North Carolina Thoracic Society
ATS Chapter

"Advancing Lung Health in North Carolina"

North Carolina Thoracic Society Newsletter

Fall 2023

NCTS EVENTS AND ANNOUNCEMENTS

New Officers

Veeranna Maddipati, MD (East Carolina University, Pulmonary) became the 2023-24 Secretary Treasurer.

Dr Maddipati is Assistant Professor with the Division of Pulmonary, Critical Care and Sleep Medicine at East Carolina University and Vidant Medical Center. He serves as a teaching faculty and as an associate program director in the pulmonary and critical care medicine fellowship program. He is also the director of pulmonary vascular diseases and pulmonary embolism response team at ECU. He practices in the ICU, as well as in the Moye Medical Center on a outpatient basis. His research includes studies in Pulmonary Hypertension, Pulmonary Embolism and COPD.

Chad Kloefkorn, MD (Duke University) became the Chapter Councilor 2023-25

Dr Kloefkorn is Assistant Professor with the Division of Pulmonary, Allergy, and Critical Care Medicine at Duke University. He received his medical degree from Eastern Virginia Medical School, his residency at Baylor University, and pulmonary fellowship at Wake Forest University. Chad is part of Duke Interstitial Lung Disease program and practices at Duke Raleigh and Duke Medical Center. While a Fellow at WFU, Chad presented at one of the first NCTS Annual meetings.

Past Meetings

2023 North Carolina Society Annual Education Conference, Saturday April 29, 2023, Embassy Suites Riverfront Wilmington, NC. About 75 lung health professionals attended the day-long educational conference. The quality of talks was exceptional, reflecting the incredible skills and

knowledge of the faculty. One focus was disease remission concerning biologics in asthma and CFTR modulators in CF – amazing what these drugs have done for patients. We had a great time afterwards at NCTS reception and dinner program at Bluewater Restaurant in Wrightsville Beach. We are so happy to be past the worst part of the pandemic and are able to learn and meet new colleagues. We learned one lesson with this meeting – if you incentivize Fellows to attend at a fun meeting location, they show up in large numbers!

NCTS ILD Specialty Conference. Sept 30, 2023 Washington Duke Inn, Durham

Stephen Nathan, MD - Keynote

Donna and Fred– Patient Support Group Leaders

NCTS and the 3 Pulmonary Fibrosis Foundation (PFF) Centers in North Carolina collaborated to plan and conduct the first educational conference on ILD – consistent with our mission to advance lung health in NC. Duke University and Lake Morrison, MD hosted the program. The keynote speaker, Stephen Nathan, MD (Inova Health, Virginia), discussed comorbidities in ILD and contributed his wisdom and experience throughout the day. From the 3 Centers, Dr Ramaswamy (Cone Health), Dr Lobo and Patel (UNC), and Dr Kloefkorn and Driehuys (Duke University) provided various lectures. There were several fellow's case presentations paired with lecture topics – great 'combo'. Lastly, two patient PFF support group leaders did a great job highlighting the needs of patients diagnosed with ILD. Also importantly, three ILD subspecialists from non-PFF Centers in NC attended (ECU, Salem Chest, Atrium Health). NCTS believes we have advanced ILD in NC.

UPCOMING MEETINGS

2024 North Carolina Society Annual Education Conference, April 26 and 27, 2024

NCTS will hold its 7th annual educational conference in Charlotte, NC on April 26 and 27, 2024. This meeting will be held at the Charlotte Motor Speedway and the meeting hotel is the Great Wolf Lodge. We are seeking to make our meetings fun and interactive, and compatible with families coming along. Cat 1 ACCME will be provided to eligible health care professionals.

We will have workshops Friday evening and again Saturday afternoon primarily directed towards critical care practice. Our lectures Saturday last until about 1PM and include MART for asthma, robotic bronchoscopy for lung cancer, new spirometry guidelines, pulmonary rehabilitation, and presentations by fellows including a pro-con debate. We strive to engage both academic- and community practice-oriented lung health professionals in our organization and meeting.

We will have a reception and dinner program Saturday evening at a local restaurant.

2025 NCTS NC/UVA Pulmonary Fibrosis Foundation Centers ILD Specialty Meeting
NCTS will collaborate with the three NC PFF Centers and the UVA PFF Center to hold an ILD conference in 2025 – hosted by Murali Ramaswamy, MD at Cone Health. Unbelievable talent that will be at that meeting!!

UPDATE ON NC RESPIRATORY CARE BOARD ADVANCED PRACTITIONER

Bill Croft, Ed.D., Ph.D., RRT, RCP, FAARC – Executive Director, NC Respiratory Care Board

On March 9, 2023, House Bill 316, the Respiratory Care Modernization Act, was introduced in the NC General Assembly. This bill seeks to add the Advanced Respiratory Care Practitioner (ARCP) to Article 38 of the Respiratory Care Practice Act as a licensed healthcare practitioner separate from the respiratory therapist. The ARCP will be a physician extender with a master's degree working under the supervision of a licensed physician.

Following the introduction of H316, the Executive Director of the NCRCB spent the next 45 days negotiating with the NC Medical Board, the NC Society of Anesthesiology, and the Health Committee in the NC House of Representatives. Between April 27 and May 2, 2003, HB 316 rapidly passed through the Health, Judiciary, and Rules Committee onto the House Floor for a final vote. On May 2, 2023, HB 316 passed the House and was sent to the Senate that night, where it passed the first reading and was sent to the Rule and Operations of the Senate. For the next month, we spent our time attempting to get out of the Rules and Operations of the Senate Committee. On June 20, 2023, we conferred with the Health Committee Chair, Senator Burgin, about moving the bill to the Health Care Committee. HB 316 was withdrawn from Rules and placed in Health later that day. As of today, H316 remains in the Health Committee of the Senate and will be heard in committee during the start of the short session. We are five votes from passing the bill into law, so the NCRCB would like to thank all the members of the NCTS for their efforts. It made a huge difference in our success.

UPCOMING RESOURCE FOR PULMONARY CLINICS

Roy Pleasants, PharmD and other NCTS members are developing a web-based training program on aerosol drug delivery. It will be piloted at selected sites by summer 2024. I think we would all agree there is a major gap in the knowledge of aerosol drug delivery, beginning at the trainee level. The target audiences of this web-based program are prescribers and office staff in outpatient clinics. Basically, participants will learn about the 'What', the 'Why', and the 'How' of aerosol drug delivery to understand the clinical science behind teaching proper use of inhalers and nebulizers.

While there are numerous sources of individual videos for specific inhalers ("How"), there are essentially no available resources that teach the background to understand optimizing aerosol drug delivery ("What" and "Why").

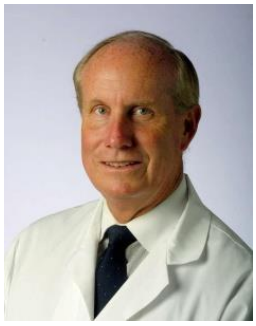
This web-based, self-paced learning will be available on the NCTS website. It consists of 4 one-hour modules: Videos 1 and 2 on the clinical science for prescribers, Video 3 on the basics of lungs and aerosol drug delivery for office staff, and Video 4 on the how to with explanations for common inhalational devices.

RENEWING MEMBERSHIP TO NCTS IN 2024

Beginning in January 2024, the process to join or renew membership will change. For ATS members, when renewing ATS membership online, you can join NCTS for 2024 by "checking" the box asking if you want to join your state society. There is no charge to join through this pathway. Non-ATS members will need to complete a form provided to them to join NCTS. In lieu of a membership fee, we will charge $50 to all attendees for each NCTS conference. We will have 2 conferences in 2024 (Fall 2024 TBA).

CLINICAL TOPICS

Spirometry Update: Neil Macintyre, MD (Duke University)



Spirometry is the oldest clinical test still in use today, first described in 1846 by John Hutchinson. Over the years, spirometry has been used widely around the world to assess lung function and performance standards have been set by the ERS and ATS.

The most recent ERS/ATS spirometry publication has been a standardized approach to interpretation (Eur Respir J. 2022 Jul 13;60(1):2101499). Another important development has been the ATS recommendation to eliminate race adjustments in spirometry reference equations (Am J Respir Crit Care 2023; 207:978). There are two big reasons for this: 1) Self identified race is not an objective

quantifiable measurement; 2) While non-Caucasians do have lower spirometric values, the reasons for this appear to be more influenced by modifiable disease risk factors (eg environmental exposures, health care access etc that are more prevalent in non-Caucasians) than clearly identifiable genetic factors.

In looking at the future of spirometry, the use of artificial intelligence (AI) to analyze the entire flow volume tracing holds considerable promise. Traditionally, spirometric interpretation is focused on only the FEV1 and FVC while the bulk of flow data during exhalation is ignored. This is often termed the spirometric "silent zone" but it likely contains a wealth of information, especially regarding small airway function. AI may be the key to opening up this zone (JCI Insight 2020;5:132781).

An Update On The Use Of Preventive Oral Azithromycin In COPD: Roy Pleasants, PharmD (aka Roy the Inhaler Guy)

Preventive, chronic azithromycin has been used substantively in COPD since the 1 year studies by Albert in 2011 and Uzun in 2014. Its immunomodulatory effects on neutrophils, effects on mucus and anti-infective effects are beneficial in COPD to decrease flares.

It is cheap (<$25/month), drug interactions are highly unlikely, and is generally well-tolerated. A recent Ann ATS study reported substantial cost savings. Side-effects with chronic use include auditory loss, GI upset, and bacterial resistance.

Use in Current Smokers?
Smokers with COPD have high rates of exacerbations. The 2024 GOLD Report suggests not to use chronic preventive azithromycin in current smokers. This is based on a post-hoc analysis of the Albert study by Han, that found no decrease in flares in this subset of COPD patients. Since that published analysis, some studies included current smokers and reported benefits on exacerbations.(Uzun, Naderi) Several animal studies report that azithromycin attenuates smoking-induced lung injury.

In the clinic setting, I suggest an N=1 to help determine possible benefits of azithromycin in a current smoker with recurrent exacerbations, a high-risk population. Risks of azithromycin are likely no different than in ex-smokers.

Hearing Loss?
Based on the literature, hearing loss is uncommon and typically sub-clinical, and is likely reversible if the drug is stopped. Most studies report stopping it in such patients.

Prolonging the QTc?
ECG's are often obtained when initiating preventive azithromycin, largely because of the FDA's response to a retrospective 2012 study in the Tennessee Medicaid population study, with a

resultant warning in the PI - and that the 'macrolide' drug class prolongs QTc. Well, azithromycin, an azalide, behaves differently on cardiac conduction than the macrolide clarithromycin – animal models show it has minimal effects on QTc. Two recent large retrospective studies in COPD patients show it did not cause more cardiac events compared to a B-lactam.

I do not recommend an EKG at baseline unless the patient is also on other notable QTc-prolonging drugs, has substantial heart disease, using pneumonia doses of IV azithromycin in the hospital (500 mg IV qd), or a h/o of prolonged QTc.

Dosing?
Azithromycin accumulates and achieves very high levels in lung tissue and extensively penetrates various inflammatory cells. The half-life of azithromycin in tissues is days-long.

The GOLD Report recommends preventive azithromycin 250 mg daily or 500 mg 3Xweekly. Recent studies found 500 mg 3Xweekly was no better than 250 mg 3Xweekly for exacerbations. (Pomares, Naderi) – The GI side-effects are dose-dependent, so a lower dose will be better tolerated.

Bacterial Resistance?
Yes, it happens according to Albert and others, such as streptococci and H. flu. It can also increase macrolide resistance to NTM, so some recommend testing for this prior to prescribing, esp if bronchiectasis is present.

Drug interactions (DDI)?
Azithromycin, unlike erythromycin and clarithromycin, is unlikely to impair metabolism of other drugs. Its effects on QTc are quite small. Unfortunately, too often DDI databases rely upon drug classes(macrolides) to make recommendations on DDI. In contrast, we should be concerned with DDI with claritho- and erythromycin because of altered drug metabolism.

How long does it work?
Data is now out to 3 years showing efficacy.

Summary
Preventive azithromycin decreases exacerbations in COPD in patients on maintenance inhalers! It's cheaper than any other such strategy, other than quitting smoking. Based on my assessment of the literature, preventive azithromycin can be used in smokers, can be dosed at 250 mg three times weekly, and most patients do not need an EKG performed at the time of prescribing. Consider bacterial resistance with azithromycin monotherapy, particularly NTM. See refs at end of newsletter.

LITERATURE REVIEW

Efzofitimod for Pulmonary Sarcoidosis (Ethan Armour, Steve Tilley, MD, UNC-CH)

Editors Note: Ethan is a recent graduate on the path to becoming an orthopedic surgeon. In his gap year prior to medical school, he is working with Dr Tilley on a sarcoid project to develop a white paper. Steve is the immediate Past Chapter Councilor for NCTS (Thanks Steve!).

Efzofitimod (ATYR1923) is an Fc fusion protein with an active moiety corresponding identically to the N-terminal domain of the extracellularly active histidyl-tRNA synthetase (HARS). Similar to the endogenously produced anti-inflammatory molecule HARS, efzofitimod binds selectively to neuropilin-2 (NRP2), a cell-surface receptor highly expressed by macrophages in sarcoid granulomas. In mouse models of sarcoidosis and hypersensitivity pneumonitis, treatment with efzofitimod significantly reduced lung inflammation (1).
This pre-clinical data prompted a phase 1b/2a study (NCT03824392) which examined the safety and efficacy of efzofitimod in a randomized, double-blind, placebo-controlled study published in CHEST (2).

Efzofitimod (1, 3, or 5 mg/kg) or placebo was administered intravenously every 4 weeks for 20 weeks to 37 pulmonary sarcoidosis patients requiring prednisone 10-25 mg/d. Two weeks after study start, prednisone was gradually tapered. The primary end point was incidence of adverse events (AEs); secondary end points were steroid reduction, change in lung function, and patient-reported outcomes (PROs). No deaths or serious drug-related AEs were observed, and the proportion of patients with AEs was similar between placebo and efzofitimod groups. A dose-dependent trend towards steroid reduction was observed, with a 22% reduction in prednisone dose seen in participants treated with 5 mg/kg efzofitimod compared to placebo. Three patients treated with 5 mg/kg efzofitimod were able to taper completely off steroids. Drug treatment also showed trends toward improved lung function and statistically and clinically significant improvement in some PROs. Post-hoc analysis found that 7.7% of patients in the pooled 3.0 and 5.0 mg/kg efzofitimod group relapsed following steroid taper, compared to 54.4% in the pooled placebo and efzofitimod 1.0 mg/kg group (p=0.017) (ERS 2023).

A phase 3 trial (NCT05415137) evaluating the efficacy of efzofitimod at reducing steroid burden in patients with pulmonary sarcoidosis is currently enrolling, including 2 sites in North Carolina (Duke, ECU). Contact information for enrollment: efzofit@cssienroll.com or 877-596-6699.

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