



Pityriasis (tinea) Versicolor

- Fluconazole 200 mg daily for 5-7 days
- Flu 300 mg once weekly for 2 weeks (98% cure rate)
- Itraconazole 200 mg daily for 5 days (100% cure rate)
- Oral terbinafine and griseofulvin are not effective
- Topical ketoconazole 2% shampoo and cream daily for 2 weeks
- Ketoconazole has best MICs for *Malassezia*

Bologna textbook

KETOCONAZOLE TABLETS

- July 2013 FDA withdrew indications for ketoconazole tablets
- Drug is still available, but no longer indicated for cutaneous fungal infections
- Does not effect ketoconazole cream or shampoo
- Substitute with another azole antifungal drug

KETOCONAZOLE TABLETS

- European Medicines Agency (CHMP) suspended usage of drug due to the conclusion that risk of liver injury is greater than benefit of antifungal treatment. July 2013
- Triggered by French authorities suspending the drug after a 2 year review

KETOCONAZOLE TABLETS



DO NOT ORDER



What about OTC treatment?

News Those ugly scars and Tinea Versicolor

Skin care matters

with Michelle Vernon

Sunday, February 14, 2016 4 Comments

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Home Remedies for Tinea Versicolor



Aloe vera
Coconut oil
Tea tree oil
Yogurt
Garlic

Home Remedies



Growth of *Malassezia furfur* on Sabouraud's dextrose medium in various oils

Fatty Substance	Growth of <i>M. furfur</i>
Butter	++++
Corn oil	+++
Flaxseed oil	+++
Coconut oil	+++
Castor oil	++
Oleic acid	++
Without oil	+

Key: ++++ = excellent growth +++ = good growth ++ = fair growth + = poor growth

Adapted from: Vijayakumar R, Muthukumar C, Kumar T, Saravananmuthu R. Characterization of *Malassezia Furfur* and its control by using plant extracts. Indian J Dermatol 2006;51:145-8.

Growth of *Malassezia* is Enhanced With Certain Oils



Adapted from: Vijayakumar R, Muthukumar C, Kumar T, Saravananmuthu R. Characterization of *Malassezia Furfur* and its control by using plant extracts. Indian J Dermatol 2006;51:145-8.

Malassezia Folliculitis



PITYROSPORUM FOLLICULITIS

- Differential diagnosis of acne
- Acneiform pruritic monomorphic pustules on upper back and chest, occasionally face
- Diagnosis confirmed by skin biopsy showing organism in yeast state below level of epidermis

Malassezia Folliculitis



- Itraconazole 200 mg daily for 2 weeks – is lipophilic
- Fluconazole 200 mg daily for 2 weeks- not lipophilic
- Avoid oils to skin

Seborrheic Dermatitis



- Ketoconazole shampoo and cream

AVOID OILS TO FACE AND SCALP



Cutaneous Candidiasis



Fluconazole 200 mg for 5 to 7 days



CHRONIC PARONYCHIA-OFTEN CAUSED BY CANDIDA

ACUTE PARONYCHIA CAUSED BY BACTERIA

CANDIDA PARONYCHIA

- Fluconazole 200 mg daily for 5 days then once weekly for 8 weeks (or until clear)
- Topical antifungal cream
 - Ciclopirox, ketoconazole or other azole cream
- Avoid cuticle manipulation to prevent recurrence

AVOID KETOCONAZOLE TABLETS

NEW DEVELOPMENTS IN ONYCHOMYCOSIS THERAPY



CURRENT TREATMENT OF ONYCHOMYCOSIS

ORAL DRUGS	TOPICAL DRUGS
<ul style="list-style-type: none"> Terbinafine Itraconazole Fluconazole* 	<ul style="list-style-type: none"> 10% efinaconazole solution 5% tavaborole solution 8% ciclopirox lacquer
<h4>ORAL NEW DEVELOPMENTS</h4> <p>*not FDA approved VT-1161</p>	

TOPICAL ANTIFUNGALS

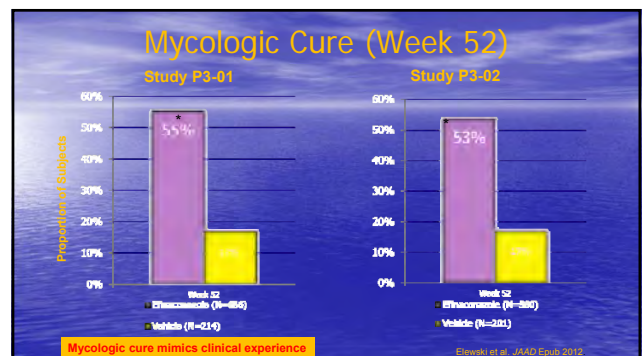
TOPICAL ONYCHOMYCOSIS TREATMENT

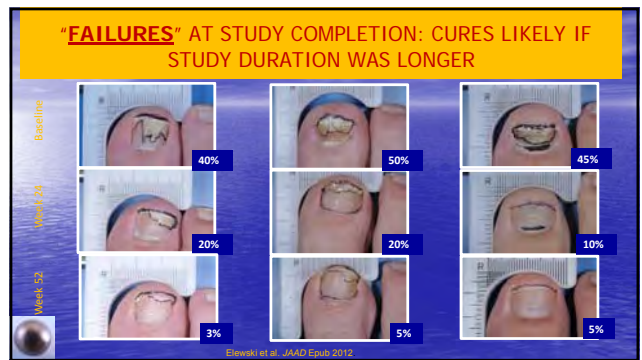
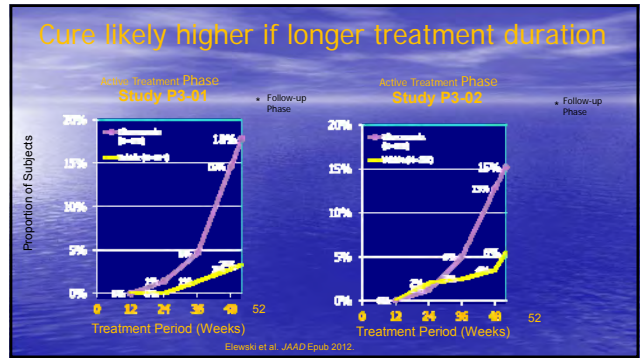
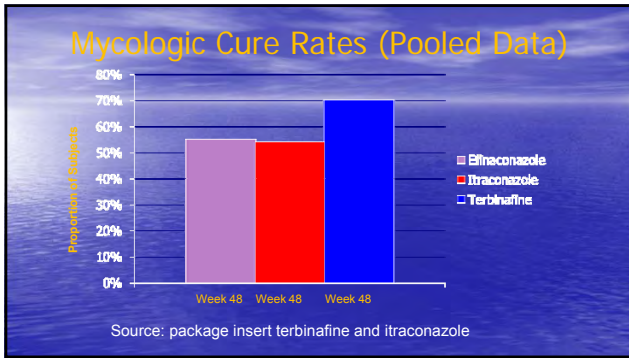
- SOLUTIONS:
 - Efinaconazole 10%
 - Tavaborole 5%
- Non-lacquer alcohol based therapies can be delivered on, under and around the nail bed

EFINACONAZOLE

(2R,3R)-2-(2,4-difluorophenyl)-3-(4-methylenepiperidin-1-yl)-1-(1H-1,2,4-triazol-1-yl)butan-2-ol

- Triazole** antifungal
 - New molecule
- Broad spectrum antifungal with activity against yeasts, molds and dermatophytes





TAVABOROLE: TOPICAL ANTIFUNGAL SOLUTION

AN2690
5-Fluoro-1,3-dihydro-1-hydroxy-2,1-benzoxaborole

Anti-fungal activity

- Crystal structure shows that AN2690 binds with an enzyme critical to fungi growth phase
- It is a new class of anti-fungal agent

Physical properties

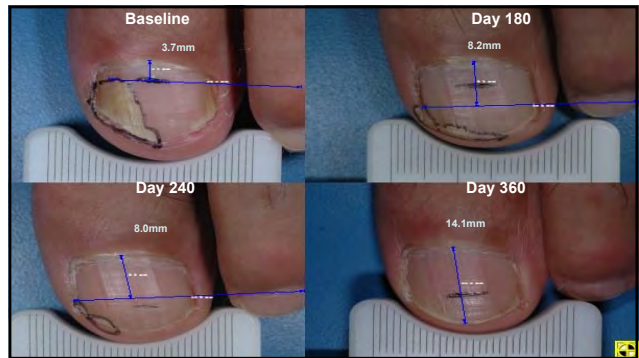
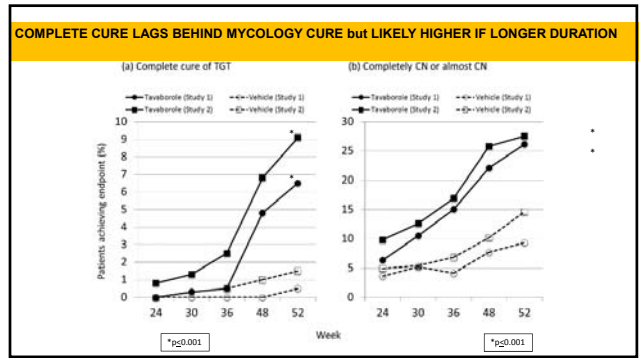
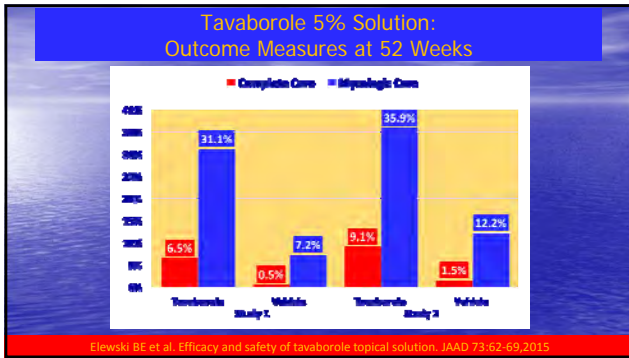
- AN2690 is designed with the physical properties required for nail penetration

BORON IS FOUND IN FOODS: FRUITS, VEGETABLES AND NUTS

Tavaborole Study Design

- Similar to eflinaconazole- applied once daily for 48 weeks in mild to moderate disease
- Differences in studies:
 - No upper age limit in tavaborole study
 - Nails were 20-60% involved in tavaborole vs. 20-50% in eflinaconazole

Elewski BE et al. Efficacy and safety of tavaborole topical solution. JAAD 73:62-69,2015



ORAL ANTIFUNGAL THERAPY FOR ONYCHOMYCOSIS

Onychomycosis: Terbinafine



Toenail / Fingernail

3 MONTHS DAILY FOR TOENAILS, AND 6 WEEKS FINGERNAILS

JAAD 1997;37:740-45 Drake et al
38% cure rate for 3 months

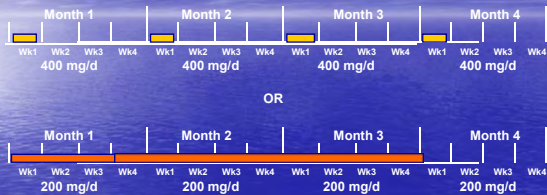
Terbinafine Pulse Dosing

- Zais and Rebell published 250 mg daily for one week for every other OR Third month until nail is healthy
 - Arch Dermatol 2004;140 (6):691-695
- Other dosing regimens: 500 mg daily for one week repeated monthly for 3 months or "pulses"
 - JAAD 2005;53 (4): 578-584

ALCOHOL ANALOGY

OFF LABEL THERAPY

Onychomycosis: Itraconazole



OR

Toenail/Fingernail

14% COMPLETE CURE

*Pulse dosage not approved for toenails

Onychomycosis: Fluconazole

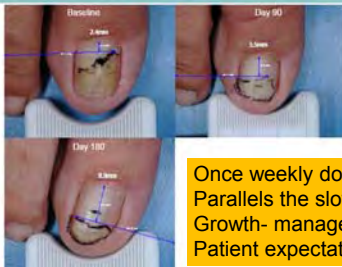


- 48% complete cure 450 mg/week
- 46% complete cure 300 mg/week
- 37% complete cure 150 mg/week

JAAD 1998; 38:S77-86 Scher R. et al

NOT FDA APPROVED FOR THIS INDICATION

Fluconazole



Once weekly dosing
Parallels the slow nail
Growth- manages
Patient expectations



**NOT ALL PATIENTS CURED WITH
CURRENT SYSTEMIC AGENTS**

PHASE 3 CLINICAL STUDIES

	COMPLETE CURE	MYCOLOGIC CURE
Terbinafine	38%	70%
Itraconazole	14%	54%
Meltrex itra	22%	44%
Fluconazole	37-48%*	47%-62%*

NOT ALL PATIENTS ARE CURED

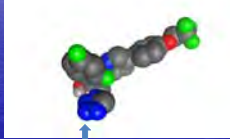
Data Per Package label*

** Fluconazole not FDA approved for onychomycosis Complete cure= normal nail, myc cure

VT-1161

- Next-generation oral antifungal
- Very high penetration into nail
- Favorable oral PK profile; once-weekly dosing
- Robust safety profile to date
- EXCELLENT results thus far in phase 2 onychomycosis study

TETRAZOLE



Novel "Tetrazole" Metal Binding Group

VT-1161 IS A CYP51 INHIBITOR

- Novel potent inhibitor of fungal lanosterol demethylase (CYP51) and binds more tightly to fungal CYP51 than human CYP51
- Less potential for drug interaction than azoles due to less inhibition of P450 enzymes
- Broad spectrum activity- dermatophytes, Candida and molds



Onychomycosis: Fill in the Gaps

- **VT-1161** Has activity against dermatophytes, Candida and molds and is more potent than itraconazole
- Intermittent dosing similar to fluconazole
- **Phase 3 study coming soon**
- **Likely to offer a viable option to patients with onychomycosis, particularly those who failed or did not respond to oral terbinafine.**

What About Diagnosis? Is There a Gap?

- Empiric treatment with terbinafine for patients with suspected onychomycosis is more cost effective than confirmatory testing with minimal effect on safety
- Confirmatory testing before efinaconazole will reduce costs across a range of disease prevalence

TREAT EMPIRICALLY WITH ORAL TERBINAFINE

Mikallov A et al JAMA Derm 2015 online Dec 23

Laboratory Monitoring

- Hepatic risk for Terbinafine: 1:50K to 120K
- Trend away from routine monitoring
 - Isotretinoin
 - Spironolactone
 - Terbinafine

Mikallov A et al JAMA Derm 2015 Kanzler MK JAMA Derm 2015 online Dec 23

Laboratory Monitoring

- Baseline hepatic panel and CBC for terbinafine, itraconazole and fluconazole: is this needed?
 - Trend is away from routine monitoring
 - Liver injury is very rare
 - Most common cause of drug induced hepatitis is trimethoprim-sulfamethoxazole
 - Pulse dosing likely safer- alcohol analogy

Kanzler MK JAMA Derm 2015 online Dec 23

KEY POINTS

- Oral ketoconazole should not be used at all!
- Avoid topical oils in patient with Malassezia
- Topical efinaconazole and tavaborole are effective
- VT-1161 is an oral tetrazole antifungal with excellent potential in onychomycosis
- Empiric oral terbinafine is cost effective
- Side effects can occur so choose your treatment with care

**THE
END**

