Now What?

A look at what's now, what's next, and how dermatology practice continues to evolve with drugs, technologies, and opportunities.

PIPELINE WATCH: GUSELKUMAB FOR PSORIASIS

Guselkumab, which is in development by Janssen, is an injectable that targets interleukin 23 (IL-23). Data have been promising, including from the VOYAGE 1 trial, which showed significantly higher proportions of patients receiving guselkumab achieved cleared/minimal disease compared with patients receiving placebo. The trial also included an active comparator arm evaluating guselkumab versus adalimumab. Guselkumab was superior to adalimumab across major study endpoints and through 48 weeks of treatment.

Andrew Blauvelt, MD, MBA, President of the Oregon Medical Research Center, presented findings from the first of three pivotal Phase 3 studies evaluating guselkumab at the 25th European Academy of Dermatology and Venereology (EADV) Congress.

Could you briefly give some context on the IL-23 pathway, specifically, and how guselkumab may fit into the armamentarium?

Dr. Blauvelt: Ustekinumab (Stelara) blocks IL-12 and IL-23, so selective inhibition of IL-23 by guselkumab is simply a variation on ustekinumab, which dermatologists know well. IL-23, and not IL-12, turns out to be one of the key drivers of inflammation in psoriasis. Selective targeting of this psoriasis-associated cytokine offers high degrees of efficacy combined with high degrees of safety.

How did guselkumab perform compared to adalimumab? What was your reaction to these findings?

Dr. Blauvelt: Guselkumab easily beat adalimumab by all measures and at all time points. These data follow a trend of recent results in psoriasis where newer biologics that block IL-17A and IL-23 have demonstrated superior efficacy to older biologics that block TNF.

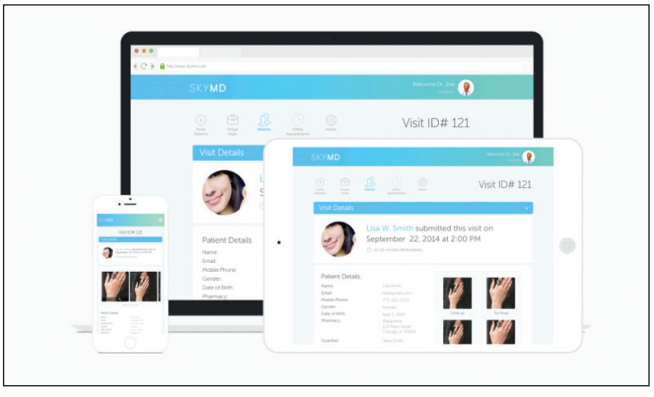
In addition to efficacy, you presented some QoL findings. Of the data shared, what is most striking?

Dr. Blauvelt: Yes, 56.3 percent of guselkumab-treated patients demonstrated DLQI scores of 0 or 1 at week 16 compared to 38.6 peercent of adalimuamb-treated patients. This score indicates that psoriasis had no impact on quality of life for these patients, which is a remarkable achievement given that psoriasis is such an impactful disease.

What do you still want to learn about guselkumab?

Dr. Blauvelt: Long-term safety still needs to be determined, although I am optimistic about this issue, given that long-term safety of ustekinumab, a related drug, has been so good.

EYE ON THE SKY: AN EMERGING APPROACH TO TELEDERM



A growing number of dermatologists are expressing interest in teledermatology, and the market is responding with new technologies and platforms to meet and create patient demand. SkyMD is a company focused on teledermatology specifically, with the goal of helping dermatologists expand their local reach by providing teleconsults for dermatologic needs. Eric Price, Co-Founder & CEO of SkyMD, talked about the service.

Tell us a little bit about the SkyMD concept and how it works for dermatologists.

Mr. Price: SkyMD is a telehealth platform designed for dermatology. The company is committed to empowering dermatologists to provide quality care to their patients anytime, anywhere. On SkyMD, patients connect securely with their dermatologist, fill out a specialty-specific questionnaire, and take photos of their skin, hair, or nail condition. Their dermatologist responds with a personalized treatment plan

including over the counter skincare recommendations and prescriptions, if necessary.

How is the SkyMD approach different from other telemedicine or teledermatology platforms?

Mr. Price: One of the most important things that sets us apart from other telehealth platforms is our specialty-specific approach. The workflows and requirements can differ dramatically from one medical specialty to another. For example, video doesn't work well as a medium for treating dermatologic problems, because the resolution of a video is not as high as that of a digital image. SkyMD was designed by a team of dermatologists to be optimized for the unique needs of their specialty, enabling our dermatologists to deliver more efficient and effective online care.

What is integration/participation like for a dermatologist? Do they need equipment, support, etc.?

Mr. Price: SkyMD is a cloud-based platform, and no hardware installation is required. Dermatologists and patients can access the web based platform from any smartphone, tablet, or desktop computer. All it takes to get started is a brief onboarding session. Each dermatologist receives a dedicated SkyMD client success manager that trains their staff, helps them market the service to new and established patients, and provides ongoing customer support.

What do you see as the most important innovations in the SkyMD platform? What's next?

Mr. Price: One of the key innovations in the SkyMD platform is the proprietary specialty specific questionnaires and templates. Our adaptive patient questionnaires gather the minimum number of data points required to make an accurate evaluation for their specific condition. Our evidence based templates include patient education and instructions for 85+ of the most common dermatologic conditions. These features are important contributors to the platform's industry leading efficacy, efficiency, and customer satisfaction.

Over the coming months, we plan to integrate several new and exciting features into the platform. SkyMD already integrates with many EHR systems, and we will continue to invest in these integrations to further streamline workflows. We will also be adding the option to supplement a SkyMD visit with a secure video call where appropriate.

What are existing dermatologist users saying? How do you measure success?

Mr. Price: We track a variety of metrics to measure success. Here are some the key metrics we are excited to share:

1. Efficacy: 90 percent of SkyMD visits are evaluated online, and only 10 percent are triaged into the office.

2. Efficiency: SkyMD reduces treatment time by more than 75 percent, compared to an office visit.

3. Patient Satisfaction: Our clients experience 98 percent patient satisfaction.

AC5 TOPICAL HEMOSTATIC DEVICE™: A POTENTIAL TOOL FOR DERMATOLOGIC SURGERY

By Terrence W. Norchi, MD

Dermatologic surgery involves relatively few risks, yet complications related to hemostasis can occur during both the intraoperative and postoperative periods. According to a review article in *Dermatology Research and Practice*, minor bleeding complications are the most frequently encountered complications of cutaneous surgery, which can predispose the patient to hematoma formation, increased risk of infection, skin graft necrosis, and wound dehiscence.

A variety of hemostatic modalities are available for surgical procedures, with use dependent on the surgeon's preference, efficacy and ease of use, expense, and bleeding risks of the particular patient. One of the more compelling approaches involves the use of topical agents applied to a wound. These have traditionally included both caustic agents (e.g. zinc chloride, ferric subsulfate, aluminum sulfate) as well as non-caustic agents (e.g. gelatin, polyethylene glycol, microporous polysaccharide spheres, microfibrillar collagen, cellulose, thrombin, fibrin sealant, octyl-2-cyanoacrylate), each with its specific mechanism of action as well as advantages and potential side effects.

One of Arch Therapeutics' product candidates, a liquid synthetic peptide called the AC5 Topical Hemostatic Device™, locally self-assembles into a nanofiber structure that provides a physical barrier on the tissue. The resulting barrier is designed to mechanically seal the wound in order to stop substances, such as blood, from leaking while supporting an environment that permits normal healing.

Based on testing to date, Arch believes AC5™ has several characteristics that may help make it user-friendly. For instance, it conforms to irregular wound geometry, does not require cold or frozen storage, and can be easily applied. Additionally, AC5 is not sticky or glue-like, which Arch believes may not only contribute to a favorable safety profile but may also enhance its utility in the settings of microsurgery. AC5 is transparent, which should make it easier for surgeons and other health care providers to maintain a clearer field of vision during a procedure. AC5 can be applied rapidly to a bleeding wound and potentially prophylactically so that additional bleeding is prevented just as it starts.

Arch recently met the objectives of its recently completed

GOLDEN OPPORTUNITIES: MICHAEL GOLD RECOGNIZED FOR EDUCATION, CONTRIBUTIONS

For his contributions to the specialty, his dedication to education, and his clinical innovations, Michael H. Gold, MD was recognized this month at the Cosmetic Surgery Forum in Las Vegas. Presented with the Lifetime Contribution to Aesthetics Award by CSF Founder Joel Schlessinger, MD, Dr. Gold shared his perspective as a global educator and practitioner. Dr. Gold, cofounded the Music City SCALE meeting and DASIL and is President of the 5-Continent Congress (5CC).

"I've been very fortunate in dermatology to do some really exciting things, from all the lasers and IPLs and radiofrequency devices that I've helped bring to the market to silicone gel sheeting to photodynamic therapy to all the injectable work that I've done. It's been an incredible ride," Dr. Gold said of his award. "I always tell people I have the best job in the world," Dr. Gold added.

The meeting Dr. Gold co-chairs with Brian Beisman, MD, Music City SCALE, takes place in May in Nashville (Get info online: tnlasersociety.com). "We are in year 12. We bring some of the most incredible faculty from the US to that meeting. We do lots of teaching and hands-on education," Dr. Gold explains. The popular 5CC, which started on the French Riviera has relocated to Barcelona, and this fall DASIL goes to Shanghai.

Watch the interview with Dr. Gold online at DermTube.com. CSF 2017 returns to the Bellagio November 29 to December 2, 2017.

single-center, randomized, single-blind prospective clinical study of AC5 in skin lesion patients with bleeding wounds. This was the first study assessing the safety and performance of AC5 in humans.

The study enrolled 46 patients, including 10 who were taking antiplatelet therapy. Each patient had bleeding wounds created as a result of the excision of at least two skin lesions under local anesthetic in the same setting. On a randomized basis, one lesion received treatment with AC5 and the other(s) received a control treatment consisting of standard therapy plus a sham. Each subject was followed-up for safety assessment on Day 7 and again on Day 30, which marked the end of the patient's participation in the clinical study.

The objectives of the study were to evaluate the safety and performance of AC5 in patients scheduled to undergo excision of skin lesions on their trunk or upper limbs. The primary endpoint was safety throughout the surgical procedure and until the end of a 30-day follow-up period post procedure. Safety of the device was determined by monitoring for treatment-related adverse events. The primary objective was met, as the safety outcomes of both the AC5 treatment group and the control group were similar. No serious adverse events were reported.

A secondary endpoint was performance as assessed by time to hemostasis. The median time to hemostasis of wounds in the AC5 treatment group was 41 percent faster than for those in the control group. The median time to hemostasis for wounds treated with AC5 was less than 30 seconds for the overall study group and in each for the subset of patients taking anti-platelet therapy. These top-line data support that AC5 is safe and performed as expected in the patients enrolled in the study throughout the completion of the patient assessments post-treatment.

It is important to consider hemostasis when performing dermatologic surgery. The eventual addition of AC5 to the surgeon's toolkit could potentially strengthen the choice of options for successful cessation of bleeding and its complications.

Terrence W. Norchi, MD is President and CEO of Arch Therapeutics, Inc., a medical device company developing a novel approach to stop bleeding (hemostasis) and control leaking (sealant) during surgery and trauma care.

DIGITAL PATHOLOGY: A NEW FRONTIER?

Digital technology could change the way that dermatologists read and share pathology findings. At least, that's what developers of a newly-studied platform believe. Michael N. Kent, PhD, Laboratory Manager/Translational Scientist, Dermpath Lab of Central States (DLCS), presented data at the Digital Pathology Association's Pathology Visions conference in San Diego this fall on the company's Laboratory Information System platform Clearpath™ 3.0. Study results show that, with nearly 500 slides to review, pathologists had greater than 90 percent consensus on diagnosis, commensurate with experience. Dr. Kent talked about the platform and its performance.

Could you briefly describe what Clearpath 3.0 is and how it is intended to benefit practitioners?

Dr. Kent: Clearpath 3.0 is the first software solution to bring digital pathology directly to the dermatologist in a format that's easy, flexible, and compatible with existing workflows. From reviewing digital whole slide images (WSI) to generating custom diagnostic reports and signing out cases, Clearpath 3.0 streamlines workflows and helps practicing clinicians realize greater efficiency.

The uniqueness of the system is two-fold. First, it is the only digital platform specifically designed for the dermatol-

ogy market allowing dermatologists to view their own slides from their practice site (as opposed to sending their biopsies to a lab and waiting for a pathologist to read it for them). The benefits of this are efficiency, full control of patient cases, and additional revenue (since they can now bill for the reading the case after confirming with a glass read). Second, its intuitive patented design works on touch enabled tablets making the process easy, workflow compatible, and remote access friendly for review of a slide.

What is it not? What are known or expected limitations of Clearpath 3.0?

Dr. Kent: First, until the FDA approves digital scanner technology for primary diagnosis, there will always be trepidation around reading just a digital image even though the concordance studies between digital and glass slides demonstrate equivalence. Currently the FDA has approved digital diagnosis for seondary consults only. Although the FDA does not directly oversee pathology, we encourage all users of Clearpath to either put a disclaimer on their reports that says the FDA has not approved digital slide reading for primary diagnosis or simply confirm all cases by glass before releasing results. We manage this issue by always sending glass slides back to the dermatologist. The practice of pathology is not currently regulated by the FDA, but falls under separate oversight of CMS via CLIA (Clinical Laboratory Improvement Amendments). The key requirement today to reading any slides (glass or digital) is doing it in a CLIA-certified environment and if reading digitally, validating cases against glass. The CAP (College of American Pathology) published detailed guidelines for validating whole slide imaging for diagnostic purposes, which we follow and provide to our clients to validate their systems with.

The second concern revolves around willingness of dermatologists to read their own slides in the first place. What is unique about derms among medical subspecialties, is that they are the only specialty that must pass their pathology boards to get their degree. Therefore they are qualified right out of school. However, most derms would prefer to use an outside lab for many reasons. These objections are slowly going away as digital imaging becomes more prevalent and the process easier.

Tell us about the current research, what it set out to show, and what the findings were.

Dr. Kent: We're conducting what is to our knowledge the largest study in dermatopathology comparing diagnosis from WSI with diagnosis from traditional glass on the microscope. Our hypothesis is that reading from digital slides is not inferior to reading from glass. It's a type of study commonly applied to pharmaceuticals to show a new treatment is no worse than what's currently available. This minumum standard of meeting the current reference is the benchmark for all studies like this. It's about patient care and safety.

We took 499 cases proportionally representing the scope of diagnoses seen in our large volume lab and added melanocytic lesion cases to ensure that melanoma was covered. Consensus, or "ground truth", diagnoses were established for each case by three board-certified dermpaths. Three different dermpaths read the cases by digital slides. After four weeks washout, they read the same cases by traditional glass slide microscope. We are comparing the findings by each method for agreement between the two methods, and agreement with the "ground truth." We are analyzing any discrepancies for significance to patient care.

We're still crunching some numbers, but the preliminary findings we found and presented at the DPA's Pathology Visions mtg. were that diagnosis from digital images and traditional microscopy agreed 93 percent of the time. The seven percent discrepancy between glass and digital is consistent between pathologists using just glass. In other words, digital reads are no more discrepant from "ground truth" than traditional microscopy reads.

What, to you, is most significant in the findings?

The take home message is that this large and well represented study of dermatopathology cases is showing that for patient care, digital pathology is not inferior to traditional glass microscopy in the derm specialty. There are many other reasons to adopt digital pathology but eliminating this overriding question is critical. We expect our findings to significantly contribute to the body evidence supporting the adoption of digital pathology, even if one specialty at a time.

RNA INTERFERENCE SHOWING PROMISE FOR SCARS

With Geert Cauwenbergh, PhD

Hypertrophic scarring is common following surgery and is associated with patient dissatisfaction, negative impact on quality of life, and in many cases, physical discomfort with or without functional impairment. Researchers are currently investigating potential methods to block the proteins that form scar tissue through the use of RNA interference (RNAi) technology. RXi Pharmaceuticals is investigating RXI-109 as a potential treatment to prevent hypertrophic scars. Biologist Craig C. Mello, PhD, who chairs the company's Scientific Advisory Board, won the Nobel Prize for his work on RNAi.

RXI-109, is designed to reduce the expression of connective tissue growth factor (CTGF), a critical agent of scar formation, at a post-wound surgical site. Trials involving RXI-109 have resulted in positive results to date. In an ongoing

Phase 2 study of subjects with surgically revised hypertrophic scars, a section of one scar is treated with RXI-109 while an adjacent area of the scar is left untreated. Preliminary data from the initial two cohorts of the study shows that use of RXI-109 is associated with a reduction in scar visibility after six doses over the course of three months.

Geert Cauwenbergh, PhD, President and CEO of RXi Pharmaceuticals, spoke with *Practical Dermatology®* magazine about the potential for RNAi in dermatology. Importantly, he notes that the company is focused on development using proprietary platforms that are more "drug like" to facilitate topical delivery of the technology. This introduces a level of reproducibility into treatment development.

The treatment, when applied locally, should act locally and not produce systemic exposure. This enhances efficacy while improving safety. In fact, if various areas of investigation prove successful, topically-applied RNAi treatments could be used in place of injectable TNA-alpha blockers for psoriasis, for example.

Each RNAi-based approach to treatment must be developed for a specific protein target and a specific intended result, Dr. Cauwenbergh explains. In addition to TNF-alpha, potential targets for RNAi approaches include collagen and tyrosinase. Treatments could be developed for warts and alopecia areata.

ENBREL APPROVED FOR PEDS

The FDA this fall approved the supplemental Biologics License Application (sBLA) for the expanded use of Amgen's Enbrel (etanercept), making it the first and only systemic therapy to treat pediatric patients (ages 4-17) with chronic moderate-to-severe plaque psoriasis.

The approval is based on results from a Phase 3 one-year study and its five-year open-label extension study to evaluate the safety and efficacy of Enbrel in pediatric patients, ages 4 to 17, with chronic moderate-to-severe plaque psoriasis. In addition to demonstrating significant efficacy, the adverse events were similar to those seen in previous studies in adults with moderate-to-severe plaque psoriasis.

Amy Paller, MD and colleagues published a study on the safety and efficacy of etanercept for childen and adolescents with plaque psoriasis (*J Am Acad Dermatol*;74(2):280-7).

The data for etanercept in pediatric patients are robust, she emphasized in an interview with *Practical Dermatology®*, noting that they are derived from a large patient population. And they echo findings from years of on-label pediatric use of etanercept to manage juvenile idiopathic arthritis.

Dr. Paller expects other biologics to pursue indications in pediatric psoriasis. Key to long-term safe use will be the establishment of registries to monitor any safety signals and provide robust data. She encourages industry to support the registries and practitioners to participate.

STEM CELL GUN AIMS TO REPLACE SKIN GRAFTING

Amid much discussion of the use of stem cells in the clinical setting, RenovaCare is seeking to develop CellMist™ and SkinGun™ technologies for isolating and spraying a patient's own stem cells onto burns and wounds for rapid self-healing. The new approach is aimed at replacing skin grafting for the management of burn and surgical wounds.

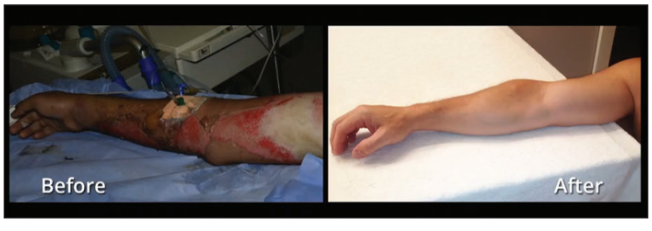
The treatment requires the harvesting of a skin sample as little as a square inch, from which the patient's regenerative stem cells are derived. Within about 90 minutes, the cells are prepared to be sprayed onto the wound, where the data to date demonstrate a 97 percent survival rate. The result, says Thomas Bold, President and CEO, RenovaCare, Inc., is "Thousands of small regenerative islands within the wound." Whereas wounds naturally heal from outside edges to the middle, these regenerative islands encourage healing throughout the wound. The goal is "natural, rapid healing with the patient's own skin that looks and functions like the original skin."

A primary benefit of the process is that it avoids the need for skin grafting, which may not take, could produce scarring, and may be slow to heal.

The CellMist/SkinGun process is relatively simple. "You don't need a bioactivator," says Mr. Bold. "The skin is the bioactivator."

The technique has been successfully used in patients, including for a State Police Trooper who sustained burns over one-third of this body. His treatment and scar-free recovery are documented on the RenovaCare website.

Mr. Bold believes the technology could have applications for all types of wounds, including from in-office surgical and cosmetic procedures. ■



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