective induction therapy with itraconazole,⁶⁴ highlighting the importance of using the more potent drug amphotericin B as induction therapy. Based on case series that included very few patients and on clinical experiences, voriconazole is an alternative therapy for patients who are unable to tolerate amphotericin B induction treatment and is an effective choice for consolidation therapy given its higher oral bioavailability **(BII)**.

Disease relapse is associated with higher mortality⁶⁴ and occurs mainly in patients who are not adherent to ART or have virologic failure, as well as in those who are not adherent to itraconazole consolidation or maintenance therapy. Therapy adherence counseling and TDM for itraconazole and voriconazole, if available, are recommended **(BIII)**.

Preventing Recurrence

When to Start Chronic Maintenance Therapy

A double-blind, placebo-controlled study conducted in Chiang Mai, Thailand, demonstrated that people not on ART who discontinued oral itraconazole 200 mg daily had a talaromycosis relapse rate of 57% compared to 0% in those who continued itraconazole therapy ($P < 0.001$).⁶⁵ All patients who successfully complete induction and consolidation treatment for talaromycosis should receive chronic maintenance therapy with oral itraconazole 200 mg/day until they reach criteria for stopping maintenance therapy **(AI)**.

When to Stop Chronic Maintenance Therapy

No randomized controlled study has been conducted to evaluate the safety of discontinuation of secondary prophylaxis for talaromycosis. However, a retrospective cohort study⁵⁶ reported no relapse of talaromycosis after itraconazole was discontinued in patients receiving ART whose CD4 counts were ≥ 100 cells/mm³. Therefore, chronic maintenance therapy for talaromycosis can be discontinued in patients who are ART adherent and have CD4 counts ≥ 100 cells/mm³ for at least 6 months **(BII)**. In settings where CD4 monitoring is not possible, secondary prophylaxis can be reasonably discontinued in patients with sustained virologic suppression for at least 6 months while on ART **(BIII)**.

Chronic maintenance therapy should be reintroduced if the CD4 count decreases to < 100 cells/mm³ **(BIII)**.

Special Considerations During Pregnancy

During pregnancy, the diagnosis and treatment of talaromycosis is similar to that in other adults with HIV, with the following considerations regarding antifungal use in pregnancy. There are limited data regarding the natural history of talaromycosis and its effect on maternal and fetal outcomes in pregnancy. Clinicians treating talaromycosis during pregnancy should take several factors into considerations. Amphotericin B has not been shown to be teratogenic in animals, and no increase in

fetal anomalies has been seen with its use in humans. There remain significant gaps in determining optimal dosing of amphotericin B in pregnancy; a review of dosing strategies in pregnancy recommended use of ideal body weight rather than total body weight to minimize risk of adverse effects to the fetus while maintaining efficacy.⁷⁵ Neonates born to women on chronic amphotericin B at delivery may be at increased risk for renal toxicity and electrolyte abnormalities and should be appropriately evaluated as newborns.⁷⁶

Itraconazole at high doses has been shown to be teratogenic in animals, but because humans lack the metabolic mechanism accounting for these defects, animal teratogenicity data are not applicable to humans. Prospective cohort studies of over 300 women with first-trimester itraconazole exposure did not show an increased risk of congenital malformations, but these studies report on varying doses and durations and have low power to detect differences.^{77,78}

Voriconazole (at doses lower than recommended human doses) is teratogenic (cleft palate and renal defects) in rats and embryotoxic in rabbits; no adequately controlled studies have assessed their teratogenicity and embryotoxicity in humans.

Azole antifungals **should be avoided** during the first trimester of pregnancy unless the benefit is felt to outweigh risk (**BIII**). Amphotericin B should be used instead of high-dose azoles in the first trimester for treatment of acute infection (**BIII**). After the first trimester, treatment with itraconazole should be considered for consolidation or maintenance therapy (**AIII**). Women on maintenance therapy with itraconazole or other azoles should postpone pregnancy until their CD4 counts have been restored with ART, such that prophylaxis can be discontinued (**BIII**). If a woman becomes pregnant while receiving itraconazole prophylaxis, the decision as to whether to continue should be individualized based on current CD4 count, virologic suppression, and patient preference. Voriconazole is **not recommended** for use during pregnancy, especially in the first trimester (**AIII**).

References

1. Vanittanakom N, Cooper CR, Jr., Fisher MC, Sirisanthana T. Penicillium marneffei infection and recent advances in the epidemiology and molecular biology aspects. *Clin Microbiol Rev*. 2006;19(1):95-110. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16418525>.
2. Hu Y, Zhang J, Li X, et al. Penicillium marneffei infection: an emerging disease in mainland China. *Mycopathologia*. 2013;175(1-2):57-67. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22983901>.
3. Le T, Wolbers M, Chi NH, et al. Epidemiology, seasonality, and predictors of outcome of AIDS-associated Penicillium marneffei infection in Ho Chi Minh City, Viet Nam. *Clin Infect Dis*. 2011;52(7):945-952. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21427403>.
4. Ranjana KH, Priyokumar K, Singh TJ, et al. Disseminated Penicillium marneffei infection among HIV-infected patients in Manipur state, India. *J Infect*. 2002;45(4):268-271. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12423616>.
5. Samson RA, Yilmaz N, Houbraken J, et al. Phylogeny and nomenclature of the genus Talaromyces and taxa accommodated in Penicillium subgenus Biverticillium. *Stud Mycol*. 2011;70(1):159-183. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22308048>.
6. Cao C, Liang L, Wang W, et al. Common reservoirs for Penicillium marneffei infection in humans and rodents, China. *Emerg Infect Dis*. 2011;17(2):209-214. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21291590>.
7. Huang X, He G, Lu S, Liang Y, Xi L. Role of Rhizomys pruinosus as a natural animal host of Penicillium marneffei in Guangdong, China. *Microb Biotechnol*. 2015;8(4):659-664. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25824250>.
8. Le T, Jonat B, Kim Cuc N, al E. The exposure and geospatial risk factors for AIDS-associated penicilliosis in Vietnam. Presented at: Conference on Retroviruses and Opportunistic Infections; 2015. Seattle, WA. Available at: <https://www.croiconference.org/wp-content/uploads/sites/2/posters/2015/843.pdf>.
9. Chariyalertsak S, Sirisanthana T, Supparatpinyo K, Praparattanapan J, Nelson KE. Case-control study of risk factors for Penicillium marneffei infection in human immunodeficiency virus-infected patients in northern Thailand. *Clin Infect Dis*. 1997;24(6):1080-1086. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9195061>.
10. Chariyalertsak S, Sirisanthana T, Supparatpinyo K, Nelson KE. Seasonal variation of disseminated Penicillium marneffei infections in northern Thailand: a clue to the reservoir? *J Infect Dis*. 1996;173(6):1490-1493. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8648227>.
11. Wang YF, Xu HF, Han ZG, et al. Serological surveillance for Penicillium marneffei infection in HIV-infected patients during 2004-2011 in Guangzhou, China. *Clin Microbiol Infect*. 2015;21(5):484-489. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25677258>.
12. Antinori S, Gianelli E, Bonaccorso C, et al. Disseminated Penicillium marneffei infection in an HIV-positive Italian patient and a review of cases reported outside endemic regions. *J Travel Med*. 2006;13(3):181-188. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16706952>.
13. Cristofaro P, Mileno MD. Penicillium marneffei infection in HIV-infected travelers. *AIDS Alert*. 2006;21(12):140-142. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17191362>.
14. Castro-Lainez MT, Sierra-Hoffman M, J LL-Z, et al. Talaromyces marneffei infection in a non-HIV non-endemic population. *IDCases*. 2018;12:21-24. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29942740>.
15. Hermans F, Ombelet S, Degezelle K, et al. First-in-man observation of Talaromyces marneffei-transmission by organ transplantation. *Mycoses*. 2017;60(3):213-217. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27687582>.

16. Hilmarisdottir I, Coutellier A, Elbaz J, et al. A French Case of Laboratory-Acquired Disseminated *Penicillium marneffei* Infection in a Patient with AIDS. *Clinical Infectious Diseases*. 1994;19(2):357-358. Available at: <https://doi.org/10.1093/clinids/19.2.357>.
17. Jiang J, Meng S, Huang S, et al. Effects of *Talaromyces marneffei* infection on mortality of HIV/AIDS patients in southern China: a retrospective cohort study. *Clin Microbiol Infect*. 2019;25(2):233-241. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29698815>.
18. Larsson M, Nguyen LH, Wertheim HF, et al. Clinical characteristics and outcome of *Penicillium marneffei* infection among HIV-infected patients in northern Vietnam. *AIDS Res Ther*. 2012;9(1):24. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22897817>.
19. Wu TC, Chan JW, Ng CK, Tsang DN, Lee MP, Li PC. Clinical presentations and outcomes of *Penicillium marneffei* infections: a series from 1994 to 2004. *Hong Kong Med J*. 2008;14(2):103-109. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/18382016>.
20. Feng RF, Ma Y, Liu ZF, et al. [Specific causes of death among 381 AIDS patients who died in hospitals]. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2013;34(12):1237-1241. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24518028>.
21. Nga TV, Parry CM, Le T, et al. The decline of typhoid and the rise of non-typhoid salmonellae and fungal infections in a changing HIV landscape: bloodstream infection trends over 15 years in southern Vietnam. *Trans R Soc Trop Med Hyg*. 2012;106(1):26-34. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/22137537>.
22. Qi T, Zhang R, Shen Y, et al. Etiology and clinical features of 229 cases of bloodstream infection among Chinese HIV/AIDS patients: a retrospective cross-sectional study. *Eur J Clin Microbiol Infect Dis*. 2016;35(11):1767-1770. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27502930>.
23. Supparatpinyo K, Khamwan C, Baosoung V, Nelson KE, Sirisanthana T. Disseminated *Penicillium marneffei* infection in southeast Asia. *Lancet*. 1994;344(8915):110-113. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7912350>.
24. Narayanasamy S, Dat VQ, Thanh NT, et al. A global call for talaromycosis to be recognised as a neglected tropical disease. *Lancet Glob Health*. 2021;9(11):e1618-e1622. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34678201>.
25. Chan JF, Lau SK, Yuen KY, Woo PC. *Talaromyces* (*Penicillium*) *marneffei* infection in non-HIV-infected patients. *Emerg Microbes Infect*. 2016;5:e19. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26956447>.
26. Ning C, Wei W, Xu B, et al. Global distribution, drivers, and burden of talaromycosis, 1964-2018. Presented at: Conference on Retroviruses and Opportunistic Infections; 2020. Boston, MA. Available at: https://www.croiconference.org/wp-content/uploads/sites/2/posters/2020/1430_8_Ning_00749.pdf.
27. Son VT, Khue PM, Strobel M. Penicilliosis and AIDS in Haiphong, Vietnam: evolution and predictive factors of death. *Med Mal Infect*. 2014;44(11-12):495-501. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25391487>.
28. Kawila R, Chaiwarith R, Supparatpinyo K. Clinical and laboratory characteristics of penicilliosis *marneffei* among patients with and without HIV infection in Northern Thailand: a retrospective study. *BMC Infect Dis*. 2013;13:464. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24094273>.
29. Sirisanthana T. *Penicillium marneffei* infection in patients with AIDS. *Emerg Infect Dis*. 2001;7(3 Suppl):561. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11485672>.
30. Le T, Huu Chi N, Kim Cuc NT, et al. AIDS-associated *Penicillium marneffei* infection of the central nervous system. *Clin Infect Dis*. 2010;51(12):1458-1462. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21054180>.
31. Narayanasamy S, Dougherty J, van Doorn HR, Le T. Pulmonary talaromycosis: a window into the immunopathogenesis of an endemic mycosis. *Mycopathologia*. 2021;186(5):707-715. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34228343>.

32. Chen J, Zhang R, Shen Y, et al. Clinical characteristics and prognosis of penicilliosis among human immunodeficiency virus-infected patients in eastern China. *Am J Trop Med Hyg*. 2017;96(6):1350-1354. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28719279>.
33. Zheng J, Gui X, Cao Q, et al. A clinical study of acquired immunodeficiency syndrome associated *Penicillium marneffei* infection from a non-endemic area in China. *PLoS One*. 2015;10(6):e0130376. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26083736>.
34. Venugopalan S, Nguyen T, Bloss K, et al. Clinical validation of a novel point of care Mp1p antigen lateral flow immunoassay to diagnose *talaromyces marneffei* infection. *Open Forum Infectious Diseases*. 2023;10. Available at: https://www.researchgate.net/publication/375955757_988_Clinical_Validation_of_a_Novel_Point_of_Care_Mp1p_Antigen_Lateral_Flow_Immunoassay_to_Diagnose_Talaromyces_marneffei_Infection.
35. Kinnamon DS, Heggstad JT, Liu J, et al. Environmentally resilient microfluidic point-of-care immunoassay enables rapid diagnosis of talaromycosis. *ACS Sens*. 2023;8(6):2228-2236. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/37279466>.
36. Pruksaphon K, Intaramat A, Simsiriwong P, et al. An inexpensive point-of-care immunochromatographic test for *Talaromyces marneffei* infection based on the yeast phase specific monoclonal antibody 4D1 and *Galanthus nivalis* agglutinin. *PLoS Negl Trop Dis*. 2021;15(5):e0009058. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33945531>.
37. Supparatpinyo K, Sirisanthana T. Disseminated *Penicillium marneffei* infection diagnosed on examination of a peripheral blood smear of a patient with human immunodeficiency virus infection. *Clin Infect Dis*. 1994;18(2):246-247. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8161635>.
38. Deng Z, Ribas JL, Gibson DW, Connor DH. Infections caused by *Penicillium marneffei* in China and Southeast Asia: review of eighteen published cases and report of four more Chinese cases. *Rev Infect Dis*. 1988;10(3):640-652. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/3293165>.
39. Supparatpinyo K, Chiewchanvit S, Hirunsri P, Uthammachai C, Nelson KE, Sirisanthana T. *Penicillium marneffei* infection in patients infected with human immunodeficiency virus. *Clin Infect Dis*. 1992;14(4):871-874. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/1315586>.
40. LoBuglio KF, Taylor JW. Phylogeny and PCR identification of the human pathogenic fungus *Penicillium marneffei*. *J Clin Microbiol*. 1995;33(1):85-89. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/7699073>.
41. Pornprasert S, Praparattanapan J, Khamwan C, et al. Development of TaqMan real-time polymerase chain reaction for the detection and identification of *Penicillium marneffei*. *Mycoses*. 2009;52(6):487-492. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19207847>.
42. Hien HTA, Thanh TT, Thu NTM, et al. Development and evaluation of a real-time polymerase chain reaction assay for the rapid detection of *Talaromyces marneffei* MP1 gene in human plasma. *Mycoses*. 2016;59(12):773-780. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27453379>.
43. Dankai W, Pongpom M, Vanittanakom N. Validation of reference genes for real-time quantitative RT-PCR studies in *Talaromyces marneffei*. *J Microbiol Methods*. 2015;118:42-50. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26327538>.
44. Khanh DH, Brown L, My PTH, et al. Optimization and clinical evaluation of a 5.8S rRNA quantitative PCR assay for the diagnosis of talaromycosis. *Med Mycol*. 2025;63(4). Available at: <https://pubmed.ncbi.nlm.nih.gov/40240298/>.
45. Huang YT, Hung CC, Liao CH, Sun HY, Chang SC, Chen YC. Detection of circulating galactomannan in serum samples for diagnosis of *Penicillium marneffei* infection and cryptococcosis among patients infected with human immunodeficiency virus. *J Clin Microbiol*. 2007;45(9):2858-2862. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17596363>.

46. Chen X, Ou X, Wang H, et al. Talaromyces marneffei Mp1p antigen detection may play an important role in the early diagnosis of talaromycosis in patients with acquired immunodeficiency syndrome. *Mycopathologia*. 2022;187(2-3):205-215. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/35237935>.
47. Thu NTM, Chan JFW, Ly VT, et al. Superiority of a novel Mp1p antigen detection enzyme immunoassay compared to standard BACTEC blood culture in the diagnosis of talaromycosis. *Clin Infect Dis*. 2021;73(2):e330-e336. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32564074>.
48. Thu NTM, Dat VQ, Chan JFW, et al. Asymptomatic Talaromyces (Penicillium) marneffei Antigenemia and Mortality in Advanced HIV Disease. Presented at Conference of Retroviruses and Opportunistic Infections 2019. Available at: https://www.croiconference.org/wp-content/uploads/sites/2/posters/2019/1430_Thu_0710.pdf.
49. Ly VT, Thanh NT, Thu NTM, et al. Occult Talaromyces marneffei Infection Unveiled by the Novel Mp1p Antigen Detection Assay. *Open Forum Infect Dis*. 2020;7(11):ofaa502. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33269295>.
50. Borman AM, Fraser M, Szekely A, Johnson EM. Rapid and robust identification of clinical isolates of Talaromyces marneffei based on MALDI-TOF mass spectrometry or dimorphism in Galleria mellonella. *Med Mycol*. 2019;57(8):969-975. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30649411>.
51. Lau SK, Lam CS, Ngan AH, et al. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry for rapid identification of mold and yeast cultures of Penicillium marneffei. *BMC Microbiol*. 2016;16:36. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26965891>.
52. Li L, Chen K, Dhungana N, Jang Y, Chaturvedi V, Desmond E. Characterization of clinical isolates of Talaromyces marneffei and related species, California, USA. *Emerg Infect Dis*. 2019;25(9):1765-1768. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31441765>.
53. Lau AF, Drake SK, Calhoun LB, Henderson CM, Zelazny AM. Development of a clinically comprehensive database and a simple procedure for identification of molds from solid media by matrix-assisted laser desorption ionization-time of flight mass spectrometry. *J Clin Microbiol*. 2013;51(3):828-834. Available at: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3592033/>.
54. Chariyalertsak S, Supparatpinyo K, Sirisanthana T, Nelson KE. A controlled trial of itraconazole as primary prophylaxis for systemic fungal infections in patients with advanced human immunodeficiency virus infection in Thailand. *Clin Infect Dis*. 2002;34(2):277-284. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/11740718>.
55. Chaiwarith R, Fakthongyoo A, Praparattanapan J, Boonmee D, Sirisanthana T, Supparatpinyo K. Itraconazole vs fluconazole as a primary prophylaxis for fungal infections in HIV-infected patients in Thailand. *Curr HIV Res*. 2011;9(5):334-338. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21916838>.
56. Chaiwarith R, Charoenyos N, Sirisanthana T, Supparatpinyo K. Discontinuation of secondary prophylaxis against penicilliosis marneffei in AIDS patients after HAART. *AIDS*. 2007;21(3):365-367. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17255744>.
57. Ly V, Thu N, Thanh NT, et al. Superior accuracy of the Mp1p antigen assay over cultures in diagnosing talaromycosis - a prospective study. Presented at: Conference Retrovirus Opportunistic Infections; 2020. Boston, MA. Available at: https://www.croiconference.org/wp-content/uploads/sites/2/posters/2020/1430_9_Vo_00750.pdf.
58. Supparatpinyo K, Nelson KE, Merz WG, et al. Response to antifungal therapy by human immunodeficiency virus-infected patients with disseminated Penicillium marneffei infections and in vitro susceptibilities of isolates from clinical specimens. *Antimicrob Agents Chemother*. 1993;37(11):2407-2411. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/8285625>.

59. Sirisanthana T, Supparatpinyo K, Perriens J, Nelson KE. Amphotericin B and itraconazole for treatment of disseminated *Penicillium marneffei* infection in human immunodeficiency virus-infected patients. *Clin Infect Dis*. 1998;26(5):1107-1110. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9597237>.
60. Ouyang Y, Cai S, Liang H, Cao C. Administration of voriconazole in disseminated *Talaromyces* (*Penicillium*) *marneffei* infection: a retrospective study. *Mycopathologia*. 2017;182(5-6):569-575. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28108867>.
61. Supparatpinyo K, Schlamm HT. Voriconazole as therapy for systemic *Penicillium marneffei* infections in AIDS patients. *Am J Trop Med Hyg*. 2007;77(2):350-353. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/17690411>.
62. Supparatpinyo K, Chiewchanvit S, Hirunsri P, et al. An efficacy study of itraconazole in the treatment of *Penicillium marneffei* infection. *J Med Assoc Thai*. 1992;75(12):688-691. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/1339213>.
63. Huang W, Li T, Zhou C, Wei F, Cao C, Jiang J. Voriconazole versus amphotericin B as induction therapy for talaromycosis in HIV/AIDS patients: a retrospective study. *Mycopathologia*. 2021;186(2):269-276. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33616828>.
64. Le T, Kinh NV, Cuc NTK, et al. A trial of itraconazole or amphotericin B for HIV-associated talaromycosis. *N Engl J Med*. 2017;376(24):2329-2340. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28614691>.
65. Supparatpinyo K, Perriens J, Nelson KE, Sirisanthana T. A controlled trial of itraconazole to prevent relapse of *Penicillium marneffei* infection in patients infected with the human immunodeficiency virus. *N Engl J Med*. 1998;339(24):1739-1743. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/9845708>.
66. Lau SK, Lo GC, Lam CS, et al. In vitro activity of posaconazole against *Talaromyces marneffei* by broth microdilution and est methods and comparison to itraconazole, voriconazole, and anidulafungin. *Antimicrob Agents Chemother*. 2017;61(3). Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28031205>.
67. Lei HL, Li LH, Chen WS, et al. Susceptibility profile of echinocandins, azoles and amphotericin B against yeast phase of *Talaromyces marneffei* isolated from HIV-infected patients in Guangdong, China. *Eur J Clin Microbiol Infect Dis*. 2018;37(6):1099-1102. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29536323>.
68. Thu NTM, Borda H, Vitsupakorn S, et al. Development and validation of a colorimetric antifungal susceptibility testing method for the dimorphic fungus *Talaromyces marneffei*. *Med Mycol*. 2023;61(11). Available at: <https://www.ncbi.nlm.nih.gov/pubmed/37994652>.
69. Qin Y, Zhou Y, Liu S, et al. HIV-associated talaromycosis: does timing of antiretroviral therapy matter? *The Journal of Infection*. 2021;84(3):410-417. Available at: <https://europepmc.org/article/med/34963636>.
70. Hall C, Hajjawi R, Barlow G, Thaker H, Adams K, Moss P. *Penicillium marneffei* presenting as an immune reconstitution inflammatory syndrome (IRIS) in a patient with advanced HIV. *BMJ Case Rep*. 2013;2013. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23362074>.
71. Liu X, Wu H, Huang X. Disseminated *Penicillium marneffei* infection with IRIS. *IDCases*. 2015;2(4):92-93. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26793468>.
72. Thanh NT, Vinh LD, Liem NT, et al. Clinical features of three patients with paradoxical immune reconstitution inflammatory syndrome associated with *Talaromyces marneffei* infection. *Med Mycol Case Rep*. 2018;19:33-37. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29379703>.
73. Bahr NC, Rolfes MA, Musubire A, et al. Standardized electrolyte supplementation and fluid management improves survival during amphotericin therapy for cryptococcal meningitis in resource-limited settings. *Open Forum Infect Dis*. 2014;1(2):ofu070. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25734140>.

74. Stott KE, Le T, Nguyen T, et al. Population pharmacokinetics and pharmacodynamics of itraconazole for disseminated infection caused by *Talaromyces marneffei*. *Antimicrob Agents Chemother*. 2021;65(11):e0063621. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34370587>.
75. O'Grady N, McManus D, Briggs N, Azar MM, Topal J, Davis MW. Dosing implications for liposomal amphotericin B in pregnancy. *Pharmacotherapy*. 2023;43(5):452-462. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/36862037>.
76. Pharma A AmBisome® (amphotericin B) liposome for injection. Astellas Pharma; 2015. www.astellas.com/us/system/files/AMBISOME.pdf
77. De Santis M, Di Gianantonio E, Cesari E, Ambrosini G, Straface G, Clementi M. First-trimester itraconazole exposure and pregnancy outcome: a prospective cohort study of women contacting teratology information services in Italy. *Drug Saf*. 2009;32(3):239-244. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/19338381>.
78. Bar-Oz B, Moretti ME, Bishai R, et al. Pregnancy outcome after in utero exposure to itraconazole: a prospective cohort study. *Am J Obstet Gynecol*. 2000;183(3):617-620. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/10992182>.