SSF Advancing Forward: Promoting Clinical Trial Development

by Theresa Lawrence Ford, MD, FACR
Chair, SSF Clinical Trials Consortium; Chair, SSF Medical and Scientific Advisory Board; and CEO and Medical Director, North Georgia Rheumatology Group, PC, Lawrenceville, Georgia

What a journey this has been. It hardly seems possible that three years ago we began directing efforts promoting the development and availability of clinical trials for patients suffering from Sjögren’s disease. We are very proud of the progress made by the Sjögren’s Syndrome Foundation (SSF) Clinical Trials Consortium (CTC) which first convened in May of 2014. I serve as the Chair of the CTC which is an international initiative whose mission is to increase the availability and the accessibility of therapies for treating Sjögren’s. We started with a small international steering committee. However, we have expanded to include many members who are leaders in the Sjögren’s community. Three major goals were developed to accomplish our mission:

- To support and promote objectives that facilitate the design of clinical trials;
- To increase industry partnerships with the SSF;
- To engage in dialogue with government agencies that oversee therapy approval. (i.e. FDA, EMA).

Clinical Trials and This Practicing Rheumatologist

by Herbert S. Baraf, MD, FACP, MACR
Arthritis and Rheumatism Associates, P.C., Wheaton, Maryland

With a career spanning almost forty years, it’s time for me to look back upon those things that have given me professional satisfaction and draw advice from those experiences to pass on to my younger colleagues.

I have worked in a private practice setting since completing a rheumatic disease fellowship at Duke University in 1978. Duke, a premier center for basic and clinical research for decades, was a great place to be. As a fellow, however, my goal was to take care of patients, eventually in a community practice setting, and not to
The latest initiatives of the SSF CTC are currently underway. The SSF is excited to be launching the first-ever online platform to train clinical trial investigators and, eventually, educate clinicians from multiple specialties who manage and treat Sjögren’s patients. Called STEP, or “Sjögren’s Training and Education Platform,” this unique program will lead to more clinical trials in Sjögren’s and higher quality trials. Ultimately, this new program will lead to greater interest in developing new therapies in Sjögren’s on the part of pharmaceutical companies, because internationally-accepted training and models for trial execution will be easily available and accessible.

Currently, pharmaceutical companies must develop their own training programs for investigators leading their clinical trials. This approach takes a great deal of time and money and most often does not lead to the best and most consistent training. With STEP, clinical trial investigators will share the same training. The STEP program will offer an online portal for clinical trial investigators to take an online course to learn how to collect data for clinical trials.

The design of this online platform will ultimately help speed the training of investigators and ensure that all investigators, no matter which clinical trial they are working on, will be collecting data in the same manner. Consistency in the way clinical trials are executed from one center to another and even from one trial to another is critical for determining if a therapy really works. Better methods for training was clearly identified by our corporate members and the SSF Clinical Trials Consortium.

**STEP Initiatives Move Forward**

Under STEP, we plan to:

1) Develop an online training program for current Sjögren’s-specific outcome measures

STEP participants will be trained to use the leading international model for objective measurements in Sjögren’s (ESSDAI) and its counterpart for patient-reported measurements (ESSPRI) that were recently developed specifically for Sjögren’s. These measures are now the most frequently used indexes to gauge the effectiveness of therapies for Sjögren’s. **This initial phase will be launched in the late fall or early next year.**

Once the basic platform is developed, the SSF will partner with pharmaceutical companies to develop personalized platforms for each company and its clinical trials. Investigators will take the online qualifying test to ensure that they meet the requirements for rating disease activity in Sjögren’s patients according to standard testing devised by our SSF key opinion leaders and, in addition, according to requirements for a company’s specific trial.

2) Develop online training programs for additional outcome measures that can be used in Sjögren’s trials

Future plans to expand our offerings through the STEP platform include training on multiple outcome measures that might be used in clinical trials in Sjögren’s. For example, outcome measures already exist for specific symptoms in Sjögren’s, such as fatigue and cognitive function (or “brain fog”), and our hope is to add these to our online training either as they currently are or changed slightly to better fit Sjögren’s. This will greatly expand our educational offerings to companies and clinical trial investigators to ensure successful clinical trial design.

3) Offer educational videos demonstrating how to perform Sjögren’s-specific tests that can be used for clinical assessment of patients in a clinician’s office and/or for use in clinical trials

Gaining knowledge and consistency in conducting Sjögren’s-specific tests is critical for healthcare professionals. Properly and consistently performing tests such as a lip biopsy (and reading these biopsies), the Schirmer’s test to measure dry eye, unstimulated and stimulated salivary flow measures, and skin biopsies for small fiber neuropathy will help medical providers in their diagnosis and treatment of Sjögren’s.
Online Forum Will be Launched for Clinical Trials

A fourth priority set by the SSF CTC is to create an online communication forum for physicians and other support staff who are engaging in clinical trials. We are excited about this special venue for discussions among those involved in executing clinical trials and those who are considering becoming a clinical trial site. The SSF expects to launch this forum this fall.

SSF National Survey Spreads Awareness and Assesses Burden of Illness

An important part of the overall effort to ensure new therapies are developed for Sjögren’s patients has been to increase education and awareness in the healthcare professional sector. In addition, a major goal has been to work closely with the pharmaceutical industry to demonstrate the tremendous disease burden that Sjögren’s patients suffer and encourage them to investigate potential therapies for Sjögren’s and engage in clinical trials. To demonstrate the challenge of the signs and symptoms experienced and the resulting functional limitations for patients, the Sjögren’s Syndrome Foundation (SSF) conducted an extensive national patient survey.

The “Living with Sjögren’s” survey was conducted in the United States by Harris Poll on behalf of the SSF between May 11 and July 11, 2016. Nearly 3,000 patients (96% women), aged 18+ years in the U.S. and who reported having been diagnosed with Sjögren’s by a medical professional or doctor, shared their experiences with the disease and its physical and emotional effects on their lives. This nationwide survey examined the variety and severity of experiences Sjögren’s patients have and the impact on their quality of life. Not only the physical but the mental and financial burdens were addressed as well. The survey was highlighted during Sjögren’s Awareness Month in April 2017, and a summary of findings can be viewed on the SSF website at http://www.sjogrens.org/home/about-sjogrens/living-withsjogrens.

SSF Five-Year Breakthrough Goal Makes Major Progress

The SSF Five-Year Breakthrough Goal “to shorten the time to diagnose Sjögren’s by 50% in 5 years!” started in 2012, and, four years into the goal, a 2016 survey showed that for patients diagnosed in 2015, the time to receive an accurate diagnosis of Sjögren’s was brought down substantially from six years to three. In addition to increasing education and awareness in the healthcare professional sector, SSF initiatives have included increasing awareness in the public domain and increasing involvement from industry, stakeholders and partners. Our goals center around ensuring that Sjögren’s patients are recognized by physicians for diagnosis and treatment and, subsequently, that Sjögren’s patients are considered for clinical trials.

SSF Clinical Trials Consortium Paves the Way

To accomplish our goals, the CTC has engaged in regular discussions to assess barriers to clinical trials in Sjögren’s. We scheduled teleconferences, as we did for our first meeting in May 2014, and face-to-face meetings, as we have done during the past three November SSF luncheon meetings during the American College of Rheumatology (ACR) annual conferences. The CTC met twice last fall, during the Biologic and Targeted Therapeutics in Sjögren’s (BATTS) conference in Oklahoma at OMRF.
and again at ACR to discuss the SSF meeting with the FDA and the needs of companies and KOLS. New priorities were set as a result and included the development of the online educational platform called STEP.

In March 2016, we hosted a face-to-face CTC meeting of U.S. members and SSF corporate partners. During that meeting, launching a dialogue with the FDA was set as the initial top priority. The SSF built on discussions begun at a November 2014 SSF meeting during the ACR, when a regulatory update was given by the FDA and ensuing discussion raised the need for an FDA guidance document for drug approval in Sjögren’s. Continuing the dialogue with the FDA last July, we discussed numerous options with the FDA that we could pursue with their input. Flexibility was encouraged.

The SSF CTC currently meets regularly with KOLs around the world to determine barriers to clinical trials in Sjögren’s and strategies to tear down those barriers. Many barriers exist in getting new therapies to market, but tremendous progress has been made and current initiatives are underway. There has been increased interest and subsequent plans for new clinical trials. Development of biomarkers and novel diagnostics are in the pipeline and a priority for SSF research grant support. We now have internationally-accepted classification criteria, and internationally-accepted outcomes measures are being utilized with ongoing updates and improvements. (Clinical trial design for Sjögren’s has made a major leap forward with the final validation of the EULAR-endorsed outcome measures, ESSDAI and ESSPRI.)

**Industry Lends a Hand**

Our industry partnerships are increasing as well as awareness that we can assist from the earliest stages of initial interest and discussions through identification of potential therapies, trial design, introduction to KOLs and potential trial sites and subsequent patient recruitment. Also, the SSF can help companies navigate government agency processes and post-approval marketing.

In turn, companies have offered critical input into the SSF CTC goals and initiatives. They bring a unique perspective to the barriers we all face, help us develop strategies to address them, and provide support for our efforts.

This journey has been both challenging and rewarding. Through the efforts of many, we are actively moving forward getting closer to our goals. The SSF thanks each one of you for your support in our continuing efforts.

---

**Learn more about Clinical Trials in Sjögren’s!**


**Links on this page take you to:**

- An article by Theresa Lawrence Ford, MD, the SSF Medical and Scientific Advisory Board Chair and Chair of the SSF Clinical Trials Consortium
- A list of clinical trials in Sjögren’s that are currently recruiting Sjögren’s patients

**Let the SSF know if you are interested in incorporating clinical trials into your practice.**

If so, we would like to learn more about you and your practice. We also often share potential clinical trial sites with our pharmaceutical members when those sites and patient populations fit the needs of a specific company and trial. Please contact us at sq@sjogrens.org if you currently engage in clinical trials or are interested in doing so.
**FOR PATIENTS WITH SJÖGREN’S SYNDROME**

**A PROVEN TREATMENT FOR DRY MOUTH**

90% OF PATIENTS REPORTED IMPROVEMENT IN SWALLOWING*

---

*N30 patients with varying degrees of xerostomia symptoms rinsed with NeutraSal® 2-3 times a day for 28 days. Subjective patient self-assessment using Dry Mouth Questionnaire assessed severity of symptoms on Day 1 vs Day 28.

NeutraSal® is clinically proven to help restore the oral environment*

Nonsystemic oral rinse:
- Neutralizes pH
- Reduces *S. mutans* population
- No known contraindications or medication interactions

Clinical study patients with varying degrees of dry mouth symptoms* who used NeutraSal® reported improvements in speaking, eating, drinking, swallowing, and taste disorders.¹

**INDICATIONS**

NeutraSal® is indicated for dryness of the mouth (hyposalivation, xerostomia) and dryness of the oral mucosa due to drugs that suppress salivary secretion. NeutraSal® may be used for relief of dryness of the oral mucosa when hyposalivation results from Sjögren’s syndrome.

**IMPORTANT SAFETY INFORMATION**

- Not intended to prevent xerostomia or oral mucositis
- Patients should avoid eating or drinking for at least 15 minutes after use
- Solution should not be swallowed but be spit out
- Not intended for systemic use to treat any diseases of the throat or upper gastrointestinal tract
- Not intended for use as an antacid
- No adverse events anticipated if swallowed accidentally
- Contains sodium; consult with patients on a low sodium diet
- No known interactions with medicinal or other products

---

REFERENCES:

NeutraSal is a trademark of Valeant Pharmaceuticals International, Inc. or its affiliates.

©2017 Valeant Pharmaceuticals North America LLC  NSL.0055.USA.17

Learn more at Neutrasal.com/Sjogrens  
Continued on page 10 ▼
become an academician or a researcher.

Like many colleagues interested in gaining clinical skills from a premier university whose focus and reputation are based on its research “chops,” I found myself “hiding under the radar.” My hope was to avoid appearing disinterested in a pathway towards an academic career, all the while clearly focused on leaving to begin a practice.

In my final year of fellowship, I was required to choose a research project and pursue its goals to completion. As I had no experience or interest in “bench” research, I sought out a clinical project. Duke is, and has been, a leading center in uric acid research and the treatment of gout and hyperuricemia. As a Southern medical institution, it served an interesting clientele with a storied culture, at least from the perspective of a city boy from the Northeast.

There was a tradition in the more rural areas of North Carolina of brewing whiskey locally. This tradition antedated prohibition. The so-called “moonshine” produced in home-fashioned distilleries, or stills, was the favored source of alcohol by some and had at least been sampled at one time or another by a large portion of the population. The distillation process was, and likely remains, not up to the standards of the major commercial distilleries. This was reflected in the presence of certain contaminants that entered the finished product - particularly lead - during distillation.

Lead in moonshine had been imputed to be the reason why so many who consumed moonshine in North Carolina developed gout. The focus of my research project was to determine whether moonshine consumption caused chronic lead intoxication which then led to gout. What I found was that gout, in the 38 patients I studied, was more likely related to the alcohol in moonshine and not the lead. Only 2 of the 38 patients had evidence of elevated lead stores.

Thus began my initially reluctant career in clinical research. In 1978, I entered private practice in 1978. Four years later, I participated in my first clinical trial. It was a study of a new NSAID for rheumatoid arthritis. Ironically, as of this writing and since that first trial, I have been involved in more than 400 clinical trials in rheumatology, mostly as a principal investigator. What had been a reluctant first step to engage in clinical research, became something of an obsession, not to mention a major source of satisfaction in my work.

During the ensuing years, I have been witness to the development of important therapies that did not exist at the start of my training. Even more rewarding, I have contributed to the development of many of these treatments.

My years in rheumatology have seen rheumatoid arthritis treatment move from gold salts to methotrexate and then to biologics. Aspirin and indomethacin have given way to safer and more convenient anti-inflammatories (the debacle of the Vioxx withdrawal notwithstanding). Revolutionary new treatments for gout and osteoporosis, improved options for lupus, for Sjögren’s, psoriatic arthritis and ankylosing spondylitis have all become available. There is barely an area in rheumatology that has not been affected by the work that thousands of others like myself have done in the clinical trials arena.

The personal rewards of engaging in clinical trials are enormous. My clinical trials experience has expanded my horizons and given me a national and international perspective on rheumatology and the varied work that rheumatologists do in their clinics. Further, I have worked closely with peers from all over this country and can point to friendships I’ve developed with at least one rheumatologist in almost every state of the Union. Rheumatologists who participate in clinical trials are extremely well networked.

Important relationships with scientists, statisticians and investigators in industry have also grown from my years as a clinical trialist as well as productive associations with highly respected academicians in our field. We all learn from one another, clinicians, academicians and physicians and other scientists in industry about the trials process and the science and utility of new treatments. Further, to do clinical trials provides important perspectives on the importance of sound study design – not just for a specific study but for the broader world of therapeutics in rheumatology. Thus, participating in an active clinical trials program has enriched my experiences in rheumatology and broadened my horizons.

Perhaps most importantly, on a day-to-day basis, being involved in clinical trials has improved the care that I provide. When there are no viable existing treatment options, participation in a clinical trial has given patients new and effective therapies. In many instances, the clinical trials program in our practice has provided our patients with access to expensive new treatments which would otherwise be economically prohibitive. In addition, my participation in clinical trials has enabled me to confidently offer newer treatments to my patients, as I have frequently had significant experience with such treatments prior to their approval.

As a result of my involvement in clinical research, I have had the opportunity to present results at national and international meetings in poster and in oral presentation formats, and I have authored or coauthored several papers that were published in peer-reviewed journals. These activities have been particularly satisfying to me and valuable to the wider medical community.

Continued on page 8 ▼
With July being Dry Eye Awareness Month, we wanted to use the summer issue of the Sjögren's Quarterly to showcase a new product available for dry eye, some of the latest dry eye research that is underway and could potentially lead to new dry eye treatments, a major July event highlighting dry eye, and the publication of the massive and game-changing report – TFOS DEWS II.

The Sjögren’s Syndrome Foundation worked with Minnesota Senator Mark Dayton to have July proclaimed Dry Eye Awareness Month in Congress in 2006. SSF Minnesota members were instrumental in obtaining Senator Dayton’s support, and the National Women’s Health Resource Center partnered with the SSF on this important national effort. In his declaration, the Senator stated that “…dry eye and Sjögren’s seriously endanger women’s health.” Since that time, numerous organizations have joined with the SSF to highlight dry eye during July.

New OTC Eye Drop is Now Available

A new over-the-counter lubricant eye drop is now available for Sjögren’s patients who suffer from dry eye. The product, ROHTO DRY-AID™, was introduced in July by the Mentholatum Company. The company reports that the eye drop:
- Helps restore natural tear film by working on all three layers of the tear
- Is clinically shown to improve signs and symptoms of Dry Eye Disease
- Delivered significant improvements in quality of life measures in clinical study

NIH-Funded Research in Dry Eye Might Lead to New Therapies

In this section, we cover 2017 National Eye Institute (NEI), National Institutes of Health (NIH) grants in dry eye research that address corneal nerve sensation, omega fatty acids and ocular drug delivery. In future issues of the Sjögren’s Quarterly, we will continue taking a look at the latest grants awarded by U.S. government agencies for studies focusing on dry eye and other aspects of Sjögren’s.

Corneal Nerve Sensation

One current hot topic in the field of Dry Eye Disease (DED) involves corneal nerve sensation and the ability of those nerves to sense basal tear evaporation and subsequently spark the production of tears. Normally, only a one-tenth degree of ocular surface cooling is needed to trigger tearing, but this does not happen in a dry eye due to the number, length and function of corneal nerve stimulators being reduced in DED. Research funded by the NEI at the NIH is centered around finding a way to promote corneal nerve growth. Hiramitsu Hirata, PhD, of Weill Cornell Medical College, New York received the 2017 grant for the project “Tear Hyperosmolarity, Corneal Nerves and Dry Eye Disease.” Hirata and colleagues at Cornell and at the University of Chicago-Illinois School of Medicine, Illinois, discovered that enhanced responses from stromal nerves might be related to abnormal corneal sensation and found that axons to which nerve terminals in the
epithelial layers are connected play a role in sensory mechanisms.1 Earlier, Hirata et al reported that tear hyperosmolarity significantly reduces ocular nerve sensation leading to diminished tears.2 These studies potentially could lead to new therapeutics in dry eye.

Another NEI-funded study is underway to determine the impact that the novel therapeutic Lacripep™, the active component of lacritin, has on maintaining and promoting functional innervation of the cornea and lacrimal gland. Sarah M. Knox, PhD of the University of California, San Francisco is a 2017 NIH grant recipient for her study, “Defining the Role of the Nervous System in Aqueous-Deficient Dry Eye.” Her goal is to define the neuroregenerative potential of lacrierep, investigate the mechanisms for achieving this, and see if lacrierep restores tear secretion by increasing functional parasympathetic innervation of the lacrimal gland. Her first grant for this project was awarded in 2015.

In the spring issue of the Sjögren’s Quarterly, we reported on Phase I/II trials that are underway using Lacrierep™ in Sjögren’s patients with dry eye. The tear protein lacritin was discovered by Gordon Laurie, PhD at the University of Virginia, Charlottesville, Virginia. He found that lacritin is highly deficient in the tears of Sjögren’s patients and formed a company, Tear Solutions, Inc., to produce Lacrierep™.

Laurie’s NEI grant for his study, “Lacritin Regulated Ocular Surface Homeostasis,” has been renewed in 2017. Having found that lacritin is a key regulator of corneal sensory nerve activity for basal tearing, Laurie is further investigating a smaller synthetic form of lacritin and further characterizing how lacritin promotes basal tearing, restores ocular surface health, and could prove to be an important therapy for dry eye.

Another approach to corneal nerve health might be through plasmacytoid dendritic cells (pDCs). Pedram Hamrah, MD of Tufts University in Boston is studying the potential benefits of these immune cells in neuronal health regeneration in his project, “Role of Plasmacytoid Dendritic Cells in Corneal Nerve Health and Regeneration.” Because pDCs link innate and adaptive immune responses and Hamrah’s initial studies show that pDCs are important to the maintenance and function of corneal nerve health, this investigation could lead to novel treatments not only for dry eye but eventually for other nerve disorders, including peripheral neuropathies. Hamrah’s grant was first funded by NEI in 2016 and a renewal grant awarded in 2017.

Mark Rosenblatt, MD, PhD, University of Illinois at Chicago, received a 2017 NEI grant to pursue “Mechanisms of Corneal Nerve Repair.” His project will investigate a new role for corneal nerve regeneration via the well-characterized vascular endothelial growth factor (VEGF) signaling pathway. Rosenblatt plans to delineate the mechanisms by which VEGF ligands mediate corneal nerve repair.

A study by Krystel Huxlin, PhD, University of Rochester, New York, also is looking into the basic mechanisms involved in corneal nerve regeneration. Her NEI-funded project, “Corneal Wound Healing and Nerve Regeneration,” started in 2004 and was renewed in 2017. Her project is based on preliminary data showing abnormalities of re-innervation in different nerve layers and an inhibitory influence by myofibroblasts in regenerating nerves. Further investigation could prove a potential avenue for a new therapy.

**Omega Fatty Acids**

Penni Asbell, MD, Professor of Ophthalmology and Director of the Cornea Service and Refractive Surgery Center at Icahn School of Medicine at Mount Sinai, New York, is leading the NEI-funded “Dry Eye Assessment and Management Study (DREAM).”
DREAM marks the first large, independent multi-site study of omega-3 fatty acids in dry eye. Her grant started in 2013 and has been renewed each year, with the most recent grant awarded in 2017.

Jason Nichols, OD, MPH PhD also has been investigating omega fatty acids through an NEI grant funded starting in 2016. His project, “The Role of (O-ACYL)-Omega-Hydroxy Fatty Acids in Human Lipid Layer Structure and Function in Health and Meibomian Gland Dysfunction,” focuses on Meibomian Gland Dysfunction which can lead to structural and functional changes in the tear film. Nichols is Assistant Vice President for Industry Research & Professor, Office of the Vice President for Research; Office of Industry Engagement; Director of Multisite Study Support and the Trial Innovation HUB Liaison Team, Center for Clinical and Translational Science, at the University of Alabama at Birmingham. He aims to quantitate and identify these fatty acids which are purported to be decreased in the meibum and tear film in Meibomian Gland Dysfunction (MGD) as well as determine the structural and functional impact of decreased OAHFAs.

**Ocular Drug Delivery**

In his 2017 NEI-funded study, Ghanashyam S. Acharya, PhD of Baylor College of Medicine, Houston, Texas is investigating methods for successful drug delivery to the eye. In “Ocular Drug Delivery Nanowafer Therapeutic to Treat Corneal Neovascularization,” Acharya is looking at a nanowafer that can be applied to the cornea with a fingertip to deliver a drug in a controlled-release manner for several weeks. While being developed specifically for corneal neovascularization, this method could be used for a wide range of ocular conditions including dry eye.

**July, as Dry Eye Awareness Month, Brings a Congressional Briefing and the Publication of the TFOS DEWS II Report**

“Dry Eye: An Updated Definition, A greater Impact on Vision Health,” was the title for a Congressional Briefing held this summer to recognize Dry Eye Awareness Month. Held in the U.S. House Rayburn building, the program was hosted by the Alliance for Eye and Vision Research (AEVR) along with AEVR coalition partners, including the Sjögren’s Syndrome Foundation, and the Tear Film and Ocular Surface Society (TFOS).

The program highlighted the impending release of the 2017 TFOS DEWS II report. This publication marks the culmination of efforts by 150 clinical and basic research experts from 23 countries over a two-and-half-year period and reports on everything having to do with dry eye from epidemiology to clinical diagnosis and management. The first TFOS DEWS (Dry Eye Workshop) project came out in 2007 and had an astounding impact on the interest in and subsequent progress in the area of dry eye. We are pleased that the latest 2017 report has just been made publicly available and is a free downloadable report (http://www.tearfilm.org/accreports-access_tfos_dews_ii_report/126_126/eng/). TFOS Founder David Sullivan, MS, PhD will provide a summary in an upcoming issue of the Sjögren’s Quarterly.

Congressional Briefing panelists included moderator Paul Karpecki, OD, Director, Cornea Services, Kentucky Eye Institute, Lexington Kentucky; David Sullivan, MS, PhD, Senior Scientist, Schepens Eye Research Institute, and Associate Professor, Department of Ophthalmology, Harvard Medical School; Susan Vitale, PhD, MHS, Research Epidemiologist, Clinical Trials Branch, National Eye Institute, NIH; and Janine Austin-Clayton, MD, Associate Director for Research on Women’s Health, and Director, Office of Research on Women’s Health, NIH.

Anat Galor, MD, MSPH, a 2017 SSF research grant recipient, presented the poster entitled “Why is dry eye disease painful?” Galor is in the Department of Ophthalmology, Miami Veterans Administration Medical Center, and the Department of Ophthalmology, Bascom Palmer Eye Institute and Department of Anesthesiology, Perioperative Medicine and Pain Management, University of Miami Miller School of Medicine. Galor recently published her study correlating eye pain and dry eye severity covered
Sjögren’s in the News!

This April the Foundation reached our largest audience yet during Sjögren’s Awareness Month thanks to our #ThisIsSjögrens awareness campaign that focused on both traditional and social media stories.

When working with traditional media, our goal was to increase awareness among the public and healthcare professionals by promoting the results of our recent patient survey “Living with Sjögren’s.” The SSF used the survey results to demonstrate the physical and emotional burden of the disease.

The SSF worked with an outside consulting agency to create media-specific materials for this campaign, including the “Living with Sjögren’s: Summary of Major Findings” infographic, and a host of press materials, including press releases, and informational fact sheets on Sjögren’s and the Sjögren’s Syndrome Foundation. Utilizing the new materials, the Foundation focused outreach to Health/Lifestyle and Medical Professional media sources and organized both national and local interviews having doctors explain the disease and patients share their stories.

Thanks to the combined effort of our volunteers who spoke to the media, we were able to receive more coverage for Sjögren’s Awareness Month than ever before! Below are only a few highlights of the media stories that featured Sjögren’s this April.
Media Highlights:

- **U.S. News & World Report**
  “Sjögren’s Syndrome: Most common autoimmune condition you’ve never heard of”

- **Fox29 TV Philadelphia**
  “How to identify what is Sjögren’s”

- **Philly Inquirer/Philly.com**
  “Sjögren’s, a disease you probably can’t see or pronounce, wreaks havoc on women”

- **The Rheumatologist**
  “Sjögren’s Awareness Month: Educate Patients, Families, Caregivers”

- **Registered Dental Hygienist**
  “Sjögren’s Awareness Month: During April Hygienists held screenings for xerostomia”

- **Sirius XM Radio**
  Rehabilitative Medicine Doctor Radio Live Show with Host Dr. Jonathan Whiteson “Overview of Sjögren’s”

- **Dentistry Today**
  “Sjögren’s Syndrome Is About Much More Than a Dry Mouth”

- **Healthy Women**
  “You’ve Probably Never Heard of my Disease”

- **Men’s Health Network**
  “Sjögren’s Awareness Month”

- **Healio Primary Care Optometry News**
  “First OD Chairman for Sjögren’s Foundation”

- **eNewsRheum**
  (American College of Rheumatology) “Sjögren’s Awareness Month”

- **Professional Eye Care Associates of America (PECAA)**
  “Sjögren’s Awareness Month Living with Sjögren’s”

- **Healio Rheumatology**
  “Patients with Sjögren’s reported visiting almost five health professionals per year”

- **Vision Monday**
  “Sjögren’s Awareness Month”

- **OptometryWeb**
  “SSF Releases Results of Living with Sjögren’s Survey”

- **Dentistry Today**
  “April is Sjögren’s Awareness Month”

- **DentistryIQ**
  “Sjögren’s Survey Reveals Deep Impact on both health and lifestyles”
This symposium is designed to facilitate precision medicine practices in all aspects of clinical care, including patient diagnosis, prognosis, therapeutic responses, and prevention. This pioneering conference specifically seeks to bring together leaders from the Sjögren’s/autoimmune research community to enhance translation of novel discoveries into clinical practice. Practitioners must embrace the advances and new technology to ensure their practice evolves with the field, ultimately improving patient care, quality and safety. Based on recent research, literature review, faculty perception, expert opinion and reviews from previous activity evaluation and outcome survey data, this 2.5 day activity will bring together science, technology, evidence-based medicine and leaders in the field to provide updates to an international audience, narrowing the gaps in knowledge.

Dates & Location

Wednesday, April 18, 2018 4:00 PM - Saturday, April 21, 2018 12:00 PM
Capital Hilton Hotel, Washington, DC

Visit
http://tinyurl.com/ISSS2018

for the most up-to-date program and registration information.
Healthcare Professionals

Call to order complimentary materials to share with your patients!

Brochures

Dry Eyes
Dry Mouth
What is Sjögren’s syndrome?

DVD

Booklet

Contact us for more information: 800-475-6473 • www.sjogrens.org
Reducing the Risk of Hydroxychloroquine Toxic Retinopathy

Hydroxychloroquine (HCQ) is commonly used for its anti-inflammatory properties in the treatment of Sjögren’s, because it is well-tolerated and rarely needs to be discontinued for adverse systemic reactions. However, HCQ may cause irreversible damage to the retina, especially if taken in high doses or if used for many years. We studied nearly 2,500 patients who were on HCQ for more than five years, which gave us the opportunity to make new observations about the risk factors for retinal toxicity and recommendations to reduce the risk. Overall, we found that retinal toxicity is not as rare as once believed (7.5% in our population), but this number reflects a population of long-term users, of which many were being given too high a dose. We’ll show below how simple calculations and awareness of how to screen patients can keep the risk of toxicity low for many years—and, in essence, make the drug safer than ever.

Our results showed that retinal toxicity was strikingly associated with high daily dosage and long exposure. Older literature had recommended keeping the daily dose of HCQ under 6.5 mg/kg of ideal weight, but this number was derived from anecdotal reports. We found that regular body weight was actually a better predictor of the risk of toxicity (especially for small women who use the drug). The best balance of therapeutic effective-
ness with a low risk of toxicity was to keep daily HCQ intake below 5.0 mg/kg, a number that corresponded to the actual usage of most of our patients and should be therapeutically suitable for most patients.

**Figure 1**

![Figure 1](image)

Figure 1. Kaplan–Meier for risk of toxicity by different daily usage. Note the marked increase in risk at daily consumption of over 5 mg/kg regular body weight. Reprinted from [1] by permission.

**Figure 2**

![Figure 2](image)

Figure 2. Smoothed response risk curves, showing the annual risk of developing toxicity for an individual patient who has been free of retinopathy up to that point. Reprinted from [1] by permission.

It is important for the prescribing physician to know these dose recommendations and insure that long-term HCQ users are getting the proper screening. Few patients complain of visual symptoms as retinopathy begins, since the damage is off-center, and the only insurance against progression of damage to severe and permanent vision loss is early recognition. This is critical as there is no treatment for HCQ retinopathy once it develops. Because the risk is so low in the initial few years of use (assuming proper dosing and no other risk factors), annual screening can be deferred for the first 5 years—but it is critical thereafter.

What are the signs of HCQ toxicity? The classical textbook sign of HCQ toxicity is a ring of depigmentation near the foveal center (i.e., in the parafovea) termed bull’s eye retinopathy (Figure 3d, right). This lesion produces a corresponding ring scotoma. However, the idea that these findings are “characteristic” comes from older literature and a time when retinopathy was not easily confirmed until a bull’s eye was visible. Furthermore, patients of Asian descent may show early toxicity further away from the fovea. With automated visual field testing and modern retinal imaging technology, signs of toxicity can (and should) be recognized years before the bull’s eye stage and before a patient has any visual symptoms. Figure 3 shows the evolution of HCQ retinopathy with these examination techniques. The 10-2 visual field examines the central 10 degrees, where early damage is most often seen in patients of European descent, but wider fields are needed for Asian patients. Spectral density optical coherence tomography (SD-OCT) is a new imaging modality (but widely available now) that shows individual retinal cell layers and can recognize damage long before the pigment layers are affected to make retinopathy visible.

**Figure 3**

![Figure 3](image)

Figure 3: Progressive stages of hydroxychloroquine retinopathy from normality (top) to visible bull’s eye retinopathy (bottom). The SD-OCT test shows individual retinal layers, and the arrows point to regions of parafoveal thinning of the photoreceptors. These can be recognized before there is bull’s eye retinopathy. Reprinted from [1] by permission.

Ideal annual screening should include both visual fields and SD-OCT and be done by a practitioner familiar with the early signs of toxicity. Note that fundus exams or photographs are not sensitive to early toxicity and are...
Transitions... 

Dr. Tim Niewold Moves to NYU

Timothy Niewold, MD, FACR is moving from the Mayo Clinic in Rochester, Minnesota to a new position at NYU. Dr. Niewold will direct the Stewart and Judith Colton Center for Autoimmunity, a free-standing center within the Department of Medicine dedicated to autoimmune disease research. The goal is to integrate efforts across the various divisions of medicine that are focused on autoimmunity, and, ultimately, to understand the causes of human autoimmune disease and develop innovative treatment strategies and disease monitoring tools. He will be the inaugural Stewart and Judith Colton Professor of Medicine and Pathology, and his lab will work toward understanding autoimmune disease genetics and human immunology.

Dr. Niewold has most recently been an Associate Professor in the Division of Rheumatology and Department of Immunology at the Mayo Clinic in Minnesota. He is a member of the Board of Directors of the Sjögren’s Syndrome Foundation.

Clinical Trials for Dry Eye

Clinical trials for dry eye garnered a hit of 644 studies listed online at ClinicalTrials.gov. Of these, 142 either are actively recruiting, ongoing but no longer recruiting, or about to be launched. These trials include testing therapeutics for dry eye from multiple causes, including Sjögren’s, and also include testing for potential treatments for systemic disease and contain an outcome measure for dry eye.

The Sjögren’s Quarterly will provide a table of active clinical trials in Sjögren’s in a future issue. You can always visit the SSF website at http://www.sjogrens.org/news/486-sjogrens-s-clinical-trials to view trials that are currently recruiting patients with the SSF.
Refer Your Patients to the SSF for Education and Support!

Complimentary What is Sjögren’s? brochures are available for you to distribute to your patients so that they can learn about the many resources available from the SSF.

By referring your Sjögren’s patients to the Sjögren’s Syndrome Foundation, you are helping them stay up to date and connected to information about managing their disease.

By connecting with the SSF, patients will discover how they can receive:

- The Moisture Seekers newsletter: This 10 issue a year print newsletter contains the latest information on Sjögren’s, practical tips for daily living, and answers to medical questions from the experts.
- Helpful educational brochures, patient fact sheets as well as our sought-after Product Directory, which lists products that patients find helpful in treating their Sjögren’s.
- Access to a network of knowledgeable volunteers and local support groups.
- Exclusive access to the patient member-only section of www.sjogrens.org, featuring resources unavailable to other site visitors such as archives of the most popular newsletter articles, our online product guide and access to our online community.
- Discounts on a variety of products and services such as The Sjögren’s Book and registration for our educational conferences.

Patients can either visit www.sjogrens.org or call the Foundation at 301-530-4420 to get connected! Information on membership is also available in the SSF’s What is Sjögren’s? brochure. Receive complimentary copies for your office by calling us today!
Probing the Conundrum of Cracked Teeth

Nothing like a toothache to ruin a good meal. Every bite you take makes you cringe—and a sip of something cold? You don’t want to go there. But you do want to go to your dentist, even if the pain isn’t constant. Your painful tooth may have a crack in it.

Getting a crack in your tooth is relatively easy—even just grinding your teeth puts you at risk. In fact, more than two-thirds of dental patients have at least one tooth with a crack in it. But finding that crack can be difficult. **Cracks in teeth often don’t show up on an x-ray and many are too shallow to hurt, although they still pose a risk to your tooth.**

So dentists in the National Dental Practice-Based Research Network studied a large group of patients to see which teeth and which patients are most likely to develop a crack. They are also looking at how quickly a cracked tooth can change.

**Common features of teeth that get cracks**

Armed with an array of sophisticated tools including high-powered magnifiers and lights that can illuminate the inside of a tooth, the researchers found that:

- Patients who had a painful cracked tooth were somewhat more likely than others to clench or grind their teeth, be female, and under age 65
- Having a filling doesn’t affect whether a cracked tooth will be painful, but having a molar that is more worn from grinding makes it more likely that a cracked tooth will be painful
- Cracks that are stained (say, from your coffee habit) were the least likely to cause pain or sensitivity.

**What to do about a cracked tooth**

The best time and way to treat a cracked tooth is still being investigated in the study. Most of the time, cracked teeth can be treated with a filling or crown; more involved treatment such as a root canal or pulling the tooth is needed much less frequently.

**If your dentist tells you that you have a cracked tooth, it’s very important to see your dentist on a regular basis so they can monitor the tooth for changes.** This will give your dentist the opportunity to recommend treatment to help prevent further problems that require more extensive treatment.


To ensure excellent dental care, the Network carries out our studies in real-world settings—like your dentist’s office—with regular patients like yourself who volunteer to participate. The studies wouldn’t be possible without the involvement of our wonderful patients.

Thanks to everyone who participated in this and all of our studies!
Clinical trials provide the means for evaluating a new or existing treatment in patients to see if the treatment, usually a drug, is safe and effective and at what dose. Clinical trials are necessary before a therapy can be approved and offered on the market. Before enrolling in a clinical trial, always discuss participation with your doctor.

Why Consider Participating in a Clinical Trial?

Patients participating in a trial will:

- Help ensure a new treatment is developed to control symptoms or overall outcome of their disease or disorder.
- Gain access to a promising treatment that may provide unique benefit or meet unmet need.
- Get access to care at no cost.
- Help other patients.
- Participate in helping to advance science/medicine.

Am I Eligible to Participate in a Clinical Trial?

- Clinical studies are performed according to a plan design called a protocol which is unique to each project.
- Protocols define eligibility criteria of participants who can be enrolled. These criteria relate to such factors as age, gender, duration of illness, prior treatments and other medications you might be taking, etc.
- Eligibility criteria fall into two categories:
  - Inclusion criteria which define the population of patients to be studied
  - Exclusion criteria which disqualify certain volunteers from participating due to age, other medical problems or other factors

Is it Safe to be in a Clinical Trial?

- Before participating, you will be provided with a document called an informed consent outlining risks and benefits and the study design (features of the protocol such as length of the study and number of visits). After reviewing that document, you might have questions, all of which should be answered.
- You have the right to withdraw from a study at any time and for any reason as is explained in all informed consent documents and by the personnel conducting the trial.
- The clinical trials program typically is monitored by an independent institutional review board that approves the study design and sites where the study is conducted.
- Most trials of new medications performed at multiple sites across the country are monitored on an ongoing basis by a data safety monitoring board.
- The FDA has oversight for the clinical trials process and periodically conducts audits at sites where trials are performed.

Please see the Patient Education Sheet on “Understanding Clinical Trials” for more information on clinical trials. This sheet is available online on the SSF website at http://www.sjogrens.org/home/about-sjogrens/brochures-and-fact-sheets. Additional information and a list of specific trials currently available for enrollment can be viewed by visiting http://www.sjogrens.org/news/486-sjogrens-s-clinical-trials.
The world of Sjögren’s has lost a leader and giant who contributed greatly to putting Sjögren’s on the map for physicians and patients. Rolf Manthorpe, MD, Associate Professor and head of the Sjögren’s Research Center in Malmo, Sweden, died on August 24, 2016.

Dr. Manthorpe launched the first International Symposium on Sjögren’s held in Copenhagen, Denmark, in 1986. The symposium marked the first time international experts in Sjögren’s came together representing all specialties involved in clinical treatment and clinical and scientific research in Sjögren’s to share information and move the field of Sjögren’s forward. Manthorpe taped a greeting from Henrik Sjögren, a Swedish ophthalmologist for whom the disease was named, that was broadcast during the symposium. Thirteen international symposia have now been held with the 14th such symposium slated for 2018 in Washington, D.C.

A renowned world expert in Sjögren’s, Dr. Manthorpe’s interest in Sjögren’s started in 1974 when he discovered that bromhexine increased tear production in many Sjögren’s patients. He has since published many studies on all aspects of Sjögren’s syndrome. He has also mentored many current leaders in Sjögren’s and friends of the Sjögren’s Syndrome Foundation. Dr. Manthorpe was appointed Chief of Rheumatology in Malmo in 1984 and opened the first Sjögren’s research center in northern Europe. He was married to Tove Bunken.

Remembering Rolf Manthorpe

Thanks to Thomas Mandl, MD for use of photo