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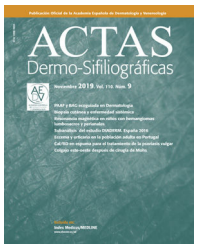

RESIDENT'S FORUM

[Translated article] RF - New Drugs for Managing Acne☆

FR - Nuevos fármacos para el manejo del acné

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PALABRAS CLAVE
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Cannabidiol

Acne vulgaris is a highly prevalent skin condition that can have a considerable impact on quality of life. Topical retinoids, benzoyl peroxide, different antibiotics, and isotretinoin have been the therapeutic pillars for decades. The recent approval of a new antibiotic by the US Food and Drug Administration for moderate to severe forms of acne, together with other new drugs that are being developed, may expand the therapeutic arsenal.

Sarecycline is a narrow-spectrum tetracycline-derived antibiotic (Table 1) with a lower probability of generating antibiotic resistance. The clinical trials SC1401 (n = 968) and SC1402 (n = 1034) included patients with moderate to severe acne, who were randomized to receive sarecycline or a placebo. The main parameter assessed was the Investigator's Global Assessment (IGA) success, equivalent to a reduction of ≥2 points on the IGA and reaching a score of 0 (no lesions) or 1 (hardly any lesions) after 12 weeks. This criterion was achieved by 21.9% and 22.6%, respectively, in the group treated with sarecycline, compared to 10.5% and 15.3% in the placebo group ($P < .0001$ and $P = .0038$). The most common adverse effects were nausea, nasopharyngitis, and headaches[1]. Clinical trial PR-10411 (n = 285) compared the effectiveness of 3 different dosages of sarecycline (0.75, 1.5, and 3 mg/kg) to a placebo and assessed the reduction in lesions at week 12. Significant results were achieved in the groups receiving 1.5 and 3 mg/kg, with a reduction of lesions greater than 50%; no differences were observed between the 2 groups with higher dosages[2]. These studies led to the approval of sarecycline, the first systemic drug approved for acne by the US Food and Drug Administration in more than 40 years. Another alternative novel antibiotic is 4% topical minocycline, a tetracycline antibiotic with bactericidal action against *Cutibacterium acnes*, and practically no systemic absorption. Randomized trial FX2017-22 (n = 1488) compared minocycline with a placebo,

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Table 1 Characteristics of the new drugs approved or under development for the treatment of acne.

Drug	Therapeutic target	Mechanism of action	Route of administration	Frequent adverse effects	FDA approval	EMA approval
Sarecycline Tetracycline derivative	*C. acnes* (anaerobic gram-positive)	Inhibits bacterial protein synthesis by binding to the 30S ribosomal subunit. Also has an anti-inflammatory effect	1.5 mg/kg once daily, orally	Nausea, nasopharyngitis, and headache	Yes, in October 2018	No
Clascoterone Antiandrogen	Cutaneous androgen receptor	Blocks androgen action by competing with dihydrotestosterone to bind to the receptor, thus inhibiting transcription of androgen-sensitive genes.	1% topical cream Twice daily	Erythema and pruritus at the application site	No	No
Tazarotene Third-generation topical retinoid	Cutaneous retinoid receptor (RAR)	Regulates gene expression by modulating cell proliferation, hyperplasia, and differentiation, thus preventing the formation of hyperkeratotic plugs in the pilosebaceous follicles.	0.1% topical foam, once daily	Dry an irritated skin at the application site	Yes, in 2012 Recently relaunched on the market	No
Topical minocycline Antibiotic (FMX101 4%)	*C. acnes*	*Broad-spectrum antibiotic, bactericide, inhibits protein synthesis in C. acnes*	4% topical foam Once daily	Irritation at the application site	No	No
Cannabidiol Nonpsychotropic cannabinoid (BTX 1503)	Cutaneous endocannabinoid system (CB1/CB2 receptors)	Activates CB1 and CB2 epidermal receptors, increasing DNA methylation of the keratinocytes via MAP kinase p38, and inhibits their proliferation. Also regulates sebum production via the TRPV4 pathway in the sebaceous gland	Topical liquid Once or twice daily	Local erythema	No	No
Olumacostat glasaretil Antiandrogen (DRM01)	Antiandrogen	Prevents synthesis of saturated fatty acids by inhibiting the acetyl coenzyme A carboxylase; indirectly prevents the growth of *C. acnes*	7.5% topical gel Twice daily	Dry an irritated skin at the application site	No	No
Epigallocatechin-3-gallate Catechin	Seboregulator and anti-inflammatory	Inhibits proliferation of sebocytes and lipid synthesis via IGF-1, reduces inflammation by inhibiting NF-κB and activator protein-1	1% topical solution Twice daily	Local erythema	No	No

Abbreviations: *C. acnes* indicates *Cutibacterium acnes*; EMA, European Medicines Agency; FDA, US Food and Drug Administration; IGF-1, growth factors similar to type-1 insulin; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; RAR, retinoic acid receptor.

with significant reduction in inflammatory lesions at week 12 ($P < .0001$) and improvement of the IGA score ($P < .0001$) in the intervention group[3].

Greater understanding has recently been achieved of sebum production, which is modulated by androgens, the endocannabinoid system, and multiple proinflammatory mediators such as histamine and leukotrienes, and this has opened up new areas of therapeutic research. Among topical treatments, clascoterone, a competitive antagonist of the androgen receptor, showed superiority compared to placebo in 2 phase-III trials, evaluated by means of the IGA score[4]. Clascoterone would be the first antiandrogen without systemic hormonal effects and could be used in men. Cannabidiol is a nonpsychotropic cannabinoid with anti-inflammatory, sebostatic, and antimicrobial action, which has been shown to be well tolerated in phase-Ib trials. A phase-II trial (drug BTX1503) is currently finishing that evaluated the effectiveness of topical cannabidiol in acne. In systemic treatments, a randomized clinical trial (n = 100) showed that the combination of levocetirizine (a nonsedating antihistamine) and isotretinoin was superior and had fewer adverse effects than treatment with isotretinoin alone[5]. Similar results have been obtained using desloratidine[6]. Antihistamines modulate sebum production and reduce the adverse effects of the retinoids.

The development of these new drugs may change the treatment of acne. It is essential to be aware of them and to achieve greater efficacy and safety in the treatment of this condition.

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