SCHOOLS IN PHARMACOLOGY

Noah Scheinfeld MD
St. Luke's-Roosevelt Hospital Center, New York, NY

Schools in Pharmacology is a new feature in that will appear periodically. It will explicate the dermatologic uses and side effects of new medications and devices. It follows medications mentioned in the Pipeline Previews into their approval and use in clinical practice.

Dutasteride, Cantharidin, Atopiclair, Cetuximab, Sirolimus, AC-11 and Dimericine Reviewed in Brief

Dutasteride and Hair Loss

Dutasteride 0.5 mg is the generic name for Avodart. FDA clearance for Avodart or dutasteride was granted to GlaxoSmithKline on October 9, 2002 for the treatment of benign prostatic hypertrophy. It appears that oral dutasteride might have a role in treating male and female types of alopecia. The following wholly discusses off-label use of dutasteride.[1]

Dutasteride is a synthetic 4-azasteroid compound. It is the first FDA-approved medication that can inhibit both types of 5-alpha reductase (5AR), an enzyme that is commonly believed to be responsible for the conversion of testosterone to 5 alpha-dihydrotestosterone (DHT). DHT appears to be the main androgen responsible for prostate growth as well as male pattern baldness. Type I is found in the skin and hair of men and women; therefore, it should be an effective medication for treating androgenetic alopecia in women avoiding pregnancy. Finasteride 1 to 5 mg (Propecia and Proscar) only lowers the DHT by 64% to 67%. Finasteride only blocks Type II, 5-alpha reductase found in the prostate gland and thus has little effect on alopecia in females.

Dutasteride standard dosage is 0.5 mg of the active ingredient dutasteride per soft gelatin capsule. The capsule is compounded by dissolving 0.5 mg of dutasteride in a combination of mono-di-glycerides caprylic/capric acid and butylated hydroxytoluene. Other ingredients include BSE-free bovine gelatin, glycerin, and yellow ferric oxide.

It takes several months for dutasteride to flush out of the body and if a woman were to take it during a pregnancy while she was carrying a male fetus it would come out looking female. The penis doesn't start to develop until the third trimester so there is some lead time in case a pregnancy develops while on therapy. There is some evidence to show that DHT may be needed to develop a male brain and that blocking DHT could cause birth effects at an earlier stage of development.

It has been suggested that if dutasteride is obtained in its raw form, one might even be able to compound their own dutasteride topical solution. It was reported in Avodart's prescribing information that the medication is absorbed through the skin as well. Dutasteride in its raw form is a white-yellowish powder. It is insoluble in water but can easily be dissolved in ethanol (44mg/mL), methanol (64 mg/mL), and polyethylene glycol 400 (3mg/mL). No data regarding its utility for its topical role in hair loss treatment has been clinically established.

Research has assessed dutasteride effects on DHT at daily dosages of 0.01 mg, 0.05 mg, 0.5 mg, 2.5 mg, and 5.0 mg per day. Scientists noted that the highest suppression of DHT was achieved with 2.5 mg or 5.0 mg per day. At a daily dosage of 2.5 mg or 5.0 mg, Dutasteride suppresses close to 100% of the DHT whereas 5.0 mg daily dosage of Finasteride only suppresses close to 70% of the DHT. According to information provided by GSK, the level of DHT suppression does not seem significantly different between 2.5 mg and 5.0 mg, and at a daily dose of 0.5mg DHT inhibition is close to 90%.

The role of dutasteride is a promising agent for the treatment of alopecia whose full utility and safety profile has yet to be defined.

Cantharidin

Cantharidin, an extract of the blister beetle, a highly effective therapy in eliminating molluscum will legally be available in the US. Cantharidin was removed from the market by the Food and Drug Administration in 1962 when its manufacturer failed to submit evidence of efficacy. The FDA has included cantharidin in a proposed list of bulk substances that physicians and pharmacists are permitted to compound for use in individual patients.

Cantharidin is typically compounded in a colloidin solution which sometimes results in sol. One retrospective study assessed cantharidin for treating molluscum in 300 children. Ninety percent of the children had complete clearing, and an additional 8% improved after an average of 2.1 treatments. While many of the children experienced temporary burning, pain, pruritus, and erythema, 95% of parents said they would proceed with another treatment if warranted.[2]

Atopiclair

Atopiclair is a hydrolipidic cream that has been developed for the management of atopic dermatitis (AD). The putative active ingredients of Atopiclair are hyaluronic acid, telmesteine, Vitis vinifera, and glycyrrhetinic acid. A 5-week study in 30 adult patients with mild to moderate AD showed that MAS063D offered significant benefits over a vehicle-only control. MAS063D improved the total body area affected (17.2% to 13.2%, $p<.001$), itch score (2.7 to 1.3 on a 10-point scale, $p=.001$) and EASI score (28.3 to 24.3, $p=.024$) after 22 days treatment compared to baseline. The patients' opinion of Atopiclair (patients' view of itch control, and view of study substance) was rated by participating patients as significantly better than control ($p=.008$, $p=.042$, respectively). Based on these preliminary results in a small scale study, it is suggested that Atopiclair is a possible new treatment option for improving signs and symptoms in adults with mild to moderate AD.[3]

No peer-reviewed American studies have been published yet on Atopiclair. Atopiclair has no medically active ingredients—it was approved as a "medical device," not a medication. Its ultimate utility has yet to be established. However, as large molecules such as those contained in Atopiclair can complex with large amounts of water, it should be able to effectively moisturize the skin or at the very least act as a medical wet dressing.

Two Drugs, Cetuximab and Sirolimus, Have Been Reported to Cause Acne

Sirolimus is a new immunosuppressive agent used to prevent rejection in renal allograft recipients in order to reduce the need of potentially nephrotoxic calcineurin inhibitors (cyclosporine, tacrolimus). Cases of follicular acneiform eruptions induced by sirolimus in renal allograft recipients have been reported, which were severe and difficult to treat, and resolved only after discontinuation of sirolimus. One large study noted an array of eruptions of the pilosebaceous apparatus involvement, including acne-like eruptions (46%), scalp folliculitis (26%), and hidradenitis suppurativa (12%); edematous complaints, including chronic edemas (55%) and angioedema (15%); mucous membrane disorders, including aphthous ulceration (60%), epistaxis (60%), chronic gingivitis (20%), and chronic fissure of the lips (11%); and last, nail disorders including chronic onychopathy (74%) and periungual infections (16%).[4]

Cetuximab is a member of a new family of antineoplastic agents that inhibit epidermal growth factor receptor (EGFR). Eight-five percent of patients treated with it developed acneiform eruptions after a mean interval of 10 days; 31% severe. Comedones were never found and acne involved nonclassical sites in 3 of 11 patients. Antibiotic treatment was given to 4 and local treatment to 2 patients which was always effective.[5]

AC-11 and Dimericine Two DNA Repair Enhancers

Two new substances, AC-11 and Dimericine, appear to enhance the DNA repair capacity of cells. These substances might have use in treating patients with xeroderma pigmentosa and in enhancing the ability of sun blocks to prevent ultraviolet-induced cellular damage.

AC-11 is the successor compound to C-MED-100® the first nutraceutical having FDA permission to claim natural DNA repair activity. AC-11 is a Cat's Claw (Uncaria tomentosa) water extract that is claimed to be a highly effective anti-aging treatment of skin because of several mechanisms: NF-kB inhibition blocking inflammatory cytokine production (eg, TNF alpha), antioxidant properties via electrophilic scavenging and NF-kB inhibition reducing surface peroxides, and enhancement of DNA repair by reducing macromolecular expression and damage and decreasing cellular replication of damaged DNA. When AC-11 is applied topically to skin it decreases the number of "sun burnt cells" and pathogenic DNA dimers induced by ultraviolet light. AC-11 can be taken orally or applied topically. It is made by Optigenex Inc.

Dimericine, made by Applied Genetics Inc. Dermatics, is a bacterial enzyme—T4 endonuclease V—that has been known for decades to repair damaged DNA strands in a test tube enveloped in a fat bubble called T4N5 liposome, which can penetrate a skin cell. When creams using Dimericine are incorporated into creams, these creams can reduce UV induced skin damage and can impede the development of actinic keratoses.

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