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### **The efficacy and safety of pulse versus continuous therapy for dermatophyte toenail onychomycosis**

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**Background:** Oral antifungals can be administered continuously or intermittently. We systematically reviewed the literature to conduct a network meta-analysis (NMA) on efficacy and adverse events (AEs).

**Methods:** We compared the mycologic cure (MC) and AE rates of terbinafine 250 mg continuous for 12, 16, and 24 weeks, 500 mg pulsed for 3 or 4 months; itraconazole 200 mg daily for 12 weeks, 400 mg pulsed for 3 or 4 months; fluconazole 150, 300, or 450 mg once weekly for 9-12 months.

**Results:** There were no significant differences in MC between continuous 12-week terbinafine and continuous 12-week itraconazole. There was no significant difference between 3-pulse itraconazole and 3-pulse terbinafine. There was no significant difference in MC between the continuous 12-week terbinafine and 500 mg pulsed terbinafine for 3 months. Continuous 12-week itraconazole was less effective than continuous 24-week terbinafine (RR = 0.613,  $P < .05$ ). The fluconazole regimens were less effective than continuous 24-week terbinafine (RR = 0.582,  $P < .05$ ). No treatments were significantly different from placebo in likelihood of causing AEs.

**Conclusions:** The most effective regimen was continuous terbinafine 250 mg for 24 weeks. Terbinafine 250 mg for 12 or 16 weeks and pulsed terbinafine 500 mg for 3 months were not significantly different in MC. Continuous itraconazole 200 mg for 12 weeks was not significantly different in MC from pulsed itraconazole 400 mg for 3 or 4 months. Fluconazole regimens were the least efficacious. All the regimens were safe with no significant difference in AEs compared with placebo.

*Commercial disclosure: None identified.*



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### **Progression of cutaneous T-cell lymphoma after dupilumab: Case review of 6 patients**

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**Background:** Dupilumab is a monoclonal antibody that inhibits IL-4 and IL-13 signaling pathways and is approved for treatment of moderate to severe atopic dermatitis (AD). Cutaneous T-cell lymphoma (CTCL) is similar to AD in its clinical presentation, role of  $T_H2$  cells, and skin-barrier disruption. We identified six patients who were treated with dupilumab, and shortly after were either diagnosed with CTCL following initial diagnosis of AD, or experienced progression of previously diagnosed CTCL.

**Results:** Six patients (33.3% female; overall median age 66 [range 58-77] years) were identified. Dupilumab was initiated for clinically presumed AD in three patients and off-label use in recalcitrant CTCL (stages II-III) with severe pruritus in three patients. Patients showed initial improvement of pruritus and skin involvement ( $n = 5$ , mean 11.4 weeks), followed by worsening of body surface area ( $n = 6$ ), pruritus ( $n = 4$ ), lymphadenopathy ( $n = 2$ ), systemic symptoms ( $n = 3$ ), and development of blood involvement in all three with previously diagnosed CTCL. Mean duration of dupilumab treatment was 7.3 months (range 3-24 months). After stopping dupilumab, all 3 stage IV patients developed higher Sézary counts (2 died of disease), and 1 stage III and 1 stage IB patient experienced skin improvement with narrowband UVB and topical steroids. The remaining patient, with stage IA disease, continued dupilumab given atopic benefits but weighed discontinuation.

**Conclusions:** Our experience raises concern about the use of dupilumab in CTCL patients and patients with atypical recalcitrant AD without proper exclusion of CTCL. We found that although these cohorts may improve initially with dupilumab, clinicians must monitor closely for sudden progression of CTCL.

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### **Efficacy of nonsurgical treatments for androgenetic alopecia in men and women: A systematic review with network meta-analyses, and an assessment of evidence quality**

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**Introduction:** Although the etiology of androgenetic alopecia (AGA) is unclear, there exist various therapies for this condition, including 5% minoxidil, platelet-rich plasma (PRP) and low-level laser therapy (LLLT). We systematically reviewed the literature to identify nonsurgical treatments for AGA and performed network meta-analyses (NMAs) to determine the treatments' relative effectiveness.

**Methods:** Only randomized controlled trials (RCTs) were included; the evidence was critically appraised and NMAs were conducted separately for men and women. Outcome was quantified as mean change in hair count from baseline, in hairs per square centimeter (hairs/cm<sup>2</sup>).

**Results:** Eight comparators were identified for men (ie, 5% minoxidil, 2% minoxidil, PRP, LLLT, 0.5 mg dutasteride, 1 mg finasteride, bimatoprost, and placebo/sham), while four comparators constituted the network for women (ie, LLLT, 5% minoxidil, 2% minoxidil, and placebo/sham). In the male and female networks, platelet-rich plasma and LLLT had the highest surface under the cumulative ranking (SUCRA) curve, respectively, thus implying that these are the two most effective treatments. However, the risk of bias across studies that compared each of these two treatments was high.

**Conclusions:** Although recent technologies like PRP and LLLT may appear to be more effective than older treatments like 2% and 5% minoxidil, 0.5 mg dutasteride (men) and 1 mg finasteride (men), the efficacy of the newer treatments should be further investigated using RCT designs with lower risk of bias.

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### **Darier disease: Long-term treatment with systemic retinoids at a tertiary hospital**

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**Darier disease (DD)** is a rare autosomal dominant genodermatosis, which main feature is the hyperkeratotic papule, mainly in seborrheic areas. Studies with systemic retinoids show efficacy in disseminated DD, but there are no large studies on the effects and safety of long-term treatment in these patients. We performed a retrospective study with 32 patients with DD from the University of São Paulo Medical School, during a period of 10 years, from 2007 to 2017. Out of 32 patients, 18 were treated with systemic retinoids (56.2%). Fourteen patients received acitretin, with median time of 78.7 months, and maximum of 209 months and 7 received isotretinoin, with an average of 64.4 months, and maximum of 287 months. All patients presented improvement and there was no case of withdrawal of medication due to therapeutic failure or severe side effects. To our knowledge, there are only few studies with long-term use of retinoids in DD. In 1984, Christiansen et al published a study with 25 patients in use of etretinate up to 60 months. More recent studies describe shorter treatment courses with isotretinoin and alitretin up to 18 months. We found a much longer course of treatment then previously described, up to 17 years with acitretin and 24 years with isotretinoin. In our dermatology service, we have 28 years of positive experience with systemic retinoids in DD. This study demonstrates that prolonged use of systemic retinoids in low doses is safe and effective for patients with moderate to severe DD.

*Commercial disclosure: None identified.*

