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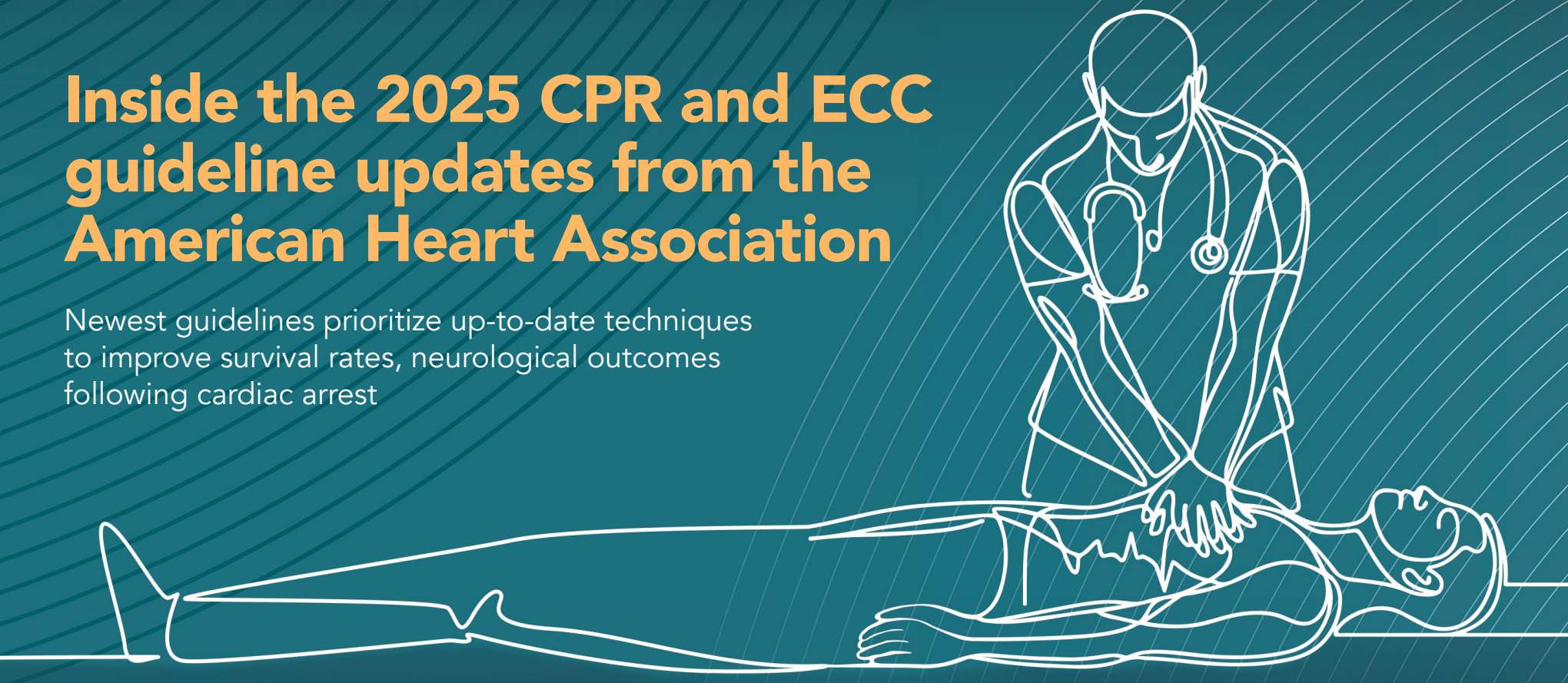
Newest guidelines prioritize up-to-date techniques to improve survival rates, neurological outcomes following cardiac arrest



BY TAYLOR FITHIAN

Late last year, the American Heart Association (AHA) released updated guidelines for CPR and emergency cardiovascular care (ECC). The recommendations build on years of ongoing evidence analysis informed by the International Liaison Committee on Resuscitation and its member organizations. The guidance reinforces the importance of high-quality chest compressions, early defibrillation, and the integration of advanced resuscitation techniques.[1]

"The 2025 update process began when the 2020 guidelines were completed—even then, we were already thinking about the next phase," said Ashish Panchal, MD, PhD, Professor of Emergency Medicine at The Ohio State University Wexner Medical Center and Chairperson of the AHA-led Emergency Cardiovascular Care Committee. "Understanding where the gaps in knowledge are—and identifying the questions that need to be addressed for each chapter—guided the conceptual framework for how we approached these updates."

// continued on page 21

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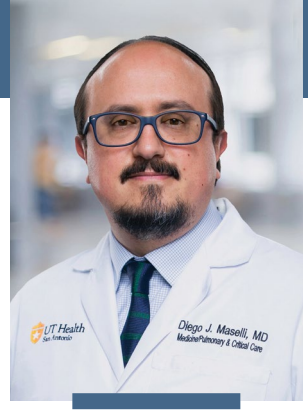
From the Editor



Dear colleagues,

Let me introduce myself: My name is Diego J. Maselli, MD, FCCP, and I will be serving as the Editor in Chief of *CHEST Physician* for the next three years. I am a Professor of Medicine and Chief of the Division of Pulmonary Diseases and Critical Care at UT San Antonio, as well as a longtime volunteer within CHEST.

I am honored and grateful for the trust placed in me, and I look forward to working alongside our Editorial Board, the CHEST Editorial Team, contributors, and readers as we continue to advance the mission of *CHEST Physician*.

First and foremost, I would like to extend my sincere thanks to my predecessor, Angel Coz, MD, FCCP. During the past four years, he elevated *CHEST Physician* to its current form. The editorial infrastructure he helped build strengthened the publication; and through his leadership, the magazine expanded its reach to a broader range of practitioners across pulmonary, critical care, and sleep medicine. I joined the Editorial Board in 2022 under his stewardship and had the opportunity to experience firsthand his unwavering dedication and commitment.

In recent years, the publication has undergone meaningful evolution. We have introduced new perspectives, expanded representation, and established additional forums for dialogue that more accurately reflect the breadth and complexity of our field. As I assume this role, my objective is to continue strengthening the growth and reach of *CHEST Physician*. I remain committed to scientific rigor, accuracy, and ethical standards, and to the improvement and innovation that have defined this publication.

For 2026, I am delighted to report that we expanded our already robust Editorial Board to include a wider range of providers, ensuring that diverse perspectives are represented in our rapidly evolving field, particularly in areas of technology and informatics. *CHEST Physician* will continue to serve as a gateway to keep you abreast of all things happening at the CHEST organization and as a nexus connecting the *CHEST*® journal portfolio, the CHEST Annual Meeting, and our broader educational offerings. In addition, we aim to provide a stronger voice for all members on our medical teams, including trainees, advanced practice providers, respiratory therapists, pharmacists, and others.

The team and I look forward to continuing to deliver timely, relevant, and high-quality content at a time when accurate information is more essential than ever. As a practicing pulmonary and critical care physician, I am keenly aware of the multiple complexities of our medical systems. We will build upon this strong foundation while maintaining the highest standards of scientific rigor, inclusivity, and clinical relevance, ensuring that this publication remains an impactful resource for our community.

Warm regards,

Diego J. Maselli, MD, FCCP
Editor in Chief, *CHEST Physician*

In memoriam

CHEST has been informed of the following deaths of CHEST members. We remember our colleagues and extend our sincere condolences.

Walter Baigelman, MD

James M. McKenna, MBBS

Mark P. Scott, MD

Alfred Soffer, MD, Master FCCP
Former Editor in Chief of the journal CHEST® *and Executive Director* (see obituary, page 11)

Charles C. Yockey, MD

CHEST Physician®

American College of Chest Physicians (CHEST)

chestphysician@chestnet.org

CHEST Physician, an official publication of the American College of Chest Physicians, provides cutting-edge reports on timely news, research, and clinical advances in the world of chest medicine. Regular columns feature the areas of pulmonary, critical care, and sleep medicine, as well as association news and updates from CHEST leadership.

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Inside

CHEST Puzzler Key

Scan the QR code to access the answer key to the crossword puzzle on page 23.

Navigating AI's emerging role in critical care

How predictive and generative tools are reshaping the ICU and medical education

BY LT ASHNA MANHAS, MD, MC, USN; LCDR MEREDITH L. OLSEN, MD, MC, USN

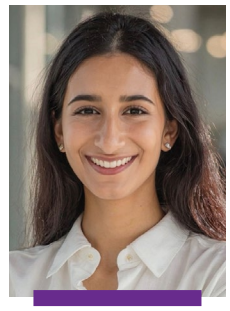
Disclaimer: The views expressed in this article reflect the opinions of the authors and do not necessarily reflect the official policy or position of the US Department of the Navy, US Department of Defense, or the United States government.

Ready or not, artificial intelligence (AI) is here. And it's already changing the landscape of medicine as we know it.

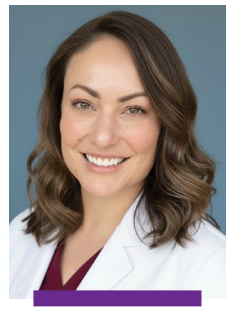
Though this is far from the first time that technological advancements have caused a monumental shift in society, AI's black box nature has triggered notable mistrust—especially when considering its potential incorporation into health care. This is, however, reminiscent of the skepticism that computers and the advent of electronic health records (EHRs) received in the 1960s.

AI is a large umbrella term for systems designed to mimic human intelligence. It can be broadly categorized as either predictive or generative in function. To simulate human intelligence, AI deconstructs it into six basic pillars: natural language processing (communication); knowledge representation (understanding); automated reasoning (thinking); machine learning (learning); computer vision (sight); and robotics (movement).[1] Machine learning (ML) is best defined as identifying patterns and structures within a dataset. It is the domain in which recent advancements have made AI as a whole gain significant attention.

Truthfully, AI has had direct applications in medicine for decades.[1] With the continued advancement of AI and its readily accessible nature with systems like OpenEvidence, there are many promising opportunities to apply AI as a new tool in critical care medicine and in medical education.



LT Ashna Manhas, MD, MC, USN



LCDR Meredith L. Olsen, MD, MC, USN

CRITICAL CARE MEDICINE

Critical care medicine has predominantly been defined by reactive processes as opposed to proactive ones. Interventions are generally pursued after clinical deterioration; whereas most of the recent AI advancements in the medical field rely on its predictive function. Research has been conducted on ML models that can predict sepsis, respiratory distress, and other conditions commonly seen in the ICU.[2]

Among the AI studies currently being conducted in ICU settings, 22.2% predict complications, 20.6% predict mortality, and 18.4% improve prognostic models. Unfortunately, most of these have not progressed to the point of practical application.[3] A notable exception is a validated severe sepsis prediction algorithm developed in Hayward, California. An ML algorithm using a patient's vital signs and age was able to predict sepsis with significantly more accuracy than the Sequential Organ Failure Assessment, the Systemic Inflammatory Response Syndrome, and the Modified Early Warning Score. The ML algorithm significantly decreased both the primary outcome of length of hospitalization and secondary outcome of in-hospital mortality; length of hospitalization decreased by 20%, and in-hospital mortality by 12.4%.[4]

Impressively, a few AI algorithms have already been integrated into clinical practice after US Food and Drug Administration (FDA) clearance, such as the Analytic for Hemodynamic Instability software.[5] Designed for patients receiving continuous telemetry, it can analyze a single lead of an electrocardiogram in tandem with intermittent noninvasive blood pressure monitoring to assess hemodynamic status and thus identify early evidence of hemodynamic instability. It is important to note that ML is being studied as tools for clinicians

to use in tandem with clinical acumen, rather than as a replacement.

AI, like any other instrument, has its limitations. ML algorithms undergo "training" based on existing data. For ICU-based algorithms, this training is often done on large, publicly accessible databases such as the Medical Information Mart for Intensive Care-III, eICU, and AmsterdamUMCdb.[2]

Systems trained on homogenous datasets can result in biased AI and can negatively affect patient outcomes for underrepresented populations. In one instance, an AI algorithm that was initially developed to predict length of hospital stay was found to identify less affluent zip codes as a variable and consequently predicted longer hospitalizations for patients based on their addresses.[5]

A large area of interest in AI application within medicine is automating existing health care tasks. AI can potentially automate up to 45% of administrative tasks in health care, allowing physicians to focus more directly on patient care.[5] By far, EHR maintenance is often cited as a leading cause of physician burnout, actively limiting patient interactions and sometimes affecting patient care negatively.

While predictive analytics rely on advancements in ML, another subcategory of AI called natural language processing (NLP) has also demonstrated significant advancements in recent years. There are many different AI-powered software programs on the market that have automated clinical notes based on patient interaction transcription.[1] While NLP algorithms have predominantly been tested in the outpatient setting, there is the clear extrapolation in using it for inpatient rounding notes, goals of care discussions, and procedure notes.

Currently, most of the technology used in health care focuses on clinical support services as opposed to direct patient application. Of the 1,247 FDA-cleared, AI-enabled medical devices, more than 75% are radiology-based and focus on triaging emergent cases or acting as second readers.[6] While AI has transformative potential for critical care medicine, it will likely be a few more years before such technology is commonplace in ICU settings.

MEDICAL EDUCATION

The way that we think, learn, and interact with educational material has constantly adapted to technological advancements. From transitioning from written text to PDFs, the amount of knowledge we have access to has only continued to grow. In fact, the amount of medical research published annually doubles every five years.[7] It is no surprise that with the full-scale buy-in to the advent of AI, the medical educational environment will once again undergo another seismic shift. Whereas most AI applications discussed in the previous clinical section are predictive in nature, there are many ways to apply its generative functions in the realm of medical education.

Large language models (LLMs) are complex algorithms that use a combination of the AI domains to generate humanlike text.[8] One LLM that has been making waves in the medical community is the previously referenced OpenEvidence. A free and unlimited tool for health care professionals, OpenEvidence aims to improve medical literature accessibility and synthesis. Content agreements with *The New England Journal of Medicine*, the *Journal of the American Medical Association*, and the National Comprehensive Cancer Network allow the model to provide users with evidence-based summaries, links to articles, and up-to-date information on clinical guidelines, diagnostic criteria, and management approaches.[9-10]

OpenEvidence can be a valued resource for medical students and resident physicians alike for study preparation. Its ability to direct nearly any peer-reviewed resource to a user's phone is unparalleled. This ready access to clinically relevant content helps directly integrate learning with clinical practice.

Notably, within two years of its launch, OpenEvidence became the first AI platform to score 100% on all three Steps of the United States Medical Licensing Exam.[8]

However, overreliance on OpenEvidence can diminish critical thinking skills necessary for independent practice.

While commending its uses, it is also important to note OpenEvidence's potential pitfalls. Though all LLMs encode billions of parameters, none are unlimited in knowledge. When LLMs are asked questions for which it has no knowledge, many produce replies that are not based on reality. This occurrence is known as an "AI hallucination" and remains a mathematical inevitability based on the training process that rewards conjecture as opposed to honest uncertainty.[9] This, consequently, can cause mislearning. For this reason, like all other tools, OpenEvidence is best used as an adjunct rather than as a substitute for critical thinking and clinical acumen.

From an educator's perspective, OpenEvidence and other large LLMs have notable benefits that are hard to ignore. With its ability to craft curated objectives and challenging multiple-choice questions based on blueprints and medical topics, it can augment curriculum-building. Like all other tools, all questions and answers should be reviewed before being implemented as part of a course. OpenEvidence also has "Trending" and "New evidence" tabs within its "Feed" section that offer trending and cutting-edge research. These can be filtered by medical specialty for a more curated selection of journal articles.[10]

As AI continues to evolve, future high-yield applications will include personalized medical instruction to better suit learners of all levels. Another area in critical care medicine education where AI will prove invaluable is simulation.[9] Already a cornerstone of medical student and resident education alike, simulation allows for clinical practice in a safe environment. High-acuity ICU scenarios are often difficult to simulate realistically, and LLM-based simulations could generate dynamic, patient-specific cases that better mirror real-world complexity.

LLMs have the potential to completely alter how medical education is pursued by learners and educators alike. But while there are many benefits to having a tool to consolidate knowledge and research articles, LLMs have limitations and should be used as supplements instead of substitutions for primary literature review and clinical expertise.

ADAPTING TO CHANGE

AI's ubiquity will only continue to grow. As clinicians, it is important to welcome this change to the medical landscape early on and to incorporate it into our practices and teachings as we see fit so as not to be left behind by the wave of technology.

In the same vein, it is important to ensure that our learners are aware of the role AI should have in their respective medical educations and to promote using it responsibly.

For the practicing intensivist, most of AI's presence has yet to be felt. However, when AI inevitably integrates into critical care practice, we look forward to having another tool in our toolbelts. ●

All references are available online at chestphysician.org.

Brinsupri®
(brensocatib) tablets, 10 mg·25 mg

THE FIRST FDA-APPROVED TREATMENT INDICATED FOR

NON-CYSTIC FIBROSIS BRONCHIECTASIS: PROVEN TO REDUCE EXACERBATIONS

Primary endpoint: In a 52-week study, BRINSUPRI reduced the annualized rate of pulmonary exacerbations vs placebo (10 mg: 1.02 [rate ratio=0.79; 95% CI: 0.68-0.92]; 25 mg: 1.04 [rate ratio=0.81; 95% CI: 0.69-0.94]; placebo: 1.29)[1]

BRINSUPRI is one pill, once a day[1]

BRINSUPRI targets a key driver of inflammation in bronchiectasis[1,2]

INDICATION

BRINSUPRI is indicated for the treatment of non-cystic fibrosis bronchiectasis (NCFB) in adult and pediatric patients 12 years of age and older.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Dermatologic Adverse Reactions
Treatment with BRINSUPRI is associated with an increase in dermatologic adverse reactions, including rash, dry skin, and hyperkeratosis. Monitor patients for development of new rashes or skin conditions and refer patients to a dermatologist for evaluation of new dermatologic findings.

Gingival and Periodontal Adverse Reactions
Treatment with BRINSUPRI is associated with an increase in gingival and periodontal adverse reactions. Refer patients to dental care services for regular dental checkups while taking BRINSUPRI. Advise patients to perform routine dental hygiene.

Live Attenuated Vaccines
It is unknown whether administration of live attenuated vaccines during BRINSUPRI treatment will affect the safety or effectiveness of these vaccines. The use of live attenuated vaccines should be avoided in patients receiving BRINSUPRI.

ADVERSE REACTIONS

The most common adverse reactions ≥2% in the ASPEN trial included upper respiratory tract infection, headache, rash, dry skin, hyperkeratosis, and hypertension. The safety profile for adult patients with NCFB in WILLOW was generally similar to ASPEN, except for a higher incidence of gingival and periodontal adverse reactions.

Less Common Adverse Reactions

Liver Function Test Elevations
In ASPEN, there was an increase from baseline in average ALT, AST, and alkaline phosphatase levels at all time points from Week 4 through Week 56 in both BRINSUPRI 10 mg and 25 mg arms compared to placebo. The incidence of ALT >3X upper limit of normal (ULN) was 0%, 1.2%, and 0.9%; the incidence of AST >3X ULN was 0.2%, 0.3%, and 0.5%; and the incidence of alkaline phosphatase >1.5X ULN was 2.5%, 4.1%, and 4.0% in patients treated with placebo and BRINSUPRI 10 mg and 25 mg, respectively.

PRIMARY ENDPOINT

Proven to reduce the risk of bronchiectasis exacerbations[1,3,a]

BRINSUPRI 10 mg

21.1%

reduction in exacerbation risk over 52 weeks

Rate ratio vs placebo (95% CI): 0.79 (0.68-0.92); *P*=0.004.[b]

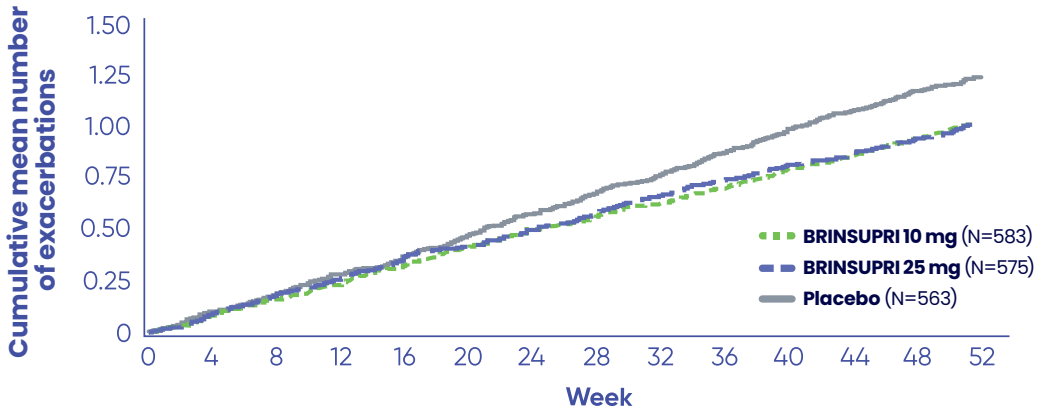
BRINSUPRI 25 mg

19.4%

reduction in exacerbation risk over 52 weeks

Rate ratio vs placebo (95% CI): 0.81 (0.69-0.94); *P*=0.005.[b]

BRINSUPRI demonstrated a significant reduction in exacerbation risk over 52 weeks



Annualized exacerbation rate: BRINSUPRI 10 mg: 1.02, BRINSUPRI 25 mg: 1.04, placebo: 1.29.

Pulmonary exacerbations were defined as a worsening of ≥3 major symptoms over 48 hours resulting in a healthcare provider's decision to prescribe systemic antibiotics. Symptoms included increased cough, increased sputum volume or change in sputum consistency, increased sputum purulence, increased breathlessness and/or decreased exercise tolerance, fatigue and/or malaise, and hemoptysis.[1]

Study design

The ASPEN study was an international, multicenter, randomized, double-blind, parallel-group, placebo-controlled Phase 3 clinical trial. Patients were 12 to 85 years of age (41 adolescents and 1680 adults) and received 1 of 2 doses of BRINSUPRI (10 mg: n=583; 25 mg: n=575) or placebo (n=563), administered orally once daily for 52 weeks. Patients in all arms were permitted to continue using their existing concomitant therapy.[1,3,4]

Explore more efficacy and safety data at BRINSUPRIhcp.com

[a]Annualized rate.[1]
[b]*P* value was adjusted for multiplicity.[3]
CI=confidence interval.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS (cont'd)

Less Common Adverse Reactions (cont'd)

Skin Cancers

In ASPEN, the incidence of skin cancers among patients treated with BRINSUPRI 10 mg and 25 mg was 0.5% and 1.9%, respectively, compared to 1.1% in placebo-treated patients.

Alopecia

In ASPEN, the incidence of alopecia among patients treated with BRINSUPRI 10 mg and 25 mg was 1.5% and 1.6% respectively, compared to 0.4% in placebo-treated patients.

USE IN SPECIFIC POPULATIONS

Pregnancy: There are no clinical data on the use of BRINSUPRI in pregnant women.

Lactation: There is no information regarding the presence of BRINSUPRI and/or its metabolite(s) in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BRINSUPRI and any potential adverse effects on the breastfed child from BRINSUPRI or from the underlying maternal condition.

Pediatric use: The safety and effectiveness of BRINSUPRI for the treatment of NCFB have been established in pediatric patients aged 12 years and older. Common adverse reactions in pediatric patients aged 12 years and older enrolled in ASPEN were consistent with those in adults. The safety and effectiveness of BRINSUPRI have not been established in pediatric patients younger than 12 years of age.

Please see additional Important Safety Information and the Brief Summary on the following pages.

insmed

References: 1. BRINSUPRI [package insert]. Bridgewater, NJ: Insmed Incorporated; 2025. **2.** Chalmers JD, et al. *Am J Respir Crit Care Med*. 2017;195(10):1384-1393. **3.** Chalmers JD, et al. *N Engl J Med*. 2025;392(16):1569-1581. **4.** Chalmers JD, et al. *N Engl J Med*. 2025;392(16)(suppl appendix):1-53.

BRINSUPRI® (brensocatib)
BRIEF SUMMARY: For complete safety, please consult the full Prescribing Information.

1 INDICATIONS AND USAGE
BRINSUPRI is indicated for the treatment of non-cystic fibrosis bronchiectasis (NCFB) in adult and pediatric patients 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage
The recommended dosage of BRINSUPRI is as follows:
• 10 mg orally once daily with or without food
or
• 25 mg orally once daily with or without food

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS

5.1 Dermatologic Adverse Reactions
Treatment with BRINSUPRI is associated with an increase in dermatologic adverse reactions, including rash, dry skin, and hyperkeratosis. Monitor patients for development of new rashes or skin conditions and refer patients to a dermatologist for evaluation of new dermatologic findings.

5.2 Gingival and Periodontal Adverse Reactions
Treatment with BRINSUPRI is associated with an increase in gingival and periodontal adverse reactions. Refer patients to dental care services for regular dental checkups while taking BRINSUPRI. Advise patients to perform routine dental hygiene.

5.3 Live Attenuated Vaccines
The concomitant use of BRINSUPRI and live attenuated vaccines has not been evaluated. It is unknown whether administration of live attenuated vaccines during BRINSUPRI treatment will affect the safety or effectiveness of these vaccines. The use of live attenuated vaccines should be avoided in patients receiving BRINSUPRI.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience
The safety data below reflect the safety of BRINSUPRI in adult and pediatric patients aged 12 years and older with NCFB. A total of 1721 patients with NCFB were randomized in a double-blind, placebo-controlled clinical trial of 52 weeks' duration (ASPEN). The safety of BRINSUPRI was based on data from 1719 adult and pediatric patients aged 12 years and older who received at least one dose of BRINSUPRI or placebo. A total of 1156 patients received at least one dose of BRINSUPRI 10 mg or 25 mg orally once daily.

Table 1 shows the adverse reactions occurring at an incidence of ≥2% and higher in BRINSUPRI-treated patients compared to placebo in the safety population from ASPEN.

Table 1 Adverse Reactions with BRINSUPRI with an Incidence of ≥2% and More Common than Placebo in ASPEN

Adverse Reaction	Placebo (N=563) n (%)	BRINSUPRI 10 mg QD (N=582) n (%)	BRINSUPRI 25 mg QD (N=574) n (%)
Upper respiratory tract infection[1]	141 (25)	157 (27)	169 (29)
Headache	39 (7)	39 (7)	49 (9)
Rash[2]	22 (4)	25 (4)	35 (6)
Dry skin[3]	8 (1)	17 (3)	25 (4)
Hyperkeratosis[4]	5 (1)	8 (1)	16 (3)
Hypertension	17 (3)	28 (5)	13 (2)

[1] Upper respiratory tract infection includes coronavirus infection, COVID-19, influenza, upper respiratory tract infection, viral infection, and viral upper respiratory tract infection.
[2] Rash includes rash, rash maculo-papular, rash pruritic, rash erythematous, dermatitis, and erythema.
[3] Dry skin includes dry skin, chapped lips, cheilitis, lip dry, skin exfoliation, skin fissures, xeroderma, and xerosis.
[4] Hyperkeratosis includes hyperkeratosis, palmoplantar keratoderma, and skin hypertrophy.

Adverse Reactions in WILLOW
A total of 256 adult patients with NCFB were randomized in the 24-week, double-blind, placebo-controlled clinical trial (WILLOW). Of those randomized, 255 adult patients received BRINSUPRI 10 mg, BRINSUPRI 25 mg, or placebo, which consisted of 170 adults treated with at least one dose of BRINSUPRI 10 mg or 25 mg orally once daily. The safety profile for adult patients with NCFB in WILLOW was generally similar to ASPEN, with the exception of a higher incidence of gingival and periodontal adverse reactions. The incidence of gingival and periodontal adverse reactions in WILLOW among patients treated with BRINSUPRI 10 mg and 25 mg were 9.9% and 10.1%, respectively, compared to 2.4% in placebo-treated patients.

Less Common Adverse Reactions

Liver Function Test Elevations
In ASPEN, there was an increase from baseline in average ALT, AST, and alkaline phosphatase levels at all time points from Week 4 through Week 56 in both BRINSUPRI 10 mg and 25 mg arms compared to placebo. The incidence of ALT >3X upper limit of normal (ULN) was 0%, 1.2%, and 0.9%, in patients treated with placebo and BRINSUPRI 10 mg and 25 mg, respectively. The incidence of AST >3X ULN was 0.2%, 0.3%, and 0.5% in patients treated with placebo and BRINSUPRI 10 mg and 25 mg, respectively. The incidence of alkaline phosphatase >1.5X ULN was 2.5%, 4.1%, and 4.0% in patients treated with placebo and BRINSUPRI 10 mg and 25 mg, respectively.

Skin Cancers
In ASPEN, the incidence of skin cancers among patients treated with BRINSUPRI 10 mg and 25 mg was 0.5% and 1.9%, respectively, compared to 1.1% in placebo-treated patients.

Alopecia
In ASPEN, the incidence of alopecia among patients treated with BRINSUPRI 10 mg and 25 mg was 1.5% and 1.6%, respectively, compared to 0.4% in placebo-treated patients.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
There are no available data on BRINSUPRI use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.

8.2 Lactation

Risk Summary
There are no data on the presence of brensocatib and/or its metabolite(s) in human milk, the effects on the breastfed infant, or the effects on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BRINSUPRI and any potential adverse effects on the breastfed child from BRINSUPRI or from the underlying maternal condition.

8.4 Pediatric Use
The safety and effectiveness of BRINSUPRI for the treatment of NCFB have been established in pediatric patients aged 12 years and older. Use of BRINSUPRI for this indication is supported by evidence from an adequate and well-controlled trial (ASPEN), which enrolled 41 pediatric patients aged 12 years and older, and additional pharmacokinetic data in pediatric patients aged 12 to 17 years.

Common adverse reactions in pediatric patients aged 12 years and older enrolled in ASPEN were consistent with those in adults.

The safety and effectiveness of BRINSUPRI have not been established in pediatric patients younger than 12 years of age.

8.5 Geriatric Use
There were 988 patients 65 years of age and older in the clinical studies for non-cystic fibrosis bronchiectasis. Of the total number of BRINSUPRI-treated patients in these studies, 676 (51%) were 65 years of age and older while 201 (15%) were 75 years of age and older. No observed differences in safety and/or effectiveness in geriatric patients compared to younger adult patients.

10 OVERDOSAGE
Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for overdose management recommendations.

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Patient Information).

Dermatologic Adverse Reactions
Inform patients that BRINSUPRI is associated with a risk of adverse skin reactions including rash, dry skin, and hyperkeratosis. Advise patients to monitor their skin and report any new rash or skin condition.

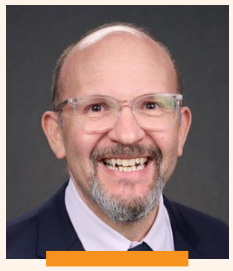
Gingival and Periodontal Adverse Reactions
Inform patients that BRINSUPRI is associated with a risk of gingival and periodontal adverse reactions. Advise patients to have regular dental checkups while taking BRINSUPRI. Advise patients to perform routine dental hygiene.

Live Attenuated Vaccines
Instruct patients to inform the healthcare provider that they are taking BRINSUPRI prior to a potential vaccination.

Column

Sotatercept in pulmonary arterial hypertension





A step-by-step approach for considering the new kid on the block

BY RODOLFO A. ESTRADA, MD, FCCP; SANDEEP SAHAY, MD, MSc, FCCP; ADRIANO R. TONELLI, MD

The US Food and Drug Administration's approval of sotatercept (Winrevair®) in March 2024 arrived with great excitement given its unique mechanism of action and proven efficacy on top of existing medications for pulmonary arterial hypertension (PAH).[1] Many providers encounter patients with PAH who are currently treated and may be candidates for sotatercept treatment. Understanding when to consider sotatercept and how to use it has become a critical part of the care of this serious condition.

WHAT MAKES IT DIFFERENT?

Sotatercept is a novel pulmonary antihypertensive. Traditional therapies like prostacyclin and its analogues, endothelin receptor antagonists, and phosphodiesterase type-5 (PDE5) inhibitors have antiproliferative benefit in addition to strong pulmonary vasodilatory properties.[3] In contrast, sotatercept inhibits activin signaling, functioning as a ligand trap for activins and growth differentiation factors.[5] PAH is characterized by reduced signaling through the bone morphogenetic protein receptor type II (BMPR2) pathway, which leads to unopposed activin activity.[5] That tilt toward pro-proliferative signaling drives smooth muscle growth, medial thickening, and the characteristic vascular remodeling observed in PAH.[6] Sotatercept counteracts these effects by rebalancing these impaired signaling pathways, favoring physiological repair rather than unchecked proliferation.[5]

TRIAL DATA

Sotatercept has met the primary trial end points in all randomized, placebo-controlled studies in which it was tested. PULSAR, the phase 2 study, showed dose-dependent effects.[7] At 0.7 mg/kg, patients saw a 34% reduction in PVR, with marked improvement in 6-minute walk distance (6MWD) and reduction in NT-proBNP levels.[1] STELLAR, the pivotal phase 3 trial, enrolled 323 patients with long-standing PAH, with nearly 60% on triple therapy and 40% on parenteral prostacyclin analogues.[3,8-9] In this context, sotatercept improved 6MWD by 34 meters and met eight of nine hierarchical secondary end points, including an 84% reduction in time to death or clinical worsening.[8]

The ZENITH trial included patients with PAH at higher risk, in World Health Organization functional class III to IV with REVEAL Lite 2 scores of ≥ 9 and on maximal conventional PAH therapy.[10] The trial was stopped early in the interim analysis for overwhelming efficacy, with a 76% relative risk reduction in the composite end point of death, transplant, or hospitalization due to PAH.[11]

The HYPERION trial, published in 2025, studied patients with a recent diagnosis (during the last year) of PAH at intermediate to high-risk, treated with double or triple PAH therapy.[12] Sotatercept produced a 76% risk reduction in the primary end point of clinical worsening (composite of death, lung transplantation, atrial septostomy, unplanned hospitalization for PAH, and deterioration in exercise performance due to PAH).[13]

Notably, sotatercept demonstrates a favorable number needed to treat (NNT): an NNT of 4 to prevent one clinical worsening event in ZENITH and an NNT of 5 in HYPERION—substantially better than historical NNTs for other PAH therapies.[14]

The SOTERIA trial, an ongoing open-label study evaluating long-term safety, tolerability, and efficacy of sotatercept in PAH, showed sustained treatment benefit at roughly 15 months of follow-up, with a low rate (2.6%) of serious adverse events.[15-16]

HOW IT FITS INTO CURRENT TREATMENT

Immediately following diagnosis, the PAH treatment algorithm is unchanged (ie, dual oral therapy for low and intermediate-risk patients and addition of parenteral prostacyclin analogues for high-risk patients).[3] Modifications occur at reassessment. For intermediate-low-risk patients who have not achieved low-risk status after three to six months of dual oral therapy, sotatercept becomes an option alongside nonparenteral prostacyclin pathway agents or replacing PDE5 inhibitors with soluble guanylate cyclase stimulators.[14]

Given the multiplicity of options, the decision of which alternative to use remains debatable, even among experts. In this context, the STELLAR trial demonstrated robust improvements in 6MWD and reduction in clinical worsening events, mostly driven by reductions in the need for rescue therapy initiation, hospitalizations, and PAH progression.[17] In contrast, the GRIPHON (testing selexipag on a background of single or dual PAH therapy) and FREEDOM-EV (testing oral treprostinil on a background a single PAH therapy) trials were larger, longer-term studies with composite morbidity-mortality primary end points.[18-19] These trials showed a 40% and 26% reduction in clinical worsening events, respectively, but more modest 6MWD improvements.[14]

WHAT TO EXPECT AND HOW TO MONITOR TREATMENT

Patients on triple therapy, including parenteral prostacyclin analogues, had significant clinical improvements from sotatercept.[5] Sotatercept can also be added for patients on parenteral prostacyclin who remain at high risk, based on data from the ZENITH trial.[11]

Sotatercept is generally well tolerated, with only 1.8% of patients discontinuing therapy for adverse effects in STELLAR.[8] Common adverse effects include epistaxis, telangiectasias, headache, dizziness, rash, and diarrhea. Hemoglobin elevations and thrombocytopenia occurred in roughly 6% of patients. Bleeding events were reported in about 21% of study patients and were usually mild and manageable.[17]

Pericardial effusion has emerged as an important real-world side effect. Recent case series report new or worsening pericardial effusions, particularly in patients with connective tissue disease associated PAH, an underlying effusion, and those treated with prostacyclin analogues.[20-22] Interestingly, STELLAR and ZENITH did not show an increase in pericardial effusions compared with placebo.[20,23] SOTERIA supports a generally stable, long-term safety profile without an increase incidence of pericardial effusion.[16] In practice, if a pericardial effusion is thought to be associated with sotatercept, it is reasonable to pause sotatercept and consider reintroduction at a lower dose once the effusion has resolved or stabilized, in the context of close echocardiographic monitoring.

IN MEMORIAM

Remembering a giant of chest medicine: Alfred Soffer, MD, Master FCCP

Alfred Soffer, MD, Master FCCP

On November 19, 2025, our community lost a monumental leader and great physician, Alfred Soffer, MD, Master FCCP. A renowned expert in cardiopulmonary medicine, Dr. Soffer, 103, served as Editor in Chief of the journal *CHEST*® for 25 years from 1968 to 1993 and led the American College of Chest Physicians (CHEST) as its Executive Director for 23 years from 1969 to 1992. He earned the distinction of Master Fellow of the College of Chest Physicians in 1992 and was named *CHEST's* first "Giant in Chest Medicine" in 2013. His efforts have had a profound impact on the organization and on the journal.

During his leadership, CHEST transitioned from an organization founded in 1935 by Murray Kornfeld, who was a patient with TB, to an international organization of more than 18,000 chest physicians—pulmonologists, cardiologists, chest surgeons, and critical care physicians—in more than 100 countries. The annual scientific meeting, the international meetings, and the continuing medical education courses drew physicians and scientists from multiple disciplines that treat patients with chest diseases, including pediatrics, anesthesiology, allergy, pharmacy, and hematology. CHEST became the international leader in clinical pulmonary education programs.

Under Dr. Soffer's leadership, the organization helped to educate the public about chest diseases, and it became the international leader in the campaign to reduce the prevalence of smoking.

During his tenure, CHEST was one of the first medical organizations to convene expert conferences that produced evidence-based practice guidelines published in *CHEST* or as supplements to *CHEST*. These guidelines have been widely accepted and have improved the quality of care for patients with pulmonary disease throughout the world.

When the journal was first published as *Diseases of the Chest* in 1935 under the sponsorship of the Federation of American Sanatoria (now CHEST), its goal was "to be of material aid to the general practitioner in dealing with his tuberculosis patients." In 1970, Dr. Soffer led the name change of the journal to *CHEST* and refocused its mission to serve all pulmonary diseases and critical care.

He introduced peer review to the journal, and when he turned over the editorship to the late Jay Block, MD, Master FCCP, the journal had more than 8,000 peer reviewers. As *CHEST* became the premier clinical pulmonary journal, the number of manuscripts submitted per year increased 700% from 300 in 1967 to 2,400 in 1993.

When asked in 2009 what made the journal so successful, Dr. Soffer said:

"During my tenure, I also ensured that every article we published was the best it could possibly be. Upon submission, the majority of articles would undergo at least one revision, incorporating suggestions from the editorial board, the editor, and out-of-office consultants. In most cases, these suggestions were welcomed by the authors and helped make the articles much stronger and, thus, strengthening the image of the journal."

In addition to his positions at CHEST, he served as Editor of the American Medical Association's *Archives of Internal Medicine* from 1976 until 1986 and founded *Heart & Lung: The Journal of Cardiopulmonary and Acute Care.*

Part of Dr. Soffer's success as a leader was his outgoing personality and enthusiasm. At every annual meeting, he made it a point to meet with as many attendees as he could (especially the youngest attendees) and welcome them to CHEST. Many of the young attendees who became active members and leaders of CHEST did so because Dr. Soffer welcomed them into the fold.

Dr. Soffer's years as Editor in Chief of *CHEST* and Executive Director had a major impact on graduate medical education and the quality of care for patients with pulmonary diseases throughout the United States and the world. His legacy is honored yearly at the CHEST Annual Meeting through the Alfred Soffer Award for Editorial Excellence, which goes to someone who has made significant contributions to CHEST. Recipients are often world experts in their fields, have written numerous papers and abstracts, have served as primary investigators, and/or have served as a department editor of *CHEST*.

Beyond CHEST, Dr. Soffer left a mark far surpassing his career. He was an authority on Jewish medical ethics and the works of Maimonides, and he lectured extensively on both subjects. He was a founding president of Solomon Schechter Day School in Northbrook, Illinois; served as Chief Medical Scientist for the State of Israel from 1973 to 1974; and, accompanied by an armed guard, visited Gaza during the Yom Kippur War to teach local physicians cardiology and internal medicine. Dr. Soffer was also an avid fisherman, skilled golfer, and nationally ranked tennis player who competed well into his 80s. Dr. Soffer was a beloved husband to the late Isabel Soffer. He is survived by his children—Jonathan (Margaret) Soffer, Joshua, and Gil (Becky) Soffer—and grandchildren—Talia (Daniel), Jacob, Gabriela, and Mia Soffer. ●

Read the full obituary online for "Kindling a career: How Dr. Alfred Soffer ignited Dr. Richard Irwin's life's work."

SO WHAT IS OUR ROLE?

Sotatercept represents real progress, but the efficacy of the medication depends on the adequate recognition and treatment of patients with PAH. Underdiagnosis and undertreatment remain common challenges in PAH. It remains essential to adequately distinguish PAH from other forms of pulmonary hypertension in which sotatercept, or other PAH therapies, has not been studied or are not beneficial. High-risk patients not on parenteral prostacyclin need timely treatment with prompt initiation of aggressive PAH therapies to improve outcomes. Comorbidities such as obesity, hypertension, diabetes, and atrial fibrillation are common but do not contraindicate PAH therapy.[14]

Real-world phenotypes like multimorbidity and heart failure with preserved ejection fraction overlap remain understudied; however, the phase 2 CADENCE trial in patients with combined post- and pre-capillary pulmonary hypertension reported meaningful PVR reductions, offering early proof of concept for group 2 disease and prompting phase 3 studies.[24-25]

For now, sotatercept offers clinicians a novel therapy that meaningfully improves outcomes. Using it thoughtfully, integrating it into risk-based care, and ensuring timely referral to expert centers are the ways pulmonologists can make a big difference in patients' lives. ●

The full version of the article and all references are available online at chestphysician.org.

Biologic therapies in asthma: From foundation to the future

BY DIEGO J. MASELLI, MD, FCCP; DHARANI NARENDRA, MD, FCCP; MEGAN CONROY, MD, MAEd, FCCP
EDITED BY JOY CURZIO

Asthma affects approximately 350 million people of all ages worldwide, with approximately 5% to 10% of those experiencing severe disease.[1-2] Type 2 mediated disease accounts for the vast majority—up to 80%—of cases.[2-3] Biologic therapies have had a profound impact on disease management in patients with moderate to severe asthma. These agents have been shown to decrease exacerbations and the reliance on oral steroids, improve lung function and quality of life in a subset of patients, and even reduce the need for inhaled corticosteroid maintenance therapy.[4-8]

Overall, this has led to a paradigm shift in asthma management goals from control to remission across patients with varying levels of disease severity. Achieving remission has become an aspirational goal for asthma management. However, only about one-third of patients receiving biologics can achieve remission.[9-10] Thus, there is still a need to improve the approach for patients with severe asthma.

Despite the lack of comparative effectiveness trials across currently available biologic therapies, a new CHEST guideline on use of biologics for severe disease was created to assist with therapeutic decision making based on individual patient characteristics.[11] As research continues to demonstrate enduring efficacy for these agents, clinicians should be encouraged to make greater use of biologic therapies for their patient populations, especially for those with more severe disease or with comorbid conditions such as chronic rhinosinusitis with nasal polyps.

More recently, radiographic findings have been found to be important for identifying phenotypes in asthma. For example, mucus plugging seen on chest CT scans has been linked to severe asthma and acute exacerbations, sometimes resulting in death.[12] Patients who have evidence of mucus plugging have been shown to have greater type 2 inflammation and more frequent severe exacerbations.[13-14]

Novel research, such as the VESTIGE trial, has shown that biologic therapies may have a greater response for these patients.[15] Such research demonstrates how the addition of radiographic assessments can further advance patient care.[16] Looking ahead, ultra-long-acting biologics are poised to change the treatment paradigm in severe asthma and may provide sustained control of type 2 inflammation with less frequent dosing.[17-18] (see "Adding to the toolkit: Depemokimab")

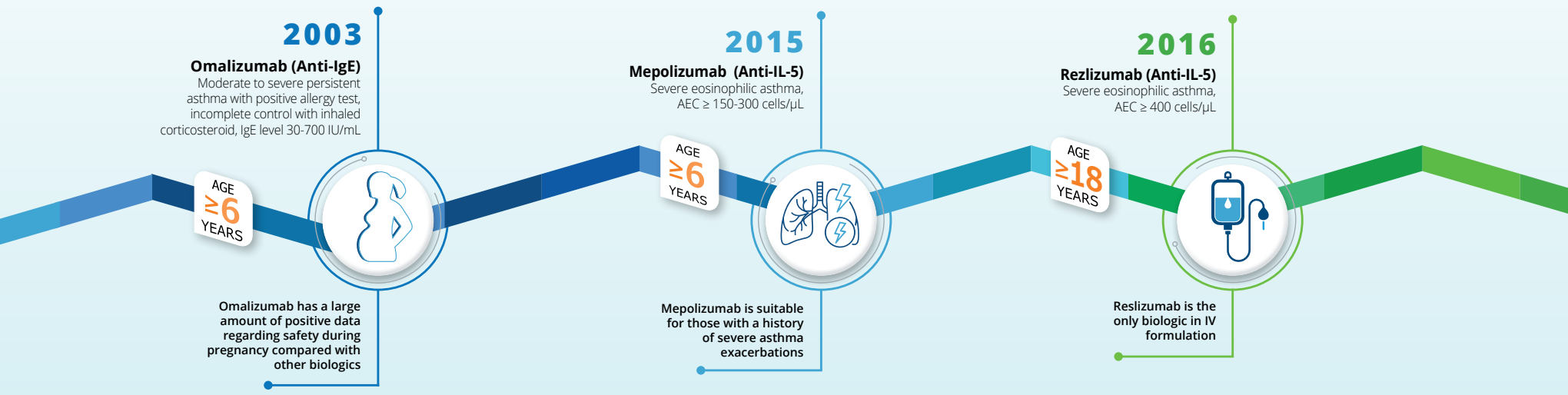
ADDING TO THE TOOLKIT: DEPEMOKIMAB

Depemokimab, an interleukin-5 (IL-5) targeted agent was recently approved (December 2025) for use by the US Food and Drug Administration and is the first ultra-long-acting biologic approved for severe asthma.

In the phase 3A, randomized, placebo-controlled replicate SWIFT-1 and SWIFT-2 trials, the pooled annualized rate of exacerbations was 0.51 (95% CI, 0.43-0.60) compared with 1.11 (95% CI, 0.92-1.33) for placebo. In addition, the every-six-month dosing is expected to result in improved patient quality of life.[17-18]

All references are available online at chestphysician.org.

BIOLOGIC APPROVALS IN ASTHMA



AGENTS IN DEVELOPMENT

AMLITELIMAB[19]

Target
OX40

Trials

NCT06033833 (active, not recruiting): Evaluating long-term safety and efficacy of amlitelimab for adults with moderate to severe asthma who completed amlitelimab treatment in RIVER-ASTHMA

TIDE-Asthma (NCT05421598; completed): Phase 2, randomized, double-blind, placebo-controlled, dose-ranging trial to evaluate efficacy and safety of amlitelimab over 60 weeks

VEREKITUG[21-22]

Target
TSLP

Trials

VALIANT (NCT06196879; active, not recruiting): Phase 2, randomized, double-blind, placebo-controlled, multicenter, dose-ranging trial evaluating the safety and efficacy of verekitug in adults with severe asthma

VALOUR (NCT06966479; recruiting): The long-term extension study of VALIANT

HBM9378 / WIN378[23]

Target
TSLP

Trials

POLARIS (NCT07120503, recruiting): Phase 2, global, randomized, double-blind, placebo-controlled trial to evaluate dosing, efficacy, and safety in patients with asthma; initial data are expected this year

ASTEGOLIMAB[20]

Target
ST2 receptor

Trials

ZENYATTA (NCT02918019; completed): Phase 2b, randomized, placebo-controlled, double-blind, multicenter trial to determine efficacy and safety of astegolimab in patients with severe asthma compared with placebo

NCT05878769 (recruiting, COPD)
NCT05595642 (recruiting, COPD)

TOZORAKIMAB[24-25]

Target
IL-33

Trials

NCT06932263 (recruiting): Studying dose-finding, safety/efficacy for patients with uncontrolled asthma on medium to high dose of inhaled corticosteroids

FRONTIER-3 (NCT04570657: completed): Phase 2a, randomized trial to evaluate the safety and effect of tozorakimab vs placebo on lung function in patients with moderate to severe asthma who were diagnosed before age 25

TILREKIMIG[28-29]

Target
IL-4 / IL-13 / TSLP trispecific

Trials

NCT06675188 (active, not recruiting): Phase 1, randomized, double-blind, third-party open, placebo-controlled, single-dose trial to evaluate safety, tolerability, pharmacokinetics/pharmacodynamics, and immunogenicity

NCT06977581 (recruiting): Phase 2 trial is recruiting for patients with moderate to severe asthma

LUNSEKIMIG[26-27]

Target
TSLP / IL-13

Trials

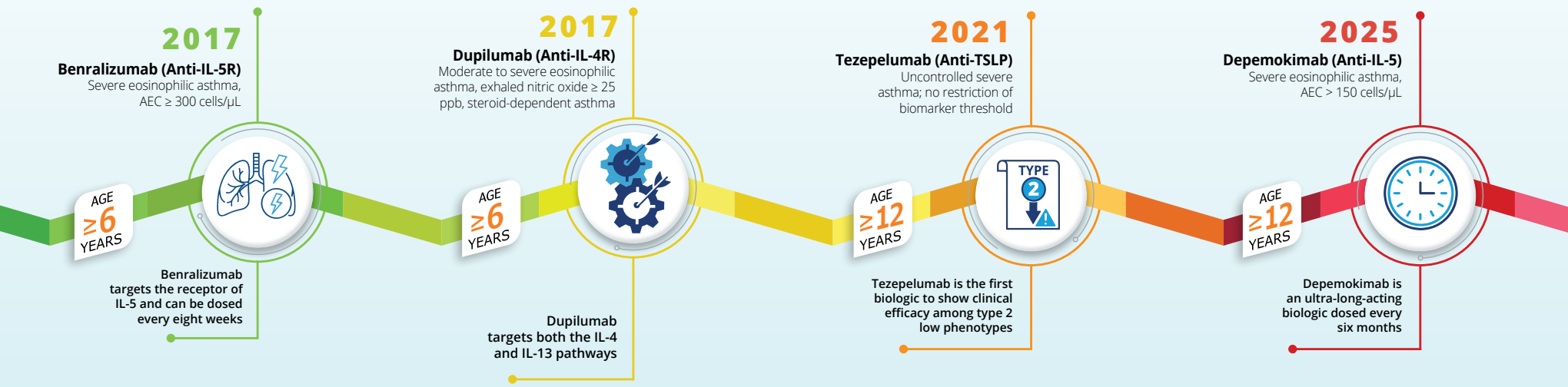
AIRLYMPUS (NCT06676319; recruiting): Phase 2, parallel-group, randomized, double-blind, placebo-controlled, two-arm study to assess the efficacy, safety, and tolerability of add-on therapy with lunsekimig compared with placebo in adults with asthma who are not eligible for biologic treatments

AIRCULES (NCT06102005; active, not recruiting): Phase 2b, global, multicenter, randomized, double-blind, placebo-controlled, parallel group, dose-ranging study to assess the efficacy, safety, and tolerability of add-on therapy with lunsekimig in adults with moderate to severe asthma

Lunsekimig is a NANOBODY® molecule, which is about 10 times smaller than a monoclonal antibody and is highly stable. Multiple nanobodies can be mixed and matched to address multiple targets in a single drug molecule. Lunsekimig is the first such agent under study.

This approach may further the understanding of how to manipulate multiple levers in severe asthma. In a world where clinicians strive for clinical remission in asthma, this approach may further advance this goal.

Early data show a single dose of lunsekimig was well tolerated. Additionally, type 2 inflammation was significantly suppressed, and lung function was improved in patients with mild to moderate asthma.



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DUPIXENT® (dupilumab) injection, for subcutaneous use Rx only
Brief Summary of Prescribing Information

1 INDICATIONS AND USAGE

1.2 Asthma

DUPIXENT is indicated as an add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma *[see Clinical Studies (14)]*.

Limitations of Use

DUPIXENT is not indicated for the relief of acute bronchospasm or status asthmaticus.

4 CONTRAINDICATIONS

DUPIXENT is contraindicated in patients who have known hypersensitivity to dupilumab or any excipients of DUPIXENT *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Hypersensitivity reactions, including anaphylaxis, serum sickness or serum sickness-like reactions, angioedema, generalized urticaria, rash, erythema nodosum, and erythema multiforme have been reported. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT *[see Adverse Reactions (6.1, 6.2, 6.3)]*.

5.3 Eosinophilic Conditions

Patients being treated for asthma may present with serious systemic eosinophilia sometimes presenting with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis, conditions which are often treated with systemic corticosteroid therapy. These events may be associated with the reduction of oral corticosteroid therapy. Healthcare providers should be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients with eosinophilia. Cases of eosinophilic pneumonia were reported in adult subjects who participated in the asthma development program and cases of vasculitis consistent with eosinophilic granulomatosis with polyangiitis have been reported with DUPIXENT in adult subjects who participated in the asthma development program as well as in adult subjects with co-morbid asthma in the CRSwNP development program. A causal association between DUPIXENT and these conditions has not been established.

5.4 Acute Symptoms of Asthma or Acute Deteriorating Disease

DUPIXENT should not be used to treat acute symptoms or acute exacerbations of asthma. Do not use DUPIXENT to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with DUPIXENT.

5.5 Risk Associated with Abrupt Reduction of Corticosteroid Dosage

Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of therapy with DUPIXENT. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a healthcare provider. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

5.7 Arthralgia

Arthralgia has been reported with the use of DUPIXENT with some patients reporting gait disturbances or decreased mobility associated with joint symptoms; some cases resulted in hospitalization *[see Adverse Reactions (6.1)]*. In postmarketing reports, onset of arthralgia was variable, ranging from days to months after the first dose of DUPIXENT. Some patients' symptoms resolved while continuing treatment with DUPIXENT and other patients recovered or were recovering following discontinuation of DUPIXENT.

Advise patients to report new onset or worsening joint symptoms to their healthcare provider. If symptoms persist or worsen, consider rheumatological evaluation and/or discontinuation of DUPIXENT.

5.8 Parasitic (Helminth) Infections

Patients with known helminth infections were excluded from participation in clinical studies. It is unknown if DUPIXENT will influence the immune response against helminth infections.

Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. If patients become infected while receiving treatment with DUPIXENT and do not respond to anti-helminth treatment, discontinue treatment with DUPIXENT until the infection resolves. Adverse reactions of helminth infections (5 cases of enterobiasis and 1 case of ascariasis) were reported in pediatric patients 6 to 11 years old who participated in the pediatric asthma development program *[see Adverse Reactions (6.1)]*.

5.9 Vaccinations

Consider completing all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with DUPIXENT. Avoid use of live vaccines during treatment with DUPIXENT. It is unknown if administration of live vaccines during DUPIXENT treatment will impact the safety or effectiveness of these vaccines. Limited data are available regarding coadministration of DUPIXENT with non-live vaccines *[see Clinical Pharmacology (12.2) in the full prescribing information]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity *[see Warnings and Precautions (5.1)]*
- Arthralgia *[see Warnings and Precautions (5.7)]*
- Parasitic (Helminth) Infections *[see Warning and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Asthma

Adults and Pediatric Subjects 12 Years of Age and Older with Asthma

A total of 2888 adult and pediatric subjects 12 to 17 years of age with moderate-to-severe asthma (AS) were evaluated in 3 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks duration (DRI12544, QUEST, and VENTURE). Of these, 2678 had a history of 1 or more severe exacerbations in the year prior to enrollment despite regular use of medium- to high-dose inhaled corticosteroids plus an additional controller(s) (DRI12544 and QUEST). A total of 210 subjects with oral corticosteroid-dependent asthma receiving high-dose inhaled corticosteroids plus up to two additional controllers were enrolled (VENTURE). The safety population (DRI12544 and QUEST) was 12-87 years of age, of which 63% were female, and 82% were White. DUPIXENT 200 mg or 300 mg was administered subcutaneously Q2W, following an initial dose of 400 mg or 600 mg, respectively.

In DRI12544 and QUEST, the proportion of subjects who discontinued treatment due to adverse events was 4% of the placebo group, 3% of the DUPIXENT 200 mg Q2W group, and 6% of the DUPIXENT 300 mg Q2W group.

Table 7 summarizes the adverse reactions that occurred at a rate of at least 1% in subjects treated with DUPIXENT and at a higher rate than in their respective comparator groups in DRI12544 and QUEST.

Table 7: Adverse Reactions Occurring in ≥1% of Adult and Pediatric Subjects 12 Years of Age and Older with Asthma in the DUPIXENT Groups in DRI12544 and QUEST and Greater than Placebo (6 Month Safety Pool)

Adverse Reaction	DRI12544 and QUEST		
	DUPIXENT 200 mg Q2W N=779 n (%)	DUPIXENT 300 mg Q2W N=788 n (%)	Placebo N=792 n (%)
Injection site reactions[a]	111 (14%)	144 (18%)	50 (6%)
Oropharyngeal pain	13 (2%)	19 (2%)	7 (1%)
Eosinophilia[b]	17 (2%)	16 (2%)	2 (<1%)

[a] Injection site reactions cluster includes erythema, edema, pruritus, pain, and inflammation.

[b] Eosinophilia = blood eosinophils ≥3000 cells/mcL, or deemed by the investigator to be an adverse event. None met the criteria for serious eosinophilic conditions *[see Warnings and Precautions (5.3)]*.

Injection site reactions were most common with the loading (initial) dose.

The safety profile of DUPIXENT through Week 52 was generally consistent with the safety profile observed at Week 24.

Pediatric Subjects 6 to 11 Years of Age with Asthma

The safety of DUPIXENT was assessed in 405 pediatric subjects 6 to 11 years of age with moderate-to-severe asthma (VOYAGE). The safety profile of DUPIXENT in these subjects through Week 52 was similar to the safety profile from studies in adult and pediatric subjects 12 years of age and older with moderate-to-severe asthma with the addition of helminth infections. Helminth infections were reported in 2.2% (6 subjects) in the DUPIXENT group and 0.7% (1 subject) in the placebo group. The majority of cases were enterobiasis, reported in 1.8% (5 subjects) in the DUPIXENT group and none in the placebo group. There was one case of ascariasis in the DUPIXENT group. All helminth infection cases were mild to moderate and subjects recovered with anti-helminth treatment without DUPIXENT treatment discontinuation.

Specific Adverse Reactions for Asthma

Hypersensitivity Reactions

Hypersensitivity reactions were reported in <1% of DUPIXENT-treated subjects. These included anaphylaxis, serum sickness or serum sickness-like reactions, generalized urticaria, rash, erythema nodosum, and erythema multiforme *[see Contraindications (4), Warnings and Precautions (5.1), and Clinical Pharmacology (12.6)] in the full prescribing information]*.

Eosinophils

Dupixent-treated subjects with asthma had a greater initial increase from baseline in blood eosinophil count compared to subjects treated with placebo. In adult and pediatric subjects 12 years of age and older with asthma (DRI12544 and QUEST), the mean and median increases in blood eosinophils from baseline to Week 4 were 130 and 10 cells/mcL, respectively. In subjects 6 to 11 years of age with asthma (VOYAGE), the mean and median increases in blood eosinophils from baseline to Week 12 were 124 and 0 cells/mcL, respectively.

Across the trials for AD, asthma, and CRSwNP indications, the incidence of treatment-emergent eosinophilia (≥500 cells/mcL) was similar in DUPIXENT and placebo groups.

Treatment-emergent eosinophilia (≥5000 cells/mcL) was reported in <3% of DUPIXENT-treated subjects and <0.5% in placebo-treated subjects (SOLO 1, SOLO 2, and AD-1021; DRI12544, QUEST, and VOYAGE; SINUS-24 and SINUS-52; PRIME and PRIME2; BOREAS and NOTUS). Blood eosinophil counts declined to near baseline or remained below baseline levels (PRIME and PRIME2; BOREAS and NOTUS) during study treatment *[see Warnings and Precautions (5.3)]*.

Cardiovascular Thromboembolic Events

In the 1-year placebo-controlled trial in adult and pediatric subjects 12 years of age and older with asthma (QUEST), CV thromboembolic events (CV deaths, non-fatal myocardial infarctions [MI], and non-fatal strokes) were reported in 1 (0.2%) of the DUPIXENT 200 mg Q2W group, 4 (0.6%) of the DUPIXENT 300 mg Q2W group, and 2 (0.3%) of the placebo group.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of DUPIXENT. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency

or establish a causal relationship to drug exposure. *Immune system disorders:* angioedema *[see Warnings and Precautions (5.1)]*
Skin and subcutaneous tissue disorders: Facial skin reactions, including erythema, rash, scaling, edema, papules, pruritus, burning, and pain

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy.
Healthcare providers and patients may call 1-877-311-8972 or go to https://mothertobaby.org/ongoing-study/dupixent/ to enroll in or to obtain information about the registry.

Risk Summary

Available data from case reports and case series with DUPIXENT use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, DUPIXENT may be transmitted from the mother to the developing fetus. There are adverse effects on maternal and fetal outcomes associated with asthma in pregnancy *(see Clinical Considerations)*. In an enhanced pre- and post-natal developmental study, no adverse developmental effects were observed in offspring born to pregnant monkeys after subcutaneous administration of a homologous antibody against interleukin-4-receptor alpha (IL-4Rα) during organogenesis through parturition at doses up to 10-times the maximum recommended human dose (MRHD) *(see Data)*. The background risk of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-fetal Risk

In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preeclampsia in the mother and prematurity, low birth weight, and small for gestational age in the neonate. The level of asthma control should be closely monitored in pregnant women and treatment adjusted as necessary to maintain optimal control.

Data

Animal Data

In an enhanced pre- and post-natal development toxicity study, pregnant cynomolgus monkeys were administered weekly subcutaneous doses of homologous antibody against IL-4Rα up to 10 times the MRHD (on a mg/kg basis of 100 mg/kg/week) from the beginning of organogenesis to parturition. No treatment-related adverse effects on embryo-fetal toxicity or malformations, or on morphological, functional, or immunological development were observed in the infants from birth through 6 months of age.

8.2 Lactation

Risk Summary

There are no data on the presence of dupilumab in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited systemic exposure to dupilumab on the breastfed infant are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for DUPIXENT and any potential adverse effects on the breastfed child from DUPIXENT or from the underlying maternal condition.

8.4 Pediatric Use

Asthma

The safety and effectiveness of DUPIXENT for an add-on maintenance treatment in patients with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma have been established in pediatric patients 6 years of age and older. Use of DUPIXENT for this indication is supported by evidence from adequate and well-controlled studies in adult and pediatric patients 6 years and older *[see Clinical Studies (14.2) in the full prescribing information]*.

Pediatric Subjects 12 to 17 Years of Age:

A total of 107 pediatric subjects 12 to 17 years of age with moderate-to-severe asthma were enrolled in QUEST and received either 200 mg (N=21) or 300 mg (N=18) DUPIXENT (or matching placebo either 200 mg [N=34] or 300 mg [N=34]) Q2W. Asthma exacerbations and lung function were assessed in both pediatric subjects 12 to 17 years of age and adults. For both the 200 mg and 300 mg Q2W doses, improvements in FEV_1 (LS mean change from baseline at Week 12) were observed (0.36 L and 0.27 L, respectively). For the 200 mg Q2W dose, subjects had a reduction in the rate of severe exacerbations that was consistent with adults. Dupilumab exposure was higher in pediatric subjects 12 to 17 years of age than that in adults at the respective dose level which was mainly accounted for by difference in body weight *[see Clinical Pharmacology (12.3) in the full prescribing information]*.
The adverse event profile in pediatric subjects 12 to 17 years of age was generally similar to the adults *[see Adverse Reactions (6.1)]*.

Pediatric Subjects 6 to 11 Years of Age:

A total of 408 pediatric subjects 6 to 11 years of age with moderate-to-severe asthma were enrolled in VOYAGE, which evaluated doses of 100 mg Q2W or 200 mg Q2W. Improvement in asthma exacerbations and lung function were demonstrated *[see Clinical Studies (14.2) in the full prescribing information]*.
The effectiveness of DUPIXENT 300 mg Q4W in subjects 6 to 11 years of age with body weight 15 to <30 kg was extrapolated from efficacy of 100 mg Q2W in VOYAGE with support from population pharmacokinetic analyses showing higher drug exposure levels with 300 mg Q4W *[see Clinical Pharmacology (12.3) in the full prescribing information]*. Subjects who completed the treatment period of the VOYAGE study could participate in the open-label extension study (LTS14424). Eighteen subjects (≥15 to <30 kg) out of 365 subjects were exposed to 300 mg Q4W in this study, and the safety profile in these eighteen subjects was consistent with that seen in VOYAGE. Additional safety for DUPIXENT 300 mg Q4W is based upon available safety information from the pediatric atopic dermatitis indication *[see Adverse Reactions (6.1) and Clinical Pharmacology (12.3) in the full prescribing information]*.
Safety and effectiveness in pediatric patients younger than 6 years of age with asthma have not been established.

8.5 Geriatric Use

Of the 1977 subjects with asthma exposed to DUPIXENT, a total of 240 subjects were 65 years or older. Efficacy and safety in this age group was similar to the overall study population.

10 OVERDOSAGE

There is no specific treatment for DUPIXENT overdose. In the event of overdosage, contact Poison Control (1-800-222-1222) for the latest recommendations and monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately.

12.6 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease.
For these reasons, comparison of the incidence of antibodies to dupilumab in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

Asthma

Approximately 5% of subjects with asthma who received DUPIXENT 300 mg Q2W for 52 weeks developed antibodies to DUPIXENT; approximately 2% exhibited persistent ADA responses, and approximately 2% had neutralizing antibodies. Similar results were observed in pediatric subjects 6 to 11 years of age with asthma who received either DUPIXENT 100 mg Q2W or 200 mg Q2W up to 52 weeks.
Approximately 9% of subjects with asthma who received DUPIXENT 200 mg Q2W for 52 weeks developed antibodies to DUPIXENT; ~ 4% exhibited persistent ADA responses, and ~ 4% had neutralizing antibodies.
[see Warnings and Precautions (5.1)].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Pregnancy Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy. Encourage participation and advise patients about how they may enroll in the registry *[see Use in Specific Populations (8.1)]*.

Administration Instructions

Provide proper training to patients and/or caregivers on proper subcutaneous injection technique, including aseptic technique, and the preparation and administration of DUPIXENT prior to use. Advise patients to follow sharps disposal recommendations *[see Dosage and Administration (2.1) in the full prescribing information and Instructions for Use]*.

Hypersensitivity

Advise patients to discontinue DUPIXENT and to seek immediate medical attention if they experience any symptoms of systemic hypersensitivity reactions *[see Warnings and Precautions (5.1)]*.

Eosinophilic Conditions

Advise patients to notify their healthcare provider if they present with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis *[see Warnings and Precautions (5.3)]*.

Not for Acute Symptoms of Asthma or Acute Deteriorating Disease

Inform patients that DUPIXENT does not treat acute symptoms or acute exacerbations of asthma. Inform patients to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with DUPIXENT *[see Warnings and Precautions (5.4)]*.

Reduction in Corticosteroid Dosage

Inform patients to not discontinue systemic or inhaled corticosteroids except under the direct supervision of a healthcare provider. Inform patients that reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy *[see Warnings and Precautions (5.5)]*.

Arthralgia

Advise patients to report new onset or worsening joint symptoms to their healthcare provider *[see Warnings and Precautions (5.7)]*.

Parasitic (Helminth) Infections

Advise patients to notify their healthcare provider if they present with clinical features consistent with helminthic infection *[see Warnings and Precautions (5.8)]*.

Vaccinations

Advise patients that vaccination with live vaccines is not recommended immediately prior to and while they are receiving DUPIXENT. Instruct patients to inform their healthcare provider that they are taking DUPIXENT prior to a potential vaccination *[see Warnings and Precautions(5.9)]*.

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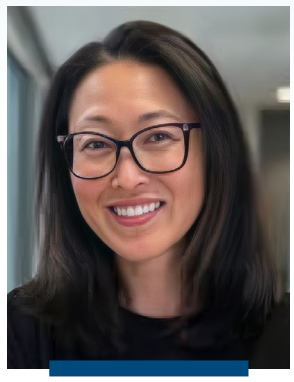
A 'central' issue in sleep medicine

Reviewing new AASM guidelines on management of central sleep apnea

BY PARVATI SINGH, MD, MS; CHRISTINE WON, MD, MS

The treatment of central sleep apnea (CSA) can be challenging. An American Academy of Sleep Medicine (AASM) task force recently performed an extensive review of published data and developed guidelines on CSA management. This article provides a summary of those recommendations, including the challenging decision of whether adaptive servo-ventilation (ASV) is a safe option in these patients.



Christine Won, MD, MS

Parvati Singh, MD, MS

BACKGROUND

Per the International Classification of Sleep Disorders (ICSD), central sleep apnea is defined by five or more central apneas and/or hypopneas per hour, with > 50% of events being central in nature and associated symptoms such as sleepiness or insomnia.[1] While the ICSD categorizes CSA into six diagnostic categories (primary CSA, CSA with Cheyne-Stokes respiration [CSR], CSA due to a medical disorder without CSR, CSA due to medication or substance, treatment-emergent CSA, and CSA due to high altitude), the task force opted to group studies that evaluated similar treatments across the different CSA subtypes.[1-2] They did this for the following reasons: there is a limited number of studies available; many studies do not differentiate CSA subtypes; and CSA, while triggered by different pathways, shares a common final pathway that involves post-hyperventilation hypocapnia (equifinality).[2]

OVERVIEW OF NEW GUIDELINES

Task force members reviewed relevant research published before February 2025 using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.[3] They looked for a clinically meaningful effect of the intervention on what was determined to be critical outcomes: disease severity (as measured by apnea-hypopnea index [AHI], central apnea index [CAI], central apnea hypopnea index [CAHI], and oxygen desaturation index [ODI]), symptoms, function, and clinical outcomes (eg, hospitalizations and mortality).[2] Based on the quality of evidence available, all the recommendations the task force made on the various interventions were marked as conditional—suggesting that providers offer these treatments to patients with an individualized approach, based on clinical context.[2]

The guidelines emphasize that CSA treatment should focus on reducing respiratory events and improving symptoms, as well as addressing its underlying etiology.[2] Potential options for treating CSA include PAP therapy, supplemental oxygen, acetazolamide, and transvenous phrenic nerve stimulation (TPNS).[2] Rather than proposing a specific algorithm, the guidelines suggest that if one intervention does not work then it is reasonable to try another intervention.[2] (See **Table 1** for the specific GRADE recommendations for each intervention by the task force.)

CPAP is a reasonable initial treatment for most types of CSA since it has been shown to reduce AHI and is readily available.[2] Use of BiPAP without a backup rate (BUR) is not advised, however, since it has the potential to induce central apneas.[2] On the other hand, a conditional recommendation for BiPAP with a BUR was given for treatment of CSA (except when secondary to heart failure and high altitude, due to lack of evidence in these subgroups).[2] This was based on their analysis of six randomized controlled trials (RCTs) that found BiPAP with a BUR improved sleepiness, AHI, CAI, CAHI, left ventricular ejection fraction (LVEF), and heart rate.[3] The guidelines also tackled a controversial management challenge in sleep medicine—the use of adaptive servo-ventilation (ASV)—ultimately giving it a conditional recommendation for management of most types of CSA.[2]

Low-flow supplemental oxygen received a conditional recommendation for the treatment of CSA due to heart failure and high altitude.[2] In CSA due to heart failure, supplemental oxygen has been shown to improve AHI, CAI, sleep quality, and hospitalizations.[2] In CSA related to high altitude, supplemental oxygen reduces the ODI.[2] Practically, however, insurance coverage may be a barrier in using supplemental oxygen to treat CSA.[2]

Acetazolamide was the only intervention that received a conditional recommendation for all six classifications of CSA, with doses ranging from 250 mg to 1,000 mg shown to reduce the AHI.[2] The task force determined that the potential side effects of acetazolamide were mild (paresthesia, change in taste, kidney stones, etc) when compared with potential benefits.[2] However, there were concerns on the changes in acid-base status, ventilation, and electrolytes, as well as questions on the dosage and duration of therapy.[2-3] Most studies reported only short-term outcomes.[2] The task force suggests that if using acetazolamide for treatment, there should be close monitoring of symptoms and side effects as well as repeat testing.[2]

Transvenous phrenic nerve stimulation (TPNS) was given a conditional recommendation for management of primary CSA and CSA secondary to heart failure, driven primarily by a single RCT showing that this therapy

	SPECIFIC INTERVENTION							
		CPAP	BIPAP w/ BUR	BIPAP w/o a BUR	ASV	Low-flow oxygen	Acetazolamide	TPNS
TYPE OF CENTRAL SLEEP APNEA	Primary CSA	Conditional for (low)	Conditional for (very low)	Against (conditional, very low)	Conditional for (low)		Conditional for (low)	Conditional for (very low)
	CSA due to heart failure	Conditional for (low)		Against (conditional, very low)	Conditional for (low)	Conditional for (low)	Conditional for (low)	Conditional for (very low)
	CSA due to medication or substance use	Conditional for (low)	Conditional for (very low)	Against (conditional, very low)	Conditional for (low)		Conditional for (low)	
	Treatment-emergent CSA	Conditional for (low)	Conditional for (very low)	Against (conditional, very low)	Conditional for (low)		Conditional for (low)	
	CSA due to a medical condition or disorder	Conditional for (low)	Conditional for (very low)	Against (conditional, very low)	Conditional for (low)		Conditional for (low)	
	High altitude					Conditional for (very low)	Conditional for (very low)	

Table 1: A summary of the AASM 2025 CSA guidelines

improved sleepiness, reduced CAI by 80%, increased 6-minute walk test distance, and decreased arousal index.[3] Of note, TPNS has not been shown to reduce mortality or improve LVEF.[3] Feasibility of TPNS implantation can be challenging, however, given limited expertise, availability, the need for coordination with other specialties, and overall cost (> $50,000).[3]

Compared with the 2016 guidelines, some of the major changes were the addition of TPNS and comments on ASV.[2,4] Other changes were related to the task force's determination that based on available data they could not comment on the use of hypnotics in the treatment of CSA as well as BiPAP with a BUR for CSA due to heart failure; previous guidelines gave an "option" recommendation.[2,4] Similarly, there were no longer any comments regarding treatment of CSA in patients with end-stage renal disease.

CONDITIONAL RECOMMENDATION FOR ASV

The decision on the use of ASV to treat CSA in heart failure with reduced ejection fraction (HFrEF) has been a major challenge in the sleep medicine world for over a decade. The 2016 guidelines recommended against the use of ASV in symptomatic heart failure patients with LVEF of < 45%.[4] This stemmed from the Treatment of Predominant Central Sleep Apnoea by Adaptive Servo Ventilation in Patients With Heart Failure (SERVE-HF) trial, which found a 34% increased risk of cardiovascular death in CSA patients with LVEF of < 45% who used ASV.[5] However, publication of the 2024 Effect of Adaptive Servo Ventilation (ASV) on Survival and Hospital Admissions in Heart Failure (ADVENT-HF) trial caused many to consider this recommendation. The ADVENT-HF data found no increase in mortality on three- to six-year follow-up when using an ASV from a different manufacturer with a peak flow target to treat both obstructive and central sleep apnea in patients with HFrEF.[6]

After SERVE-HF, BiPAP with a BUR became the frequent go-to in treating CSA with HFrEF. However, the new guidelines do not provide any recommendation on BiPAP with a BUR for CSA treatment in patients with heart failure. Instead, the guidelines suggest ASV to treat heart failure patients with CSA without a specific LVEF cutoff.[2] This may pose some problems with some payors who, in our experience, will cover ASV only when BiPAP with a BUR has been tried and fails to control CSA.

The task force members' recommendations on ASV were based on the analysis of 12 RCTs.[3] Their analysis found that ASV resulted in > 70% reduction in AHI, CAI, CAHI, and/or ODI.[3] They did find an increased signal of hospitalization in patients using ASV but deemed this not to be clinically meaningful.[3] When pooling the data from four trials (including SERVE-HF and ADVENT-HF), the task force found that the use of ASV in HFrEF patients was not associated with increased mortality.[3] In weighing the risks and benefits of ASV therapy, they determined that since the ASV device used in the SERVE-HF trial that showed increased mortality is no longer manufactured, the benefits of ASV as a class outweigh the risks; thus, ASV received a conditional recommendation for use with low certainty of evidence.[2]

The conditional recommendation on ASV was presented with some caution.[2] It was acknowledged that ASV devices are made by different manufacturers and that each has a different algorithm.[2] Since the task force looked at ASV as one general class rather than by brand, it could not recommend a specific ASV brand.[2] For these reasons, the task force emphasized that the use of ASV involves shared decision-making with the patient, close follow-up, and utilization by experienced centers.[2]

FUTURE DIRECTIONS

One clear theme that emerged from the newly released AASM guidelines is that more data is needed to be able to provide strong recommendations. Some of the limitations in the current data are that studies sometimes lumped different CSA disorders together when evaluating an intervention and that central hypopneas were often not adequately measured or identified in the studies.[3] Other considerations that affect treatment recommendations are that comorbid OSA can make it difficult to recognize and treat CSA and that a class of device might work differently based on the manufacturer.[3]

There is need for future research concerning targeted therapies based on etiology or pathophysiology, analysis of whether CSR is a nonharmful compensatory mechanism, understanding when and how CPAP improves CSA, looking at the use of multimodal therapy, comparing different treatment modalities, and treatment strategies that improve mortality.[3]

As we await new research, the task force has provided a helpful step forward addressing interventions that sleep medicine providers can consider for patients with CSA. ●

All references are available online at chestphysician.org.

Column

Beyond the blueprint

Early outcomes from the CHEST Critical Care APP certification exam

BY CORINNE YOUNG, MSN, FNP-C, FCCP

In critical care, confidence is built one decision at a time. It is shaped by long shifts, complex cases, and the responsibility of caring for patients at their most vulnerable. For many advanced practice providers (APPs), professional certification represents far more than a credential; it is a reflection of commitment, growth, and pride in practice.

The 2025 CHEST Critical Care APP (CCAPP) certification exam marked another meaningful step forward in the evolution of advanced practice in critical care. Strong participation, high pass rates, and thoughtful candidate feedback provided insight into why APPs pursue certification, how they experience the process, and how the program can continue to grow.

WHY APPs PURSUE CERTIFICATION

When applicants were asked why they chose to pursue the CCAPP certification, their responses reflected a shared professional mindset rather than a single motivation. Certification was not viewed as a formality but as an intentional step toward professional excellence.

Many candidates described seeking validation of their knowledge and skills in an environment where complexity and acuity demand constant growth. Others emphasized lifelong learning, viewing certification as a way to remain engaged, current, and challenged in their practice. Advancing the APP profession itself was another common theme, with certification seen as a way to strengthen the credibility and visibility of APPs within interdisciplinary teams.

Leadership, recognition, and career advancement also played important roles. For some candidates, certification represented an opportunity to influence practice, mentor colleagues, or pursue new professional roles. Underlying these motivations was a strong sense of personal pride, the satisfaction of meeting a high standard, and knowing that achievement carries meaning.

One applicant summarized this perspective powerfully: *"As a critical care NP, I strive to be a lifelong student and to continually elevate my practice. Pursuing this certification will be a reflection of that professional drive to practice at the highest level, provide the best care for my patients, and set myself apart from my peers."*

Another applicant highlighted credibility and patient safety as key drivers: *"I would like to take the CHEST exam to enhance professional credibility among colleagues and to continue to contribute to patient safety and best patient outcomes. I believe this is a great learning opportunity and will also give me personal satisfaction in my career development by passing this test."*

Together, these voices underscore an important reality: APPs pursue certification not only for themselves but for their patients, their teams, and the profession as a whole.

WHO TOOK THE EXAM IN 2025

A total of 172 APPs sat for the 2025 exam, representing a broad range of professional backgrounds and experience levels.

Nurse practitioners comprised the majority of test takers, with 130 candidates accounting for 76% of the total group. Physician assistants/associates made up the remaining 42 candidates, representing 24%.

Most candidates brought substantial clinical experience to the exam; 110 test takers (64%) reported having six or more years of experience. Another 53 candidates (31%) had three to five years of experience, while a smaller group of nine candidates (5%) were early in their careers, with six months to two years of experience.

This distribution highlights that while many APPs pursue certification after establishing themselves clinically, there is also growing interest among early career clinicians who view certification as a foundation for long-term professional development.

EXAM PERFORMANCE AND OUTCOMES

Overall exam performance in 2025 reflected a high level of preparation among candidates. Of the 172 test takers, 154 passed the exam, resulting in a 90% pass rate. Eighteen candidates (10%) did not pass.

This strong pass rate suggests that exam content aligns well with real-world critical care practice and that candidates are approaching the certification process with seriousness and intent.

LOOKING AHEAD

The inaugural round of the CCAPP exam tells a clear story: APPs are seeking meaningful validation, value lifelong learning, and want credentials that reflect the realities of modern critical care.

Strong performance outcomes, positive candidate experiences, and thoughtful feedback demonstrate a program that is both effective and responsive. With continued attention to quality, education, and engagement across career stages, the CCAPP certification is well positioned to support the next generation of APP leaders.

In a field defined by complexity and constant change, one thing remains steady: APPs continue to raise expectations for themselves and their profession, and this certification serves as a benchmark toward excellence in critical care practice. ●

APPLY TO TAKE THE EXAM IN 2026

The CCAPP exam will be offered online twice in 2026. APPs can apply for either the spring or the fall exam period.

Spring exam period: April 21 to May 8, 2026 (application deadline April 14)

Fall exam period: October 27 to November 13, 2026 (application deadline October 23)

To apply, visit chestnet.org/APP-exam

AHA guideline updates // continued from cover

A DIVERSE DEVELOPMENTAL PROCESS

The latest guideline update focuses on equitable access to lifesaving care and clarifies consistent application in real-world settings. Rather than introducing sweeping changes, the recommendations reflect targeted interventions informed by experts working through the committee, bringing diverse clinical perspectives to the guideline development process.

"The AHA always tries to diversify their committees to include pediatricians, emergency department clinicians, critical care clinicians, and other specialists," said Daniel Arellano, PhD, RN, APRN, ACNP-BC, an acute care nurse practitioner at MD Anderson Cancer Center in Houston and a member of the committee. "They do a really good job with incorporating that diverse thought."

Despite advances in resuscitation science, the incidence of cardiac arrest remains high and overall survival rates are low. Outcomes also vary widely, with lower survival rates among marginalized racial and ethnic groups and in rural areas.[1]

With these challenges in mind, the updated guidelines introduce several key changes for both lay rescuers and professional responders. The following sections highlight select updates on resuscitation strategies. Full details are available at www.heart.org.

REFINING TERMINOLOGY

Alongside clinical updates, the 2025 AHA guidelines for CPR and ECC refine the language to help improve communication and accuracy in emergency response education. For example, "rescue breaths" is no longer used; "breaths" now refers to assisted breathing during CPR or for someone with a pulse who is not breathing. "Ventilation" is reserved for mechanical respiratory support provided by professionals.[1]

The guidelines also recommend the term "lay rescuer" rather than "bystander," noting the role that nonhealth care professionals play in initiating lifesaving care. Additional terminology clarifies the distinction between return of spontaneous circulation and return of circulation, differentiating spontaneous cardiac recovery from circulation achieved through mechanical support.[1]

DEFINING THE ROLE OF MECHANICAL CPR

Mechanical CPR devices have been used to deliver consistent, automated chest compressions, particularly during prolonged resuscitation efforts or situations in which maintaining high-quality manual CPR is challenging.

However, the updated guidelines stop short of recommending routine use of mechanical CPR devices. Based on the evidence reviewed, the guidelines reaffirm manual CPR as the standard approach, with mechanical devices considered only in specific circumstances when logical factors—such as transport time, crew safety, or limited personnel—make manual compressions difficult to sustain.[2]

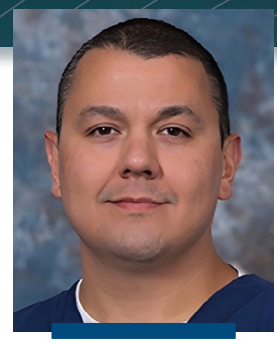
ADDRESSING EQUITY IN DEFIBRILLATOR PLACEMENT

Timely defibrillation remains a cornerstone of cardiac arrest care. But Dr. Arellano noted that uncertainty around pad placement and clothing—particularly in women—can delay care.

"Defibrillator pad placement is important because it touches on equity and access," he said. "In some cases, providers hesitate to adjust or remove clothing, such as bras. The guidelines give clearer direction to avoid it being a hindrance. We don't want women to have worse outcomes simply because of clothing like bras."

Additionally, the guidelines clarify that defibrillation pads may be placed in either an anterolateral or anteroposterior position and recommend using pads or paddles with an electrode diameter greater than 8 cm for adults.[2]

Ashish Panchal, MD, PhD



Daniel Arellano, PhD, RN, APRN, ACNP-BC

A UNIFIED CHAIN OF SURVIVAL

The essential actions for treating cardiac arrest are contained within the comprehensive framework known as the "Chain of Survival." This framework is flexible and can be adapted based on the specific context of the arrest, such as the victim's age, the cause of the event, and where it takes place.

Previously, the 2020 guidelines depicted four related but distinct chains of survival for adults and children experiencing in-hospital and out-of-hospital cardiac arrest. The 2025 guidelines place renewed emphasis on the Chain of Survival as a single, unified framework that applies across adult and pediatric patients and care settings.

With the update, the Chain of Survival is a clearer progression of events, beginning with recognition of cardiac arrest and ideally culminating in survival and recovery.[3] Each link in the chain is paired with a visual representation to reinforce key priorities:

- Early recognition and emergency activation
- High-quality CPR
- Defibrillation
- Advanced resuscitation
- Postcardiac arrest care
- Recovery and survivorship

Notably, the symbol for high-quality CPR now includes lungs alongside chest compressions, highlighting the importance of breathing—especially in pediatric patients and in opioid-related arrests.[3]

"One of the biggest aspects highlighted for me is the continued support of our initial response: Call 911, and push hard and fast," Dr. Panchal said. "When our experts revisited the Chain of Survival, we unified it into a clearer, single framework that reinforces the concept of immediate response."

BE INTENTIONAL AND IMPLEMENT

Covering topics from ethics and basic life support to advanced techniques and postarrest care, the updated guidelines prioritize clarity, consistency, and practical application. Clinicians and lay responders alike are encouraged to review the full guidelines and update their training to reflect these new recommendations.

The responsibility of providers, Dr. Panchal noted, extends beyond the hospital walls.

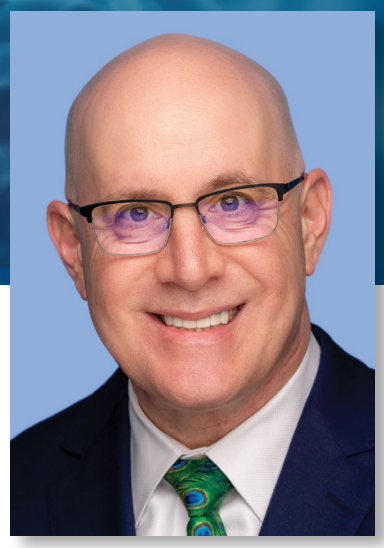
"We're not only advocates, we're also ambassadors. So many people look to us for guidance about what is the right thing to do at the right time," he said. "Take to heart the importance of your role as an ambassador to save lives because people will listen to you, and they will follow your lead in learning how to do hands-only CPR and being intentional about doing the right thing. ●

All references are available online at chestphysician.org.

FROM THE PRESIDENT

Column

Get to know 2026 CHEST President Neil Freedman, MD, FCCP



Neil Freedman, MD, FCCP

CHEST is pleased to introduce Neil Freedman, MD, FCCP, the 2026 President of the American College of Chest Physicians (CHEST). A long-time volunteer, educator, and leader within the organization, Dr. Freedman shares his perspective on the year ahead, CHEST's values, and his hopes for the future in the answers that follow.

What would you like to accomplish as President of CHEST?

I think of my presidential year as part of the CHEST organizational journey. Yes, 2026 is just one year, but—as we just celebrated at last year's meeting—this organization has been around for 90. As president, my goal is to honor that legacy by building on the strategy thoughtfully established by the Board of Regents and ensuring that we continue to move forward with clarity and purpose so that, at the end of my term, CHEST is even stronger than when I began.

Together with CHEST's leadership and members, I want to continue building on our core pillars of people, education, research, and social responsibility. Having worked in academics, private practice, and an integrated health system, I bring a range of perspectives that I believe can help us innovate and continue to be successful in the future. I am particularly excited about continuing to expand CHEST's educational offerings. This includes our ever-expanding Bridging Specialties® initiative, digital access to all our content through CHEST MedCast, and our education and certification for advanced practice providers. These efforts reflect a larger priority: We must continually assess how we deliver value and think proactively about the next decade and beyond, rather than just relying on the strengths that carried us in the past.

What do you consider to be CHEST's greatest strength, and how will you build upon this during your presidency?

CHEST's greatest strength is, without question, its people. Our volunteers, faculty, staff, executive leadership team, and Board of Regents form an incredible community. The dedication, expertise, and collaboration within this organization are what make CHEST truly exceptional.

Over the years, I have had the privilege of working closely with many of our leaders. Their commitment to clarity, accountability, and strategic direction has positioned CHEST for continued success. Equally important, our diverse perspectives help us make thoughtful decisions and ensure alignment with our values.

During my presidency, I want to continue building an environment where every member—regardless of role, stage of training, or practice setting—feels welcomed, supported, and heard. That means fostering open dialogue, nurturing emerging leaders, and living our values of community, inclusivity, innovation, advocacy, integrity, and science-based medicine in everything we do.

What are some of the challenges CHEST is facing, and how will you address them?

The challenges affecting CHEST mirror the pressures facing health care nationwide. Clinicians are facing increasing financial pressures, as reimbursement fails to keep up with rising operational and practice expenses. Burnout, compensation concerns, and the growing demands of patient care all take a toll on our members. On top of that, political and regulatory shifts are creating uncertainty that affects how we practice.

CHEST plays a critical role in supporting our members and helping them navigate these challenges. We will continue providing timely clinical education and guidelines, partnering with other societies on issues like reimbursement, oxygen access and regulatory reform, and supporting research and philanthropy during a time when federal funding is uncertain.

It is also important that we stand firm in our values. We continue to demonstrate our unwavering commitment to science, patient safety, and public health.

As we think about the future, we must also continue to innovate. CHEST is thinking differently, exploring new technologies, including artificial intelligence, and seeking out partnerships that will allow us to deliver value in new ways. To meet the needs of tomorrow, we will need both stability and bold thinking.

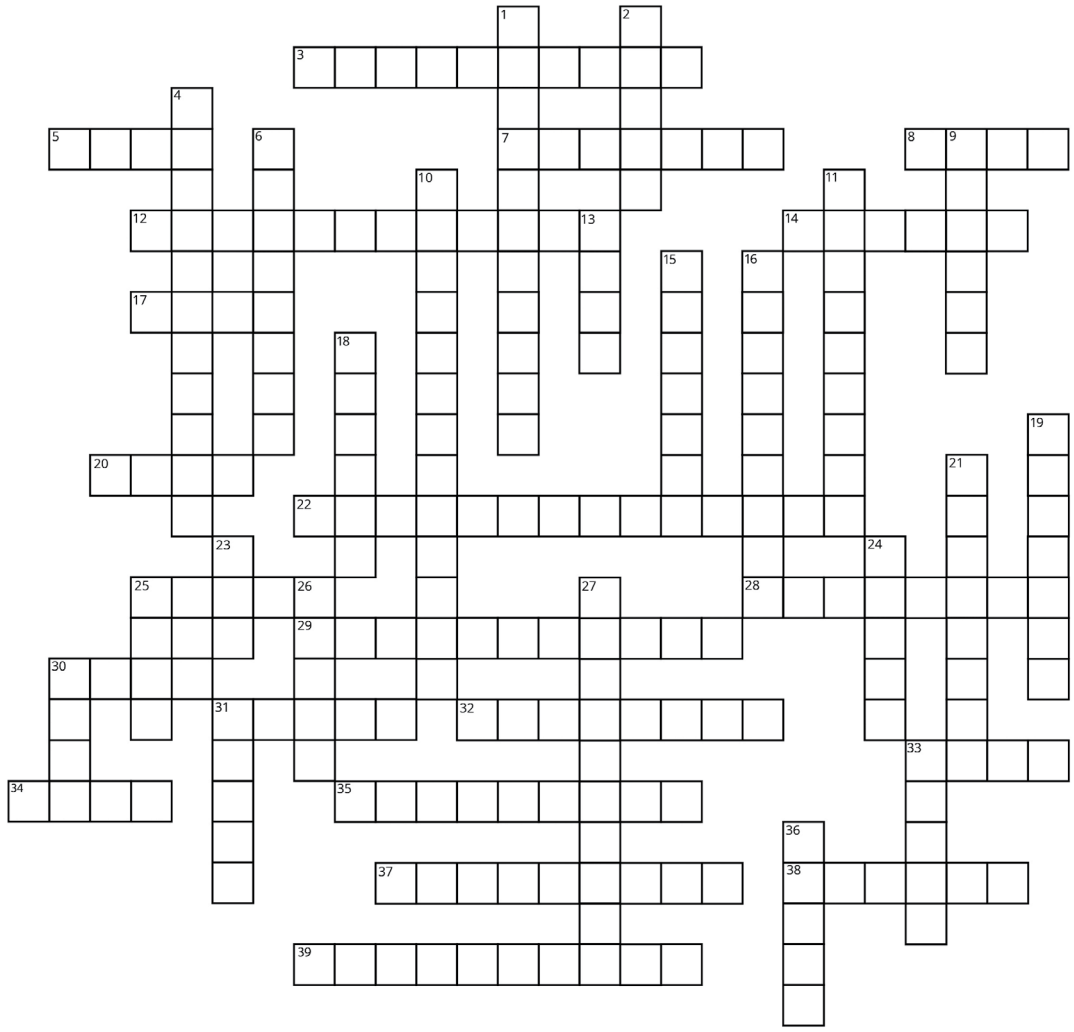
How can members support you during your presidency?

More than anything, I ask that members remain engaged with CHEST. Share your challenges, your ideas, and your successes. Communicate about the issues that matter to you in your practice. Share your feedback—both positive and constructive—so that we can continue improving to better meet your needs. We are active on social media channels, and you can contact me at **president@chestnet.org**.

I also encourage members to support CHEST philanthropy, which fuels our mission by advancing education, supporting research, and expanding initiatives that directly benefit clinicians and patients. Above all, stay connected, stay vocal, and stay committed to our mission. CHEST's strength has always come from its members; and together, we can continue building an enduring future for chest medicine. •

CHEST Puzzler

Test yourself with these clues from the October, November, and December 2025 issues of the journal *CHEST*®—compiled by William Kelly, MD, FCCP.



Scan QR code on page 4 for answer key

ACROSS

3. 19.5% of patients with ILD from _____ arthritis get admitted annually (Nov p.1163)
5. Contrast echocardiography shows bubbles after _____ heart beats if pulmonary shunt and earlier if cardiac shunt (Dec p.1474)
7. Use of this AI tool is increasing and has been proposed as way to enhance data accuracy and interpretation in meta-analyses (Nov p.1089)
8. Newly diagnosed OSA was associated with fourfold greater incidence of [acronym] in veterans (Oct p.851)
12. Persistent systemic and local _____ is a hallmark of COPD and contributes to mortality (Nov p.1073)
14. Reversible myocardial depression due to this common reason for ICU admission was first described by Parker more than 40 years ago (Dec p.1384)
17. Clinical trials have > 90% lung cancer screening follow-up; but in real-world study, less than 1 in ___ do (Oct p.1060)
20. Continent with the greatest estimated increase in indirect COPD costs by 2050 (Oct p.885)
22. Pulmonary _____ has level 1 evidence for reducing dyspnea, increasing exercise capacity, and improving quality of life (Oct p.944)
25. There are more than 50 causes of pleural effusions, and Dr. _____ shed insight on distinguishing transudates and exudates 50 years ago (Dec p.1518)
28. Clinical _____ (a physics term for "mass in motion") may reduce palliative care usage and increase persistent critical illness (Dec p.1282)
29. The TTM2 trial cast doubt on benefits of this nonpharmacological therapy after out-of-hospital cardiac arrest (Nov p.1076)
30. First-line therapy [acronym] for patients with acute, hypoxemic respiratory failure; article focuses on "liberation" (Nov p.1152)
31. In T1c lung tumors, ones that are 2 to ___ cm, segmentectomy may be viable alternative to lobectomy, though NCDB data could not evaluate for local recurrence (Dec p.1292)
32. _____ appear to have greater risk of lung cancer and KRAS mutations, not to mention more lead occupational exposure (Dec p.1529)
33. Using Canadian health databases, having used a recalled _____ device for sleep apnea was not associated with obstructive lung disease development or progression (Nov p.1231)
34. ILD experts think all graduating pulmonary fellows should be able to independently manage cryptogenic organizing pneumonia, _____-induced ILD, and sarcoidosis (Oct p.975)
35. European Society of Cardiology recommends measuring regurgitation of this valve to screen for PH (Dec p.1288)
37. This can be successful after lung transplant in women, though higher risk when unplanned (Oct p.932)
38. Two 1980s landmark trials provided evidence that _____ improves survival in COPD (Nov p.1120)
39. Multiple choice questions about managing this life-saving ICU device written by AI were indistinguishable from, and written 90% faster than, those by humans (Dec p.1425)

DOWN

1. Some individuals see 14 providers before receiving a diagnosis of this granuloma-forming condition (Dec p.1396)
2. In radiation associated with CTPA and V/Q scans, doses of < _____ mGy are considered to be negligible risk to a fetus (Oct p.1012)
4. Approved in August 2025 for non-CF bronchiectasis (Dec p.1276)
6. Preventing and assessing for this "D" is part of the ABCDEF (A2F) ICU care bundle (Oct p.927)
9. In-hospital mortality of critically ill patients receiving mechanical ventilation approaches ___% (Oct p.913)
10. Among the two most frequent non-nodule findings in lung cancer screening CT scans are emphysema and coronary artery _____ (Nov p.1265)
11. The number of CHEST simulation courses currently being offered in 2026, which is also the number of syllables in a haiku
13. Proteomic study using swabs from this body part "knows" if a 1-week-old baby may get bronchopulmonary dysplasia (Oct p.848)
15. In a secondary analysis, it may be the burden of _____ measured during the night and NOT apnea-hypopnea index that is associated with major cardiovascular/cerebrovascular events (Dec p.1481)
16. A lymphocyte proliferation test has high specificity for distinguishing this exposure from sarcoidosis (Dec p.1404)
18. Discordant pleural effusions (exudate by protein or LDH but not both) are much less likely to be due to _____ or infection (Dec p.1293)
19. Measuring this in pleural fluid and serum may help distinguish "false exudates" due to CHF or hepatic hydrothorax (Dec p.1294)
21. A "How I Do It" article outlines building a procedural "_____" for incoming PCCM fellows. The term also refers to training military recruits. (Dec p.1434)
23. GLI 2023 race-neutral lung function equations inadvertently introduced systemic distortions from this other unmodifiable demographic variable (Nov p.1081)
24. Less than one-third of the active-duty military receive the recommended _____ hours of sleep per night (Oct p.1024)
25. Screening for _____ cancer is much lower than that of breast, colon, and cervix cancers (Nov p.1260)
26. D-dimer levels naturally peak during this trimester of pregnancy (Oct p.1008)
27. The only curative treatment to improve survival and quality of life in patients with advanced irreversible lung disease (Oct p.944)
30. Authors suggest that body _____ could be one of many factors when selecting site for central venous catheter insertion... one should not take shortCUTS (Dec p.1298)
31. Tailoring discussions to the patient/surrogate's background, humanizing participation, and being transparent were three approaches that build _____ in the informed consent process for critical care research (Dec p.1364)
33. The "C" in the TOPIC questionnaire studied to differentiate its refractory form by the sensations and triggers that cause it (Dec p.1284)
36. Modern positive pressure ventilation gained momentum during this 1952 epidemic (Oct p.846)

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