Update on New Drugs in Dermatology

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Medications in dermatology are used in a variety of different methods and dosages and for numerous different diseases entities that are not approved by the US Food and Drug Administration (FDA); however, there are medications that have only recently hit the market that require our attention, as they are either FDA approved for the intended dermatologic use or could be effective in treating conditions that previously have been poorly managed.

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CenterWatch (http://www.centerwatch.com/) is an online resource that provides directories, analysis, and market research of medications that are either under clinical evaluation or available for use in patients. A list of currently approved drugs by the US Food and Drug Administration (FDA) also is available by specialty. It is important for dermatologists in-training to know about recently approved drugs and those that are in the pipeline, as these treatments may benefit patients who are unresponsive to other previously used medications. New drugs also may be useful for physicians who have a difficult time getting insurance to cover prescriptions for their patients, as most new medications have built-in patient assistance.

New Drugs in Dermatology

Actinic Keratosis—Ameluz (aminolevulinic acid hydrochloride)(Biofrontera AG) is a new drug that was approved in May 2016 for treatment of mild to moderate actinic keratosis on the face and scalp.[1] It is only intended for in-office use on patients who may not be candidates for other treatment options for actinic keratosis. The product is a gel formulation that should be applied to cover the lesions and approximately 5 mm of the surrounding area with a film of approximately 1-mm thickness. The entire treatment area is then illuminated with a red light source, either with a narrow spectrum around 630 nm with a light dose of approximately 37 J/cm^2 or a broader and continuous spectrum in the range of 570 to 670 nm with a light dose between 75 and 200 J/cm^2.[1] Similar to the previously used aminolevulinic acid treatment method for actinic keratosis, the patient may experience a burning stinging sensation throughout the treatment and the skin will then proceed to peel.

Psoriasis and Psoriatic Arthritis—Taltz (ixekizumab) (Eli Lilly and Company) was approved by the FDA in March 2016 for the treatment of moderate to severe plaque psoriasis.[2] It is a humanized IL-17A antagonist that works when IgG4 monoclonal antibodies selectively bind with IL-17A cytokines and inhibit their interaction with the IL-17 receptor. Although this injectable medication is approved for the treatment of psoriasis, it also can potentially be used off label for the treatment of psoriatic arthritis and rheumatoid arthritis. The approved dosage is 160 mg (two 80-mg injections) at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks.[2] Injectable immunomodulatory medications such as ixekizumab are ideal for patients in whom topical treatments and light therapy failed and they continue to have serious psoriatic discomfort as well as for those who have substantial body surface area coverage.

In January 2015, Cosentyx (secukinumab) (Novartis Corporation) was approved by the FDA.[3] Similar to ixekizumab, this injectable is an IgG1 monoclonal antibody that selectively binds to the IL-17A cytokine and inhibits its interaction with the IL-17 receptor. It is approved for the treatment

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of moderate to severe plaque psoriasis and psoriatic arthritis. The approved dosage for plaque psoriasis is 300 mg (two 150-mg subcutaneous injections) at weeks 0 through 4 followed by 300 mg every 4 weeks as needed until clearance.[3] Similar to ixekizumab, secukinumab may be used for the treatment of recalcitrant psoriasis or psoriasis with substantial body surface area involvement.

Melanoma—Cotellic (cobimetinib)(Genentech USA, Inc) was FDA approved in November 2015.[4] Cobimetinib is a reversible inhibitor of mitogen-activated protein kinase (MAPK)/extracellular signal regulated kinase 1. Mitogen-activated protein kinase MEK1 and MEK2 are regulators of the extracellular signal-related kinase pathway, which promotes cellular proliferation. This pathway is key, as melanomas that have a BRAF V600E and kinase mutation continue to proliferate due to the constitutive activation of MEK1 and MEK2, further promoting cellular proliferation. Cobimetinib is approved for the treatment of melanoma in patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in conjunction with vemurafenib. Zelboraf (vemurafenib)(Genentech USA, Inc), another inhibitor of BRAF V600E, also is used for the treatment of unresectable melanomas and was initially approved in 2011.[5]

BRAF is a serine/threonine protein kinase. When unregulated, it results in the deregulation of cell proliferation. According to Ascierto et al,[6] 50% of melanomas have a BRAF mutation, with nearly 90% of them with a V600E mutation. Hence, since the advent of direct chemotherapeutic agents such as BRAF inhibitors, clinical trials have shown notable reduction in mortality and morbidity of melanoma patients with BRAF mutations.[6]

Imlygic (talimogene laherparepvec)(Amgen, Inc) is a modified oncolytic viral therapy.[7] This treatment was approved by the FDA in 2015 and replicates within tumors to produce granulocyte-macrophage colony-stimulating factor protein, which promotes an antitumor immune response within unresectable cutaneous, subcutaneous, and nodal melanoma lesions. Although it is not a gene-directed therapy, the melanoma does not require a specific mutation for treatment. Again, this medication is better served in conjunction with other melanoma chemotherapeutic and surgical interventions.

Submental Fat—Kybella (deoxycholic acid) (Allergan) is a nonhuman, nonanimal, synthetically created compound that is naturally found within the human body for the breakdown and absorption of dietary fat.[8] This drug was FDA approved in 2015 for the improvement of the appearance of moderate subcutaneous fat under the chin. Patients are evaluated in clinic to determine if the submental fat would be responsive to an injectable or require more radical surgical intervention based on desired outcomes. The treatment is administered as 0.2-mL injections (up to a total of 10 mL) spaced 1-cm apart and ideally is repeated at regular intervals to evaluate for efficacy.

Basal Cell Carcinoma—Odomzo (sonidegib) (Novartis Corporation) was FDA approved in 2015 for locally advanced basal cell carcinoma.[9] Odomzo is a smoothened antagonist that inhibits the hedgehog signaling pathway. Smoothened is a transmembrane protein that allows for signal transduction of hedgehog proteins.[10] Protein patched homolog 1 binds to smoothened protein and prevents the signal transduction through the cell for Gli family zinc factor 1 to continue protein translation; however, when PTCH is mutated and can no longer bind to smoothened, tumor formation results, specifically basal cell carcinoma. Hence, sonidegib is for the treatment of basal cell carcinomas that have persisted despite radiation treatment and/or surgery as well as for patients who have multiple basal cell carcinomas that can no longer be treated with surgery or radiation.

Final Thoughts

Overall, although there are several medications that can be used in conjunction for treatment of dermatological conditions, it always is recommended to know what is in the pipeline as FDA-approved medications for dermatology.

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