AESTHETICS

Revance Therapeutics, Inc. has submitted a Biologics License Application (BLA) to the FDA for daxibotulinumtoxinA for Injection (DAXI) in the treatment of moderate to severe glabellar (frown) lines. The submission includes results from the SAKURA Phase 3 trials, which is the largest aesthetic neuromodulator clinical program ever conducted for the treatment of glabellar frown lines.

A pooled analysis of the two SAKURA 1 and 2 pivotal studies and the SAKURA 3 open label safety study, reported at the annual meeting of the American Society for Dermatologic Surgery (ASDS) 2019 Annual Meeting in Chicago, showed that the magnitude and duration of clinical efficacy of DAXI between those subjects with prior botulinum toxin A (BoNT-A) treatment and those who were treatment naïve are similar, as was the safety profile.

“I think it is quite interesting to note the results from the pooled analyses, as they illustrate that previous BoNT-A treatment may not be a factor in the clinical efficacy or duration of effect of DaxibotulinumtoxinA for Injection,” says lead author Joel L. Cohen, MD of AboutSkin Dermatology in Colorado. “These data give me confidence that DAXI will be an appropriate, effective, and predictable treatment option for patients who may switch from another BoNT-A product, as well as those who are new to neuromodulators.”

Additional data presented from the SAKURA 3 open-label safety study show that 96 percent of patients had a clinically measurable improvement (≥1 grade change) in glabellar lines at week four after treatment with DAXI. This result was sustained for at least 28 weeks in at least half of the patients.

Additionally, in the SAKURA 3 study with DAXI for glabellar lines in which more than 2600 patients were treated, the clinical responses to DAXI for both response rates and duration of effect were highly consistent from treatment cycle to treatment cycle and no new safety concerns were observed.

Allergan’s Juvéderm Voluma XC is now FDA-approved for cheek augmentation in the mid-face in adults over 21 with a TSK Steriglide cannula.

This cannula features a patented tip design with a near-tip delivery port for precise product placement. Within the Juvéderm Collection of Fillers, this is the first approval for the use of cannula.

In a multicenter, split-face, investigator-blinded, non-inferiority study to assess the safety and effectiveness of Juvéderm Voluma XC for correction of age-related volume deficit in the mid-face with the use of the new cannula versus a needle, results demonstrated comparable performance, safety profile, and patient satisfaction between cannula and needle injection.

The FDA approved Jeuveau (prabotulinumtoxinA-xvfs), the lead product from Evolus, Inc., for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults.

BTL launched Emtone to target cellulite via thermal monopolar radiofrequency and mechanical targeted pressure energy simultaneously.

This combination results in increased production of collagen and elastin to effectively address all major contributing factors to cellulite and smooth the appearance of dimpling, BTL says. Emtone can also be used on all body types with no BMI or skin color restrictions.

Studies show that Emtone is 64 percent more effective than standalone cellulite treatments for building elastin, and 59 percent more effective for building collagen, the company states. Additionally, Emtone was shown to be 50 percent faster than standalone therapies, with a 90 percent rate of patient satisfaction, BTL reports.

For best results, most patients undergo four Emtone treatments, scheduled once or twice a week. A treatment typically takes about 20 minutes, depending on the treated area.

The FDA has cleared a new indication statement for Cellfina (Merz) that notes the benefits of treatment last for five years—an increase from the previous three-year indication. Cellfina demonstrated five-year improvement in the appearance of cellulite on the buttocks and thighs of adult females. Five-year durability makes Cellfina the longest-lasting FDA-cleared treatment for cellulite on the market.

The new indication is based on observations by an independent physician using before and after patient photographs at five years post-treatment. Results showed that after a single in-office treatment, 100 percent of follow-up patients still had noticeable improvements. Follow-up studies at one, three,
and five years after a single in-office treatment showed sustained improvements.

Allergan plc’s CoolTone device received FDA clearance for improvement of abdominal tone, strengthening of the abdominal muscles, and development for firmer abdomen. CoolTone is also indicated for strengthening, toning and firming of buttocks and thighs.

Using magnetic muscle stimulation (MMS), CoolTone technology penetrates into the muscle layers and induces involuntary muscle contractions. The body responds to these contractions by strengthening its muscle fibers, resulting in improved muscle conditioning. Whether targeting abdomen, buttocks or thighs, CoolTone strengthens, tones, and firms the muscles in the treated area, resulting in a more defined and toned appearance. CoolTone has 50 percent more magnetic intensity than the leading competitor (1.35 T versus 0.9 T) at the point of contact (based on performance testing measuring magnetic field expressed in tesla [T] over the applicator surface). The clinical significance of this data has not been established.

Cutera launched the new truSculpt flex muscle sculpting platform in the US. truSculpt flex is FDA-cleared for the improvement of abdominal tone, strengthening of the abdominal muscles, and development of a firmer abdomen. It is also cleared for the strengthening, toning, and firming of buttocks and thighs.

truSculpt flex simultaneously treats eight muscle groups, covering the largest treatment area in the body sculpting industry, Cutera says. Three treatment modes in the same session simulate different workouts by replicating intensified twisting, squat, and crunch actions, the company adds.

Proprietary MDS technology involves direct delivery of electrical current to stimulate muscle contractions without energy waste and treats specific muscle groups using three treatment mode options. The device offers customizable handpiece configuration and placement locations to target multiple, specific small and large muscle groups with no downtime. These low levels of energy achieve deep, full muscle contractions at high intensity.

ACNE AND ROSACEA

The FDA is reviewing the New Drug Application (NDA) from Cassiopea SpA for clascoterone cream 1% and has set a Prescription Drug User Fee Act (PDUFA) action date of August 27, 2020.

Clascoterone is a new chemical entity and a proposed first-in-class topical androgen receptor inhibitor for the treatment of acne. It is also in late-stage development for the treatment of androgenetic alopecia in men.

Joshua Zeichner, MD provided an update on clascoterone in the October edition of Practical Dermatology® magazine, noting, “Clascoterone represents a new treatment option for acne patients. Traditional anti-androgen treatments like spironolactone are effective but cannot be used in men because of adverse events like gynecomastia. The action of clascoterone is at the site of application rather than systemically. No sexual side effects or gynecomastia, which have been seen with the use of oral anti-androgens, were observed in the study of topical clascoterone.”

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PrivatEquity

By The Numbers

184 Number of private equity-backed dermatology management groups that acquired dermatology practices from 2012 to 2018

381 Estimated number of acquired dermatology clinics as of mid-2018

12x Approximate number of takeovers in 2017 as in 2012

— JAMA Dermatol. 2019;155(9):1013-1021
La Roche-Posay’s Effaclar Adapalene Gel 0.1% Acne Treatment reached the over-the-counter market this summer. With the launch, the company now offers a topical prescription-strength retinoid (adapalene) acne treatment in addition to its existing OTC Effaclar Duo micronized benzoyl peroxide acne treatment.

La Roche-Posay also launched My Skin Track PoreScan. The tool uses artificial intelligence to make personalized skincare recommendations for those concerned with clogged pores, raised imperfections, and residual marks.

FDA is expected to make a decision this month on Ortho Dermatologic’s New Drug Application for IDP-123 (tazarotene 0.045%) Lotion for acne. If approved, IDP-123 will be the first tazarotene acne treatment available in a lotion form.

The NDA submitted for IDP-123 includes data from two successfully completed Phase 3 randomized, placebo-controlled, double-blind clinical trials in 1,614 patients with moderate to severe acne. The primary efficacy endpoints included the absolute change in the mean non-inflammatory and inflammatory lesion counts, the percentage of subjects who had a least a two-grade improvement from baseline to week 12 in the Evaluator Global Severity Score (EGSS) and who had “clear” or “almost clear” skin. In both Phase 3 studies, all primary efficacy endpoints were met with statistical significance (p<.001). IDP-123 was also shown to be well-tolerated in the clinical study population. The most common adverse events were application site pain, application site dryness and application site exfoliation.

Phase 3 study results show that Epsolay microencapsulated benzoyl peroxide cream, 5% demonstrated statistically significant improvement in efficacy and was well tolerated in patients with papulopustular rosacea. Sol-Gel Technologies’ patented microencapsulated technology enables a drug substance to be entrapped in porous silica microcapsules to slow the release of treatment and potentially minimize the skin irritation often associated with existing topical therapies.

Sol-Gel is planning to share top-line Phase 3 results in the first quarter of 2020 for the investigational acne treatment TWIN, a fixed-dose combination of microencapsulated benzoyl peroxide and microencapsulated tretinoin.

Sol-Gel plans to submit an NDA for Epsolay in the first half of 2020.

The FDA approved an expanded indication for Almirall’s Aczone 7.5% Gel to include patients aged 9-11. Aczone 7.5% Gel was previously approved in February 2016 to treat inflammatory and non-inflammatory acne in patients 12 and older.

The expanded approval was based on data from an open-label safety study to assess safety, pharmacokinetics, and treatment effect of Aczone Gel, 7.5% in 101 patients 9 to 11 years of age with acne vulgaris. Aczone 7.5% Gel was determined to be safe and effective in this patient population.

Sebacia microparticles continue to show benefit for the management of acne. New research presented at the ASDS 2019 Annual Meeting show that the technology helps to safely and effectively clear acne when used with or following pre-treatment with common first-line topical acne medications.

The microparticles feature a silica core covered in gold, a light-absorbing material that draws in the laser’s energy and delivers it directly to the sebaceous gland.

In the ongoing European Union real-world registry, patients were prescribed a two-to-four-week course of topical retinoid followed by three weekly in-office treatments of Sebacia microparticles at one of nine non-academic clinical practices in Europe.

Latest clinical results out to two years demonstrated:
- 92 percent average acne inflammatory lesion count (ILC) improvement at 24 months compared to baseline.
- 77 percent of patients were acne medication-free at 24 months.
- Nine percent of patients received a topical acne drug and only 14 percent received a systemic acne drug during the follow-up period.
- There were no serious or unanticipated adverse events.

The FDA approved Amzeeq (minocycline) topical foam, 4%, from Foamix Pharmaceuticals, Ltd. for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in adults and pediatric patients nine years of age and older. Amzeeq, formerly known as FMX101, is the first topical minocycline to be approved by the FDA for any...
A Clinician’s Take on Tremfya Four-year Data

New long-term data from the open-label period of the Phase 3 VOYAGE 1 clinical trial show that 82 percent of patients receiving Tremfya (guselkumab, Janssen) in the combined group of patients initially randomized to Tremfya or to placebo with crossover to Tremfya at week 16 achieved at least a 90 percent improvement in the Psoriasis Area Severity Index (PASI 90) response and an Investigator’s Global Assessment (IGA) score of cleared (0) or minimal disease (1) at week 204 (4 years). The data were presented at the 39th Fall Clinical Dermatology Conference in Las Vegas.

Additional results from the open-label extension of the VOYAGE 1 Phase 3 clinical study showed that PASI 100, IGA 0/1, and IGA 0 clear skin responses were consistent at week 52 and week 204 in the combined group of patients initially randomized to Tremfya or to placebo with crossover to Tremfya at week 16. Proportions of patients with Psoriasis Symptoms and Signs Diary (PSSD) symptom scores of 0 (no symptoms of psoriasis) were consistent at week 76 and week 204. No new safety signals were identified.

Andrew Blauvelt, MD, MBA, President, Oregon Medical Research Center, and VOYAGE 1 study steering committee member, spoke to Practical Dermatology magazine about the findings.

Obviously patients and their physicians are concerned about long-term safety and efficacy. What do you see as the value specifically of 4-year data from a long-term clinical trial?

Dr. Blauvelt: Long-term data for psoriasis patients on biologics are critical to determine whether drugs continue to work and whether any new safety signals emerge over time. Ideally, we want drugs that continue to work over time without causing any unexpected or problematic side effects.

Was there anything you were looking for in this data? Any surprises?

Dr. Blauvelt: The four-year long-term data emerging from the VOYAGE guselkumab trials are very reassuring while revealing no surprises. More specifically, efficacy is maintained in the vast majority of patients after four years of continuous guselkumab use and no new safety signals have emerged in these patients.

We know that many patients do well on biologics long-term but some lose efficacy. Can you offer some context for the degree and extent of durability seen with Tremfya?

Dr. Blauvelt: Clinical trial and real-world data with older biologics have shown that ustekinumab, an IL-12/IL-23 blocker, clearly has better efficacy durability than TNF blockers. Since guselkumab also targets IL-23 while being dosed infrequently (every two months), one would also expect guselkumab efficacy to be durable. This is exactly what we have now seen with the VOYAGE four-year data: very durable efficacy (essentially flat efficacy curves) over time.

Which patients do you believe are the best candidates for Tremfya? Has/will this data influence your prescribing?

Dr. Blauvelt: These long-term data reinforce the concept that newer biologics like guselkumab are more effective, safer, and more convenient than older biologics that block TNF. In practice, I no longer prescribe TNF blockers, and encourage providers to challenge payers who force step therapy with less effective and less safe drugs upon our patients.

condition. It is expected to be available January 2020.

The approval is supported by data from three Phase 3 clinical trials in 2,418 patients nine years of age or older. In each 12-week, multicenter, randomized, double-blind, vehicle-controlled study, subjects with moderate to severe acne vulgaris were treated once-daily with Amzeeq or vehicle. No other topical or systemic acne medication was permitted to be used by subjects during the study period. The studies each found statistically significant disease improvement with Amzeeq versus vehicle for the co-primary endpoint of absolute reduction of inflammatory lesions, while studies 2 and 3 demonstrated a statistically significant improvement in IGA treatment success. IGA treatment success was defined as a score of 0 (“clear”) or 1 (“almost clear”) and at least a two-point decrease from baseline. Amzeeq was well-tolerated and no treatment-related serious adverse events were reported. The most common adverse reaction was headache, which was reported in three percent of subjects treated with Amzeeq versus two percent of subjects treated with vehicle.

Amzeeq utilizes the proprietary Molecule Stabilizing Technology (MST) platform from Foamix to deliver minocy-
Sunscreen ingredients found in different sunscreens enter the bloodstream at levels that far exceed the FDA’s recommended threshold without a government safety inspection, a study in *Journal of the American Medical Association* suggests.

Leading dermatologists who reviewed the new findings for *Practical Dermatology* magazine caution that the benefits of using sunscreen far exceed any downsides.

“Ultraviolet radiation causes skin cancer. Therefore a comprehensive sun protective regimen which includes sunscreen, sun avoidance, and protective clothing is central to prevention,” says Adam Friedman, MD, FAAD, Professor and Interim Chair of Dermatology at George Washington School of Medicine and Health Sciences in Washington, DC, where he also serves as Residency Program Director, Director of Translational Research, and Director of Supportive Oncodermatology.

In the study, 24 participants applied one of four different kinds of sunscreen spray, lotion, or cream four times per day for four days on all areas that wouldn’t be covered by a swimsuit. Researchers then measured the concentration of avobenzone, oxybenzone, octocrylene, and ecamsule. If the blood absorption of any of these ingredients exceeds 0.5 nanograms per milliliter (ng/mL), the FDA recommends that they undergo nonclinical toxicology assessment including systemic carcinogenicity and additional developmental and reproductive studies.

The levels of all four chemicals in the participants’ bloodstream far exceeded that even within one day—and three remained there for seven days. For oxybenzone, in particular, plasma concentrations reached the threshold within two hours after a single application and exceeded 20ng/mL on day seven of the study. The FDA has previously included these four chemicals on a list of ingredients that need to be researched further before they can be considered “generally safe and effective.”

“These sunscreen ingredients have been used for several decades without any reported internal side effects in humans,” notes AAD President George J. Hruza in a statement. “Skin cancer is the most common cancer in the United States, and dermatologists see the impact it has on patients’ lives every day. Unprotected exposure to the sun’s ultraviolet rays is a major risk factor for skin cancer.”

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In an editorial for the July 2019 edition of *Practical Dermatology* magazine, Chief Cosmetic Surgery editor Joel Schlessinger, MD urged healthy skepticism.

“I have already seen countless national mentions of the importance of essentially disregarding this study that was done by the FDA under exactly the guidelines that we, as dermatologists, tell our patients to use sunscreen. To me, this challenges the limits of what we should be doing. The study raises legitimate questions, on top of the continued concern about sunscreens’ effect on coral bleaching,” Dr. Schlessinger says.

“Our primary job is to protect our patients. This study shows that diligent patients may actually achieve meaningful levels of certain ingredients (avobenzone, oxybenzone, octocrylene, and ecamsule) in the blood. The ramifications of this are not known in adults, children, or pregnant women. This alone should make us rethink our blind allegiance to manufacturers who have not done the requisite studies to determine the effects of their products on the end-user,” he says. “What is needed—sooner rather than later—is a study that corroborates or disproves the data in this study and investigation into newer forms of sunscreen. Sadly, the FDA has clearly not done the public any favors with its lack of approval of newer forms of sunscreen. This may be due to the lack of testing and rigor that was evidenced in the *JAMA* study, but if there are now concerns on the table, every effort should be made to analyze older, as well as potentially newer, sunscreens for harmful properties.”
Year in Focus

Burnout Perspectives

Although the burnout rate among physicians in the United States has dropped, new data suggest that significant room for improvement remains. The burnout rate dropped modestly in 2017 from its peak in 2014. Current burnout rates are in line with 2011 levels.

The triennial study of physician burnout by researchers from the American Medical Association (AMA), the Mayo Clinic, and Stanford University School appears in Mayo Clinic Proceedings.

The study finds that 43.9 percent of US physicians exhibited at least one symptom of burnout in 2017, compared with 54.4 percent in 2014 and 45.5 percent in 2011. In comparison, the overall prevalence of burnout among US workers was 28.1 percent in 2017, similar to levels found in 2014 (28.4 percent) and 2011 (28.6 percent).

“We like having a derm-dispensed option in our office,” says Florida-based dermatologist Leslie Baumann, MD. “I believe there is a link between an office visit and compliance when the patient can leave with the recommended medication in hand. Life is full of distractions and making a drug available in the office helps to ensure that the patient will use it in the way it has been prescribed. And, there is an enhanced possibility that use of the drug will begin that day. This means the patient will be able to see results sooner. We dispense several brands in our office, specifically for this reason and I suspect it is a strong trend.”

The FDA approved Galderma’s Aklief (trifarotene) Cream, 0.005% for the topical treatment of acne. Aklief Cream is the only topical retinoid that selectively targets retinoic acid receptor (RAR) gamma, the most common RAR found in the skin. Trifarotene is the first new retinoid molecule to receive FDA approval for the treatment of acne in more than 20 years. Aklief Cream is the first topical treatment specifically studied and proven to treat facial (forehead, cheeks, nose and chin) and truncal (chest, shoulders and back) acne, offering healthcare professionals and acne patients another treatment option.

“Galderma came out with adapalene many years ago, which really was not irritating to the skin but had similar efficacy [to tretinoin], which was great. Fast forward, we had tazarotene. Fast forward, we had some retinoids with other indications, and now fast forward, we actually have a retinoid that targets retinoid receptor for gamma, which is very good with efficacy and very, very low with irritation,” says Sandra Johnson, MD, FAAD, an investigator in the clinical trials of Aklief Cream and a dermatologist at Johnson Dermatology in Fort Smith, AR. “The tolerability of trifarotene is much better than that of prior topical retinoids, if you can compare them. Trifarotene in this new topical retinoid is also the first one that has been studied for both truncal and facial acne. So that is a new thing in our dermatology market.”

The approval of Aklief Cream is supported by data from the two pivotal Phase 3 clinical trials of once-daily Aklief Cream in patients with moderate acne on the face and trunk. The two identical 12-week, randomized, multicenter, parallel group, double-blind, vehicle-controlled clinical trials of 2,420 patients showed that Aklief Cream significantly reduced inflammatory lesions as early as two weeks on the face and four weeks on the back, shoulders and chest compared to vehicle (p<0.05). Aklief Cream was well tolerated when used on the face, back, shoulders and chest. The most common adverse reactions (incidence >1%) included application site irritation, application site pruritus, and sunburn.

generally favorable and consistent throughout the clinical development program.

Also last month, Foamix Pharmaceuticals Ltd. and Menlo Therapeutics Inc. signed a definitive merger agreement to create a combined biopharmaceutical company focused on the commercialization and development of therapeutics to serve patients in the dermatology space. The boards of directors of both Foamix and Menlo have unanimously approved the transaction. The combined company will have a diversified portfolio including an approved product and three late-stage product candidates focused on dermatologic indications.

Altreno (tretinoin, Ortho Dermatologics) Lotion, 0.05%, is now available exclusively for physician dispensing in a new, large 20-gram size. Altreno Lotion is the first tretinoin available in a lotion for the treatment of acne. Dispensing through dermatologists’ offices allows dermatologists to provide patients Altreno Lotion right at the time of their appointment, avoiding issues with prescriptions not getting filled due to cost or inconvenience.
Olaregen Therapeutix, a subsidiary of Generex Biotechnology, is a regenerative medicine company focused on the development, manufacture, and commercialization of products that fill unmet needs in the current “hard to heal” cellular and/or tissue-based product market. Olaregen’s first product introduction is Excellagen, a 3-dimensional wound conforming matrix. Excellagen is indicated for the management of wounds and is topically applied. Olaregen CEO, President, and Chairman of the Board, Anthony Dolisi spoke with Practical Dermatology magazine about the product and its role in dermatology.

Excellagen is a ready to use wound solution.

Excellagen is a 510(k) FDA cleared cellular and/or tissue-based product with an indication for management of wounds including diabetic foot ulcers, venous stasis ulcers, pressure ulcers, post Mohs surgical wounds and other hard to heal wounds. It’s a three-dimensional wound conforming matrix that supports a favorable wound healing environment. It’s designated and designed to accelerate granulation tissue growth by providing a structural scaffold for cellular migration and proliferation. It activates platelets, triggering the localized release of endogenous growth factors, including platelet derived growth factor or PDGF.

Excellagen is supplied in a prefilled syringe. It’s a gel form, flowable conforming matrix that is ready to use. It’s kept refrigerated. You take it out of the refrigerator and it’s ready to apply to the patient.

Excellagen has been tested in various types of difficult to treat wounds.

In the clinical trials, we looked at the hard to heal wounds that had been around for quite some time and the providers were having difficulties managing those wounds. Hard to heal wounds include but are not limited to pressure ulcers, diabetic foot ulcers, venous leg ulcers, and wounds from Mohs surgery. They present a real insignificant challenge to wound care professionals and consume a great deal of healthcare resources around the globe.

Patients with these non-healing wounds are likely to be non-ambulatory or in some cases have been paralyzed, unable to provide self-care and/or they suffer from dementia.

Wounds are a growing health concern.

Chronic wounds impact nearly 15 percent of Medicare beneficiaries and up to two percent of the population in developed countries. The population is aging; Wounds are poised to become one of the most significant social and medical challenges of the 21st century as the number of people 60 years and older is projected to more than double in size by 2050, reaching nearly 2.1 billion. As such, chronic wounds will become an ever increasing burden on the medical community.

We believe that Excellagen can offer a solution with a better clinical and economic outcome, particularly with the ease of use and the speed at which it works. We funded a multi-center randomized controlled clinical study that showed the average number of applications to close these wounds was 1.6. Almost half the wounds closed within 12 weeks.

Excellagen consists of a highly purified dermal collagen. It's 2.6% collagen, immediately providing a structural scaffold that’s needed for repair, cell migration, and proliferation. It has those similarities with PRP, yet it still remains different. Furthermore, in dermatological procedures, such as deep chemical peels and microneedling, where post-procedure bleeding occurs, Excellagen will activate those blood platelets, resulting in the release of key stimulatory growth factors, all without the need for the blood draw and the processing that’s required with PRP.

We’re applying a direct collagen, which up regulates the platelet derived growth factors. So there are similarities, but there are differences. Again, no blood draw, no processing required.

Dermatologic and aesthetic applications are under investigation.

We believe that the immediate acceleration of healing following a single application of Excellagen observed in the Wagner Grade 1 DFU study bodes well for post Mohs surgery and the use in aesthetic dermatology. These procedures also create partial thickness wounds and rapid healing is desirable to reduce the patient’s downtime and reduce the potential for complications, including infection. We strongly believe that in those areas there’s going to be an uptake and we’re going to meet several needs for the clinician and the patient.

Excellagen is FDA cleared for the management of post Mohs surgical wounds.

ECZEMA

Dupixent (dupilumab) from Regeneron Pharmaceuticals, Inc. and Sanofi SA received expanded approval to include patients aged 12 through 17 whose eczema is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.

The FDA evaluated the Dupixent application under Priority Review. Dupixent was also granted Breakthrough Therapy designation by the FDA for inadequately controlled
moderate to severe atopic dermatitis in adolescents. The Breakthrough Therapy designation was created to expedite the development and review of drugs developed for serious or life-threatening conditions.

In the pivotal Phase 3 trial evaluating Dupixent monotherapy in adolescent patients with uncontrolled moderate to severe atopic dermatitis, the safety and efficacy were generally consistent with that previously seen in adult studies. At 16 weeks the average improvement in the Eczema Area and Severity Index (EASI) from baseline was approximately 66 percent compared to 24 percent for placebo.

The safety profile of Dupixent in the adolescent trial was similar to the safety profile from trials in adults with atopic dermatitis, and consistent through 52 weeks. The most common adverse events were injection site reactions, eye and eyelid inflammation including redness, swelling, and itching, oropharyngeal pain, and cold sores in the mouth or on the lips.

“This is a really big deal because there are so many adolescents and children with eczema,” says Emma Guttman-Yassky MD, PhD, Vice Chair for Research in the Department of Dermatology and Director of the Center for Excellence in Eczema at Mount Sinai Hospital in New York City. “For many of these patients, topicals aren’t enough and phototherapy isn’t feasible.”

“Dupixent is a very safe treatment, and we hope in the future, its use will be expanded to include early childhood.” Dr. Guttman-Yassky’s research and clinical trials helped lead to FDA approval in adults and children and adolescents.

MELANOMA

Clinical data from the ongoing Phase 3 MAVIS (Melanoma Antigen Vaccine Immunotherapy Study) Study—a multicenter, double-blind, placebo-controlled adaptive trial to assess the safety and efficacy of seviprotimut-L—show benefit for CK Life Sciences’ investigational melanoma vaccine candidate. Primary endpoints of the study are recurrence-free survival (RFS) and overall survival (OS) in patients with American Joint Committee on Cancer (AJCC) Stage IIB/C, IIIA, IIB/C melanoma at high risk of recurrence after definitive surgical resection.

Interim analysis of subgroups suggested enhanced RFS for seviprotimut-L among those with AJCC stage IIB/IIC melanoma, as well as those under age 60. Seviprotimut-L was well-tolerated with treatment-emergent adverse events (AEs) similar to patients given placebo.

The Know Now Testing Program, an initiative from Novartis in collaboration with Quest Diagnostics, offers genetic mutation testing at no cost for all patients with stage III or stage IV melanoma. Nearly half of all advanced melanoma patients carry the BRAF mutation. BRAF status is key for assessing treatment options.

Results from tests completed under the Know Now Testing Program are available approximately 48 hours after a Quest Diagnostics laboratory receives a sample, which could lead to timely and optimal treatment decisions, Novartis says. To access the Know Now program and its no-cost test-

Rosacea Impact
By The Numbers

76% Percentage of rosacea patients who saw at least some improvement in their skin after receiving treatment.

40% Percentage of rosacea patients who had improvement who also said that treatment had improved their psychological well-being.

24% Percentage of rosacea patients who had minimal improvement with therapy who reported improved psychological well-being.

— National Rosacea Society survey of 1,044 rosacea patients

Biologics to Grow the Derm Drugs Market

$34.5 Billion The predicted value of the dermatology drugs market by 2023, a new report from Research and Markets suggests. Biologics are expected to be the fastest growing category, advancing at CAGR of 9.1% during the forecast period.

The dermatology drugs market saw the highest revenue generated from psoriasis drugs during the historical period evaluated. The category generated revenue of $142 billion in the market in 2017.
Year in Focus

**Who’s Who in Aesthetic Marketing?**

Brooke Shields, Drew Barrymore, Paula Abdul, and Viola Davis have joined the ranks of Christie Brinkley, partnering with WarmSculpting (formerly SculpSure), BTL’s Emsculpt, InMode’s BodyTite and FaceTite technologies, and L’Oréal Paris, respectively. Ms. Brinkley has partnered with Merz Aesthetics’ Ultheraphy and Xeomin since 2017.

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**PSORIASIS**

The International Psoriasis Council (IPC) hopes a new method to classify psoriasis severity can determine the appropriate course of treatment. The new method is described in a paper published in the *Journal of the American Academy of Dermatology*.

“There’s a lot of unnecessary suffering among psoriasis patients due to ’under-classifying’ the severity of the disease. This new approach to assess psoriasis severity developed by an IPC-led Delphi exercise aims to help providers everywhere start their patients on the appropriate treatment, and sooner,” says Bruce Strober, MD, PhD, assistant clinical professor at Yale University, head of Central Connecticut Dermatology Research and secretary-treasurer of the IPC Board of Directors. Dr. Strober is lead author on the new consensus paper.

The International Psoriasis Council method of assessing psoriasis severity is a treatment-first approach that significantly simplifies the process of getting psoriasis patients on the right medication for their disease level. The IPC method calls for classifying patients as candidates either for topical therapy or systemic therapy.

To qualify for systemic therapy, patients must meet one or more of the following criteria:

1. Psoriasis lesions on 10% or more of their body surface; OR
2. Psoriasis lesions on sensitive areas of the body (i.e., hands/feet, face, genitals, scalp); OR
3. Topical therapy failed to control symptoms.

Amgen has entered into an agreement with Celgene Corporation in connection with its previously announced merger with Bristol-Myers Squibb Company to acquire worldwide rights to Otezla (apremilast), the only oral, non-biologic treatment for psoriasis and psoriatic arthritis, and certain related assets and liabilities, for $13.4 billion in cash, or approximately $11.2 billion, net of the present value of $2.2 billion in anticipated future cash tax benefits.

Otezla is currently approved for three indications in the US—the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy; adult patients with active psoriatic arthritis; and adult patients with oral ulcers associated with Behçet’s Disease.

Sales of Otezla in 2018 were $1.6 billion driven by strong volume growth. Amgen has stated previously that it will focus on medicines that can deliver sustained, long-term volume driven growth and the company believes there is a significant opportunity to grow Otezla through global expansion and new indications, with expectations for Otezla to realize at least low double-digit sales growth, on average, over the next five years.

Anti-inflammatory biologic therapies used to treat moderate to severe psoriasis can significantly reduce coronary inflammation in patients with the chronic skin condition. Scientists said the findings are particularly notable because of the use of a novel imaging biomarker, the perivascular fat attenuation index (FAI), that was able to measure the effect of the therapy in reducing the inflammation.

The study published online in *JAMA Cardiology*, has implications not just for people with psoriasis, but for those...
Year in Focus

Improved Onboarding Tools: Aiming to Boost Adherence to Self-Injection

By Alex Catino

Patients living with psoriasis and atopic dermatitis often rely on biologic therapies that require self-injection of medication at home. Even with the rise in self-injection biologics, research published in the *Journal of the American Academy of Dermatology* suggested that nearly half of patients skip or altogether avoid these self-injections due to anxiety or fear of several aspects of self-injecting, including needles or injecting improperly. Because of this, robust training and onboarding solutions are critical for patients who self-inject.

Unfortunately, a significant fraction of healthcare providers (HCPs) neither receive training themselves, nor train their own patients on how to properly administer a self-injection. As a result, it is useful to assess and understand the importance of improving strategies for training to boost patient adherence rates to therapies. It is also imperative to recognize the need to provide training devices for both HCPs to train patients in-office and for patients to use in the home setting for practice between injections.

**THE PROBLEM: CHANGES ARE NEEDED TO THE CURRENT TRAINING PARADIGM**

The dermatology patient population states dissatisfaction with the current training paradigm. For example, results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey (MAPP), released in 2014, showed that “about half of patients indicated that biologics were burdensome, primarily because of anxiety/fear of injections and physical preparation for self-injection, inconvenience, and adverse effects.” In patients who had received biologics, “fear, anxiety, and/or physical preparation of injections were cited as burdensome by 31 percent of current users, while inconvenience was cited by 20 percent of current users.”

Most psoriasis or atopic dermatitis patients complete one initial in-office training session with their new injectable when it is prescribed to help manage their disease. Afterward, they are unfortunately left on their own for the course of their at-home treatment. How successfully they self-inject in the privacy of their homes varies significantly as HCPs are not there to offer support. What’s more, patients may seek alternate training methods such as YouTube videos, that may offer incorrect information.

Research suggests adherence success may depend on whether the prescribed treatment is supported by training materials that go beyond an introductory in-office session and the standard Instructions for Use (IFU) provided by the drug manufacturer. Studies also find that patients’ own natural memory decay, coupled with longer periods of time between injections, further highlights the need for training devices in the home to use throughout treatment and not just one time in an HCP office.

A recent longitudinal study conducted by Noble—whereby researchers sought to understand how patients interact with training devices—uncovered encouraging statistics for the ongoing use of trainers. One hundred percent of study participants who were given training devices to practice with at home (before coming back into the testing center to self-inject) successfully completed all crucial self-injecting steps after the two-week practice period. In contrast, more than half of participants who did not receive training devices to practice with at home made critical errors in the self-injection process.

One study found that 92 percent of patients preferred to receive and practice with training devices at home to help them feel more confident during the actual self-injection; and with even more support, such as formal patient support programs, adherence rates to therapies rose to a staggering 94 percent.

How, specifically, can technology be integrated most effectively? Training devices and onboarding solutions have been developed to help patients not only with the initial device training and onboarding, but also with continuous training throughout disease management. The goal of these initiatives is to build confident self-injecting patients to counteract training decay in order to improve adherence and ultimately patients’ overall health outcomes.

**THE SOLUTION: REALISTIC TRAINING FEATURES ARE DESIGNED TO PROMOTE PATIENT ADHERENCE**

Training devices are built to replicate the actual drug delivery device patients will use for their self-injection. They are strategically implemented to give patients the most realistic training experience possible prior to actually self-injecting. Important replicated features include accurate plunger resistance and breakout forces that simulate the actual injection device and drug viscosity, as well as needle insertion technologies that simulate needle sensation and force. These features habituate patients early on to the feel of the injection, enhancing its familiarity.

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The training devices’ error-correcting features are complemented by several additional multisensory features designed to provide patients with the most realistic simulation possible, including:

- plunger speed simulation, with preconfigured components;
- actuation force simulation with adjustable audible feedback that has been developed to simulate the auditory feedback and resistance of variable-step actuated devices;
- agitator needle simulation tips, designed to replicate the feel and forces involved for insertion systems;
- resettable safety systems, with the trainer’s cap doubling as a reset mechanism allowing users to train multiple times prior to an actual injection;
- and device replication, designed to simulate all aspects of the patient experience—including design form, color adjustments, window size, tactile feedback, cap removal force, actuation force, and more.

Training devices that are as close in form and function to the true drug delivery device are vital for both HCPs and patients. Reinforcing proper self-injecting techniques throughout a patient’s course of therapy can help HCPs ensure patients stay the course. When patients are adherent to their self-injection regimen, they see an overall better quality of care—and thus, of health outcomes.

TRAINING DEVICES CAN HELP HCPS ACHIEVE BETTER PATIENT OUTCOMES

Studies have indicated the importance of HCPs taking extra steps to promote patient adherence to medications, including improving patient education on how to use self-injection medications properly. Studies suggest it is important for HCPs to demonstrate proper use of delivery systems to improve the effectiveness of therapy. The use of realistic training devices can play a role here by offering an improvement in the quality of self-injection programs that are initiated by HCPs, which have been shown to increase medication adherence.

Evaluating the effectiveness of patients’ self-injection medication once those patients are sent home with their therapies is a major challenge for HCPs. It is important for HCPs to understand whether patients are using their self-injection devices properly. Even so, this is extremely difficult to do as they are constrained by the lack of available information other than patient self-reporting, which has been known to be one of the least reliable ways to gather feedback. Additionally, if patients believe they are utilizing their devices correctly when, in fact, they are not, it can affect the analysis of the medication and disease management, potentially forcing patients to needlessly alter or end their current treatment.

A dermatology patient who practices with realistic training devices is more likely to adopt proper technique from the start and continue good habits when self-administering the medication at home, ensuring more effective drug delivery. Because of this, improving the current standard of onboarding and training options for dermatology patients could ultimately result in more favorable treatment outcomes. Stakeholders in the field would undoubtedly agree that harnessing technology in this way is a goal well worth pursuing—one that helps create better patient outcomes all around.

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with other chronic inflammatory diseases, such as lupus and rheumatoid arthritis. These conditions are known to increase the risk for heart attacks and strokes. The study was funded by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health.

The researchers analyzed 134 patients who suffered moderate to severe psoriasis and had not received biologic treatment for at least three months before starting on the study’s therapy. Fifty-two of these patients who chose not to receive the biologic therapy, were treated with topical or light therapies only and served as the control group. Patients underwent CT scans at the start of the study and again a year later to assess coronary inflammation using the perivascular FAI. (See images on following page.) Researchers found a significant reduction in coronary inflammation among those receiving biologic therapy, but there was no change in the control group. Even patients with preexisting coronary artery plaque saw a reduction in coronary inflammation following biologic therapy.

Positive results from BE READY, the second of three phase 3 studies this year to report findings on the investigational treatment bimekizumab, were released last month. BE READY evaluated the efficacy and safety of UCB’s IL-17A and IL-17F inhibitor in the treatment of adults with moderate-to-severe plaque psoriasis. This randomized withdrawal study met its co-primary endpoints of at least a 90 percent improvement in the Psoriasis Area and Severity Index (PASI 90) and Investigator Global Assessment (IGA) response of clear or almost clear (IGA 0/1) at week 16, compared to placebo.

Among key secondary endpoints, bimekizumab was statistically superior to placebo in achieving total skin clearance (PASI 100) at week 16. In addition, bimekizumab was statistically superior to placebo in patient-reported reductions in itch, pain and scaling, as well as clear or almost clear scalp (scalp IGA), at week 16. Bimekizumab was also statistically superior to placebo in achieving rapid response, defined as PASI 75 at week 4. Furthermore, after an initial week 16 response, continued treatment with bimekizumab resulted in a statistically superior response at week 56 compared to placebo, during the randomized withdrawal period of the study. The initial data assessment indicates that the safety profile of bimekizumab was consistent with earlier clinical studies. Full BE READY results will be presented at a scientific congress in 2020.

The safety and efficacy of bimekizumab are also being evaluated in psoriatic arthritis (PsA), ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA).

The FDA has approved Mayne Pharma Group Limited's Sorilux (calcipotriene) Foam, 0.005% in adolescents 12 years and older.

The FDA approved Sorilux in 2010 based on evidence from two eight-week placebo controlled clinical trials in patients with mild to moderate plaque psoriasis of the body and one eight-week placebo controlled clinical trial in patients with moderate plaque psoriasis of the scalp. Further data was obtained in a follow-on open label study in patients aged 12 to 17 years of age with psoriasis.

Ortho Dermatologics’ Duobrii (halobetasol propionate and tazarotene) Lotion, 0.01%/0.045% received FDA approval for the topical treatment of plaque psoriasis in adults. Duobrii is the only topical lotion that contains a unique combination of halobetasol propionate and tazarotene in one formulation. In a year-long safety study, patients used Duobrii Lotion for up to 24 weeks of continuous use and up to 52 weeks of as-needed use.

Skyrizi (risankizumab-raa), an interleukin-23 (IL-23) inhibitor from AbbVie, received FDA approval for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. In clinical trials, Skyrizi produced high rates of durable skin clearance with 82 and 81 percent of treated patients in two trials, respectively, achieving PASI 90 at one year. The majority (56 and 60 percent, respectively) achieved complete skin clearance or PASI 100.

The recommended dose for Skyrizi is 150mg administered by two subcutaneous injections every 12 weeks following two initiation doses at week 0 and 4. Skyrizi can be administered in-office or by self-injection after training.

“The complex nature of psoriasis and the variability or
loss of treatment response over time can prevent some patients from achieving their treatment goals,” said Kenneth B. Gordon, MD, a principal investigator for the ultIMMa-1 pivotal trial and professor and chair of dermatology at the Medical College of Wisconsin. “In clinical trials, risankizumab demonstrated high levels of skin clearance that persisted through one year. I’m pleased the dermatology community now has a new option that can help patients achieve and maintain a high level of treatment response.”

Skyrizi is part of a collaboration between Boehringer Ingelheim and AbbVie, with AbbVie leading development and commercialization of Skyrizi globally.

The FDA approved Tremfya One-Press, a single-dose, patient-controlled injector for adults with moderate to severe plaque psoriasis. Tremfya (guselkumab) from the Janssen Pharmaceutical Companies of Johnson & Johnson is the first FDA-approved medication of its kind to offer the One-Press patient-controlled injector. One-Press fits comfortably in the hand and offers a controlled injection that hides the needle throughout the process. Tremfya is administered as a 100mg subcutaneous injection once every eight weeks, after starter doses at weeks 0 and 4.

INFECTIONS AND INFESTATIONS
Even though fungal diagnostic preparations can assist the accurate diagnosis of cutaneous fungal infections, a survey

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Kesha Buster, MD, FAAD, and Ekene Ezenwa, BS
from a team at the George Washington University (GW) led by Adam Friedman, MD identifies barriers that prevent their consistent use. The study is published in the Journal of Drugs in Dermatology.

Direct microscopy using potassium hydroxide (KOH) or other stains provide an inexpensive method to diagnose fungal infections. However, this requires clinics to have the Clinical Laboratory Improvement Amendment (CLIA) certification. Previously published research from Dr. Friedman on the difficulty of distinguishing between skin fungal infections and other inflammatory skin diseases highlights the importance of using laboratory-based tools to aid in patient care.

The new survey was distributed via email to participants of the Orlando Dermatology Aesthetic and Clinical Conference, and the data was compiled in a web-based platform. Of the respondents, around 21 percent indicated they rarely/never perform fungal preparations and about 20 percent reported they sometimes do, often because they think clinical diagnosis is adequate or because fungal preparations take too long. Additionally, about 21 percent of respondents reported not having CLIA certifications, mostly because the process requires too much work or because they do not know how to apply. Of the providers who have CLIA certification, more than 25 percent reported that it was difficult to obtain.

What’s the best defense against Clostridiodes difficile? Clorox may be the best bet, but it’s not 100 percent effective, according to results of a new study published in the Antimicrobial Agents and Chemotherapy journal of the American Society for Microbiology.

Overall, Clorox, Cidex OPA, and Virex were most effective at killing C. diff spores. Clorox and OPA were also effective at killing total vegetative cell growth, the cellular stage responsible for causing infections. Virex was found to be ineffective against vegetative cell growth in biofilms. Clorox and Virex were most effective in reducing biomass followed by Nixall, Cidex OPA and Vital oxide.

VP-102 (cantharadin film) from Verrica is now under FDA review for the treatment of molluscum. Data from a pooled analysis of the Phase 3 CAMP-1 and CAMP-2 clinical studies showed that treatment with VP-102 brought about a statistically significantly higher rate of complete lesion clearance at Day 84 (primary endpoint) compared to vehicle. Complete clearance of all molluscum lesions at the end of study (EOS) visit occurred in 50 percent of subjects treated with VP-102, as compared to 15.6 percent for vehicle (p<0.0001). In addition, mean lesion counts decreased by 76 percent for subjects in the VP-102 group, compared to a 0.3 percent decrease in the vehicle arm by the EOS visit (p<0.0001). VP-102 was well-tolerated, and adverse events were primarily mild to moderate in intensity. Rates of discontinuation of study medication due to an adverse event were low (1.9% for VP-102; 0.5% for vehicle).

A second pooled analysis of the CAMP studies evaluated the time course and percentage of subjects with >75 percent and >90 percent reduction in lesions at the EOS visit in the intent-to-treat population. Data demonstrated that as early as Day 21, >75 percent and >90 percent lesion clearance rates were statistically significantly higher with VP-102 treatment as compared to vehicle (p<0.0001). At EOS, 77.7 percent of VP-102 subjects achieved >75 percent reduction in lesions compared to 34.9 percent for vehicle, and 65.8 percent of VP-102 subjects achieved >90 percent reduction of lesions compared to 27.1 percent for vehicle (p<0.0001 respectively).

TECHNOLOGY

Nextech Systems has launched a new partnership with RxPhoto, a collaborative medical imagery solution. This partnership integrates RxPhoto’s patient photography app within Nextech’s existing technology workflows for plastic surgery, dermatology and medical spa clients.

When Nextech software is partnered with the HIPAA compliant, image-capturing app, both help to create a replicable patient experience that simultaneously improves patient flow and retention. RxPhoto’s on-screen positioning guides and patented photo ghosting, paired with Nextech’s EMR charting and information input, offer opportunities for further education, expectation management and marketing activities within practices. Further, the integration ensures all patient photos are consistently captured at the same angle, distance and rotation within their EMR. Annotation tools allow for precise treatment, procedure and mole tracking to assist with better charting and patient satisfaction.

Pulse Biosciences, Inc. presented results of three clinical studies demonstrating high clearance rates across its benign skin lesion portfolio during the ASDS 2019 Annual Meeting in Chicago. The company’s proprietary CellFX System harnessing Nano-Pulse Stimulation (NPS) technology is under FDA review for the management of Sebaceous Hyperplasia lesions. Non-thermal, cellular-specific NPS technology was featured at the opening Plenary Session, which highlights cutting-edge science and emerging therapies in dermatologic surgery. NPS technology delivers nano-second pulses of electrical energy to non-thermally clear cells while sparing adjacent healthy, non-cellular tissue.

In prior studies, investigator assessments concluded that the NPS procedure met efficacy endpoints in 99.5 percent of Sebaceous Hyperplasia lesions and 82 percent of Seborrheic Keratosis lesions along with normal and expected skin recovery periods.