Eastern Pulmonary Conference
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Scientific Posters F1-F44 will be on display in the Ponce 5&6, and Ponce Foyer during the coffee break, 10:30-11:15am, Friday September 9, 2022

Not for CME Credit

R1

Tuberculosis Infections in the USA During the COVID-19 Pandemic

Kushinga M. Bvute, Feyikemi Ogunfuwa, Hadeer Sinawe, Michael A. DeDonno

Background: The Covid-pandemic disrupted international Tuberculosis (TB) services, decreasing international cases; however, there is no report analyzing the impact of Covid on TB in the USA. This study compares TB between 2019 (Pre-pandemic) and 2020 (Pandemic).

Method: We used publicly available data from the Center for Disease Control and Prevention that reported TB in the USA. We extrapolated data from tables; age, ethnicity, geography, reasons for testing, risk factors, and genotype. We excluded data aggregated by metropolitan statistical areas. We used SPSS to examine the statistical variables. The project was exempt from IRB approval.

Results: There was a statistically significant decrease in TB cases from 2019 (n = 8916, M = 177.84, SE = 48.833) to 2020 (n= 7174, M = 143.10, SE = 38.638). The same top five states with the most TB cases remained the same with all showing decreased cases from 2019 to 2020; California (n=2,113 vs 1,705), Texas (n=1,159 vs 884), New York (n= 754 vs 606), Florida (n= 558 vs 412), and New Jersey (n= 311 vs 245). The median age in the five states ranged from 34.8 to 42.2 years.

Significantly more people in 2019 underwent TB testing due to symptoms (M =99.24± SD 206.96 vs. 81.02±166.98*), abnormal chest x-ray (M=36.28± SD 67.91 vs. 27.00± 57.43**), targeted testing (M= 8.32 ±29.61 vs. 4.96 ±17.41*), immigrant examination (M= 3.56± SD 7.73 vs. 1.64±4.28**), and administrative testing (M =0.94± SD 1.77 vs. 0.52 ±1.16*).
*= p<0.5, **p<0.01.

Conclusion: Although global TB cases decreased by 20%, we cannot attribute the reduction to mask-wearing or lockdowns versus reduced access to care. TB cases in the USA decreased in 2020 similar to global trends. However, the acute reduction does not exclude or confirm the effect of mask-wearing.

R2

Radiographic edema does not predict mortality in patients with COVID-19 requiring mechanical ventilation

Daniel Kotok, Christine Girard, Jose Rivera Robles, Andrew Kim, Shruti Shettigar, Allen Lavin, Samantha Gillenwater, Anas Hadeh

Background: Baseline radiographic edema on chest X-ray (CXR) in patients with COVID-19 presenting to the emergency department has been associated with need for hospital and intensive care unit (ICU) admission as well need for mechanical ventilation and 30-day mortality. Whether this is true for radiographic edema quantified after initiation of mechanical ventilation is unclear. We sought to evaluate this question using a well-validated scoring system (the Radiographic Assessment of Lung Edema [RALE] score) using data over 6 months from a large, multi-hospital healthcare system including all adult (age >= 18) patients.

Methods: We collected CXRs performed in patients soon after endotracheal intubation for COVID-19 associated hypoxemic respiratory failure between March and September 2020. We quantified severity of radiographic edema using the RALE score. Two independent reviewers quantified radiographic edema using the RALE scoring system. We examined the association of radiographic edema with time from hospital admission to intubation and 30-day mortality.

Results: 65 patients were identified (median age 68, 40% female). Inter-rate agreement for RALE score was excellent (ICC = 0.84, 95% CI 0.82 - 0.87, p < 0.0001). Mortality at 30 days was 54% (n = 35). There was no association between RALE scores and time to ICU admission from ED presentation (r = -0.14, p = 0.27). RALE scores were not different in survivors and non-survivors (8 [4-17] and 7 [5-15], p = 0.92 respectively). When adjusted for age and history of diabetes, there was no difference in the likelihood of survival in 30-day mortality between the lowest and highest RALE quartiles (HR 0.67 [0.24 - 1.85], p = 0.44).

Conclusions: In unvaccinated, untreated patients with COVID-19 hypoxemic respiratory failure requiring mechanical ventilation there is no association between baseline (time of intubation) radiographic edema as captured by CXR and 30-day mortality. Larger observational studies accounting for vaccination status, oxygenation strategies and medical therapy are needed.

R3

Prone positioning in severe ARDS due to COVID-19

Ana Suarez MD, Jennifer Perez MD, Heidy Izquierdo MD, Sabrina Arshed MD

Introduction: Early application of prone-positioning in ARDS significantly decreased mortality. Our goal is to evaluate the effect of early prone-positioning on COVID ARDS patients.

Methods: A multicenter, retrospective observational analysis with a total of 1,335 patients with COVID ARDS that underwent prone positioning from 1/1/2020- 6/20/2021. ARDS was defined using the Berlin criteria. Logistic regression was used to predict the likelihood of in-hospital all-cause mortality early vs late prone-positioning. Secondary outcomes: age, MAP, days on ventilator and ICU length of stay.

Results: From January 1, 2020 through June 20, 2021, 3,407 patients with COVID ARDS were admitted to the participating facilities. 1,335 patients were included in the final analysis. Patients were 51-80 years old (77%), male (61.5%), white (55.4%), all admitted to ICU on mechanical ventilation. In-hospital all-cause mortality was significantly lower in the shorter time to prone group (<16 hours) than the longer time to prone group (>16, >24 hours), (p <0.001, Exp(B) = 1.119, 95% C.I. [1.088, 1.151]). Mortality rate <16 hours (46.53%), >16 hours (55%) vs >24 hours (68.1%). Patients that were prone in <16 hours were less likely to experience an in-hospital mortality than those prone >16 hours (X2 (1, N= 1513) = 19.051, p <0.001). Days on the ventilator were associated with a decreased likelihood of in-hospital mortality. For each one-day increase in days on vent the likelihood of mortality is 0.978 times as likely. (p < 0.01, Exp(B) = 0.978, 95% C.I. [0.968, 0.989]). Expired and hospice rate by time to prone <16 hours (55.45%) vs >16 hours (79.69%). For each one-year increase in age, patients are 1.045 times as likely to experience an in-hospital mortality (p < 0.001, Exp(B) =1.045, 95% C.I. [1.033,1.056]).

Conclusions: Time to prone had a statistically significant relationship to in-hospital all-cause mortality. Patients with COVID ARDS benefit from early prone treatment.

R4

Procalcitonin as a surrogate for culture positive ventilator-associated pneumonia in COVID-19

Andrew Kim MD, Amy Van MD, Jose Rivera Robles MD, Sikandar Khan MD, Lewjain Sakr MD, Milad Heydari MD, Anas Hadeh MD

Introduction: Procalcitonin has been traditionally used to de-escalate antibiotics in a variety of infections. The initial procalcitonin ventilator-associated pneumonia (VAP) investigations showed that procalcitation use resulted in a significant reduction of days of antibiotic use. Most recently, procalcitonin is being assessed to differentiate between gram-negative, gram-positive, and fungal infections. The goal of this study is to observe if procalcitonin use can be used as a surrogate for bacterial VAPs in COVID-19.

Methods: In this retrospective study, 287 patient records were selected based on the diagnosis of positive SARS-CoV-2 by PCR test and patients requiring mechanical ventilation. Lab values were obtained on admission and during ventilator-associated events (VAE) or sputum collections.

Results: A total of 93 culture-positive VAP were identified in patients with gram-negative bacilli 58 (63%), gram-positive bacteria 19 (20%), and fungal infections 16 (17%). There was a significant difference in the procalcitonin level of gram-negative VAP (42.5 ng/mL, 95% CI 18.5-60.0, p<0.001) and gram-positive VAP (6.8 ng/mL, 95% CI 0.2-6.8, p=0.037) in comparison to culture-negative VAE (3.2 ng/mL). There was no significant difference in fungal VAP procalcitonin (1.135 ng/mL, p=0.185). Additionally, there was no significant difference in admission procalcitonin in gram-negative VAP (0.9 ng/mL, p=0.245), gram-positive VAP (0.9 ng/mL, p=0.53), and fungal VAP cohorts (2.1 ng/mL, p=0.74) in comparison to the culture-negative VAE cohort (1.7 ng/mL).

Conclusions: Gram-negative VAP and gram-positive VAP had a significantly higher correlation with procalcitonin than culture-negative VAE. Conventionally, antibiotic initiation is based on clinical judgement, especially in unstable patients regardless of procalcitonin levels. Thus far, there have been no randomized controlled trials to assess if procalcitonin can be used to escalate therapy in ventilated patients. Our study contributes that there may be a role in using procalcitonin to initiate antibiotic therapy in VAP, with larger increases in procalcitonin for gram-negative and gram-positive bacterial pneumonias.

R5

Influence of Right Ventricular Structure and Function on Hospital Outcomes in COVID-19 Patients

Jozef Oweis, MD; Ali H. Al-Tarbsheh, MD; Annie Leamon, BS; Katharine Goodspeed, BS, MS; Paul Feustel, PHD, Ciril Khorolsky, MD; Anupama Tiwari, MD; Amit Chopra, MD, Mikhail Torosoff, MD

Background: Impact of Right ventricular dysfunction (RVD) noted on outcome has not been well investigated in hospitalized patients with COVID-19 infection.

Objectives: The main aim of our study was to investigate in-hospital outcomes including mortality, ICU admission, mechanical ventilation, pressor support, associated with RV dilatation, and RV systolic dysfunction in COVID-19 patients without a history of pulmonary hypertension.

Methods: It was a single academic tertiary center, retrospective cohort study of 997 PCR-confirmed COVID-19 patients.194 of those patients did not have a history of pulmonary hypertension and underwent transthoracic echocardiography at the request of the treating physicians for clinical indications. Clinical endpoints which included mortality, ICU admission, need for mechanical ventilation or pressor support were abstracted from the electronic charts.

Results: Patients' mean age was 68+/-16 years old and 42% of the study population were females. COPD was reported in 13% of the study population, whereas asthma was 10%, and CAD was 25%. The mean BMI was 29.8+/-9.5 kg/m2. Overall mortality was 27%, 46% in ICU patients, and 9% in the rest of the cohort. There were no significant differences in co-morbidities between expired patients and the survivors (Table 1).
A total of 19% of patients had evidence of RV dilatation and 17% manifested decreased RV systolic function. RV dilatation or decreased RV systolic function were noted in 24% of the total study population (Table 2).
RV dilatation was significantly more common in expired patients (15% vs 29%, p=0.026) and was associated with increased mortality in patients treated in the ICU (HR 2.966, 95%CI 1.067-8.243, p=0.037), who did not need require positive pressure ventilation, IV pressor support or acute hemodialysis (Table 3 and Figure 1).

Conclusions: In hospitalized COVID-19 patients without a history of pulmonary hypertension, RV dilatation is associated with a 2-fold increase in in-patient mortality and a 3-fold increase in ICU mortality.

F6

Hidden Primary Malignant Melanoma of the Lung: A Case of Tumor Seeding Along Biopsy Tract

Khan, S. MD , Gillenwater, S. MD , Gonzalez, M. MD , Rivera, J. MD , Lavina, A. MD, Woytanowski, J. MD, AlShelli, I. MD

Introduction: Percutaneous transthoracic needle biopsy (PTNB) of the lung can help guide therapy in patients with abnormal lung findings. Although tumor seeding along the PTNB route has been reported, it is a relatively rare complication1,2. We present a case of a primary malignant melanoma of the lung with a malignant pleural effusion, likely a result of tumor seeding through the PTNB tract. Further studies are required to adequately risk-stratify and help guide treatment in the future.

Case Report: 77 year old male never-smoker with a history hypertension and coronary artery disease presented to the emergency department complaining of cough and dyspnea on exertion. Computed tomography (CT) of the chest showed a right lower lobe bronchopneumonia as well as multiple discreet lung nodules measuring up to 11 millimeters (mm). He was treated with antibiotics and followed up in pulmonary clinic with repeat CT Chest three months later showing increased size of previous pulmonary nodules. He underwent navigational Bronchoscopy with biopsy of a left upper lobe (LUL) nodule. Pathology showed focal chronic inflammation and occasional eosinophils. Cultures were negative and cytology was negative for malignant cells. He subsequently underwent a CT guided lung biopsy of a 12 mm nodule within the left lingula (figure A). Pathology revealed malignant melanoma. He presented 4 weeks later for worsening dyspnea and was found to have a large left sided pleural effusion (figure B). Fluid cytology was positive for metastatic melanoma. Positron emission tomography (PET) scan showed increased uptake within the lung nodules, proximal stomach, and inguinal lymph nodes. He subsequently had rapid progression of his malignancy and passed away a few months later.

Discussion: Tumor seeding along the needle biopsy tract is a relatively rare complication of PTNB. A study by Tomiyama N. et al in 2006 evaluated 9,783 lung biopsies from 124 centers in Japan, out of which 0.061% had tumor seeding along the biopsy route3. Interestingly, our patient had no known history of melanoma and no skin lesions to suggest a primary skin melanoma. Cases of malignant melanoma dissemination through needle tract routes have been reported in the skin, eyes (ocular melanoma)4, and GI tract5. However, Pleural inoculation of melanoma after a lung biopsy is rare and has been reported only once to the best of our knowledge6,7.

Conclusion: Although the incidence of tumor seeding may be underestimated due to the relatively late presentation of such complications, further studies are needed to help establish standard of care and assist physicians in avoiding such complications in the future.

F7

The Outlier: The Unsuspected Case of Pulmonary Adenocarcinoma

Zadesha Gordon MD, Kushinga Bvute MD, Danielle Little MD

Introduction: About 10 – 20% of lung cancers occur in non-smoking adults in the US; the pathology of 50% – 60% of these is adenocarcinoma. Lung cancer screening is recommended at age 50 to 80 for those who have a 20-year smoking history who currently smoke or quit within 15 years. However, those without the risk factors for screening may be overlooked. This case illustrates a patient with incidental findings of lung adenocarcinoma

Case Presentation: A 65-year-old female with history of osteoporosis, Rheumatoid Arthritis, Methotrexate induced pulmonary fibrosis, and congenital left ureter duplication with left ureteral reimplantation, presented to an outpatient clinic for management of recurrent MDR UTI. She was referred to urology who deemed her eligible for nephrectomy. Pre-operative Chest X-ray showed a 3 cm right lateral lung region of abnormal density. A follow up Chest CT showed a pleural-based, right upper lobe, spiculated nodule suspicious for malignancy, and bibasilar interstitial fibrosis with honeycombing. A lung biopsy revealed a well-differentiated adenocarcinoma with mixed acinar and lepidoc pattern. Six months after her nephrectomy, she underwent an uncomplicated right-pulmonary wedge resection with surgical pathology confirming adenocarcinoma with non-necrotizing epithelioid granulomata of uninvolved lung tissue. The patient returned to the outpatient clinic for a follow-up. Additional risk factors for lung cancer were explored, and she denied a smoking history, second-hand smoking, family history, or environmental risks associated with lung cancer.

Discussion: Although there are well established risk factors for lung cancer, there are some patients with lung cancer who miss the criteria for screening. Lung adenocarcinoma comprises 50 -60% of lung cancers in nonsmokers, with 65 as the mean age of diagnosis. Perhaps age, along with other risk factors for lung cancer, could be included or considered in the guidelines for lung cancer screening as early detection is associated with improved clinical outcomes.

F8

All that infarcts is not clot: A rare case of Pulmonary Epithelioid Angiosarcoma.

Rajaganesh Rajagopalan MD, Tulsi Shah MD, Ali Jiwani MD and Guillermo Garrido-Rosa MD.

Introduction: Angiosarcoma of the lung is very rare. We present a patient with a pulmonary infarct who was subsequently diagnosed with an epithelioid angiosarcoma.

Case presentation: A 22 year old female presented to the pulmonary clinic with an incidentally noted lung consolidation on a CT abdomen & pelvis done to evaluate abdominal pain. The patient denied respiratory and constitutional symptoms. The remainder of her history was non-contributory except for OCP use and daily use of nicotine vapes. Repeat imaging done 3 weeks later revealed obstruction of the right superior lobar pulmonary artery and worsening right lower lobe consolidation. Bronchoalveolar lavage of the right lower lobe superior segment and Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) at stations 7 and 11R were non diagnostic. 3 weeks later, she had worsening right lower lobe consolidation. Robotic Navigational Bronchoscopy (Ion ™) guided biopsies revealed organizing thrombus with infarctive necrosis. EBUS-TBNA at stations 4R, 7 and 11R was non diagnostic. Therapeutic anticoagulation was initiated to treat a biopsy proven pulmonary infarct. 3 weeks later, she was readmitted for pleuritic chest pain with progression of right lower lobe consolidation and right pulmonary artery thrombosis. Video Assisted Thoracoscopic right middle and lower lobectomy with mediastinoscopy was performed. 99% of the specimen was necrotic and was sent to Brigham and Women's Hospital. Epithelioid angiosarcoma was diagnosed.

Discussion: Angiosarcoma can mimic thrombosis and is usually diagnosed after metastases. Our patient was diagnosed with a pulmonary infarct based on radiological findings corroborated by pathological findings from bronchoscopic tissue sampling. The histopathological findings required to diagnose an angiosarcoma may not be discernible on transbronchial biopsies or needle aspirations and may necessitate a larger specimen.

Conclusion:Pulmonary angiosarcoma should be considered as a differential diagnosis in patients with a pulmonary infarct. Prompt surgical intervention may expedite the diagnosis of pulmonary angiosarcoma.

F9

Invasive group B Streptococcus from a periprosthetic joint abscess leading to mitral valve endocarditis and severe ARDS

Czarina Teano, MD, Lyanne Rolon Rosario, MD, Alfonso Manotas, MD, Mauricio Danckers, MD, Daniel Heller, MD

Introduction: Acute Respiratory Distress Syndrome (ARDS) can be a complication of severe sepsis typically involving infections of the pulmonary system. Skin and joint infections are less frequently associated with the development of ARDS, with an incidence of less than 6%. Invasive Group B Streptococcus (GBS) leading to ARDS is rare in nonpregnant adults with a mortality rate of up to 90%. We report an unusual case of ARDS from invasive GBS, treated with antibiotics and hip revision.

Case Description: A 58-year old female with cirrhosis and recent hip arthroplasty presented with altered mental status. She developed progressive hypoxemia requiring endotracheal intubation and initiation of mechanical ventilation. Her arterial blood gas revealed a P/F ratio of 77, consistent with ARDS. CT of the chest/abdomen revealed multifocal pneumonia and partially visualized right hip/thigh fluid collection. Blood cultures resulted in GBS. She was treated with ceftriaxone for 3 weeks and lung protective ventilation as per ARDSNet protocol. Further history revealed that the patient had complaints of hip pain prior to arrival. Ultrasound of the hip revealed a large 12.7 x 8.7 x 6.2 cm complex fluid collection, which was drained, resulting in GBS. Persistent bacteremia prompted a transesophageal echogram, revealing a 1.3 cm vegetation on the mitral valve. She underwent washout and revision of the hip, revealing a large amount of purulent liquid deep in the hip fascia. Her repeated chest imaging and oxygenation improved, and was extubated on Day 14 and later discharged to a long-term care facility on Day 28.

Conclusion: ARDS caused by GBS bacteremia is rare in nonpregnant adults. Prompt identification and source control is crucial in the management of critically ill patients. Our case illustrates the importance of careful history in the guidance of proper workup.

F10

Severe Acute Flash Pulmonary Edema in Patient with Solitary Lung Following AV Nodal Ablation and Dual-Chamber Pacemaker Placement

Hadeer Sinawe M.D., Joseph Salami M.D., Suhad Al Omaishi M.D., Khalil Nassar B.S., Maryellen Campbell MS4

Introduction: Severe flash pulmonary edema is a rarely noted sequelae of atrioventricular node ablation and pacemaker placement. If not treated promptly with utmost concern for airway protection and aggressive diuresis, the consequences are dire. In this case, we present a middle-aged female with a solitary lung and paroxysmal atrial fibrillation who underwent nodal ablation and pacemaker placement complicated by subsequent flash pulmonary edema, requiring endotracheal intubation.

Case: A 62-year-old female with a past medical history of atrial flutter on Apixaban, hypertension, and left pneumonectomy following a gunshot wound in 1981 presents to the emergency room with palpitations, tachycardia, and dyspnea. She states that she felt her heart racing, which prompted her to manually check her heart rate. She was scheduled to receive a planned pacemaker placement in the afternoon following failed medical management, multiple ablations, and loop recorder placement but instead presented to the emergency room due to her symptoms. She denied any presyncope, syncope, lightheadedness, dizziness, weakness, or fatigue. She reports dyspnea on exertion. She is regularly seen outpatient by electrophysiology and cardiology, and discontinued flecainide and apixaban in preparation for procedure. The patient was found to be tachycardic at 113. EKG revealed sinus tachycardia. Following atrioventricular nodal ablation and dual-chamber pacemaker placement, the patient was found to be hypoxic and in acute severe respiratory distress; chest radiograph revealed severe flash pulmonary edema. The patient was intubated and subsequently extubated in 24 hours following aggressive diuresis in the ICU. Resolution was tracked by a series of chest radiographs and clinical course.

Discussion: This case highlights the rare and underreported risk of atrioventricular nodal dyssynchrony with flash pulmonary edema during an atrioventricular nodal ablation and dual-chamber pacemaker placement. Prompt airway protection and aggressive diuresis can protect the patient in the interim from this dangerous complication, especially in this patient with a solitary lung.

F11

A national public health threat: A case of *Carbapenem-resistant Acinetobacter baumannii* pneumonia

Danielle Little, M.D., Lashea Johnson, M.D., Naren Bhupatiraju, M.D., Zadesha Gordon M.D.

Introduction*: Carbapenem-resistant Acinetobacter baumannii (CRAB)* is a multidrug resistant pathogen found in healthcare environments, with pneumonia as the primary site of infection. The Centers of Disease Control and Prevention lists *CRAB* as an urgent public health threat, requiring immediate and aggressive action to control potential outbreaks. Risk factors include prolonged stays in healthcare facilities and contaminated medical devices, such as catheters. Unfortunately, few treatments exist to treat *CRAB* infections, leading to substantial morbidity and mortality rates. This case illustrates the high mortality associated with *CRAB* pneumonia.

Case: 77-year old male with a past medical history of recurrent pleural effusions treated with an indwelling pleural catheter presented to the ED from a skilled nursing facility with respiratory distress. Upon arrival, the patient was severely hypoxic and urgently intubated. Chest x-ray showed a large right pleural effusion, which was promptly drained. Blood, pleural fluid, and sputum cultures were obtained, and he was started on broad spectrum antibiotics. Sputum cultures grew *CRAB* sensitive to cifedecoral on day 4 of hospitalization. Antibiotics were changed to polymyxin B and cifedecoral, but despite this, the patient further deteriorated and ultimately expired four days later.

Discussion*: CRAB* is a national nosocomial threat. Due to its resistance to most antibiotics, including carbapenems, *CRAB* infections are challenging to treat. In 2017, there were 8,500 cases of *CRAB*-related infections among hospitalized patients in the US, resulting in 700 deaths. Therapeutic options for *CRAB* infections are limited and have uncertain efficacy. Although polymyxin B is the preferred therapeutic agent, there are no randomized trials addressing its efficacy in *CRAB* infection. Some isolates of *CRAB* have shown susceptibility to cifedecoral, but there is only limited data showing improved clinical outcomes. Given the high morbidity of *CRAB* infections and the few drug options available, further investigation of treatment is warranted.

F12

Calm after the storm? Post-COVID Thromboprophylaxis Failure

Claudia Tejera, MD, Jessica Baek, MD, Gustavo Avila, MD, Andrew Fischer, MD.

Introduction: Venous thromboembolism (VTE) is a leading cause of morbidity and mortality worldwide and this high incidence is often secondary to thromboprophylaxis failure more than omission. Studies have demonstrated that an extensive pro-inflammatory and hypercoagulable state is present in COVID-19 patients, however the duration of this state post-infection is unclear. Early identification of additional risk factors for thromboprophylaxis failure warrants a closer follow up.

Case Description: We present a 47-year-old man with past medical history of obesity, recent COVID-19 pneumonia and subsequently ventilator dependent respiratory failure (VDRF) who presented with one-day history of worsening abdominal pain and bloating due to pneumoperitoneum secondary to PEG tube placement 9 days prior. Patient was discharged after a prolonged admission for management of respiratory failure in the setting of COVID-19 infection that was complicated with severe hemodynamic compromising, subsequently managed with mechanical ventilation and V-V ECMO. Patient received standard DVT prophylaxis since admission. On presentation, patient was tachycardic in moderate respiratory distress and had an oxygen saturation of 94% on 75% FiO2. Further work-up revealed COVID PCR negative, elevated Ferritin of 1130 ng/mL, elevated NT-proB type Natriuretic peptide (NT-Pro BNP) of 467 pg/mL and elevated D-Dimer of 914 ng/mL. ABG revealed decreased partial pressure of oxygen and elevated A-a gradient. Computed tomography angiogram revealed moderate sized right upper lobe pulmonary embolism with no evidence of right heart strain. Patient was started on heparin drip during admission and then switched to Apixaban upon discharge.

Discussion : The development of VTE despite prophylaxis is not uncommon. The rates of DVT in the absence of prophylaxis range between 40 and 60% and 2-5% in its presence. It is pertinent learning to identify high risk patients to develop this condition and consider anticoagulation at a higher dose or for a longer period of time even after discharge. Patients with COVID-19 infection possess and additional risk from the underlying hypercoagulable state and a worse outcome is expected. The high risk of thrombosis in COVID-19 is demonstrated by the increase in d-dimer, which was found to be the most significant change in coagulation parameters in these group, suggesting increased thrombin production and activation of fibrinolysis. There is therefore a need to identify the increased risk of VTE at an early stage and to prevent thrombotic events and organ damage as far as possible.

Conclusion: More data is needed on how long this hypercoagulability period persists and how long should we continue DVT prophylaxis in this special population. This case aims to bring more awareness about being attentive on thrombotic complications and consider extending DVT prophylaxis in patients with higher prothrombotic risk.

F13

Dyspnea and wheeze due to central airway metastatic endometrial carcinoma in the absence of abdomino-pelvic spread

Jay S. Maizes, MD, FCCP. Ali Mustafa, DO.

Introduction: Many patients are diagnosed with lung cancer as an incidental finding or after the onset of overt symptoms which commonly include dyspnea, cough, and/or hemoptysis. Often, patients who present with symptomatic pulmonary carcinoma face a poor prognosis. Metastatic carcinomas of endometrial origin are rarely associated with pulmonary metastasis in the absence of abdominopelvic spread.

Case: We report a case of a 62-year-old female presenting to the emergency department with progressively worsening dyspnea, cough, and wheezing worked up for possible asthma and/or COPD. She has a remote history of endometrial carcinoma which was treated 6 years ago via a total hysterectomy with bilateral salpingectomy and oophorectomy followed by radiation therapy. Chest CT Angiography showed a subcarinal mass with what appears to be contiguous invasion into the bronchi and associated narrowing into the bilateral mainstem, and also right lower lobe cavitary lesion, and left lower lobe nodule. Subsequent PET-CT imaging showed a hypermetabolic subcarinal lesion (2.7 cm), hypermetabolic right lower lobe cavitary lesion (3 cm), and minimally metabolic left lower lobe nodule (12 mm). No intra-abdominal spread was observed on PET-CT. The patient was initially treated with bronchodilators and steroids before undergoing bronchoscopy which revealed a mass growing into the main proximal airways at the level of the carina. Intraoperative pathology was suspicious for possible small cell carcinoma. The thoracic surgeon performed a debulking procedure. The patient was discharged with instructions to follow up outpatient with thoracic surgery, medical oncologist, and radiation oncologist.

Discussion: The final pathology analysis came back with endometrial carcinoma invasion into the airway. This case demonstrates two significant points: 1.) Evaluation of wheezing due to central airway disease 2.) Evaluating of gynecologic origin of pulmonary metastasis, even in the absence of any intra-abdominal spread.

F14

Spontaneous pneumothorax: A rare complication of septic pulmonary emboli in a patient with infective endocarditis

Lyanne Rolon-Rosario, MD, Czarina Teano, MD, Shany Quevedo, MD, Michael Vempala, MD, ,Livasky Concepcion Perez, MD

Introduction: Septic pulmonary emboli (SPE) is a common complication that results from infective endocarditis (IE). SPE can also result from septic thrombophlebitis and other infectious processes. A rare, but serious complication of SPE is the development of spontaneous pneumothorax (SPX). To date, only seven cases have been identified in literature with 6 out of the 7 involving males.

Case Description: A 32-year-old female with a history of depression, anxiety, polysubstance abuse and intravenous drug abuse presented with a 1-week history of abdominal pain and cough. On presentation, the patient was febrile and hypoxic. Physical exam findings were significant for a new systolic murmur, chest wall tenderness, and diffuse abdominal pain. Echocardiogram revealed vegetations affecting the tricuspid, aortic and pulmonic valves. CT chest revealed multifocal pneumonia with bilateral innumerable septic emboli and loculated pleural effusions. Blood cultures were positive for MRSA. By Duke's criteria, the patient was subsequently diagnosed with infective endocarditis. On the fifth day of admission, patient became tachypneic and chest x-ray revealed a left-sided pneumothorax, a rare complication of septic pulmonary emboli. Patient was monitored clinically and serial chest x-rays were obtained while remaining on antibiotic therapy. Pneumothorax remained stable, the patient eventually improved and was safely discharged without surgical intervention.

Discussion: Although rare, SPX can develop from SPE. Cases identified in literature report the development of SPX to be as early as day of admission up to the fifteenth day. Prompt recognition of this complication by intensivists is crucial in prevention of further lethal complications in patients presenting with sudden onset dyspnea or hemodynamic instability in the setting if SEP.

F15

Hemoptysis from Angiosarcoma

Naren Bhupatiraju MD, Fatima Ahson MD, Luisa Barrueto DO, Teresa Koger MD, Ibrahim Ali MD

Introduction: Angiosarcoma is a cancer that can form in blood or lymphatic vessels. When involving the lung, it is usually secondary to metastasis and is quite rare. Here we present a case of angiosarcoma in the lung secondary to metastasis.

Case Presentation: 47 year old female with past medical history of hypothyroidism presented for shortness of breath. Stated she had an associated cough for several days but had an episode of hemoptysis the day of admission. CT scan showed right perihilar mass occluding pulmonary arterial branch to right upper lobe, invasion of right main pulmonary artery, right apical mass as well as enlarged right axillary lymph nodes, left chest wall mass, and multiple sclerotic osseous lesions. Biopsy of left chest wall mass showed angiosarcoma. Her hospital course was complicated by hemithorax and underwent thoracoscopic decortication, parietal pleurectomy and pleurodesis. Patient was discharged with follow up with a sarcoma specialist.

Discussion: Angiosarcoma of the lung is usually secondary to metastasis and is rare. Risk factors include anything that changes DNA in blood vessels or lymph nodes. These involve factors such as radiation, edema of lymph nodes causing vessel damage, toxic chemicals such as vinyl chloride and arsenic. There does seem to be a genetic component to it as well given patients with neurofibromatosis and the BRCA mutations are more likely to develop angiosarcoma. Presentation involving the lung is often similar to the case presented, involving nonspecific symptoms such as cough, hemoptysis and dyspnea. CT chest commonly shows multiple lesions. Treatment can involve chemotherapy, radiation, or immunotherapy but unfortunately the prognosis of angiosarcoma of the lung is grim and has nearly a 100% mortality a few months after diagnosis.

F16

Bilateral ground glass opacities aren't always what they seem: A reminder that COVID-19 is not the only thing that can take your breath away

Teresa Koger MD, Andrew Arteaga DO, Steven Shiba M.S., Luisa Barrueto DO, Fatima Ahson MD

In the midst of the all-encompassing COVID-19 pandemic, it is reasonable to have high suspicion in a patient presenting with respiratory symptoms and classic radiologic findings of bilateral ground glass opacities of the COVID-19 viral illness. But what about all of the other potential differentials with similar presentations to COVID-19? We present a case of Pneumocystis pneumonia with superimposed Stenotrophomonas pneumonia in the setting of newly diagnosed HIV infection with a severely decreased CD4 count. This is a case of a 53-year-old female who presented with complaints of shortness of breath over the course of three weeks that failed to improve with outpatient management consisting of prednisone, albuterol, and doxycycline. On admission, a computed tomography (CT) of the chest revealed superimposed diffuse ground glass opacities bilaterally, features suggestive of COVID-19 pneumonia. Even though initial COVID-19 RNA Rapid ID was negative, there was still high suspicion of COVID-19 given the patient's lack of response to treatment with IV antibiotics and their significant hypoxemia. It was several days before the patient's HIV-1 antibody test came back positive and the CD4 count was found to be 18. It was then that the patient underwent a diagnostic and therapeutic bronchoscopy. Unfortunately, even though she was started on the appropriate treatment with Bactrim, her respiratory status continued to deteriorate, and she had to be intubated for worsening hypoxic respiratory failure. Although presently it feels like COVID-19 is everywhere we turn, we cannot neglect other pathogens that may present with similar clinical, laboratory, and radiologic findings. Our case supports the need to explore these differentials in order to provide the appropriate treatment regimen in a timely manner.

F17

Hepatopulmonary syndrome: A frequently overlooked diagnosis

Toni-Ann Smith MD, Jessica Baek MD, Yeiniel Rodriguez Torrado MD, Sheyla Paredes Aller MD

Introduction: Hepatopulmonary syndrome (HPS) is a disorder characterized by dilation of pulmonary vasculature in the presence of liver disease or portal hypertension, which causes a reduction in arterial oxygen saturation (PaO_2). It is the most common cause of respiratory insufficiency in patients with chronic liver disease.

Case Description: Patient is 59-year-old male with history of alcoholic cirrhosis who was transferred from an outside facility for liver transplant evaluation. Prior to transfer, patient underwent cardiac catheterization due to concern for HPS and severe pulmonary hypertension in the setting of acute hypoxemic respiratory failure. Patient was found to have low right sided pressures with high PaO_2. Transthoracic echocardiogram was performed, which showed late appearing bubbles to left heart suggestive of extracardiac shunt. Ventilation-perfusion scan revealed extrapulmonary shunt fraction of 39.7%. CT chest was negative for any large central pulmonary emboli. Shortly upon arrival, patient's condition deteriorated, requiring intubation. Given his worsening clinical condition, the family opted for hospice care.

Discussion: HPS is commonly associated with portal hypertension due to chronic liver disease but can also be seen in portal hypertension without any underlying liver disease. HPS is often missed or diagnosed late as dyspnea is the predominant symptom, which is very nonspecific and common in patients with underlying liver disease. The most specific presentation is platypnea, defined as breathlessness in the upright position, improved in recumbent position. However, as many as 88% of HPS patients also present with orthodeoxia, which is defined as a decrease in PaO2 or SpO_2 when moving from supine to standing position. In the absence of an alternative explanation, HPS should be suspected in chronic liver disease patients who present with respiratory failure. Currently, no effective medical therapy for HPS exists. Liver transplantation is the only successful treatment hence early diagnosis is important to prevent morbidity and ultimately mortality from this syndrome.

F18

Diffuse alveolar hemorrhage in the setting of COVID pneumonia

Davide Fox, MD, Gustavo Lagrotta, MD, Daniel Heller, MD, Danial Arshed MD

Introduction: Diffuse alveolar hemorrhage (DAH)1 is a cause of respiratory failure that is diagnosed with Bronchoalveolar lavage (BAL) with a mortality rate roughly 20%2. It is usually caused by autoimmune disorders or viral infections, but has to the best of our knowledge not been described in the setting of COVID-19. Presented below is a case of DAH as the initial presentation of COVID-19 pneumonia.

Case: A 21 year old male presented obtunded and in acute respiratory distress. An ABG showed marked hypoxemia with a pO2 of 51, and the patient was intubated for acute respiratory distress syndrome (ARDS). A COVID test was ordered and was found to be positive. CT scan upon admission showed coalescing consolidations of the bilateral lung bases concerning for diffuse alveolar damage. A bronchoscopy performed was consistent with a diagnosis of DAH. The patient was treated with low tidal volume ventilation per ARDS protocol, high dose systemic dexamethasone, and baricitinib. His oxygenation requirements improved after the initiation of the systemic glucocorticoids and he was subsequently liberated from the ventilator and discharged.

Discussion: COVID-19 has been associated with a wide variety of clinical symptoms with a wide spectrum of severity. Its management has been compared to other viral illnesses and is mainly supportive although moderate dose steroids have been shown to be beneficial in cases of hypoxemia3. However, high dose steroids have not been shown to be beneficial 4. Although Influenzae5 has been well documented in the literature as a cause of DAH, after extensive literature review we were not able to find reported cases of DAH in the setting of SARS, MERS, or COVID-19 pneumonia. Hemoptysis is usually a presenting symptom in DAH, however up to 20% of patients with DAH may lack hemoptysis1, such as in our case. BAL findings confirmed in our case confirmed DAH. Rapid initiation of steroids and immunologic agents may improve outcomes2.

Closing: Physicians should maintain a high index of suspicion for DAH when treating patients with acute hypoxemic failure due to COVID-19 pneumonia with characteristic signs of DAH on imaging. Rapid initiation of high dose systemic steroids and other immunomodulators may be useful, however further studies are necessary.

F19

A case of severe obstructive ventilatory impairment due to alveolar septal amyloidosis

Omair Tahir, Aditya Sahay, Adil Bhutta, Hassan Baig

Background: Amyloidosis is a heterogeneous group of diseases characterized by the deposition of amyloid fibrils in the extracellular matrix of tissues and organs. Diffuse alveolar septal amyloidosis is a form of pulmonary amyloidosis, which is associated with systemic AL amyloidosis. This is characterized by parenchymal destruction due to amyloid fibril deposition, which results in restrictive ventilatory impairment on pulmonary function tests. We describe an unusual case of progressively worsening obstructive ventilatory impairment, which is related to significant cystic destruction from alveolar septal amyloidosis.

Case report: 52-year-old African American female with history significant for remote seizure disorder who was initially evaluated for progressive shortness of breath in 2020. Initial pulmonary evaluation showed preserved spirometry. The patient was noted to have exertional hypoxemia, requiring 2LPM. CT scan of chest showed mid to lower lung field predominant bilateral cystic changes. Laboratory tests included serum protein electrophoresis and free light chains. A surgical lung biopsy showed "Diffuse alveolar septal pattern of amyloidosis, that is associated with extensive multinucleated giant cell reaction." The patient was evaluated in an amyloidosis clinic and started systemic therapy. Unfortunately, she has experienced a progressive decline in her pulmonary function, despite treatment. Subsequent pulmonary function tests have shown worsening obstructive ventilatory impairment. As one might expect, bronchodilator challenge did not demonstrate significant response in this patient. CT scans show worsening cystic changes.

Discussion: We describe this case to highlight that alveolar septal amyloidosis can be associated with obstructive ventilatory impairment in some situations. We hypothesize that this is a result of diffuse progressive cystic changes. It is sometimes presumed that obstruction is related to bronchial or bronchiolar deposition of amyloid fibrils, however, this was not observed in pathology specimens. No obvious tracheobronchial lesions were seen on chest CT scan either.

F20

Apixaban associated leukocytoclastic vasculitis complicated by TRALI

Yeiniel R. Torrado M.D., Jessica Baek M.D., Toni-Ann Smith M.D, Rathakrishnan, Ranga M.D

Introduction: Leukocytoclastic vasculitis (LCV) is an immune complex-mediated vasculitis of small vessels that usually presents with palpable purpuric skin lesions in the lower extremities. Many different classes of drugs have been implicated as causes of this condition; however, apixaban is only described in a few case reports as the potential cause. Herein, we describe a case of apixaban-associated LCV, complicated by a transfusion-related acute lung injury (TRALI).

Case Presentation: Patient was a 72-year-old male with history of chronic atrial fibrillation on apixaban, who presented with 2-week history of purpuric papules in the bilateral upper and lower extremities. Patient underwent right lower extremity skin biopsy, which showed findings consistent with IgA vasculitis, confirmed with direct immunofluorescence. Identified as the potential cause, apixaban was discontinued immediately and treatment with steroids was started. Hospital course was further complicated by worsening renal function and anemia, requiring transfusion. However, shortly after the transfusion with leukoreduced and irradiated blood, patient developed acute hypoxic respiratory failure due to suspected transfusion-related acute lung injury, illustrated on chest radiograph as new interstitial opacities. Patient refused any aggressive life sustaining measures and subsequently expired from cardiac arrest.

Discussion: Although rare, multiple anticoagulant drugs have being reported to be associated with cutaneous small vessel vasculitis, including warfarin, heparin, and streptokinase. 40% of LCV are drug-induced with anticoagulants occupying only a small portion. As described in this case, TRALI was an unexpected complication that was not reported in previous cases of LCV. Although the exact pathogenesis of TRALI is unclear, one of the proposed mechanisms is via a two-hit mechanism involving neutrophil sequestration, priming, and activation. There is currently no data showing increased risk of TRALI in patients with LCV. The only recommended management for TRALI is supportive care after the discontinuation of transfusion. Since TRALI is the leading cause of transfusion-related fatalities, further studies are warranted to determine the pathophysiology and proper management of such complications.

F21

Concomitant tracheal bronchus with tracheomalacia: Coincidence or association?

Jessica Baek MD, Armando Rodriguez MD, Claudia Tejera MD, Christopher Wood MD, Adam Friedlander MD

Introduction: Tracheal bronchus is an anatomical variant in which a congenital accessory bronchus arises from the trachea. It is a common finding in pigs, which is why it is sometimes referred to as "pig bronchus." Even though it is usually diagnosed in childhood, incidental findings in adulthood have been reported.

Case description: A 65-year-old woman with history of diastolic heart failure, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea, and recurrent pneumonia was hospitalized for worsening shortness of breath. Patient was initially managed with diuresis and non-invasive ventilation. Due to worsening hypercarbic hypoxemic respiratory failure, patient required endotracheal intubation and mechanical ventilation. Flexible bronchoscopy showed severe tracheobronchomalacia. Patient was also found to have an accessory bronchus visualized 0.5cm proximal to the carina. After a prolonged hospital course, patient was discharged to a long-term acute care facility.

Discussion: Tracheal bronchus occurs more commonly on the right side and has been associated with other congenital anomalies, such as tracheal stenosis, Down syndrome, lobar emphysema, cyanotic cardiac lesions, and tracheal hypoplasia. Two main types have been described: supernumerary and displaced. Common complications in the pediatric population include recurrent pneumonias, stridor, respiratory distress, and atelectasis. Its association with acquired tracheomalacia is not very well understood in adults and may pose challenges in patients that require emergent intubation. Tracheomalacia, which refers to softening of the tracheal cartilage, clinically manifests as an excessive dynamic airway collapse during expiration and is most commonly due to recurrent mechanical or biological insult to the airway. It is common in patients with prolonged mechanical ventilation, tracheostomies, bronchiectasis, and COPD, as shown in this case. This case suggests that presence of tracheal bronchus could contribute to recurrent pneumonias and ultimately lead to the development of tracheomalacia. Further study is warranted to determine proper treatment of the concomitant conditions.

F22

Acute inflammatory demyelinating syndrome post Covid-19 infection: A case report

Gonzalez, M. MD, De Salvio, F. MS, Khan, S. MD, Gillenwater, S. MD

Introduction: The novel coronavirus disease 2019 (COVID-19) has caused over 278 million cases and just under 5.4 million deaths since it was initially recognized in Wuhan, China, on December 31, 2019 (1). COVID-19 is characterized by the development of bilateral lung infiltrates and a surge of inflammatory cytokines that lead to acute respiratory failure. Neurological complications of COVID-19 include headaches, encephalitis, seizures, anosmia, dizziness, and dysgeusia (2). A less common complication is acute inflammatory demyelinating polyneuropathy (AIDP), the most frequent variant of Guillain-Barre syndrome (3). This case report presents a patient with progressive ascending flaccid paralysis and dysesthesia in the lower extremities immediately following COVID-19 pneumonia.

Case Presentation: A 69 year-old male presented to the emergency department reporting one week history of worsening dyspnea and new-onset progressive weakness, paraesthesia, and pain involving the bilateral upper and lower extremities. Significant past medical history included deep vein thrombosis and recent recovery from COVID-19 pneumonia 14 days prior. He was treated with monoclonal antibody casivirimab-imdevimab and dexamethasone. Vital signs were unremarkable. Muscle examination was significant for bilateral lower and right upper extremity weakness (4/5 right deltoid, 2/5 bilateral hip and 3/5 bilateral distal lower extremity). Deep tendon reflexes were 2/4 in the upper extremities and absent in the lower extremities. At baseline, patient reported being very active and independent. He reported neither weakness during nor immediately following COVID-19 pneumonia. Laboratory analysis was unremarkable. Cervical and brain magnetic resonance imaging and computed tomography showed no evidence of acute intracranial pathologies. Lumbar puncture was performed and showed albuminocytologic dissociation with a protein level of 57 mg/dL with no evidence of infection. Diagnosis of AIPD was made. The patient underwent five sessions of plasmapheresis with drastic improvement of peripheral weakness and paresthesias and was ultimately discharged to acute rehab.

Discussion: Although the etiology is still not well understood, GBS and its variants are immune-mediated neuropathies (4). Molecular mimicry is one of the most accepted hypotheses to explain this phenomenon (5). Antecedent viral or bacterial infections have been found in over 70% of cases of GBS. The immune response triggers antibody production during the infection that attacks the gangliosides in the host nerves. This cross-reactivity can damage both myelin and axons of peripheral nerves, ultimately causing neuropathic symptoms characteristic of GBS (5). COVID-19 has been linked in numerous case series to AIDP. Which patients are most susceptible to post-COVID AIDP is not fully understood. There appears to be a higher prevalence amongst males (6-7). To our knowledge there have been no cases of casivirimab-imdevimab associated AIDP.

Conclusion: We add to the growing body of literature establishing a causal relationship between COVID-19 and AIDP. The link between COVID-19 and AIDP is not well understood. However, given the increasing number of reports, physicians should suspect AIDP following COVID-19 infection in patients with appropriate symptoms.

F23

COVID-19 associated encephalopathy in a kidney-transplant patient

Richard Shalmiyev, MD, MPH, Lyanne Rolon Rosario, MD, Ana Martinez, MD, Raiko Diaz, DO, Daniel Heller, MD

Introduction: Encephalopathy is a well-documented sequela of SARS-CoV2 infection; however, few cases have been reported in transplant patients, and to our knowledge, none in kidney-transplant patients.[1,2] This report describes a case of COVID-19 associated encephalopathy in an immunosuppressed kidney-transplant patient.

Methods: Data was collected during the admission.

Results: A 50-year-old male with a history of diabetes, poorly-controlled hypertension, left renal transplant in 1988 on Tacrolimus and Mycophenolate, and COVID-19 infection 15 days prior to this admission presented with an acute change in mental status - fully independent the night prior but now only arousable to pain. Stroke work-up came back negative but labs were significant for WBC 17e3, blood glucose 1622 mg/dL, anion gap of 17, positive acetones, negative COVID NAA/PCR, positive COVID IgG, CRP 6.3 mg/dL, ESR 43 mm/hr, negative urine toxicology, and CSF with an elevated protein of 82 mg/dL. Home immunosuppressive agents included Mycophenolate 180mg twice daily and Tacrolimus 4mg twice daily, which showed a trough level of 17.1 ng/mL. He was admitted for acute encephalopathy secondary to multiple possible etiologies. Mycophenolate was continued but Tacrolimus was stopped until he was within his goal range of 3-5 ng/mL. His chemistry was corrected but he remained altered and ultimately intubated for airway protection. All further testing came back negative, including syphilis, CMV, hepatitis, HSV, HIV, VZV and an extensive rheumatologic workup. MRI showed minimal hyperintense foci with no acute findings and no evidence of PRES. MRA/MRV showed no thrombosis. He unexpectedly began improving on day 10 and was discharged home 4 weeks after admission.

Conclusion: Few studies exist describing the association surrounding COVID-19 encephalopathy and patients on immunosuppression.[2] While their symptoms may mimic other neurologic conditions such as PRES, COVID-19 associated encephalopathy should be considered in altered solid-organ transplant patients on immunosuppression.

F24

HSV pneumonia with generalized rash- A rare entity

Mahapatra S ,Railwah C Mehta J

Introduction: Data suggest that severe pulmonary involvement in HVS1 infection associated with immunocompetent individual is very rare and the diagnosis is challenging as it has similar presentation like other pneumonia. It is associated with significant mortality in critically ill patients. We present a unique case of HSV pneumonia with diffused rash and myopathy.

Case summary: The patient is a 59 y/f with history of Fibromyalgia, cervical and lumbar radiculopathy s/p spinal surgery who was admitted for worsening LE weakness since 2016 along with urinary and fecal incontinence and diffuse macular and petechial rash. History is negative for any malignancy or immunosuppression. He also noticed off late weak hand grips and difficulty chewing and swallowing which prompted him to use Decadron off label x 3 weeks before admission with no improvement. Shortly after admission he developed new onset acute hypoxemic respiratory failure requiring 2L NC on rest, Initial imaging showed multifocal areas of GGOs throughout both lungs with associated interlobular septa thickening and was started on empiric coverage for CAP. During the course his SOB worsened and rash became more erythematous. Antibiotics was broadened with no improvement. Repeat imaging of the chest showed interval worsening of the GGOs along with increasing b/l effusion. Steroid's dosage was also increased with no improvement. Comprehensive autoimmune workup was negative for any autoimmune pathologies or vasculitis. Pneumonia workup for typical and atypical was negative as well. Skin and Bronchial biopsy showed viral cytopathic changes conclusive of herpes cutaneous infection and HSV PCR positive. She was started on Acyclovir and discharged on valacyclovir. We were able to wean her off from the oxygen and rash improved. Extensive work up for myopathy including myasthenia gravis was negative. Myopathy was steroid induced.

Discussion: Given its rarity and atypical findings its of paramount importance to have HSV pneumonia as one of the differentials in immunocompetent patients. Unlike other case reports of HSV pneumonia our patient. Our patient significantly improved with antivirals.

F25

Review of pathophysiology of respiratory failure in hepatopulmonary syndrome

Shivani Desai, DO; Alyssa Gries, DO; RaeAnn Tourangeau-Young, MD

Introduction: We review a case and the underlying pathophysiology of respiratory failure secondary to hepatopulmonary syndrome due to chronic cirrhosis.

Case Presentation: A 59-year-old male with significant past medical history of liver cirrhosis presented to the ED from a LTACH to undergo a left and right heart catheterization. Patient reports he had been having worsening shortness of breath over the last month. He is currently requiring oxygen, 6L nasal cannula. Due to his chronic cirrhosis he is pending acceptance onto a liver transplant list, therefore he is undergoing further workup with heart catheterization. Pertinent past medical history of recurrent pleural effusions, HFpEF, chronic alcohol use (in remission, 5 years), and CAD s/p 5 stents.

- Transthoracic echocardiogram (TTE) showed preserved ejection fraction, with significance for late crossing of bubbles to the left heart, suspicious for extracardiac shunting. Insufficient tricuspid regurgitation
- Right heart catheterization showed low right-sided pressures and high pulmonary artery O2 saturations (90%).
- Left heart catheterization showed patent stents and an overall high flow system with high output.

Patient ultimately transferred to the local VA hospital. Then from there, would be transferred to a tertiary center for liver transplant. At time of discharge, patient requiring high flow nasal cannula, 25L at 60% FiO2.

Discussion: Following catheterization, there was a question of intracardiac shunting. TTE confirmed shunting but of an extracardiac nature. Normally microbubbles do not make it past the capillaries, but due to dilation of pulmonary vessels and/or arterio-venous malformations, were able to reach the left ventricle.

F26

Benralizumab Associated with Reductions in Asthma Exacerbations, Healthcare Resource Use, and Medical Costs: ZEPHYR 2 Study Results

Donna Carstens MD, Diego Maselli MD, Danni Yang BA, Erin E. Cook ScD, Yen Chung PharmD

Introduction: Benralizumab has demonstrated significant reductions in asthma exacerbations in clinical trial and observational study settings. Real-world data can provide additional insights on the potential benefits of benralizumab.

Methods: This retrospective pre-post intervention cohort study used data from the PatientSource® and DiagnosticSource™ US insurance claims databases (November 2016-June 2020) to examine patients with asthma treated with benralizumab (index). Cohorts of patients aged ≥12 years, with ≥2 records of benralizumab use, and ≥2 asthma exacerbations in the 1-year pre-index period were included. Analyses evaluated reductions in asthma exacerbations and rescue and controller medication use among patients stratified by pre-index peripheral blood eosinophil (EOS) counts, who were biologic-naïve, as well as those who switched to benralizumab from omalizumab or mepolizumab. Pre-post comparisons of healthcare resource use (HRU) and medical costs associated with exacerbations were analyzed in the biologic-naïve patients.

Results: From the 8473 patients who used benralizumab, 1292 were biologic-naïve, 429 were included in the analysis by EOS, and 349 switched from either omalizumab or mepolizumab to benralizumab. All groups experienced a significant reduction in asthma exacerbations post-index vs. pre-index (biologic naïve: 59%; EOS<150 cells/µl: 52%; EOS≥150 cells/µl: 64%; EOS<300 cells/µl: 56%; EOS≥300 cells/µl: 64%; omalizumab switchers: 62%; mepolizumab switchers: 53%; all $p<0.001$) and use of short-acting beta-agonists (SABA). Significant reductions in combination inhaled corticosteroid and long-acting beta-agonists were also observed in most cohorts. The biologic-naïve group experienced significant reductions in HRU and costs of inpatient stays, emergency department, and outpatient visits; all $p<0.001$.

Conclusions: Patients receiving benralizumab experienced significant reductions in asthma exacerbations and SABA use across a wide range of EOS counts, regardless of previous biologic therapy. HRU and medical costs were also decreased in biologic-naïve patients, highlighting the real-world benefit of benralizumab therapy in patients with severe eosinophilic asthma.

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F27

Efficacy and safety of albuterol/budesonide (PT027) in mild-to-moderate asthma: Results of the DENALI study

Bradley E. Chipps, Elliot Israel, Richard Beasley, Reynold A. Panettieri Jr., Frank C. Albers, Christy Cappelletti, Robert Rees, Lynn Dunsire, Eva Johnsson, Anna Danilewicz, Alberto Papi

Introduction: Short-acting β_2-agonists (SABA) provide quick asthma symptom relief but fail to address underlying inflammation. PT027 is a fixed-dose combination of albuterol (a SABA) and budesonide (an inhaled corticosteroid) rescue inhaler, shown to significantly reduce severe asthma exacerbation risk compared with albuterol alone. The Phase 3 DENALI study (NCT03847896) evaluated contributions of the mono-components to albuterol/budesonide lung function efficacy in patients with mild-to-moderate asthma ≥4 years.

Methods: Patients ≥12 years were randomized 1:1:1:1:1 to four-times-daily albuterol/budesonide 180/160 or 180/80 µg, albuterol 180 µg, budesonide 160 µg or placebo for 12 weeks; patients 4-11 years were not included in this analysis set. Dual-primary endpoints were change from baseline in forced expiratory volume in 1 second area under the curve from 0-6 hours (FEV_1, $AUC_{0\text{-}6h}$) over 12 weeks and in trough FEV_1 at Week 12. Secondary endpoints included time to onset, as defined by a 15% improvement in FEV_1 within 30 minutes on Day 1, and duration of effect, and Asthma Control Questionnaire-7 (ACQ-7) responder (≥0.5-point reduction from baseline) analysis at Week 12.

Results: Of 1001 patients randomized, 989 were aged ≥12 years (mean age 48.9 years, 62.2% female). Change from baseline in FEV_1 $AUC_{0\text{-}6h}$ over 12 weeks was greater with albuterol/budesonide 180/160 µg (only dose tested) versus budesonide (least squares mean [LSM] difference 80.7 mL, 95% confidence interval [CI] 28.4-132.9; p=0.003). Change in trough FEV_1 at Week 12 was greater with albuterol/budesonide 180/160 and 180/80 µg versus albuterol (LSM difference 132.8 mL [95% CI 63.6-201.9] and 120.8 mL [95% CI 51.5-190.1], respectively; both $p<0.001$). Median time to onset and duration of effect on Day 1 (responders: 49.7%, 44.0% and 42.9%), was 7.5 and 7.0 minutes vs 9.5 minutes, and 186.9 and 191.4 minutes vs 168.2 minutes, respectively, for albuterol/budesonide 180/160 or 180/80 µg and albuterol. At Week 12, percentages of ACQ-7 responders were 66.5% and 65.5% vs 47.2% with albuterol/budesonide 180/160 or 180/80 µg vs albuterol (odds ratio [OR] 2.3 [95% CI 1.5-3.7] and OR 2.3 [95% CI 1.5-3.6]; both nominally significant), respectively. The safety profiles for both albuterol/budesonide doses were similar to the mono-components.

Conclusions: Both mono-components contributed to albuterol/budesonide efficacy, with the combinations demonstrating superior effects on lung function. Onset and duration of bronchodilation were similar for albuterol/budesonide vs albuterol on Day 1, and more patients experienced a nominal improvement in asthma control at Week 12. The overall clinical profile of albuterol/budesonide observed supports its potential utility as a future novel rescue therapy.

Funding: AstraZeneca

F28

A window of opportunity to prevent exacerbations in intermittent and mild persistent asthma

Miguel Lanz, Michael Pollack, Ileen Gilbert, Hitesh Gandhi, Joseph Tkacz, Njira Lugogo

Introduction: Prior to exacerbations, airway inflammation, symptoms, and short-acting β_2-agonist (SABA) use rise. This study aimed to compare SABA and maintenance therapy use patterns surrounding a serious exacerbation (SE; urgent ambulatory/emergency department visits or hospitalization for asthma) in patients treated as Intermittent or Mild Persistent (Int/M; NAEPP Steps 1/2).

Methods: We evaluated 2010-2017 IBM MarketScan administrative claims for US patients ≥12 years. Patients were indexed on a random SABA and had 1-year eligibility pre- and post-index and ≥1 post-index SABA and/or Step 2 fill. Post-index SE, and SABA and maintenance pre- and post-SE were assessed (unpaired t-test, unadjusted odds ratio [95% confidence interval]; significance $p\leq0.05$).

Results: 323,443 Int/M patients were included (62.0% female; mean(SD) age 34.9(18.2) years, SABA fills 2.7(2.7), SE 1.2(0.5); 16.0% with ≥1 SE. 30 days pre-SE, 24.6% filled SABA and 19.0% maintenance. Odds of SABA vs maintenance fills rose progressively over this period. 7 days post-SE, 62.9% filled SABA and 87.1% maintenance. Despite increased maintenance fills post-SE, 13.2% had ≥2 post-index events.

Conclusions: SE were common in patients with Int/M asthma. In the days before a SE, SABA fills are progressively greater than those for anti-inflammatory therapy. A *Window of Opportunity* to prevent SE for Int/M patients may exist if ICS and SABA were used concomitantly.

Funding: AstraZeneca

F29

Zinpentraxin alfa (PRM-151) for Idiopathic Pulmonary Fibrosis: Design of STARSCAPE, A Phase III Randomized Double-Blind Placebo-Controlled Trial

Luca Richeldi MD, Jürgen Behr MD, Tamera J. Corte MBBS PhD, Vincent Cottin MD, PhD Gisli Jenkins MD, PhD Nikhil Kamath MBBS, Yoshikazu Inoue MD, PhD Steven D. Nathan MD, Ganesh Raghu MD, Jessie Randhawa MBBS, Simon L.F. Walsh MD, PhD Fernando J. Martinez MD

Introduction: Pirfenidone and nintedanib slow the rate of forced vital capacity (FVC) decline in patients with idiopathic pulmonary fibrosis (IPF) but neither halts disease progression. Pentraxin-2 plays biologically relevant roles in wound repair and fibrosis prevention. Plasma pentraxin-2 concentrations are reduced in patients with IPF and correlate with disease severity. Zinpentraxin alfa (previously PRM-151) demonstrated clinically meaningful benefits in patients with IPF in a Phase II trial (NCT02550873). This abstract reports the design of the Phase III trial aiming to further evaluate these findings.

Methods: STARSCAPE (NCT04552899) is a Phase III, multicenter, randomized, double-blind, placebo-controlled trial. 658 patients with IPF will be randomized (1:1) to receive intravenous zinpentraxin alfa or placebo administered on Days 1, 3, and 5, and every 4 weeks thereafter over 48 weeks. The primary endpoint is absolute change from baseline to Week 52 in FVC (mL). The key secondary endpoint is change from baseline to Week 52 in 6-minute walk distance. Eligible patients are aged 40–85 years with a diagnosis of IPF confirmed centrally by high-resolution computed tomography (and lung biopsy if available), with FVC ≥45%, forced expiratory volume in 1 second/FVC ratio >0.70, and carbon monoxide diffusing capacity 30–90% during screening. Patients can receive background therapy with nintedanib or pirfenidone.
Initiating a global Phase III trial during the COVID-19 pandemic brings unique challenges. A large number of countries/sites will be included to mitigate potential regional recruitment challenges. COVID-19 serology testing will be conducted to allow exploratory analyses on the impact of COVID-19 on lung function parameters.

Conclusions: The Phase III STARSCAPE trial aims to confirm the therapeutic potential of zinpentraxin alfa by using a broad range of efficacy, safety, quality of life, pharmacokinetic, and biomarker assessments over 52 weeks. Patients completing this 52-week trial may be eligible to enroll into the open-label extension.

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F30

Asthma Impairment and Risk Questionnaire (AIRQ) at Baseline Predicts 12-Month Health-Related Quality of Life (HRQoL)

Kevin R. Murphy, MD; Bradley Chipps, MD; Robert A. Wise, MD; David A. Beuther, MD; Maureen George, PhD; William McCann, MD; Robert S. Zeiger, MD; Ileen Gilbert, MD; James M. Eudicone, MS; Hitesh N. Gandhi, MBBS; Gale Harding, MA; Melissa Ross, PhD; Joan Reibman, MD

Introduction: The Asthma Impairment and Risk Questionnaire (AIRQ) is a 10-item asthma control tool validated in patients aged ≥12 years. Scores 0-1 indicate well-controlled (WC), 2-4 not well-controlled (NWC), and 5-10 very poorly controlled (VPC) asthma. The ability of AIRQ to predict HRQoL was evaluated.

Methods: Baseline AIRQ scores and demographic/clinical characteristics were obtained from 1112 patients participating in a 12-month AIRQ longitudinal validation study. St. George's Respiratory Questionnaire (SGRQ) was completed at baseline and at 6 and 12 months. A mixed-effect model for repeated measures (MMRM) was performed using change in SGRQ total score at 12 months as the dependent variable. Covariates significantly related in a univariate analysis to patient-reported exacerbations during the study were included in the model: baseline AIRQ control level, SGRQ score, age, sex, education, BMI, sleep apnea, FeNO, and GINA-level treatment class; ≥2 prior-year oral corticosteroid courses; timing of exacerbations; and changes in treatment and AIRQ score over the study period.

Results: 71.1% were female; mean (SD) age 43.9(19.5) years. Based on AIRQ scores, 35% of patients were WC, 38% NWC, and 27% VPC. Covariates independently contributing to 12-month HRQoL included male sex, higher educational attainment, BMI, and comorbid sleep apnea. SGRQ score changes at 12 months were 18.8 points higher (indicating worsening) for patients with VPC asthma at baseline, and 7.7 points higher for NWC asthma vs WC asthma. From baseline to 12 months, for each point increase in AIRQ score, SGRQ increased 3.7 points.

Conclusions: Asthma control as measured by AIRQ may be predictive of HRQoL over 12 months.

Funding: AstraZeneca

F31

Patient preferences for biologic treatments for severe asthma: Pilot results from a discrete choice experiment

Matthew Williams, Christopher S. Ambrose, Andrew W. Lindsley, Melissa Ross, Hannah Collacott, Andrea Schulz, Yen Chung, Pooja Desai, Pallavi Rane, Heather L. Gelhorn, Tara Carr

Rationale: Multiple biologic therapies are available for treating severe asthma. Here we report the results of a pilot discrete choice experiment (DCE) to evaluate the preferences of patients for attributes of biologics for severe asthma.

Methods: In 12 experimental choice tasks, participants chose from two hypothetical treatments and a no-treatment option. Hypothetical treatments were defined by eight attributes, including three efficacy attributes (reduction in number of severe asthma attacks, reduction in number of asthma-related hospitalizations, and time to notice an improvement in symptoms) and two safety attributes (risks of severe allergic reactions and injection site reaction). The DCE was piloted in adults with self-reported severe asthma diagnosed for ≥5 years.

Results: The pilot sample comprised 50 participants. Asthma Impairment and Risk Questionnaire (AIRQ®) scores indicated that asthma was well controlled in only 4% of participants. The attributes considered most important were risk of injection site reaction (RAI=16.0%), reduction in number of severe asthma attacks (RAI=15.9%), time to notice an improvement in symptoms (RAI=14.8%), location of administration (at home versus at the clinic; RAI=14.6%), and frequency of administration (RAI=13.1%). Risk of severe allergic reactions (RAI=6.1%) was the least important attribute. Participants strongly preferred a medication that gave 70% fewer (reference level [ref.] 25% fewer; p=0.01) or 50% fewer (p=0.03) severe asthma attacks; that had a 1-week (ref. 6 months; p=0.01) or 6-week (p=0.03) time to notice an improvement in symptoms; that had a low (2%) risk of injection site reaction (ref. 45%; p=0.004); and that could be administered every 8 weeks (ref. every 2 weeks; p=0.02) at home (ref. at the clinic; p<0.001).

Conclusions: Treatment attributes most important to participants included efficacy, safety, and administration-related attributes. All RAI values were <20%, indicating that no individual attribute was markedly more important and that preferences for biologic treatments are likely heterogeneous.

Funding: AstraZeneca and Amgen, Inc.

F32

Annual inhaled corticosteroid, short-acting beta$_2$-agonist and systemic corticosteroid exposure in adolescents and adults with asthma in the United States

Njira Lugogo, Ileen Gilbert, Michael Pollack, Hitesh Gandhi, Joseph Tkacz, Miguel Lanz

Introduction: The Global Initiative for Asthma (2021) and National Asthma Education and Prevention Program (2020) recommend concomitant fast-acting bronchodilators and inhaled corticosteroids (ICS) for rescue therapy in patients ≥12 years, as this approach can reduce exacerbations requiring systemic corticosteroids (SCS). We assessed ICS, short-acting beta$_2$-agonist (SABA), and SCS exposures and compared the relative magnitude of observed SCS versus projected ICS that could occur if as-needed SABA were combined with ICS.

Methods: IBM® MarketScan® databases of 2010–2017 administrative claims for US patients ≥12 years receiving SABA for asthma were evaluated. Patients were indexed on a random SABA claim, had 12-months' continuous eligibility pre- and post-index, and filled post-index ICS-based maintenance medication totaling >32 days' supply or ≥1 additional SABA if no maintenance. Post-index ICS (µg/day fluticasone propionate [FP] equivalents), SABA (inhalations/day based on 200 inhalations/canister) and SCS (mg/year prednisone equivalents) were analyzed, assuming full claims use. As budesonide is the most-studied rescue ICS, projected as-needed ICS over the post-index year was calculated assuming each SABA inhalation contained 80 µg budesonide (50 µg FP equivalent). Maximum acceptable daily ICS ranges were derived from FDA-approved FP product labels. Statistics were descriptive and unadjusted.

Results: 577,394 patients were identified. 63% filled SABA only (41% with SCS exposure); 37% filled ICS-based maintenance (40% with SCS). For each maintenance therapy, mean post-index ICS µg/day was below the respective maximum approved levels, ranging from 24% (high-dose ICS/long-acting beta$_2$-agonist [LABA]) to 52% (low-dose ICS) of FDA approved daily doses. Mean (standard deviation) post-index SABA ranged from 2.2 (2.2) canisters (~1.2 inhalations/day, SABA only group) to 4.9 (4.8) canisters (~2.7 inhalations/day, ICS/LABA/long-acting muscarinic antagonist [LAMA] group). If each SABA inhalation was combined with 80 µg budesonide, total projected maintenance plus as-needed ICS/day would range from 36% (high-dose ICS/LABA) to 100% (low-dose ICS) of respective approved doses. For all groups, mean post-index SCS exposure exceeded 500 mg/year prednisone equivalents, ranging from 542 (1,438) mg (low-dose ICS/LABA) to 1,088 (2,148) mg (ICS/LABA/LAMA). Total annual projected mgs of ICS were 6.2 (medium/high dose ICS) to 28.0 (SABA only) times lower than mgs of observed SCS exposure.

Conclusions: Many patients ≥12 years with asthma have SCS exposures associated with the development of adverse health conditions (≥500 mg). Even if as-needed SABA with concomitant ICS remains at the same level as current SABA use, modeled ICS exposure is within the range of approved doses and patients could benefit from reduced SCS exposures.

Funding: AstraZeneca

F33

Assessment of the Long-Term Safety and Efficacy of Dupilumab in Children With Asthma: LIBERTY ASTHMA EXCURSION

Leonard Bacharier, MD; Anabelle Keohane; Jorge Maspero, MD; Constance Katelaris, MD; Alessandro Fiocchi, MD; Remi Gagnon, MD; Ines de Mir, MD; Theresa Guilbert, MD; Daniel Jackson, MD; Ning Li, Bolanle Akinlade, MD; Elizabeth Laws, PhD; Leda Mannent, MD; Jennifer Maloney, MD; Tawo, Faisal Khokhar, MD; Megan Hardin, MD; Raolat Abdulai, MD; David Lederer, MD; Lacey Robinson

Introduction: Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin-4/interleukin-13. Efficacy and safety of dupilumab in children with asthma have been demonstrated up to 52 weeks in VOYAGE. This open-label extension (OLE) study (NCT03560466) assessed dupilumab long-term safety and efficacy in children with uncontrolled, moderate-to-severe asthma who completed VOYAGE (aged 6–11 years at enrollment in parent study).

Methods: 365 patients enrolled from VOYAGE into EXCURSION, and received add-on dupilumab 100/200mg (body-weight based) every 2 weeks for 52 weeks. A subgroup of patients received 300mg every 4 weeks. Treatment-emergent adverse events (TEAE), annualized rate of severe asthma exacerbations (AER), and change from parent study baseline (PSBL) in percent predicted forced expiratory volume in 1 second ($ppFEV_1$) were assessed.

Results: Safety during the OLE was consistent with the parent study (any TEAE: 61.3% and 68.0% of dupilumab/dupilumab and placebo/dupilumab group, respectively; treatment-emergent SAE: 2.5% and 0.8%; TEAE leading to discontinuation: 1.3% and 0%; parasitic infection: 1.7% and 1.6%; eosinophilia: 3.3% and 8.0%; 0 TEAE leading to death). In type 2 patients (blood eosinophils ≥150 cells/µL or ≥20ppb fractional exhaled nitric oxide at PSBL), the low unadjusted AER/improvement in $ppFEV_1$ observed with dupilumab in the parent study were sustained in the OLE (AER: 0.118; $ppFEV_1$ at PSBL: mean [SD] 76.87 [14.30]; change from PSBL at EXCURSION Week 0: +12.50 [18.70]; Week 2: +11.28 [18.60]; Week 52: +12.60 [18.19]). Patients who switched from placebo to dupilumab also showed low AER (0.124), and $ppFEV_1$ improvement as early as Week 2 (PSBL: mean [SD] 78.72 [13.90]; change from PSBL at EXCURSION Week 0: +3.79 [14.40]; Week 2: +8.71 [15.71]; Week 52: +9.43 [16.22]).

Conclusion: Long-term use of dupilumab was well tolerated. The efficacy observed in the parent study was sustained over an additional 52 weeks in patients with type 2 asthma.

Funding: Sanofi and Regeneron Pharmaceuticals, Inc.

F34

Dupilumab Impact on Lung Function in Children With Uncontrolled, Moderate-To-Severe Asthma and Elevated Type 2 Biomarkers

Theresa Guilbert, MD; Anabelle Keohane; Leonard Bacharier, MD; Constance Katelaris, MD; Antoine Deschildre, MD; Wanda Phipatanakul, MD; Arman Altincatal, MS; Leda Mannent, MD; Nikhil Amin, MD; Elizabeth Laws, PhD; Bolanle Akinlade, MD; Xavier Soler, MD; Juby Jacob-Nara, MD; Yamo Deniz, MD; Paul Rowe, MD; David Lederer, MD; Megan Hardin, MD

Introduction: Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin-4/interleukin-13, key and central drivers of type 2 inflammation. In the phase 3 VOYAGE study (NCT02948959), add-on dupilumab vs placebo demonstrated significant improvements in percent predicted pre-bronchodilator FEV_1 ($ppFEV_1$) at Week 12 in children aged 6 to <12 years with uncontrolled, moderate-to-severe asthma, a type 2 inflammatory phenotype (baseline blood eosinophils ≥150 cells/µL or fractional exhaled nitric oxide [FeNO] ≥20ppb). This analysis evaluated dupilumab efficacy in improving lung function by assessing proportions of patients achieving $ppFEV_1$ ≥80% and ≥95%, in the type 2 population and in patients with ≥300 eosinophils (eos)/µL at baseline.

Methods: Patients were randomized 2:1 to receive add-on subcutaneous dupilumab 200/100mg every 2 weeks (q2w) based on body weight, or matched placebo q2w for 52 weeks. Proportion of patients with $ppFEV_1$ <80%, ≥80%, and ≥95% at baseline and Week 52 were analyzed.

Results: In type 2 patients who received dupilumab (n=236) vs placebo (n=114), 8.1% vs 12.3%, and 50.8% vs 48.2%, had $ppFEV_1$ ≥95% and ≥80% at baseline, respectively. At Week 52 these proportions increased in dupilumab vs placebo groups to 34.9% vs 20.8%, and 77.2% vs 66.0% with $ppFEV_1$ ≥95% and ≥80%, respectively. 22.8% vs 34.0% of patients receiving dupilumab vs placebo continued to have $ppFEV_1$ <80% at Week 52 (49.2% vs 51.8% at baseline). In the eos ≥300/µL subpopulation that received dupilumab (n=175) vs placebo (n=84), 7.4% vs 13.1% and 53.1% vs 46.4% had $ppFEV_1$ ≥95% and ≥80% at baseline, respectively. At Week 52, these proportions increased in dupilumab vs placebo to 32.9% vs 21.1% and 76.6% vs 64.5% with $ppFEV_1$ ≥95% and ≥80%, respectively.

Conclusions: Dupilumab increased the proportion of pediatric patients with improved lung function, in both the type 2 population as well as the eos ≥300/µL subpopulation.

Funding: Sanofi and Regeneron Pharmaceuticals, Inc.

F35

International, prospective study of mepolizumab in severe asthma: REALITI-A at 2 years

Cristiano Caruso PhD, Giorgio W. Canonica MD, Manish Patel PhD, Andrew Smith PhD, Mark C. Liu MD, Rafael Alfonso-Cristancho PhD, Robert G. Price MSc, Rupert W. Jakes PhD, Lydia Demetriou MSc, Antonio Valero MD, Charles Pilette PhD, Peter Howarth DM

Introduction: The real-world clinical impact of mepolizumab in severe asthma is reported but few studies assessed sustained treatment benefits; the international REALITI-A study assessed longer-term outcomes.

Aims: To report key 2-year REALITI-A outcomes.

Methods: REALITI-A was a 2 year prospective, observational study enrolling patients with asthma, newly prescribed mepolizumab 100 mg SC. Outcomes included the rate of clinically significant exacerbations (CSEs; requiring oral corticosteroids [OCS] and/or hospitalization/emergency room [ER] visit) and exacerbations requiring hospitalization/ER visits in 1 year pre- and 2 years following mepolizumab initiation, and change in maintenance OCS (mOCS) use and dose (prednisone-equivalent) in 28 days prior to (baseline) and Weeks 101–104 following mepolizumab initiation. Investigator-determined treatment-related adverse events (TRAEs) were collected.

Results: Overall, 822 patients were treated. At enrollment, mean (standard deviation) age and asthma duration (n=801) were 54 (13.6) years and 19.7 (15.68) years, respectively; 63% (n=521) of patients were female, 39% (n=320) had baseline mOCS use and geometric mean (SD log) baseline blood eosinophil count (n=614) was 350 (1.253) cells/µL. By 2 years, CSEs reduced by 74% (1.11 [n=820] vs. 4.25 [n=821] events/year; rate ratio [RR] [95% CI]: 0.26 [0.24, 0.29]; p<0.001) and exacerbations requiring hospitalization/ER visits reduced by 79% (0.19 [n=820] vs. 0.92 [n=821] events/year; RR [95% CI]: 0.21 [0.17, 0.25]; p<0.001) vs. pre-treatment. Furthermore, the median (interquartile range) mOCS dose reduced by 100% vs. baseline (0.00 [0.0, 5.0] [n=168] vs. 10.0 [5.0, 14.7] [n=297] mg/day); 57% (95/168) of patients discontinued mOCS use. 599 (73%) patients withdrew from/completed the study with mepolizumab treatment ongoing. TRAEs were observed in 90 (11%) patients; 7 (<1%) of these were serious, 1 fatal (hepatic cancer).

Conclusions: The 2-year REALITI-A data support long-term real-world clinical benefits of mepolizumab in patients with severe asthma.

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F36

Mepolizumab Treatment Leads to Clinical Remission in Patients With Severe Eosinophilic Asthma: Results From the Real-World REDES Study

Christian Domingo-Ribas MD, PhD, Ian Pavord FMedSci, DM, Robert G. Price MSc, Peter Howarth DM, John Oppenheimer MD, Liam Heaney MD, Hiroyuki Nagase MD, PhD, Emilio Pizzichini MD, PhD, David Banas Conejero MSc, Frances Gardiner MPhil

Rationale: The real-world REDES study demonstrated that mepolizumab is effective at enabling patients with severe eosinophilic asthma to achieve treatment goals such as oral corticosteroids (OCS) elimination, exacerbation reduction or symptom control. This post hoc analysis assessed the proportion of patients achieving a multicomponent treatment goal of clinical remission (based on OCS-free, exacerbation-free, and asthma control) after 1-year of treatment with mepolizumab.

Methods: The REDES study was a retrospective, observational cohort study in patients with severe eosinophilic asthma treated with mepolizumab (100 mg subcutaneous) across 24 specialized hospital asthma units in Spain. Using data from the REDES study, we report the proportion of patients achieving clinical remission 52 weeks post-mepolizumab initiation. We evaluated the following three components of clinical remission, which are also considered to be the key treatment goals in severe asthma: 1) OCS-free (yes/no); 2) exacerbation-free (yes/no); 3) asthma control test (ACT) score ≥20 (yes/no) at Week 52.

Results: Results are reported in patients who had complete data across the three components (N=260/318, 82%); 58 patients were excluded due to missing ACT score at Week 52. Overall, 96/260 (37%) patients achieved clinical remission based on our multicomponent three-way definition (meeting the OCS-free, exacerbation-free, and ACT score ≥20 criteria at Week 52). Additionally, 116/260 (45%), 107/260 (41%), and 170/260 (65%) of mepolizumab-treated patients achieved two of the components of clinical remission (OCS and exacerbation-free; exacerbation-free and ACT score ≥20; and OCS free and ACT score ≥20 respectively at Week 52).

Conclusions: Results from this post hoc analysis of the REDES study show that mepolizumab is effective at achieving a status of clinical remission, an ambitious multicomponent treatment goal comprising key clinical criteria, in patients with severe eosinophilic asthma treated in clinical practice.

Funding: GSK

F37

Impact of Baseline Treatment, Duration of Disease, and Refractory Status on Outcomes in Mepolizumab-Treated Patients With EGPA

Paneez Khoury, Praveen Akuthota, Lee Baylis, Sarah Chang, Jane Bentley, Michael E Wechsler

Rationale: Mepolizumab, an anti-interleukin-5 monoclonal antibody has been shown to increase remission duration in patients with eosinophilic granulomatosis with polyangiitis (EGPA). We investigated impact of baseline treatment, disease duration, and refractory status on mepolizumab efficacy using Phase III MIRRA study data.

Methods: Patients with relapsing/refractory EGPA, receiving stable prednisolone/prednisone (≥7.5–≤50 mg/day), were randomized (1:1) to monthly mepolizumab 300 mg or placebo subcutaneously for 52 weeks. Co-primary endpoints were total accrued duration of remission from Weeks 0 to 52 and proportion of patients in remission at both Weeks 36 and 48. Data were stratified by baseline immunosuppressant (IS) use (yes/no) and disease duration (≤4/>4 years); analyses by baseline refractory disease status (yes/no) were performed post hoc.

Results: Of 136 patients enrolled in MIRRA, 72 had baseline IS use (placebo[n=31]/mepolizumab[n=41]), 70/136 had EGPA >4 years (placebo[n=36]/mepolizumab[n=34]) and 74/136 had refractory disease at baseline (placebo[n=40]/mepolizumab[n=34]). Mepolizumab increased accrued duration in remission versus placebo, irrespective of baseline IS use (odds ratio[95%CI]; yes:3.39[1.11,10.38]; no:11.85[3.50,40.13]), EGPA duration (odds ratio[95%CI]; ≤4 years:17.08[3.41,85.54]; >4 years:4.26[1.53,11.91]) or baseline refractory disease status (odds ratio[95%CI]; yes:3.70[1.29,10.65]; no:9.25[2.44,35.08]). More patients receiving mepolizumab were in remission at Weeks 36 and 48 versus those on placebo, irrespective of baseline IS use (yes:32%[13/41] vs 6%[2/31]; no:33%[9/27] vs 0%[0/37]), EGPA duration (≤4 years:24%[8/34] vs 0%[0/32]; >4 years:41%[14/34] vs 6%[2/36]), and baseline refractory disease status (yes:24%[8/34] vs 3%[1/40]; no:41%[14/34] vs 4%[1/28]).

Conclusions: In patients with EGPA, mepolizumab was associated with increased likelihood and duration of remission versus placebo, irrespective of baseline IS use, disease duration, and baseline refractory disease status.

Funding: GSK

F38

The Impact of Comorbid Nasal Polyps on Real-World Mepolizumab Effectiveness in Patients With Severe Asthma: Results From the REALITI-A Study

Mark C. Liu MD, Diego Bagnasco MD, PhD, Andrea Matucci MD, Charles Pilette MD, Robert G. Price MSc, Aoife C. Maxwell PhD , Rafael Alfonso-Cristancho MD, Rupert W. Jakes PhD, Shibing Yang PhD, Peter Howarth DM, Amarjit S. Cheema MD

Introduction: Several Phase III clinical trials and open-label extension studies demonstrated mepolizumab reduces exacerbation rates, oral corticosteroid (OCS) use, and improves asthma symptoms in patients with severe eosinophilic asthma (SEA). In previous studies, patients with SEA with nasal polyps (NP) demonstrated greater response to mepolizumab treatment than those without NP. This study assessed the impact of NP status on real-world mepolizumab effectiveness in patients with SEA.

Methods: REALITI-A, a 2-year observational study, enrolled adults with asthma newly prescribed mepolizumab treatment (100 mg subcutaneous). Patient-reported NP status (with/without) was recorded at enrollment. Primary endpoint: rate of clinically significant exacerbations (CSE; requiring systemic corticosteroids and/or hospital/ER admission) following mepolizumab treatment (follow-up) relative to the 12-month pre-treatment period; secondary endpoints: change from baseline (28 days pre-mepolizumab) in daily maintenance OCS (mOCS) and total OCS (maintenance and rescue burst) dose during follow-up. This interim analysis assessed Week 53–56 outcomes, stratified by NP status at enrollment, in the full study population 1-year post mepolizumab treatment.

Results: Of 822 treated patients, 39% reported comorbid NP. Patients with NP experienced numerically greater reductions in rate of CSE at follow-up than those without NP (75% vs 69%). Both groups experienced reduced mOCS dose; patients with NP experienced greater percent reductions in median mOCS dose versus patients without NP (83% vs 50%). Patients with NP experienced greater reductions in median total OCS dose versus those without NP (68% vs 51%). By Week 53–56, more patients with NP had improved mOCS/total OCS use, or discontinued use, than those without NP.

Conclusions: This real-world study showed that mepolizumab reduced exacerbations and OCS use in patients with SEA, with greater impact in patients with comorbid NP. Patients with SEA and NP represent a clinically identifiable phenotype particularly suited to mepolizumab therapy.

Funding: GSK

F39

Persistent Reductions in OCS Use in Patients With Severe, OCS-Dependent Asthma Treated With Dupilumab: LIBERTY ASTHMA TRAVERSE Study

Mark Gurnell, PhD; Anabelle Keohane; Christian Domingo, MD;, Klaus Rabe, MD; Andrew Menzies-Gow, MD; David Price, MD; Guy Brusselle, MD; Michael Wechsler, MD; Changming Xia, PhD; Michel Djandji, MD; Rebecca Gall, MD; Juby Jacob-Nara, MD; Paul Rowe, MD; Yamo Deniz, MD; Shahid Siddiqui, MD

Background: Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin-4/interleukin-13, key and central drivers of type 2 inflammation. In the phase 3 LIBERTY ASTHMA VENTURE study (NCT02528214), add-on dupilumab 300mg every 2 weeks (q2w) vs placebo significantly reduced oral corticosteroid (OCS) use from baseline in patients aged ≥12 years with OCS-dependent severe asthma. LIBERTY ASTHMA TRAVERSE (NCT02134028), a single-arm, open-label extension study, evaluated long-term safety and efficacy of add-on dupilumab in patients from previous dupilumab studies, including VENTURE. Here we assessed dupilumab efficacy in patients with OCS-dependent severe asthma, stratified by baseline OCS dose during VENTURE (≤10 or >10mg/day).

Methods: Patients with OCS-dependent asthma received add-on dupilumab 300mg q2w or placebo for 24 weeks during VENTURE (parent study), then add-on dupilumab 300mg q2w for up to 96 weeks in TRAVERSE (dupilumab/dupilumab and placebo/dupilumab groups). Endpoints were OCS dose reduction from parent study baseline in TRAVERSE, annualized rate of severe asthma exacerbations (AER) during VENTURE and TRAVERSE, and pre-bronchodilator forced expiratory volume in 1 second (FEV_1) in TRAVERSE .

Results: 187 patients (≤10mg/day: placebo/dupilumab, n=61; dupilumab/dupilumab, n=60; >10mg/day: placebo/dupilumab, n=36; dupilumab/dupilumab, n=30) were included. The greater reductions in daily OCS use observed in patients on dupilumab at VENTURE study end continued during TRAVERSE in dupilumab/dupilumab patients (≤10mg/day: −82.8%; >10mg/day: −74.7% at TRAVERSE Week 48). In patients who were on placebo during VENTURE and were switched to dupilumab in TRAVERSE (placebo/dupilumab), OCS use was further reduced, irrespective of OCS use at baseline (≤10mg/day: −49.6%; >10mg/day: −66.5% at TRAVERSE Week 48). Despite these continued reductions in OCS use, AER continued to decline during TRAVERSE (range: 0.284–0.599) and pre-bronchodilator FEV_1 greatly improved (range at TRAVERSE Week 48: 1.83–1.92L).

Conclusions: Dupilumab reduced OCS dose and improved and maintained clinical efficacy outcomes of asthma, regardless of baseline OCS starting dose.

Funding: Sanofi and Regeneron Pharmaceuticals, Inc.

F40

Characterization of Asthma Patients Treated With Dupilumab in a Real-World Setting: The RAPID Registry

Njira Lugogo, MD; Anabelle Keohane; Xavier Soler, MD; Andrew Menzies-Gow, MD; Anju Peters, MD; Andréanne Côté, MD; Ole Hilberg, MD; Changming Xia, PhD; Yi Zhang, PhD; Lucia de Prado Gomez, MSc; Paul Rowe, MD; Amr Radwan, ;Juby Jacob-Nara, MD; Yamo Deniz, MD

Introduction: Up to 58% of patients with severe asthma have uncontrolled symptoms despite recommended treatment. Dupilumab is a fully human monoclonal antibody that blocks interleukin-4/-13, key and central drivers of type 2 inflammation. In phase 3 LIBERTY ASTHMA QUEST (NCT02414854), add-on dupilumab 200mg/300mg vs placebo significantly reduced severe asthma exacerbations, improved pre-bronchodilator (pre-BD) forced expiratory volume in 1 second (FEV_1) in patients with uncontrolled, moderate-to-severe asthma and evidence of type 2 inflammation, and demonstrated an acceptable safety profile. We report baseline characteristics of patients enrolled during the first six months of RAPID (NCT04287621), a global, prospective registry that characterizes patients with asthma initiating dupilumab therapy in real-world clinical practice.

Methods: The RAPID registry enrolls patients aged ≥12 years who initiate dupilumab for asthma, according to country-specific prescribing information. Signed consent is obtained (for minors, from parent/guardian).

Results: During the first 6 months, 205 patients enrolled. Characteristics included: mean age 50.10±17.41 years; female 65.4%; body mass index 30.67±7.96; 74.1% were White (including of Hispanic origin), and 13.2% were Black/African-American. 86.8% had moderate-to-severe asthma (GINA steps 3–5); 6.3% were GINA 1/2. 24.4% were current/former smokers. Severe asthma exacerbations in the previous year were recorded in 4.10±6.30 participants (median: 2.0 [min–max: 0–36, Q1–Q3: 1.0–4.0]). Pre-BD FEV_1, 2.29±1.13L; pre-BD percent predicted FEV_1, 70.34±20.29%; forced vital capacity, 3.09±1.08L; and peak expiratory flow, 356.88±169.83L/min. 6-item Asthma Control Questionnaire was 2.40±1.18, and Asthma Quality of Life Questionnaire score was 4.10±1.31. Fractional exhaled nitric oxide was 42.2±34.83ppb.

Conclusions: In this initial RAPID sample, patients initiating dupilumab treatment had asthma symptoms and a history of smoking. A small proportion had milder-than-expected asthma. Patients had a high number of exacerbations in the past year, impaired lung function, and poor asthma control and quality of life, suggesting a population with high disease burden despite standard-of-care treatment.

Funding: Sanofi and Regeneron Pharmaceuticals, Inc.

F41

EVELUT: Dyspnea and symptom burden in COPD patients switching from LABA/ICS to LAMA/LABA or LAMA/LABA/ICS

Roland Buhl, MD; Dreher M, MD; Mattiucci-Guehlke M, MD; Sebastian Eckhardt, MSc; Taube C, MD; Vogelmeier CF, MD; Asif Shaikh, MD

Introduction: The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends that chronic obstructive pulmonary disease (COPD) patients who are dyspneic despite the use of long-acting β_2-agonist (LABA) plus inhaled corticosteroid (ICS) be switched to LABA plus long-acting muscarinic antagonist (LAMA) or LAMA/LABA/ICS (triple therapy; TT). However, no prospective clinical evidence is available supporting a switch from LABA/ICS to LAMA/LABA (instead of TT) when ICS is not indicated. The EVELUT® study investigated the reduction of dyspnea and symptom burden in dyspneic COPD patients who were switched from LABA/ICS to LAMA/LABA (tiotropium/olodaterol [T/O]) or TT (fixed or free).

Methods: COPD patients with low exacerbation risk and symptoms (modified Medical Research Council [mMRC] score ≥1; COPD Assessment Test [CAT™] score ≥10) despite LABA/ICS were switched to T/O or TT (at physician's discretion) at Visit 1 (baseline) and treated until Visit 2 (~Week 12). The co-primary endpoints were changes in the mMRC and CAT scores (Visit 1 to 2) in a propensity score–matched population. The percentage of responders (ΔmMRC ≥1; ΔCAT ≥2) was a secondary endpoint.

Results: The 1:1 matched population included 121 patients per treatment arm. The mean (95% confidence interval) reduction in the mMRC score was 0.23 (0.11–0.36) with T/O and 0.25 (0.13–0.38) with TT, and the mean (95% confidence interval) reduction in the CAT score was 3.45 (2.45–4.45) with T/O and 2.51 (1.62–3.40) with TT. The percentage of mMRC responders was 25.0% with T/O and 21.8% with TT, and that of CAT responders was 67.9% with T/O and 56.3% with TT.

Conclusion: In accordance with GOLD recommendations, dyspneic patients on LABA/ICS without an indication to continue ICS can be switched to T/O LAMA/LABA, with TT showing no benefit versus T/O with regard to symptoms and health status.

Funding: Boehringer Ingelheim

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Patients in Triple Therapy Clinical Trials Compared to Real World Observational Study: An analysis of the COPD Gene Cohort.

Barry Make, MD; Carla Wilson, MS; Aaron Reed, RT, DNP; Asif Shaikh, MD, DrPH, MPH Dawn DeMeo, MD, MPH; Russell Bowler, MD, PhD

Introduction: Randomized clinical trials (RCTs) include well-defined populations determined by narrow inclusion/exclusion criteria, but the percentage of the general COPD population that would be candidates for these studies is unknown. This analysis assessed the percentage of COPD participants from the COPD Genetic Epidemiology Study (COPDGene) who would be eligible for inclusion in three trials (ETHOS, IMPACT, KRONOS) of triple therapy in COPD based on trial enrollment criteria and gender inclusion.

Methods: ETHOS, IMPACT and KRONOS enrollment criteria (age, smoking pack-years (PY), asthma history, post-bronchodilator (PBD), forced expiratory volume in 1 second (FEV1) and FEV1/ forced vital capacity (FVC), COPD Assessment Test (CAT) score, maintenance inhaler use, and exacerbation history), as well as gender inclusion, were applied to COPDGene participants' data. Proportions were calculated.

Results: COPDGene Phase 2 participants who were COPD GOLD 1 – 4 (n=2,487) had a mean age of 68 years, median 45.6 PY, mean PBD FEV1 60.6% predicted (66.4% GOLD stage 1-2, 33.6% GOLD 3-4), 67.1% CAT score ≥10, 45.7% not prescribed inhaled maintenance therapy, 10% GOLD stage D, mean eosinophil 160 cells/microliter, and 72.1% without an exacerbation in prior year. The percentage of COPDGene subjects eligible for clinical trials was low: ETHOS 10.1% (95% CI 6.6-8.4%), IMPACT 17.0% (11.3-13.9%), and KRONOS 24.5% (17-20%). History of exacerbations (25.5% for ETHOS/IMPACT) and presence of inhaled maintenance therapy (41.6% ETHOS and KRONOS, 54.3% IMPACT) contributed most to ineligibility. Female inclusion (ETHOS 40.3%, IMPACT 33.7%, KRONOS 28.8%) was low compared to COPDGene (44.6%).

Conclusions: Only 10-24% of COPDGene participants would be eligible for previously reported clinical trials of inhaled triple therapies in COPD. Trial ineligibility was driven by insufficiently frequent exacerbations and no prior inhaled maintenance therapy. These results suggest the external validity of triple therapy in the general COPD population may be low and that female inclusion is inadequate.

Funding: Boehringer-Ingelheim

F43

Brensocatib for the Treatment of Non–Cystic Fibrosis Bronchiectasis (NCFBE): Number Needed to Treat (NNT) and Number Needed to Harm (NNH)

James D. Chalmers, MB, ChB, PhD; Mark L. Metersky, MD, FCCP, Joseph Feliciano, PharmD, MS; Andrea Maes, PhD ; Anjan Chatterjee, MD, MPH, MBA

Introduction: Increased airway neutrophil elastase (NE) activity is associated with bronchiectasis progression and increased risk for pulmonary exacerbations. Brensocatib is an investigational, small-molecule, orally bioavailable, selective, and reversible dipeptidyl peptidase-1 inhibitor that blocks activation of neutrophil serine proteases, including NE. In a randomized, double-blind, placebo-controlled phase 2 study (WILLOW; NCT03218917), brensocatib prolonged time to first exacerbation in patients with NCFBE and reduced sputum NE concentrations vs placebo. This analysis evaluated NNT and NNH using data from WILLOW.

Methods: 256 adults with NCFBE were randomized 1:1:1 to receive once-daily brensocatib 10 mg or 25 mg or placebo. Primary endpoint was time to first bronchiectasis exacerbation over 24 weeks; key secondary endpoint was rate of exacerbations at week 24. NNT was calculated for the prevention of exacerbations. NNH was assessed for the risk of serious treatment-emergent adverse events (TEAEs), including and excluding exacerbations as safety events. Reciprocal of risk difference between brensocatib treatment arms and placebo was calculated for NNT and NNH.

Results: The proportion of patients with exacerbations at week 24 was lower in treatment arms (31.7%, 33.3%, and 32.5% in the brensocatib 10-mg [n=82], 25-mg [n=87], and pooled groups [n=169]) vs placebo (48.3% [n=87]), yielding NNTs for exacerbation prevention of 6, 7, and 6, respectively. Serious TEAEs across treatment arms (13.6%, 11.2%, and 12.4% in the 10-mg [n=81], 25-mg [n=89], pooled groups [n=170]) and placebo (22.4%) yielded NNHs of −11, −9, and −10, respectively, with negative NNH indicating lower risk of these events vs placebo. NNH values excluding exacerbations in the brensocatib 10-mg (11.1%), 25-mg (9.0%), and pooled groups (10.0%) compared with placebo (12.9%) were −55, −25, and −34, respectively.

Conclusions: NNT and NNH analyses indicate a favorable benefit-risk profile for brensocatib, potentially advancing bronchiectasis treatment. The ongoing phase 3 ASPEN trial aims to confirm these findings.

Funding: Insmed Incorporated

F44

Reduction in hospitalizations after initiation of amikacin liposome inhalation suspension: a retrospective cohort study of patients in real-world settings

Jasmanda Wu, PhD; Mariam Hassan, PhD; Emily Achter, MPH; Anjan Chatterjee, MD, MPH, MBA

Introduction: *Mycobacterium avium* complex lung disease (MAC-LD) is associated with substantial burden and high hospitalization rates. Amikacin liposome inhalation suspension (ALIS) is the first FDA-approved therapy for refractory MAC-LD. In clinical trials, ALIS plus guideline-based therapy improved MAC infection elimination in sputum by month 6. The objective was to assess changes in hospitalizations among patients initiating ALIS.

Methods: This retrospective cohort study (all-payer claims database, 10/2018-4/2020) evaluated patients (≥18 years) with ≥1 pharmacy claim for ALIS and ≥12 months of continuous health plan enrollment before and after ALIS initiation. All-cause and respiratory disease-related hospitalizations were compared for 12 months before and after ALIS initiation. Hospitalizations were reported for each 6-month interval, with a reference period of 6 months before ALIS initiation.

Results: 331 patients received ALIS (mean±SD age, 64.6±16.0 years; female, 77.9%; Medicare, 65.9%; commercial plans, 27.8%; COPD, 46%; bronchiectasis; 57%; US region [southern, 45.9%; northeastern, 22.4%; western, 19.0%; north central, 12.7%]). Hospitalizations were highest ≤6 months before ALIS initiation. 0-6 months before vs 0-6 and 7-12 months after ALIS initiation, all-cause (35.9% vs 26.6% and 23.0%, respectively; both $P<.01$) and respiratory disease-related (26.9% vs 19.3% and 15.4%, respectively; both $P<.01$) hospitalizations were reduced. Mean all-cause (1.2±1.8 vs 0.7±1.2 and 0.7±1.4, respectively; both $P<.001$) and respiratory disease-related (1.0±1.6 vs 0.6±1.0 and 0.6±1.2, respectively; both $P<.001$) hospitalizations per person per 6 months were reduced. ≈28% and ≈43% fewer patients had respiratory disease-related hospitalizations 0-6 and 7-12 months after ALIS follow-up, respectively. Mean respiratory disease-related hospitalizations per person per 6 months decreased by ≈40% at 0-6 and 7-12 months after ALIS follow-up. A similar trend was observed for all-cause hospitalizations.

Conclusions: Significant reductions in real-world all-cause and respiratory disease-related hospitalizations were seen within 12 months post ALIS initiation. Results provide resource utilization-related economic data to better understand the impact of ALIS treatment.

Funding: Insmed Incorporated

Eastern Pulmonary Conference
September 8-11, 2022 ~ Palm Beach, FL

Scientific Posters S1-S44 will be on display in the Ponce 5&6, and Ponce Foyer during the coffee break, 10:30-11:15am, Saturday September 10, 2022

Not for CME Credit

R1

Tuberculosis Infections in the USA During the COVID-19 Pandemic

Kushinga M. Bvute, Feyikemi Ogunfuwa, Hadeer Sinawe, Michael A. DeDonno

Background: The Covid-pandemic disrupted international Tuberculosis (TB) services, decreasing international cases; however, there is no report analyzing the impact of Covid on TB in the USA. This study compares TB between 2019 (Pre-pandemic) and 2020 (Pandemic).

Method: We used publicly available data from the Center for Disease Control and Prevention that reported TB in the USA. We extrapolated data from tables; age, ethnicity, geography, reasons for testing, risk factors, and genotype. We excluded data aggregated by metropolitan statistical areas. We used SPSS to examine the statistical variables. The project was exempt from IRB approval.

Results: There was a statistically significant decrease in TB cases from 2019 (n = 8916, M = 177.84, SE = 48.833) to 2020 (n= 7174, M = 143.10, SE = 38.638). The same top five states with the most TB cases remained the same with all showing decreased cases from 2019 to 2020; California (n=2,113 vs 1,705), Texas (n=1,159 vs 884), New York (n= 754 vs 606), Florida (n= 558 vs 412), and New Jersey (n= 311 vs 245). The median age in the five states ranged from 34.8 to 42.2 years.

Significantly more people in 2019 underwent TB testing due to symptoms (M =99.24± SD 206.96 vs. 81.02±166.98*), abnormal chest x-ray (M=36.28± SD 67.91 vs. 27.00± 57.43**), targeted testing (M= 8.32 ±29.61 vs. 4.96 ±17.41*), immigrant examination (M= 3.56± SD 7.73 vs. 1.64±4.28**), and administrative testing (M =0.94± SD 1.77 vs. 0.52 ±1.16*).
*= p<0.5, **p<0.01.

Conclusion: Although global TB cases decreased by 20%, we cannot attribute the reduction to mask-wearing or lockdowns versus reduced access to care. TB cases in the USA decreased in 2020 similar to global trends. However, the acute reduction does not exclude or confirm the effect of mask-wearing.

R2

Radiographic edema does not predict mortality in patients with COVID-19 requiring mechanical ventilation

Daniel Kotok, Christine Girard, Jose Rivera Robles, Andrew Kim, Shruti Shettigar, Allen Lavin, Samantha Gillenwater, Anas Hadeh

Background: Baseline radiographic edema on chest X-ray (CXR) in patients with COVID-19 presenting to the emergency department has been associated with need for hospital and intensive care unit (ICU) admission as well need for mechanical ventilation and 30-day mortality. Whether this is true for radiographic edema quantified after initiation of mechanical ventilation is unclear. We sought to evaluate this question using a well-validated scoring system (the Radiographic Assessment of Lung Edema [RALE] score) using data over 6 months from a large, multi-hospital healthcare system including all adult (age >= 18) patients.

Methods: We collected CXRs performed in patients soon after endotracheal intubation for COVID-19 associated hypoxemic respiratory failure between March and September 2020. We quantified severity of radiographic edema using the RALE score. Two independent reviewers quantified radiographic edema using the RALE scoring system. We examined the association of radiographic edema with time from hospital admission to intubation and 30-day mortality.

Results: 65 patients were identified (median age 68, 40% female). Inter-rate agreement for RALE score was excellent (ICC = 0.84, 95% CI 0.82 - 0.87, p < 0.0001). Mortality at 30 days was 54% (n = 35). There was no association between RALE scores and time to ICU admission from ED presentation (r = -0.14, p = 0.27). RALE scores were not different in survivors and non-survivors (8 [4-17] and 7 [5-15], p = 0.92 respectively). When adjusted for age and history of diabetes, there was no difference in the likelihood of survival in 30-day mortality between the lowest and highest RALE quartiles (HR 0.67 [0.24 - 1.85], p = 0.44).

Conclusions: In unvaccinated, untreated patients with COVID-19 hypoxemic respiratory failure requiring mechanical ventilation there is no association between baseline (time of intubation) radiographic edema as captured by CXR and 30-day mortality. Larger observational studies accounting for vaccination status, oxygenation strategies and medical therapy are needed.

R3

Prone positioning in severe ARDS due to COVID-19

Ana Suarez MD, Jennifer Perez MD, Heidy Izquierdo MD, Sabrina Arshed MD

Introduction: Early application of prone-positioning in ARDS significantly decreased mortality. Our goal is to evaluate the effect of early prone-positioning on COVID ARDS patients.

Methods: A multicenter, retrospective observational analysis with a total of 1,335 patients with COVID ARDS that underwent prone positioning from 1/1/2020- 6/20/2021. ARDS was defined using the Berlin criteria. Logistic regression was used to predict the likelihood of in-hospital all-cause mortality early vs late prone-positioning. Secondary outcomes: age, MAP, days on ventilator and ICU length of stay.

Results: From January 1, 2020 through June 20, 2021, 3,407 patients with COVID ARDS were admitted to the participating facilities. 1,335 patients were included in the final analysis. Patients were 51-80 years old (77%), male (61.5%), white (55.4%), all admitted to ICU on mechanical ventilation. In-hospital all-cause mortality was significantly lower in the shorter time to prone group (<16 hours) than the longer time to prone group (>16, >24 hours), (p <0.001, Exp(B) = 1.119, 95% C.I. [1.088, 1.151]). Mortality rate <16 hours (46.53%), >16 hours (55%) vs >24 hours (68.1%). Patients that were prone in <16 hours were less likely to experience an in-hospital mortality than those prone >16 hours (X2 (1, N= 1513) = 19.051, p <0.001). Days on the ventilator were associated with a decreased likelihood of in-hospital mortality. For each one-day increase in days on vent the likelihood of mortality is 0.978 times as likely. (p < 0.01, Exp(B) = 0.978, 95% C.I. [0.968, 0.989]). Expired and hospice rate by time to prone <16 hours (55.45%) vs >16 hours (79.69%). For each one-year increase in age, patients are 1.045 times as likely to experience an in-hospital mortality (p < 0.001, Exp(B) =1.045, 95% C.I. [1.033,1.056]).

Conclusions: Time to prone had a statistically significant relationship to in-hospital all-cause mortality. Patients with COVID ARDS benefit from early prone treatment.

R4

Procalcitonin as a surrogate for culture positive ventilator-associated pneumonia in COVID-19

Andrew Kim MD, Amy Van MD, Jose Rivera Robles MD, Sikandar Khan MD, Lewjain Sakr MD, Milad Heydari MD, Anas Hadeh MD

Introduction: Procalcitonin has been traditionally used to de-escalate antibiotics in a variety of infections. The initial procalcitonin ventilator-associated pneumonia (VAP) investigations showed that procalcitation use resulted in a significant reduction of days of antibiotic use. Most recently, procalcitonin is being assessed to differentiate between gram-negative, gram-positive, and fungal infections. The goal of this study is to observe if procalcitonin use can be used as a surrogate for bacterial VAPs in COVID-19.

Methods: In this retrospective study, 287 patient records were selected based on the diagnosis of positive SARS-CoV-2 by PCR test and patients requiring mechanical ventilation. Lab values were obtained on admission and during ventilator-associated events (VAE) or sputum collections.

Results: A total of 93 culture-positive VAP were identified in patients with gram-negative bacilli 58 (63%), gram-positive bacteria 19 (20%), and fungal infections 16 (17%). There was a significant difference in the procalcitonin level of gram-negative VAP (42.5 ng/mL, 95% CI 18.5-60.0, p<0.001) and gram-positive VAP (6.8 ng/mL, 95% CI 0.2-6.8, p=0.037) in comparison to culture-negative VAE (3.2 ng/mL). There was no significant difference in fungal VAP procalcitonin (1.135 ng/mL, p=0.185). Additionally, there was no significant difference in admission procalcitonin in gram-negative VAP (0.9 ng/mL, p=0.245), gram-positive VAP (0.9 ng/mL, p=0.53), and fungal VAP cohorts (2.1 ng/mL, p=0.74) in comparison to the culture-negative VAE cohort (1.7 ng/mL).

Conclusions: Gram-negative VAP and gram-positive VAP had a significantly higher correlation with procalcitonin than culture-negative VAE. Conventionally, antibiotic initiation is based on clinical judgement, especially in unstable patients regardless of procalcitonin levels. Thus far, there have been no randomized controlled trials to assess if procalcitonin can be used to escalate therapy in ventilated patients. Our study contributes that there may be a role in using procalcitonin to initiate antibiotic therapy in VAP, with larger increases in procalcitonin for gram-negative and gram-positive bacterial pneumonias.

R5

Influence of Right Ventricular Structure and Function on Hospital Outcomes in COVID-19 Patients

Jozef Oweis, MD; Ali H. Al-Tarbsheh, MD; Annie Leamon, BS; Katharine Goodspeed, BS, MS; Paul Feustel, PHD, Ciril Khorolsky, MD; Anupama Tiwari, MD; Amit Chopra, MD, Mikhail Torosoff, MD

Background: Impact of Right ventricular dysfunction (RVD) noted on outcome has not been well investigated in hospitalized patients with COVID-19 infection.

Objectives: The main aim of our study was to investigate in-hospital outcomes including mortality, ICU admission, mechanical ventilation, pressor support, associated with RV dilatation, and RV systolic dysfunction in COVID-19 patients without a history of pulmonary hypertension.

Methods: It was a single academic tertiary center, retrospective cohort study of 997 PCR-confirmed COVID-19 patients.194 of those patients did not have a history of pulmonary hypertension and underwent transthoracic echocardiography at the request of the treating physicians for clinical indications. Clinical endpoints which included mortality, ICU admission, need for mechanical ventilation or pressor support were abstracted from the electronic charts.

Results: Patients' mean age was 68+/-16 years old and 42% of the study population were females. COPD was reported in 13% of the study population, whereas asthma was 10%, and CAD was 25%. The mean BMI was 29.8+/-9.5 kg/m2. Overall mortality was 27%, 46% in ICU patients, and 9% in the rest of the cohort. There were no significant differences in co-morbidities between expired patients and the survivors (Table 1).
A total of 19% of patients had evidence of RV dilatation and 17% manifested decreased RV systolic function. RV dilatation or decreased RV systolic function were noted in 24% of the total study population (Table 2).
RV dilatation was significantly more common in expired patients (15% vs 29%, p=0.026) and was associated with increased mortality in patients treated in the ICU (HR 2.966, 95%CI 1.067-8.243, p=0.037), who did not need require positive pressure ventilation, IV pressor support or acute hemodialysis (Table 3 and Figure 1).

Conclusions: In hospitalized COVID-19 patients without a history of pulmonary hypertension, RV dilatation is associated with a 2-fold increase in in-patient mortality and a 3-fold increase in ICU mortality.

S6

Eosinophilic Granulomatosis with Polyangiitis and Diffuse Alveolar Hemorrhage Meets Pulmonary Fibrosis and Emphysema: A Case Necessitating Intrapulmonary Recombinant Factor VIIa and Multiple Thoracostomies

Rachel Earle M.D., Colton Hawco M.D., Lucas Goldenburg M.D., David Pendlebury, M.D., Allen Lavina M.D.

Introduction: Eosinophilic granulomatosis with polyangiitis (EGPA) is an anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Diffuse alveolar hemorrhage (DAH) is an associated complication that carries a high mortality. Our case highlights the management of EGPA complicated by ventilator-induced barotrauma with concomitant DAH treated with activated recombinant factor VII (rFVIIa).

Case Description: 55 year old male was hospitalized for hemoptysis. His CT chest was significant for pulmonary fibrosis with centrilobular emphysema. On hospitalization day (HD) #2, he was intubated followed by bronchoscopy which revealed diffuse bleeding; DAH was confirmed with serial lavages lacking color change. Subsequently, he developed a right pneumothorax refractory to placement of two 8-French chest tubes. This progressed to a tension pneumothorax resolved with insertion of a 28-French chest tube connected to wall suction. Persistent bloody secretions prompted repeat bronchoscopies with rFVIIa. On HD 5, 50mcg/kg rFVIIa was divided into 5 portions and instilled throughout all lobes. On HD 14, this was repeated with 80mcg/kg rFVIIa. Meanwhile, his workup would reveal a positive pANCA and anti-MPO consistent with EGPA for which he underwent stepwise therapies starting with pulse dose steroids, plasmapheresis, and then Rituximab. He was extubated on HD 33 and ultimately discharged with plans for a steroid taper and Mepolizumab.

Conclusion: DAH is most commonly associated with AAV. It is a life-threatening emergency that often requires intubation. Our case highlights a risk versus benefit scenario where increased intra-alveolar pressure combined with pre-existing lung disease imparts a high mortality risk with mechanical ventilation. Fortunately, complications in our patient were remediated with thoracostomies. Furthermore, bronchoscopy with bronchoalveolar lavage remains the gold standard diagnostic for DAH, and at times, is considered treatment. However, there is growing evidence in the hemostatic effect of intrapulmonary rFVIIa in this scenario and our patient's course provides support for its inclusion in the clinician's armamentarium.

S7

Started from the Bottom, Now We're Here: The Unrelenting Case of Charcot Marie Tooth Disease from Foot Drop to Recurrent Venous Thromboemboli to Ventilator Dependence

David Pendlebury, MD, Rachel Earle, MD, Lucas Goldenberg, MD, Colton Hawco, MD, Allen Lavina, MD

Introduction: Charcot Marie Tooth Disease Type 4J (CMT4J) is a rare inherited peripheral neuropathy caused by mutations of the lipid phosphatase FIG4 gene. Severe forms may lead to respiratory dysfunction.

Case presentation: A 44 year old male had an initial complaint of falls due to bilateral foot drop. Nerve conduction studies demonstrated axonal and demyelinating polyneuropathy. This raised suspicion for chronic inflammatory demyelinating polyneuropathy. He was started on intravenous immunoglobulin treatments and corticosteroids with no improvement, and soon he became wheelchair bound. 3 months after initial presentation, he developed shortness of breath and chest pain; he was diagnosed with provoked bilateral pulmonary emboli with pulmonary infarcts and started on rivaroxaban. Pulmonary function testing revealed severe restrictive lung disease with decreased respiratory muscle force necessitating a non-invasive auto-titration ventilation device (AVAPS-AE). Genetic testing performed at 4 months since initial symptoms revealed a heterozygous missense variant in the FIG4 gene consistent with CMT4J. 6 months after initial presentation, he went into cardiac arrest due to hypercapnic respiratory failure; return of spontaneous circulation was achieved, and eventually he underwent a tracheostomy and became ventilator dependent.

Discussion: CMT4J is a rapidly progressive pure motor neuron type of CMT which mimics amyotrophic lateral sclerosis. This case highlights the course of the disease as it relates to the timing of symptom onset, diagnosis, and the most crippling complication that is respiratory failure.

Conclusions: Peripheral neuropathies, especially in the benign phases, should provoke early and broad screening, genetic testing, and advanced planning with regard to the devastating sequelae of ascending neuromuscular weakness.

S8

Fat embolism syndrome in a patient with newly diagnosed HbSC: An uncommon presentation of an uncommon disease

Adderley, Patton MD; Innis, Ashley MD; Godoy-Brewer, Gala MD

Introduction: Fat embolism syndrome (FES) is an uncommon and potentially fatal complication of extensive osteonecrosis caused by chronic sickling in patients with hemoglobinopathies such as HbSS, HbSC, and HbSβ. The release of fat globules into the systemic circulation damages tissues by occluding arteries as well as inciting an intense inflammatory response. Interestingly, this condition is more prevalent in patients with milder variants of sickle cell, such as HbSC.

Case Description: 44-year-old female with history of chronic joint pain attributed to seronegative systemic lupus erythematosus presented to the hospital with syncope. Initial evaluation revealed acute hypoxic respiratory failure in the setting of bilateral pulmonary emboli, managed with therapeutic anticoagulation and supplemental oxygen via non-rebreather facemask. Her immediate hospital course was complicated by hypovolemic shock in the setting of a bleeding gastric ulcer, managed with blood transfusions and cauterization. On hospital day two, she experienced two witnessed generalized seizures requiring emergent intubation for airway protection. CT brain was unremarkable. She was transferred to the MICU and extensively worked up due to progressive multiorgan dysfunction, including transaminitis, severe thrombocytopenia, and massive ferritin elevation (40,000 micrograms per liter). Multiple differential diagnoses were sequentially ruled out, including meningoencephalitis, CNS vasculitis, lupus flare, thrombotic thrombocytopenic purpura, and hemophagocytic lymphohistiocytosis. CT abdomen and pelvis revealed a calcified spleen and osteonecrosis of bilateral hips, which prompted hemoglobin electrophoresis, revealing HbSC disease. On hospital day ten, she exhibited decerebrate posturing and tongue biting. Repeat CT brain was negative for acute changes. EEG was negative for seizures. MRI brain revealed innumerable bilateral hemispheric and infratentorial microhemorrhages in a "walnut kernel pattern", pathognomonic for cerebral fat emboli. She subsequently underwent plasma exchange and pulse steroid therapy.

Discussion: Patients with heterozygous hemoglobinopathies are more likely to develop FES. The rarity of this condition frequently results in delayed diagnosis and subsequent treatment, which may play a role in the high morbidity and mortality associated with the disease. Treatment is mainly supportive, however early red cell exchange transfusion and therapeutic plasma exchange have been shown to improve outcomes. We hope that this case will increase awareness of this lethal complication of sickle cell disease.

S9

Misdiagnosed Pulmonary Embolism in Dapsone Induced Methemoglobinemia

Polina Gaisinskaya, MD; Christopher Gebara, MD

Introduction: Hypoxia is one of the most common initial presentations to the emergency department. Life threatening conditions are always first on a physician's mind. We present an interesting case of an HIV/AIDS patient on prophylactic dapsone therapy, who presented with hypoxia resulting in a misdiagnosed and treated pulmonary embolism that was then found to have dapsone induced methemoglobinemia.

Case: A 79-year-old male with a past medical history of HIV, chronic kidney disease and chronic interstitial lung disease presented to the hospital with foot pain. The patient endorsed swelling of his right leg and an accompanying pain with movement. He also reported episodes of dizziness and one episode of falling the week prior. On arrival, he was saturating 90% with dyspnea, though he felt baseline. A V/Q scan was obtained, and showed high probability of a pulmonary embolism, but was inconclusive due to his concurrent lung disease. The patient was then started on a heparin drip. ABG after revealed increased methemoglobin level at 20.9. He recently started a new medication but did not remember the name. Upon further investigation, he was taking Dapsone. Repeat ABG showed a significant decrease in the methemoglobin level following methylene blue administration. After improvement of renal function, CTA showed no evidence of a pulmonary embolism. The patient's anticoagulation and dapsone were discontinued and he was discharged.

Discussion: Dapsone induced methemoglobinemia is found in over 10% of patients started on therapy. A thorough medical history and medication review is crucial in any patient encounter, especially with a broad differential such as hypoxia. Thorough detail could prevent inappropriate or unnecessary testing and subsequent treatment. We hope to raise awareness of the prevalence of dapsone induced methemoglobinemia, especially in vague cases such as ours to aid in proper diagnosis and prompt treatment.

S10

A case of combined pulmonary fibrosis and emphysema in a patient with chronic occupational exposure to trichloroethylene.

Huda Asif, Sydney Braman

Rationale: Trichloroethylene (TCE) is a degreasing agent previously used in aircraft industry. Chronic occupational exposure is associated with pulmonary conditions including pulmonary veno-occlusive disease. Exposure to TCE is associated with pulmonary fibrosis in mice. We present a case of a combined pulmonary fibrosis and emphysema in a veteran with chronic TCE occupational exposure.

Case presentation: 84-year-old male veteran with no significant past medical history presented in pulmonary clinic for progressively worsening shortness of breath for 2 years. Occupational history was significant for prolonged TCE exposure while working in aircrafts maintenance. Exam showed normal oxygen saturation at room air. Bilateral basal inspiratory crackles to mid lung without wheezing. Lower extremity edema was evident. Spirometry showed a normal ratio of forced expiratory volume in 1 second and forced vital capacity while a diffusing capacity of lung for carbon monoxide (DLCO) severely decreased at 24%, total lung volume was 66%. CT chest showed subpleural reticulations predominant in bases, minimal honey-coming, mild bronchiolectasis, and extensive para septal emphysema with apical bullous cystic changes. Rheumatologic work up was negative. These findings were consistent with diagnosis of combined pulmonary fibrosis with emphysema (CPFE). Patient was started on a combination long acting beta agonist (LABA) and muscarinic agonist (LAMA) inhalers and is currently being evaluated for anti-fibrotic therapy.

Discussion: The treatment of CPFE, irrespective of the etiology, is similar to that of emphysema and fibrosis with use of LAMA/LABA in addition to antifibrotic therapy. A significantly low DLCO with a normal FEV1/FVC ratio is an import que to diagnosis.

Conclusions: CPFE is an important entity in fibrotic lung diseases. Careful occupational history may help identify the offending agent. We speculate the association of prolonged exposure to TCE with development of CPFE in our patient. Treatment is essentially the same as that for emphysema and fibrosis.

S11

Hypercalcemia secondary to T-cell neoplasm from HTVL-1 infection

Alfonso Manotas, MD

Human T-cell leukemia/lymphoma virus type 1(HTLV-1) infection is endemic to regions in Japan, the Caribbean islands, areas in Central Africa, South America, Iran, Papua New Guinea, Solomon Islands and Romania. In these endemic areas, transmission occurs most often in infancy, through breast milk, however HTLV-1 can also be transmitted sexually. HTLV-1 infection demonstrates 1-5% risk for development of Adult T-cell Leukemia/Lymphoma (ATLL). A 45-year-old Haitian male with no PMHx presented with a 5-day history of progressive generalized weakness, polyuria, polydipsia and vomiting. Physical exam was remarkable for bilateral axillary lymphadenopathy. Initial lab values showed WBC 49.4, Corrected Calcium 21.5, Lactic Acid 3.5, Alkaline phosphatase 192. 25-OH Vitamin D, PTH were within normal limits. Aggressive IV hydration, calcitonin and zoledronic acid were administered. Upon further investigation, PTHrP was found to be 53 pg/mL (11-20) and 1-25 OH Vitamin D 7.6 pg/mL (19.9-79.3). CT of abdomen and pelvis findings were significant for hepatomegaly, mesenteric and bilateral inguinal lymphadenopathy and bilateral nephrolithiasis. Bone scan negative for any osteolytic or osteoblastic lesions. Flow cytometry of peripheral blood demonstrated marked lymphocytosis, composed of mostly T cells positive for CD2, CD3, CD4, CD5 and negative for CD7. Axillary lymph node biopsy findings showed tissue completely effaced by a diffuse tumor composed of small, medium and large lymphocytes, with a centroblastic appearance. Flow cytometry of the axillary node demonstrated T cells positive for CD3, CD4 and negative for Tdt. Bone marrow biopsy demonstrated hypercellular marrow with trilineage hematopoiesis, including granulocytic hyperplasia and megakaryocytic hyperplasia with atypia and approximately 25% involvement by T cell lymphoma. The patient was discharged at normal calcium levels and baseline functional status with plans for immediate outpatient oncologic follow up and treatment. The typical presentation and disease progression of ATLL includes skin lesions, lytic bone lesions, hypercalcemia, bone marrow involvement and leukemia. Severely elevated calcium that is refractory to calcium lowering interventions is a significant cause of early death for patients with ATLL. Prognosis varies based on classification, such as Acute, Lymphoma-type, Chronic, or Smoldering. A high clinical suspicion should be maintained in patients from endemic regions with HTLV-1 when presenting with isolated lab abnormalities, such as hypercalcemia. Although the prognosis of ATLL is poor, early recognition can prompt faster evaluation by hematology/oncology services where the appropriate chemotherapy regimen and/or allogeneic hematopoietic cell transplantation can be initiated.

S12

A Case of Pulmonary Tuberculosis Mimicking Community Acquired Pneumonia

Sadaf Afraz, DO, Amy Van, MD, Jose Rivera, MD, Lewjain Sakr, MD, Miquel Gonzalez, MD, Jinesh Mehta, MD.

Introduction: Pulmonary tuberculosis (TB) presenting as community acquired pneumonia (CAP) is a rare manifestation of the disease that can pose as a diagnostic challenge. The incidence of TB in patients presenting with clinical and diagnostic signs of CAP has been previously reported as 0.3-35%, based on regional prevalence and individual risk factors. We report a case of pulmonary TB presenting clinically and radiographically as CAP, leading to delay in diagnosis and treatment.

Case presentation: An 86-year-old Caucasian female without significant history presented to the emergency department for 4-month history of fever, progressive shortness of breath, and productive cough with yellow sputum. Associated symptoms included weight loss, anorexia, and malaise. Travel history was significant for missionary work in Africa 30 years earlier. Prior to admission, she was prescribed several courses of antibiotic regimens as outpatient including amoxicillin/clavulanic acid, azithromycin, and levofloxacin all of which provided temporary relief. Review of prior chest radiograph revealed patchy opacity of the right upper and middle lobe. On examination, patient was febrile with maximum temperature of 101F. Physical exam was significant for right sided decreased breath sounds without rhonchi or wheezing. Chest commuted tomography (CT) revealed right hilar and mediastinal lymphadenopathy as well as right upper and right middle lobe ground glass infiltrate and consolidation respectively. She was initiated on ceftriaxone and azithromycin for presumed CAP. Initial sputum stain and culture were negative. Her hospital course was complicated by persistent fevers and worsening hypoxia leading to escalation of antibiotic therapy to vancomycin and piperacillin/tazobactam. Due to lack of clinical improvement and relevant travel history, sputum samples were sent for acid fast bacilli (AFB) stain and culture. The *mycobacterium tuberculosis complex* (MTB) probe rapidly returned positive. The patient subsequently completed 14 days of inpatient RIPE therapy with resolution of symptoms.

Discussion: Factors leading to misdiagnosis of TB as CAP include radiographic imaging similar to acute pneumonia and atypical clinical course. Additionally, the acute presentation of TB as CAP results in treatment with standard antibiotics, many of which have antituberculosis effect leading to transient symptomatic improvement. This can delay diagnosis and subsequently prolong the disease course giving rise to increased risk for development of disseminated TB, vertical transmission, and overall increased mortality. As in our case, the patient was unnecessarily treated with several rounds of empiric antibiotics which triggered a delay of laboratory diagnosis and initiation of appropriate therapy. Therefore, it is essential for clinicians to keep TB high in their differential in patients diagnosed with CAP that are unresponsive to standard empiric therapy.

S13

Aspirating your way to eggerthia catenaformis bacteremia and parvimonas micra lung abscess

Fatima Ahson MD, Ibrahim Ali MD, Naren Bhupatiraju MD, Luisa Barrueto DO, Katrina Ramsamooj MS3

Introduction: Eggerthia catenaformis is an oral anaerobe rarely associated with human infections. E. catenaformis has been documented in literature as the causative agent of brain abscess, pleural empyema, necrotizing fasciitis, deep neck space infection, peritonitis, and septic knee arthritis however documented bacteremia due to Eggerthia catenaformis is extremely rare.

Case Presentation: We present a case report of a polymicrobial infection with oral pathogens due to aspiration in the setting of poor dentition and overdose causing loss of consciousness. A 48 year old Caucasian male with a past medical history of IVDU, recent Hepatitis C diagnosis and tobacco abuse presents from a rehab facility for fever, flank pain and a nonproductive cough. Chest X-ray found left basilar opacity. Ct chest found a 8.8 cm cavitary mass at the left costophrenic sulcus. Patient was cultured and started on antibiotics. CT surgery was consulted and patient underwent thoracoscopic decortication, parietal pleurectomy and pulmonary pneumolysis. Wedge resection of the lung was done to drain the abscess and chest tubes was placed. Surgical pathology grew parvimonas micro. His blood cultures grew Eggerthia Catenaformis. Antibiotics were changed to just pipericillin-tazobactam but despite this patient was febrile and so antibiotics were changed to ampicillin/sulbactam and was discharged with Augmentin.

Discussion: Patients that have poor dentition are prone to developing infections like pneumonia and bacteremia. Bacteremia with Eggerthia Catenaformis is exceedingly rare with only a few case reports to our knowledge. The antibiotics that have been used in the past have been amoxicillin with or without clavulanate. Other antibiotics include clindamycin, metronidazole, imipenem to name a few. The response to antibiotics is fairly good and has minimal resistance usually.

S14

Beyond the Looking Scope: A Case Report of a Missed Foreign Body Aspiration

Amy Van MD, Colton Hawco MD, Sadaf Afraz DO, Jose Rivera MD, Allen Lavina MD, Miquel Gonzalez MD, Ihab AlShelli, MD

Introduction: Foreign body aspirations (FBA) typically occur in infants and children. However, adults, especially those around the sixth decade of age, with encephalopathy, neurological disease, etc., are predisposed for an aspiration event. Radiopaque materials, like metal or teeth, can be easily identified on chest x-ray (CXR), but up to 32% can be negative during an acute aspiration event. This is because food, the most common aspirated material in adults, is difficult to spot on plain imaging. Bronchoscopy remains the gold standard for diagnostic evaluation and therapeutic intervention for FBA. However, if prompt identification and removal is delayed, granulation tissue and purulent discharge can further conceal the foreign body.

Case Presentation: A 72-year-old male with history of chronic obstructive pulmonary disease (COPD), 75-pack-year smoking history and non-small cell lung cancer status-post right upper lobe lobectomy presented to the pulmonology clinic for recurrent dyspnea and cough. Four months prior, he had night sweats without hemoptysis or tuberculosis risks and early evaluation with CXR exhibited patchy opacities at the right base. He was treated for community acquired pneumonia and COPD exacerbation, but symptoms persisted for four weeks prompting a chest computed tomography (CT). This revealed an endobronchial tumor in the right lower lobe (RLL). Subsequent bronchoscopy with biopsy showed inflammatory cells and mucopurulent debris. At this point, he was referred to our clinic for a second opinion. Repeat CT showed debris in the RLL bronchus and localized micronodular opacities.
Symptoms remained despite medical therapy until second bronchoscopy revealed an obstructing endobronchial white foreign body. The extracted intact mass was grossly consistent with chewing gum. The dyspnea and cough resolved post-procedurally and pathology was negative for malignancy.

Discussion: Patients with FBA often present with recurrent pneumonias in the same area and diagnosis is not suspected until well after initial presentation. Without a clear history of an inciting event, which are often not remembered, nonspecific respiratory symptoms may be mistakenly attributed to other medical conditions. This is especially true in our geriatric population who usually carry diagnoses such as COPD, congestive heart failure, or pneumonia all of which can symptomatically resemble FBA. In addition, patients with neurologic impairment may be unable to provide a sufficient history to prompt evaluation for FBA.
In this case, the patient's history of COPD, extensive smoking and prior cancer led to significant concern for malignancy. His inability to recall the aspiration and non-specific initial imaging did not trigger concern for FBA. This then propelled a cycle of the foreign body being hidden by granulation tissue that further delayed recognition, diagnosis, and treatment upon initial bronchoscopy. It is important to acknowledge the harm that anchoring bias, or the inclination to rely on an initial piece of information when making decisions, could have. By anchoring to malignancy, our patient may have suffered through unnecessary interventions. Pulmonologists should always have an open mind with broad differential diagnoses when encountering patients that are not improving despite treatment that at the time of evaluation is deemed correct.

S15

Impending cardiopulmonary collapse following Acupuncture

Luisa Barrueto DO, Teresa Koger MD, Fatima Ahson MD, Ibrahim Ali MD, Naren Bhupatiraju MD

Introduction: Acupuncture is a form of therapy in Traditional Chinese Medicine practiced by many worldwide and covered by Medicaid in some states (1,2). Much attention is placed on disagreements regarding recommendations on the application of Acupuncture as a form of medical therapy across professional organizations and not enough on potential complications of its practice. We present a case of an iatrogenic near tension pneumothorax following a routine acupuncture session.

Case Presentation: A 32-year-old female with no past medical history presents to the emergency room with worsening dyspnea and central pleuritic chest pain. Symptoms started at rest 2 hours following acupuncture session. Patient presented to the ED 12 hours post-acupuncture session when her symptoms rendered her unable to sleep. On arrival patient was found to be in moderate distress, tachypneic, tachycardic, with a stable blood pressure and normal SpO2%. Her trachea was midline, there was no stridor, she had decreased chest excursion on the left along with absent vocal fremitus. Chest X-ray showed a large left-sided pneumothorax with near complete collapse of left lung along with a mild shift of the mediastinum. She was immediately placed on a non-rebreather mask followed by a chest tube placement with left lung-expansion on repeat imaging. She is a lifetime non-smoker, denied recent air travel, scuba diving, and had no identifiable causes of secondary spontaneous pneumothorax. Patient shares she gets weekly sessions for stress induced neck and back pain, and this one was no different than prior with needles placed subcutaneously medial to the medial scapular border bilaterally. The chest tube was successfully removed at the 48-hour mark.

Discussion: An iatrogenic tension pneumothorax is a potentially fatal complication that can develop insidiously from Acupuncture. It has come to our attention, that acupuncture complications are poorly reported. We share this case in an effort to raise awareness as increasingly more insurances cover acupuncture treatment sessions for the management of chronic back pain.

S16

CMV Encephalitis as the First Presentation of AIDS.

Shany Quevedo, MD, Lyanne Rolon-Rosario, MD, Michael Vempala, MD, Richard Medina-Perez, MD, Yoel Tajes Leiva, MD

Introduction: Cytomegalovirus (CMV) is a double-stranded DNA virus known for causing disseminated or localized disease in immunocompromised patients. In those with HIV, typically, the cluster of differentiation (CD4) is less than 50. We present a case of CMV as the initial presentation of AIDS in a patient with CD4 T cell count greater than 50/mm3 [4].

Case Summary: A 65-year-old Haitian male without past medical history presented with two weeks of altered mental status and word-finding difficulty. Physical exam revealed cachexia, an ataxic gait and sudden urinary incontinence upon standing. Labs were unremarkable. Computerized tomography (CT) of the brain was notable for mildly dilated ventricles. Subsequent imaging revealed ventriculomegaly and scattered white matter T2 enhancing regions without hydrocephalus. Syphilis serologies and electroencephalography (EEG) were negative. Rapid HIV test resulted positive and the initial CD4 T cell count was 65/mm3. He was started on prophylactic antibiotics and later intravenous ganciclovir when an encephalitis panel resulted positive for CMV. He was scheduled to complete six weeks of therapy and later started on highly active antiretroviral therapy (HAART) and was advised to follow up outpatient.

Discussion: CMV encephalitis is a rare disease, most likely presenting in immunocompromised patients. HIV patients positive for CMV typically have CD4 counts of 50 or less, or HIV viral loads around 100,000 copies/ml of plasma. In the case of our patient, CD4 count was greater than 50. We only found one other case with similar CD4 counts, but this patient had several concurrent infections as well. Our patient presented with symptoms mimicking normal pressure hydrocephalus, consisting of confusion, gait instability and incontinence, which could have led to a missed diagnosis of CMV if not inquisitive about etiology of presentation. This case emphasizes the importance of maintaining a broad differential in patients with acute neurological symptoms.

S17

A Hidden Case of Hemophagocytic Lymphohistiocytosis Presenting Initially with Acute Respiratory Failure

Lewjain Sakr, MD. Sadaf Afraz, MD. Alex Ghorishi. Amy Van, MD. Jose Rivera, MD. Sikandar Khan, MD. Allen Lavina, MD. Justin Dolan, MD

Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a life threatening hyper-inflammatory condition due to dysregulated activation of immune cells which results in multi-organ failure and death without prompt treatment with immunosuppressive cytotoxic chemotherapy [1]. We present a case of a patient who presented with acute respiratory failure that was later found to be due to HLH.

Case presentation: 65-year-old male with no significant past medical history presented to the emergency department with fever, malaise, shortness of breath for five days. On presentation, patient was afebrile, tachycardic with an oxygen saturation of 92% on room air. Labs were significant for AST 483, ALT 275, platelets 58, D-dimer 1980, and lactic acid 2.6. Chest X-ray demonstrated possible pneumonia. A computed tomography (CT) of chest, abdomen, and pelvis were significant for enlarged spleen with multiple infarcts. Patient developed acute hypoxemic respiratory failure with worsening oxygen requirement and subsequently became hypotensive and was transferred to the intensive care unit for further management of shock – presumed septic and treated with antibiotics. Repeat imaging revealed new onset hemoperitoneum without evidence of active bleeding. Patient underwent a bone marrow biopsy due to subsequent worsening hematological disturbances and concern for disseminated intravascular coagulation and was found to have diffuse large B-cell lymphoma with HLH. He was started on chemotherapy and was progressively weaned off oxygen back to room air prior to discharge.

Discussion: Hemophagocytic lymphohistiocytosis (HLH) is a rare disorder, with an estimated yearly incidence of 1.5 per million with a 2:1 male to female ratio [2]. The innate immune system responds to infection by releasing cytolytic enzymes. In HLH, the immune cells are unable to effectively inoculate target cells with toxic enzymes, leading to increased recruitment of cytotoxic cells with elevated cytokine release to combat the persistent pathologic antigen. Hypercytokinemia overstimulates macrophages leading to hemophagocytosis and widespread inflammation with resultant organ damage [1]. Multiple systems might be affected as a result of the inflammatory insult including cardiac, pulmonary, and renal. The diagnosis of HLH can be challenging and diagnostic criteria are not always present at the same time. A diagnosis is established by the presence of 5 out of the 8 total HLH-2004 criteria which include fever, cytopenia, splenomegaly, hypertriglyceridemia +/- hypofibrinogenemia, biopsy-proven hemophagocytosis, ferritin greater than 500 ng/mL, low or absent NK-cell activity, and elevated serum soluble interleukin receptor 2 alpha levels [3]. Our patient presented with what seemed to be an acute infectious respiratory process. Differential diagnosis included COVID-19 infection given the prevalence of the infection during this time. This case highlights the importance of keeping a broad differential and recognizing the underlying signs of possible HLH that may arise later during the course of hospitalization.

S18

Distal Intestinal Obstruction with Cystic Fibrosis

Aamer Mahmood, MD; Ishna G. Poojary, MD

Introduction: Cystic Fibrosis (CF) is associated with multi-system complications. Distal intestinal obstruction syndrome (DIOS) is one such complication. We present a first-time occurrence of DIOS in a patient with multiple risk factors.

Case Description: A 44-year-old man with history of CF (homozygous ΔF508), pancreatic insufficiency, bilateral lung transplant (26 years ago) presented with two weeks of progressive dyspnea and green sputum. Vital signs were stable with a grossly normal physical exam. Bloodwork revealed a leukocyte count of 15.2 K/μL. CT Chest showed bilateral areas of patchy consolidations and left lung cavity (5.3cm x 7.9cm). Respiratory culture grew Pseudomonas aeruginosa and intravenous antibiotics were planned. For vascular access a portacath was placed and then replaced 2 days later due to malfunction under anesthesia with propofol, fentanyl and midazolam. In between, a bronchoscopy with bronchoalveolar lavage (BAL) was performed using fentanyl and midazolam. On the sixth day, patient complained of abdominal discomfort, non-bilious vomiting, constipation since admission. Examination showed hypoactive bowel sounds with right lower quadrant tenderness. Abdominal X-Ray demonstrated gas-filled small bowel loops. CT of the abdomen showed partial small bowel obstruction (SBO), dilated bowel loops (3.9 cm) and left hemi-pelvis transition point. Intravenous hydration, antiemetics, laxatives and enemas demonstrated little improvement. A nasogastric tube was attempted but not tolerated. CT abdomen repeated on day 13 showed partial SBO, worsening small bowel dilation (4.5 cm) and midline lower abdomen transition point. Exploratory laparotomy was performed with enterotomy, decompression of small bowel by evacuating inspissated feces and fecal obstruction was identified three feet from the ileocecal valve. Patient had a bowel movement 3 days post-surgery and uneventful course till discharge.

Discussion: DIOS results from thickened fecal obstruction in the small bowel due to admixing of viscous feces with thickened mucus in distal small intestine. [1] Risk factors for DIOS include homozygous ΔF508 mutation, prior meconium ileus/DIOS, dehydration, lung transplantation and Pseudomonal infections.[2] Despite having risk factors, our patient had no prior history of DIOS. We believe that the frequent procedural opiates culminated in severe DIOS. DIOS is usually managed conservatively and in rare cases like ours, surgical intervention becomes necessary.

S19

Type B Lactic Acidosis: An emerging association with Hemophagocytic Lymphohistiocytosis (HLH)

Rivera, Jose MD , Koppikar, Maekhila MS , Van, Amy MD, Afraz, Sadaf MD , Rios, Javier MD, Gonzalez, Miquel MD, Bello, Alibel MD , Zisman, David MD

Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a rare condition in which immune cells cause a cytokine storm that leads to life-threatening organ damage. In adults, it is often secondary to underlying conditions such as infection or malignancy. The clinical presentation of HLH is highly variable and nonspecific; symptoms such as fever and malaise often prompt a diagnosis of sepsis, thereby delaying care. Other findings in HLH include encephalopathy, organomegaly, transaminitis, anemia, coagulopathy, and GI upset. However, an underreported finding suggestive of HLH is lactic acidosis (LA). Here, we discuss the case of a patient diagnosed with HLH after he presented with persistent Type B LA and explore the limited existing literature about this association.

Case Presentation: A 54-year-old male with extra-nodal marginal zone B-cell lymphoma of the small bowel and secondary anaplastic large cell lymphoma on Brentuximab presented with shortness of breath (SOB). Vital signs on presentation were heart rate 97 beats per minute, blood pressure 92/72 mmHg, oxygen saturation 97%, and temperature 36.8□C. Physical exam revealed splenomegaly. ABG: 7.45/28/255 on 50% FiO2 with lactate of 8.8 mmol/L. He was placed on noninvasive mechanical ventilation. Computed tomography of the chest without contrast revealed new minimal ground glass opacities in the left upper lobe. He was admitted to ICU given his LA and possible impending respiratory arrest and started on broad-spectrum antibiotics and methylprednisolone to cover for infection and/or pneumonitis. Although his respiratory distress improved, his LA did not despite appropriate fluid resuscitation. He developed new fevers, thrombocytopenia, and anemia. Given the patient's persistent LA, alternative diagnoses were considered. An elevated serum ferritin and suspicion for HLH vs invasion of lymphoma into the bone marrow and lungs vs Warburg Effect prompted a bone marrow biopsy which showed hemophagocytosis. HLH was diagnosed. As per the patient's wishes, goals of care shifted to hospice.

Discussion: While the mechanism of Type B LA in hematologic malignancy is well established, it is difficult to attribute our patient's LA to his malignancy without exploring a possible association with his HLH due to the temporal relationship between the two. Case reports of HLH presenting as Type B LA are limited. One illustrated a patient whose persistent Type B LA led to the diagnosis of diffuse large B-cell lymphoma and presumed concurrent HLH despite negative bone marrow findings. Another case presented with Type B LA that persisted for several weeks prior to HLH diagnosis with a literature review containing five cases with similar findings. Given limited reported cases, by expanding on this literature review with our case, we support the fact that this association exists. Further investigation is needed to uncover the mechanism and prognostic value of Type B LA in HLH. Moreover, intensivists should keep their differential broad when encountering Type B LA given that the etiology could be far more sinister than expected, as in our patient.

S20

A Life-Threatening Complication of a Paraesophageal Hernia Repair

Katherine Reano, MD

Background: Hiatal hernias are a common occurrence in the geriatric population which can reduce their quality of life. In contrast, giant hiatal hernias, otherwise known as paraesophageal hernias, are rarer and is defined as a hernia with greater than 30% of the stomach translocating into the thoracic cavity.[1] These are usually associated with symptoms of severe acid regurgitation, heartburn, and decrease in appetite. Laparoscopic surgical repair is the standard of care, and although studies have shown the procedure is safe and effective, there continue to be many risks involved. Here we have a case of laparoscopic repair of paraesophageal hernia with volvulus resulting in an unexpected outcome.

Case Presentation: 86-year-old female with history of reflux and atrial fibrillation on Eliquis, presented with chronic vomiting of one month and failure to thrive. She was found to have aspiration pneumonia and bilateral pleural mild effusions on initial chest x-ray and was treated with a course of ampicillin-sulbactam. She was also noted to have a large paraesophageal hernia with partial volvulus, likely the cause of her chronic emesis. Hospitalization was complicated by upper gastric intestinal bleed requiring one unit of blood transfusion. She subsequently developed atrial fibrillation with rapid ventricular response and acute kidney injury. She was stabilized, surgery was consulted, and the patient underwent robotic hiatal hernia repair with gastropexy. The surgery was complicated by left sided capnothorax resulting in release of pleural fluid into abdominal cavity, right hemothorax, shock, and rapid atrial fibrillation. The patient received two epinephrine pushes and was transferred to the intensive care unit. She remained intubated from the procedure, a right sided chest tube was placed, she was started on piperacillin-tazobactam, norepinephrine, and amiodarone. Unfortunately, the patient continued to decline, experiencing multiorgan failure and eventual disseminated intravascular coagulation. An attempt at continual renal replacement therapy was unsuccessful and patient underwent pulseless electrical activity arrest and expired.

Discussion: Elderly patients have a higher incidence of hiatal hernias possibly due to the age-related weakening of the diaphragm. Although multiple studies have shown laparoscopic repair is safe, effective, and improves quality of life, there are still many risks involved.[2,3,4] The most common complication is left pneumothorax since the left parietal pleura is exposed during the dissection.[5] With this patient, she experienced left sided capnothorax and right sided hemothorax. It has been found that there is a higher risk associated with strangulation, volvulus, and perforation and these should be considered prior to surgery.[6] Unfortunately, in this patient, her compilations ultimately resulted in decompensation and death. Awareness of this risk needs to be adequately assessed, preventative measures both prior and during surgery should be taken, and if pneumothorax transpires, immediate correction should occur to avoid this catastrophic event.

S21

Bullous Disease Gone Viral: HTLV-1 associated Pulmonary Lymphoma with Tropical Spastic Paresis and Recurrent Pneumothorax

Veronica Williams, DO, Nydia Martinez, MD

Introduction: Human T-cell leukemia virus type I (HTLV-1) is a retrovirus affecting CD4 T-cells. The two major HTLV-1-associated diseases are adult T-cell lymphoma (ATL) and HTLV-1-associated myelopathy. Primary pulmonary lymphomas represent only four percent of all Non-Hodgkin's lymphomas. We report a unique case of primary pulmonary T-cell lymphoma associated with HTLV-1 infection presenting clinically with rapidly progressive diffuse bullous disease and recurrent pneumothoraces.

Presentation of Case: A 36 year-old male presented with 6-months duration of cough, dyspnea, fatigue, 40-pound weight loss and facial rash, complicated by multiple episodes of pneumothorax occurring after paroxysms of cough. He was initially treated with chemical pleurodesis, bullectomy and VATS. He subsequently presented with new left-sided pneumothorax following several days of upper respiratory symptoms. Medical history was notable for HTLV-1 and tropical spastic paraparesis. Physical examination demonstrated facial erythema with scaling on seborrheic areas. CBC and chemistry were normal. HTLV I/II IgG Antibodies were reactive. Alpha-1-antitrypsin, C-ANCA, P-ANCA, HIV, Hepatitis and autoimmune panel were negative. CT chest showed severe bullous emphysema, large apical bilateral bullous formation, pleural blebs, and micronodular infiltrates with interlobular septal thickening; these findings were markedly worse compared to a CT scan performed six months prior. Thorascopic lung biopsy revealed interstitial lymphoid cell population CD3+/CD25+ positive; marked nuclear atypia, subpleural bleb formation and pleural thickening. Bone marrow biopsy showed an immunophenotype consistent with partially activated T-cell population with inverted CD4:CD8 ratio and T-cell receptor rearrangement.

Clinical Course: The patient was treated with interferon and zidovudin; he gained 25 lbs over two years with no new episodes of pneumothorax and respiratory symptoms remained stable. Follow up CT one year after chemotherapy showed some progression of bullous emphysema.

Conclusions: To our knowledge, this is the first case of a Pulmonary T cell lymphoma from HTLV-1 to present with rapidly progressive bullous emphysema. The use of antiretroviral agents has shown activity in this disease with improvement in survival and response rate.

S22

A Case of Bilateral Obstructive Urolithiasis Leading to Septic Shock

Michael Vempala MD, Lyanne Rolon Rosario MD, Shany Quevedo MD, Richard Medina Perez MD, Livasky Concepcion MD

Introduction: Urolithiasis is a common condition, prevalence one in 11 people. Acute bilateral obstructive uropathy occurs in five in 10000. Presentation of obstructive urolithiasis in a patient with concomitant septic shock and triple acid-base disturbance presents a valuable teaching case.

Case Presentation: A 55 year-old male with a history of hypertension, congestive heart failure, type 2 diabetes, renal cell carcinoma, and urolithiasis presents with dyspnea. Patient noted acute left flank pain. On exam, patient was hemodynamically stable but in respiratory distress. Labs showed leukocytosis, anemia, hyperkalemia, anion-gap metabolic acidosis, lactic acidosis. Renal ultrasound showed bilateral mild hydronephrosis with left nephrolithiasis. Computed tomography of the abdomen showed large bilateral obstructing renal calculi, both causing hydronephrosis. Patient was intubated for impending respiratory failure. Urology was consulted for renal calculi management and analysis. Interventional radiology was consulted and placed bilateral percutaneous nephrostomy tubes. Patient was assessed with septic shock and started on empiric broad-spectrum antibiotics with cultures sent out. Patient required four vasopressors as well as stress steroids post-intubation and emergent hemodialysis was initiated. Patient was admitted to the intensive care unit and monitored by the ICU team. On day three of stay, the patient was extubated and removed off vasopressors. By day five, cultures resulted as negative. The patient was weaned off hemodialysis and nephrostomy tubes were removed. Urology performed cystoscopy and placed bilateral ureteral stents. On day 6 of his stay, the patient was discharged home with follow-up for shock wave lithotripsy.

Conclusion: This case provides insight into how a patient with obstructive urolithiasis can present and how they can be managed. Mainstay of treatment in patients with obstructive urolithiasis with hydronephrosis is to relieve obstruction either with nephrostomy tubes or with ureteral stents. In addition, diagnosis of the stone etiology should be done to help guide for definitive treatment and prevention of recurrence.

S23

Reverse Bernheim Phenomenon - Always a Conundrum

L.A. Wulff MD, M. Islam MD , R. Restrepo Jaramillo MD , K. Patel MD , J. D. Herazo-Maya MD , D. Bandyopadhyay MD

70-year-old male presented with dyspnea and exertional syncope. His medical history revealed diastolic heart failure and pulmonary arterial hypertension (PAH) on sildenafil and ambrisentan. Admission blood pressure was 128/55 mmHg with heart rate 81 bpm. Exam showed distended cervical veins and bibasilar crackles without ankle edema. Labs significant for BNP 1418 pg/mL and troponin 0.010 ng/L. Chest x-ray showed no abnormalities. Cardiac loop recorder showed idioventricular rhythm. An exercise echocardiogram, during which patient became symptomatic, confirmed severe RV dilatation and dysfunction with left ventricular outflow tract (LVOT) obstruction and transient low-output state, without shunt. Findings returned to baseline at rest. The patient was started on intravenous treprostenil therapy with resolution of symptoms and clinical improvement. Repeat stress echocardiogram months later showed mild RV dilatation without overt LVOT compression on exercise. We present a unique case of the Reverse Bernheim Phenomenon, where severe RV dilatation causes a leftward shift of the IVS leading to compression of the LV cavity and essentially an LVOT obstruction. This leads to distorted LV geometry and compromised LV function which clinically manifests as left heart failure and can be seen with or without LV dysfunction. To our knowledge there is only one other described case of this phenomenon where its features are only apparent with exercise while the echocardiography at rest is normal. A high index of suspicion is important for early detection as this phenomenon changes management of PAH in the clinical presentation of worsening diastolic heart failure. The common scenario of elevated LV filling pressure thought to be secondary to increased flow to the left heart leads to de-escalation of pulmonary vasodilator therapy. In the case of this phenomenon the elevated LV filling pressures can only be alleviated by reducing RV size which paradoxically is accomplished by augmentation of pulmonary vasodilators.

S24

An Unusual Case of Pulmonary Hypertension Induced by Swyer James MacLeod Syndrome

Laura Muller, MD, Keegan Plowman, MD, Jalpa Patel, DO, David Lindner, DO

Introduction: Swyer James Macleod syndrome (SJMS) is a rare condition thought to result from early pulmonary infections. The syndrome is characterized and diagnosed by CT findings of unilateral hypoplasia of pulmonary vasculature resulting in pulmonary artery hypoperfusion and reduction in size of lung parenchyma. Recurrent pulmonary infections are often seen with concomitant bronchiectasis. Typically, it is diagnosed in childhood. Progression of disease to development of Group III pulmonary hypertension is uncommon.

Case Summary: A 56-year-old female presented with progressive dyspnea. She had a past medical history of early age tuberculosis, an aspiration event, chronic hypoxemic respiratory failure, and a prior suspected pulmonary embolism. Pulmonary function tests revealed mixed obstructive and restrictive lung disease. She required 2 liters nasal cannula oxygen. BNP was 79 pg/mL. Echocardiogram findings included an ejection fraction of 60%, with 2/4 diastolic dysfunction, moderate tricuspid regurgitation, moderately enlarged right atrium and ventricle, and estimated right ventricular systolic pressure of 55-60 mmHg. High resolution CT demonstrated a small left lung, mediastinal shift with bronchiectasis, bronchial thickening, left pleural thickening and left upper lobe scarring. Right heart catheterization demonstrated a right ventricular pressure of 35/4 cmH20, pulmonary artery pressure of 35/18 cmH20 and pulmonary capillary wedge pressure of 12 cmH20 consistent with mild pulmonary hypertension, with Functional Class III and REVEAL score +7 (without 6MWT).

Discussion: This is a case of SJMS with development of significant pulmonary disease presenting in adulthood. Most importantly, it is one of only 4 case reports highlighting progression of disease to Group III pulmonary hypertension. In addition to supplemental oxygen and treatment of underlying lung disease, patients can be trialed on treprostinil to reduce symptoms. In the setting of recurrent infections, failure of medical therapy, and saccular bronchiectasis, patients may benefit from pneumonectomy.

S25

Borborygmi in the chest?

Gustavo Avila, MD, Claudia Tejera Quesada, MD, Jessica Baek, MD, Renuka Reddy, MD

Introduction: Hiatus hernia is a condition involving herniation of the abdominal cavity contents, most
commonly the stomach, through the diaphragm into the mediastinum. This may result in gastroesophageal reflux disease. Complications may include Volvulus or bowel obstruction. The incidence of Hiatal hernias increases with age; approximately 60% of individuals aged 50 or older have a hiatal hernia. Of these, 9% are symptomatic. 95% of these are "sliding" Hiatal hernias, and only 5% are the "rolling" type IV paraesophageal. This case highlights the importance of the physical exam on suspecting this entity with the auscultation of bowel sounds in the chest.

Case Presentation: 92 yo male with a medical history of dementia and Diabetes Mellitus insulin-dependent, presented to ER with abdominal pain accompanied by constipation, nausea, and vomiting. Physical Exam remarkable for Chest with audible bowel sounds posteriorly, non-tender abdominal palpation, other systems were clinically normal. Blood work significant for elevated Total Bilirubin: 2.1 and Unconjugated Bilirubin:1.4. Imaging CT Chest showed a Large hiatal hernia. The entire stomach and portions of the colon were above the diaphragm level within the hiatal hernia. Surgery evaluated the patient and stated that findings were consistent with Type IV paraesophageal hernia. Surgical intervention was offered, but the patient refused. Patient symptoms improved during hospitalization, and he was able to tolerate feeds and pass gases, for which the patient was
able to be discharged.

Discussion: Hiatal hernia has often been called the "great mimic" because its symptoms can resemble many disorders. In patients with Type IV hernia, the presence of bowel sounds in the thorax secondary to the protrusion of the intestine into the thoracic cavity can be detected, which makes the diagnosis suspicious, as occurred in the reported case. Symptomatic hiatal hernia in a patient is usually due to acid reflux. Therefore, the aim is to reduce the symptoms of gastroesophageal reflux disease (GERD) by addressing gastric acid secretion.
According to the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) surgical treatment is indicated for symptomatic patients with paraesophageal hernia (6), especially those with obstructive symptoms and gastric volvulus which require urgent surgery. Within the surgical techniques, open surgery presents a high complication rate. It requires a prolonged recovery while laparoscopic surgery has proven feasible and safe, giving a shorter hospital stay and lower complication rates.

Conclusion: The finding of bowel sounds in the thorax should make clinicians suspect the presence of this entity and reinforce the art of physical examination that should always be essential in our clinical reasoning. Imaging studies should be conducted to confirm this diagnosis, in order to carry out a timely treatment of the patient

S26

Hemolysis in patients in cardiogenic shock on VA-ECMO. Clinical implications and outcomes

Pedro Torres M.D., Baher AL Abbasi M.D., Jesus Pino M.D., Robert Chait M.D., Sajid Mirza M.D.

Introduction: The clinical implications of hemolysis in patients on veno-arterial extracorporeal membrane oxygenation (VA-ECMO) for the treatment of cardiogenic shock (CS) are unclear.

Methods: This retrospective cohort study involved patients with cardiogenic shock that underwent VA-ECMO implantation between 2/2015-6/2020 in a tertiary cardiovascular center. In high-risk patients (drop>2 g/dl in hemoglobin, increase in total bilirubin and changes in urine color), the criteria used to define hemolysis were: elevated lactate dehydrogenase(>246 U/L), increase in plasma free hemoglobin(>15 mg/dl) and decrease in haptoglobin(<50 mg/dl). Patients were stratified based on the presence of hemolysis or no hemolysis. Evaluated outcomes included in-hospital mortality, need for blood transfusion, acute kidney injury (AKI) requiring continuous venovenous hemodialysis (CVVHD), and intensive care unit length of stay (ICU LOS).

Results: 58 patients were included, of which, 34%(20/58) were female with a mean age of 53±17. Indications for ECMO were myocardial infarction(MI)-CS in 24% of patients, heart failure(HF)-CS in 43%, and post-cardiovascular surgery(CVS)-CS comprised the remaining 33%. Hemolysis occurred in 34% (20/58) of patients (4 HF-CS, 7 MI-CS, and 9 post-CVS-CS), p=0.0356. Out of the 14 patients with MI-CS, 50%(7/14) developed hemolysis vs 16%(4/25) of the HF-CS vs 47%(9/19) in the post-CVS group. 43 patients underwent VA-ECMO implantation and 15 patients underwent VA-ECMO plus Impella (ECPELLA) implantation. Hemolysis occurred in 30%(13/43) of the VA-ECMO group vs 46%(7/15) of the ECPELLA group, p=0.3453. Outcomes: In-hospital mortality was higher in the hemolysis group 80%(16/20) vs 20%(4/20) for the non-hemolysis group (p= 0.0476) OR: 3.6 (95 % CI: 1.0137-12.7843). There was no significant difference in transfusion requirement (p=0.4248), CVVHD (p=0.2749), and ICU LOS (p=0.5923) between groups.

Conclusion: Hemolysis in patients with CS on VA-ECMO is associated with a 3-fold increase in mortality. MI-CS and post-CVS-CS are at a higher risk of developing hemolysis. HF-CS patients had a significantly lower incidence of hemolysis.

S27

CAPTAIN: Effects of lung function at screening (FEV_1 % predicted) as a continuous variable on treatment outcomes

Papi A, Barnes N, Fowler A, Kerstjens H, Kerwin E, Mannino D, Nathan R, Pavord I, Pizzichini E, Slade D, Zarankaite A, Oppenheimer J

Introduction: In patients with uncontrolled asthma despite inhaled corticosteroid/long-acting β_2 agonist (ICS/LABA) therapy, the effects of adding long-acting muscarinic antagonist (LAMA) or increasing ICS dose may vary by lung function at screening. We therefore investigated whether lung function at screening predicts the response to adding umeclidinium (UMEC [LAMA]) to fluticasone furoate/vilanterol (FF/VI [ICS/LABA]) or increasing the FF dose.

Methods: CAPTAIN was a Phase IIIA, randomized, double-blind, 24–52-week, parallel-group study in adults (≥18 years) with uncontrolled asthma despite ICS/LABA. Treatment: FF/VI (100/25, 200/25 mcg) or FF/UMEC/VI (100/31.25/25, 100/62.5/25, 200/31.25/25, 200/62.5/25 mcg) once-daily. Outcomes: change from baseline in clinic trough forced expiratory volume in 1 second (FEV_1) at Week 24 (post hoc analysis using mixed-model repeated measures) and annualized moderate/severe exacerbation rate (Weeks 1–52; post hoc analysis using a negative binomial model) by FEV_1 % predicted at screening. Treatment groups were pooled by the addition of
UMEC 62.5 mcg or FF dose. For fractional polynomial (FP) modeling, models were adjusted for two FP transformations of FEV_1 % predicted at screening and their interactions with treatment.

Results: Numerically greater improvements in trough FEV_1 were seen with adding UMEC or increasing the FF dose, across the FEV_1 % predicted range; adding UMEC led to greater improvements (~100 mL) than increasing FF. Similarly, numerically greater reductions in exacerbation rate were seen with increasing FF, irrespective of FEV_1 % predicted at screening, although there was some overlap in the 95% confidence intervals; adding UMEC had minimal impact.

Conclusions: The effects of adding UMEC to FF/VI or increasing the FF dose were largely independent of lung function at screening.

Funding: GSK

S28

CAPTAIN: Effects of age as a continuous variable on treatment outcomes

Nicola A Hanania, Zelie Bailes, Neil Barnes, Louis-Philippe Boulet, Frances Gardiner, Hiromasa Inoue, Paul W Jones, Huib Kerstjens, Njira Lugogo, Robert Nathan, Reynold Panettieri Jr Emilio Pizzichini, David Slade, Edward Kerwin

Introduction: CAPTAIN showed that adding umeclidinium (UMEC) to fluticasone furoate/vilanterol (FF/VI) **improves lung function and symptom control in** patients with uncontrolled asthma on inhaled corticosteroid/long-acting β_2-agonist (ICS/LABA). A previous analysis showed that FF/UMEC/VI response may vary according to patient age (<65 vs ≥65 years). Here, we explore potential differential treatment responses using age as a continuous variable.

Methods: This Phase IIIA, double-blind, 24–52-week, parallel-group study randomized adults (≥18 years) with uncontrolled asthma despite ICS/LABA therapy (N=2436). Treatment: once-daily FF/VI (100/25, 200/25mcg) or FF/UMEC/VI (100/31.25/25, 100/62.5/25, 200/31.25/25, 200/62.5/25mcg) (ELLIPTA inhaler). Here, we report post hoc analyses of clinic trough forced expiratory volume in 1 second (FEV_1) change from baseline (Week 24; analyzed using mixed model repeated measures) and annualized rate of moderate/severe asthma exacerbations (Weeks 1–52; analyzed using a negative binomial model) by age. Treatment groups were pooled by UMEC 62.5mcg addition or FF dose. Fractional polynomial modelling was used to model effects of age per endpoint.

Results: Numerically greater improvements in trough FEV_1 (~100mL) were seen following addition of UMEC 62.5mcg to FF/VI irrespective of age. UMEC 62.5mcg addition led to numerically greater reductions in moderate/severe exacerbation rate versus FF/VI with increasing age, though with substantial 95% CI overlap. FF 200mcg was associated with numerical improvements in trough FEV_1 versus FF 100mcg across the age range, although there was some overlap in 95% CIs. Improvements in trough FEV_1 with FF 200mcg were less pronounced compared with the effect of adding UMEC. FF 200mcg was also associated with numerically greater reductions in moderate/severe exacerbation rate versus FF 100mcg across the age range. In all analyses there was greater uncertainty at the extremes due to lower patient numbers.

Conclusions: Adding UMEC to FF/VI or increasing FF dose was generally associated with numerical improvements in treatment outcomes independent of age.

Funding: GSK

S29

Continued treatment with nintedanib in patients with limited cutaneous systemic sclerosis (lcSSc) and interstitial lung disease (ILD)

Yannick Allanore, Dinesh Khanna, , Vanessa Smith, Martin Aringer, Anna-Maria Hoffmann-Vold, Masataka Kuwana, Alexandra James, Steven Sambevski, Margarida Alves, Christopher P Denton

Introduction: SENSCIS-ON is an open-label extension trial collecting data on decline in forced vital capacity (FVC) and adverse events in patients treated with nintedanib. We assessed the effects of nintedanib in patients with lcSSc and ILD.

Methods: Patients with SSc-ILD were eligible to enter SENSCIS-ON if they completed the randomized placebo-controlled SENSCIS trial (in which patients received trial drug for 52-100 weeks) or a drug–drug interaction (DDI) study of nintedanib and oral contraceptive (in which female patients received nintedanib for ≤28 days). Among patients with lcSSc, we analysed changes in FVC and adverse events over 52 weeks of SENSCIS-ON in patients who received nintedanib in SENSCIS and continued it in SENSCIS-ON ("continued nintedanib" group) and in patients who received placebo in SENSCIS or who received nintedanib for a short time in the DDI study ("initiated nintedanib" group).

Results: There were 98 patients with lcSSc in the continued nintedanib group and 127 (114 from SENSCIS) in the initiated nintedanib group. Mean (SE) changes in FVC from baseline to week 52 of SENSCIS-ON were −45.1 (19.1) mL in the continued nintedanib group, −41.5 (24.0) mL in the initiated nintedanib group, and −43.3 (15.3) mL in all patients with lcSSc, similar to the change in patients with lcSSc at week 52 of the SENSCIS trial (−39.1 [22.2] mL). The adverse event profile of nintedanib in SENSCIS-ON was consistent with that observed in the SENSCIS trial.

Conclusions: The change in FVC in patients with lcSSc and ILD who received nintedanib over 52 weeks, and the safety profile of nintedanib, in SENSCIS-ON were similar to observations in patients who received nintedanib in SENSCIS. These analyses support a continued effect of nintedanib on slowing decline in FVC and the ability to manage adverse events in patients with lcSSc and ILD over the longer term.

Funding: Boehringer Ingelheim

S30

Risk of All-cause Mortality During and After Severe Exacerbations in Patients With Chronic Obstructive Pulmonary Disease (COPD): Post Hoc Analysis of the IMPACT Trial

Manoj J Mammen MD, Tara F Carr MD, Gerard J Criner MD, Mark T Dransfield MD, David MG Halpin MD, MeiLan K Han MD, Benjamin Hartley M Math, Renu Jain PhD, Viren Kaul MD, Mitchell G Kaye MD, Monica Kraft MD, Doug Mapel MD, Dawn Midwinter MSc, Paul D Scanlon MD, Dave Singh MD, J Michael Wells MD, Robert Wise MD, David A Lipson MD

Introduction: Severe exacerbations are associated with increased risk of mortality in patients with COPD. In IMPACT, fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) triple therapy was associated with a 34% reduction in annual rate of severe exacerbations, and a 42% reduction in on-treatment all-cause mortality (ACM) risk, versus UMEC/VI in patients with symptomatic COPD and an exacerbation history. This analysis investigated risk of ACM during and following a moderate or severe exacerbation in patients enrolled in IMPACT.

Methods: IMPACT was a Phase III, 52-week trial comparing once-daily FF/UMEC/VI 100/62.5/25mcg with FF/VI 100/25mcg and UMEC/VI 62.5/25mcg. Eligible patients had symptomatic COPD and forced expiratory volume in 1s (FEV_1) <50%predicted and ≥1 moderate or severe exacerbation, or a FEV_1 50–<80% predicted and ≥2 moderate or ≥1 severe exacerbations in the prior year. This post hoc analysis analyzed risk of on-treatment ACM during and 1-90 and 91-365 days post-moderate or severe exacerbations, versus baseline using a time-dependent repeated measures Cox model. Moderate exacerbations required treatment with antibiotics or systemic/oral corticosteroids. Severe exacerbations resulted in hospitalization or death.

Results: 10,355 patients were included in the intent-to-treat population. 5034 (48.6%) patients experienced moderate/severe exacerbations. ACM risk was significantly increased during a severe exacerbation versus baseline (hazard ratio [HR]: 41.22 [95% confidence interval [CI] 26.49-64.15]; *P*<0.001). This risk decreased post-severe exacerbation, with neither time period demonstrating a significant difference in risk versus the baseline period (1-90 days: HR: 2.13 [0.86-5.29]; *P*=0.102; 91-365 days: HR: 1.15 [0.27-4.84]; *P*=0.852). ACM risk during and 1-90 days following a moderate exacerbation was elevated but not statistically significant.

Conclusions: This time-dependent model analysis demonstrates risk of death was significantly increased during a severe exacerbation event, and decreased following the event. These results emphasize the importance of preventing severe exacerbations and the need to optimize treatment in patients at risk of exacerbations.

Funding: GSK

S31

Effect of Once-daily Single-inhaler Fluticasone Furoate/Umeclidinium/Vilanterol Triple Therapy on Severe Exacerbation Rates Compared With Twice-daily Budesonide/Formoterol Dual Therapy in Patients With Chronic Obstructive Pulmonary Disease: A Post Hoc Analysis of the FULFIL Study

Reynold Panettieri Jr MD, Mohan Bangalore PhD MBA, Carlos A. Camargo Jr MD, Tariq Cheema MD, Sherif El Bayadi MD, Stanley Fiel MD, Renu G. Jain PhD, Dawn Midwinter MSc, Nashat Rabadi MD, Byron Thomashow MD, David A. Lipson MD

Introduction: The FULFIL trial showed clinically meaningful and statistically significant improvements in lung function and health-related quality of life, and reductions in moderate/severe exacerbation annualized rates in patients with chronic obstructive pulmonary disease (COPD) receiving fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) versus budesonide/formoterol (BUD/FOR). Severe exacerbations place a high burden on patients and healthcare systems. This post-hoc analysis examined treatment effects on severe exacerbation rates in FULFIL.

Methods: FULFIL was a Phase 3, randomized, double-blind, double-dummy trial in 1810 patients with symptomatic COPD and forced expiratory volume in 1s (FEV_1) <50% predicted or ≥50–<80% predicted and ≥2 moderate or ≥1 severe exacerbations in the past year. Patients were randomized to 24 weeks of treatment with once-daily FF/UMEC/VI 100/62.5/25µg (N=911) or twice-daily BUD/FOR 400/12µg (N=899). A subset of the population remained on treatment for up to 52 weeks, obtaining long-term data (extension population: FF/UMEC/VI n=210, BUD/FOR n=220). On-treatment severe (hospitalized) exacerbation rates over 24 and 52 weeks were evaluated in intent-to-treat and extension populations using a generalized linear model assuming a negative binomial distribution.

Results: Patient characteristics were similar between the intent-to-treat and extension populations. Up to Weeks 24 and 52, 12 (1%) and 5 (2%) patients on FF/UMEC/VI and 22 (2%) and 20 (9%) patients on BUD/FOR experienced severe exacerbations respectively. FF/UMEC/VI reduced severe exacerbation rates vs BUD/FOR by 51% (mean annualized rate 0.029 vs 0.059, respectively; rate ratio: 0.49 [95% confidence interval [CI]: 0.24-1.03]; *P*=0.061) up to Week 24 and by 67% (mean annualized rate 0.037 vs 0.112, respectively; rate ratio: 0.33 [95% CI: 0.13-0.85]; *P*=0.021) up to Week 52.

Conclusions: Post-hoc results suggest once-daily FF/UMEC/VI reduces severe exacerbation rates compared with twice-daily BUD/FOR, highlighting the potential benefits of triple versus dual therapy in reducing the clinical and economic burden caused by severe exacerbations in this patient population.

Funding: GSK

S32

Effect of antifibrotic therapy on survival in patients with idiopathic pulmonary fibrosis (IPF): data from the IPF-PRO Registry

Joao A de Andrade, Megan L Neely, Anne S Hellkamp, Daniel A Culver, Hyun J Kim, Timothy Liesching, Lobo LJ, Murali Ramaswamy, Shaun Bender, Craig S Conoscenti, Scott M Palmer, Laurie D Snyder on behalf of the IPF-PRO Registry investigators

Introduction: Real-world studies have shown a reduction in mortality in patients with IPF treated with antifibrotic therapy; however, the initiation or discontinuation of therapy may have introduced bias. We investigated the effect of antifibrotic therapy on mortality and other outcomes in patients with IPF using causal inference methodology.

Methods: Patients with IPF that was diagnosed or confirmed at the enrolling center in the previous 6 months were enrolled into the IPF-PRO Registry. Patients were followed prospectively, with follow-up data collected as part of routine care until death, lung transplant, or withdrawal. We used the Gran method, which accounts for differences in patient characteristics and for treatment initiations and discontinuations, to assess the effect of antifibrotic therapy (nintedanib or pirfenidone) on death, death or lung transplant, respiratory-related hospitalization, acute worsening of IPF (any health care encounter deemed due to acute worsening of IPF) and a composite of death, lung transplant, acute worsening of IPF and absolute decline in FVC ≥10% predicted. The analysis cohort was limited to patients who started antifibrotic therapy on or after the day of enrollment or had never taken it.

Results: Among 499 patients in the analysis cohort, 352 (70.5%) received antifibrotic therapy. Estimated event rates (95% CI) of death at 1 year were 6.6% (6.1%, 7.1%) for treated patients and 10.2% (9.5%, 10.9%) for controls. There were no statistically significant associations between antifibrotic drug use and any of the outcomes studied. There was a numerical reduction in the risk of death (hazard ratio [HR] 0.53 [95% CI: 0.28, 1.03]; p=0.060) and a numerical increase in the risk of respiratory-related hospitalization (HR 1.88 [95% CI: 0.90, 3.92]; p=0.091) in treated versus control patients.

Conclusions: Analyses of data from the IPF-PRO Registry suggest that patients with IPF who are treated with antifibrotic therapy may have improved survival.

Funding: Boehringer Ingelheim

S33

Effect of tezepelumab on seasonal exacerbations in patients with severe, uncontrolled asthma grouped by blood eosinophil count

Jonathan Corren, MD, Andrew Menzies-Gow, MD, Christopher S Ambrose, MD, Gene Colice, MD, Stephanie L Roseti, MSc, Åsa Hellqvist, MSc, Andrew W Lindsley, MD and Bill Cook, PhD

Introduction: Tezepelumab, a human monoclonal antibody, targets thymic stromal lymphopoietin (TSLP). In the phase 3 NAVIGATOR study (NCT03347279), tezepelumab reduced exacerbations in patients with severe, uncontrolled asthma with high or low baseline blood eosinophil counts (BECs) and across all seasons in the overall population. This pre-specified exploratory analysis evaluated the effect of tezepelumab on seasonal asthma exacerbation rates in NAVIGATOR patients grouped by baseline BEC.

Methods: NAVIGATOR was a multicentre, randomized, double-blind, placebo-controlled study. Patients (12–80 years old) were randomized 1:1 to tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks. The annualized asthma exacerbation rate (AAER) was assessed by season in patients grouped by baseline BEC.

Results: Of 1059 treated patients, 618 had a BEC of <300 cells/μL and 441 had a BEC of ≥300 cells/μL at baseline. In the placebo group, there were seasonal variations in the AAER, with a peak in winter (BEC <300 cells/μL, 2.32; BEC ≥300 cells/μL, 3.07). Tezepelumab reduced the AAER versus placebo across all seasons in patients with a BEC of <300 cells/μL (winter, 55% [95% confidence interval (CI): 36, 68]; spring, 31% [95% CI: −4, 54]; summer, 37% [95% CI: 5, 58]; fall, 43% [95% CI: 20, 59]) and in those with a BEC of ≥300 cells/μL (winter, 72% [95% CI: 57, 82]; spring, 62% [95% CI: 38, 77]; summer, 80% [95% CI: 67, 88]; fall, 66% [95% CI: 49, 77]).

Conclusions: Tezepelumab reduced exacerbations versus placebo across all seasons in adults and adolescents with severe, uncontrolled asthma with high or low baseline BECs, consistent with the overall NAVIGATOR population.

Funding: AstraZeneca and Amgen Inc.

S34

Characterization of a former smoker phenotype in Chronic Obstructive Pulmonary Disease (COPD) from an Electronic Health Records Database

Nicola A Hanania. MD, MS., Dave Singh. MD., Michel Djandji. MD., Danen Cunoosamy. PhD., Richard Stanford. PharmD, MS., Xavier Soler. MD, PhD., Amr Radwan MB, BChir, FFPM., Juby A Jacob-Nara MD, DHSc, MPH., Michael J Asmus. PharmD., Thomas J Ferro. MD.

Introduction: In a phase 2 study, Itepekimab, an IL33 blocker, added to maintenance inhaled therapy significantly reduced COPD exacerbations in former smokers with COPD. To further characterize former smokers' phenotype, we investigated demographics, peripheral blood eosinophils (EOS) and maintenance therapy in former smokers from a US electronic health records (EHR) cohort of patients with COPD.

Methods: Patients with COPD were identified from an EHR database using ICD-10 and ICD-9-CM codes and natural language processing (NLP) techniques based on a modification of the previously validated eMERGE criteria. All subjects were ≥40 years of age at initial COPD diagnosis (first occurrence of ≥2 ICD-9-CM or ICD-10 defined COPD) from 2003-2020. Smoking history was determined using NLP filters to search the most recent patient self-reported smoking data found in each subject's EHR free-text data. The highest EOS level in the most-recent 3-year period for each subject were reported. COPD maintenance treatment was determined based on therapy prescribed in the most recent 12 months.

Results: 20,614 former smokers were identified (49% of EHR COPD cohort 41,239) during 2003-2020. The median time since quitting was 7.6 (range 2-16) years. 16,215 former smokers (>6 months quit) also had EOS (cells/μL) data available in the most recent 3-year period (5% EOS <100; 62% EOS 100-300, 33% EOS >300). 47% of former smokers were using ICS/LABA as maintenance medication; 28% on LAMA; 15% on ICS/LABA/LAMA; 8% on LABA/LAMA and only 1% on LABA only. 28% of this former-smoker COPD cohort also had comorbid asthma.

Conclusion: This is one of the first studies to assess EOS levels and maintenance inhaler use in former smokers with COPD. Most of the former smokers had EOS above 100 cells/μL with a large majority currently using an ICS based maintenance treatment, either ICS/LABA or ICS/LABA/LAMA.

Funding: Sanofi and Regeneron

S35

Chronic Obstructive Pulmonary Disease (COPD) Stratified by Tobacco Use and Blood Eosinophils from an Electronic Health Records Database Cohort

Nicola A Hanania. MD, MS., Dave Singh. MD., Jigna Heble. PharmD., Michel Djandji. MD., Danen Cunoosamy. PhD., Richard Stanford. PharmD, MS., Xavier Soler. MD. PhD., Amr Radwan. MB, BChir, FFPM., Juby A Jacob-Nara. MD, DHSc, MPH., Michael J Asmus. PharmD., Thomas J Ferro. MD.

Introduction: Smoking status and peripheral blood eosinophil (EOS) levels are important factors to consider when selecting COPD maintenance therapy. We examined data from a large electronic health records (EHR) database encompassing 17 years (2003 – 2020) from 3 US geographies (Northeast, Southeast, Midwest) to assess EOS and smoking history

Methods: We identified the COPD cohort using the International Classification of Disease (ICD-10 and ICD-9-CM) codes plus natural language processing (NLP) techniques using a validated eMERGE criteria (Su Chu, et al. Sci Rep. 2021;11(1):19959). Subjects were age ≥ 40 years old at COPD diagnosis (first occurrence of ≥ 2 ICD-9-CM or ICD-10 defined COPD). Smoking history was determined using NLP filters to search the most recent patient self-reported smoking data found in each subject's EHR free-text data. We selected the highest EOS level reported in the most recent 3-year period for each subject.

Results: 41,239 patients met criteria for COPD. 33,160 (80%) had ≥ 1 EOS measurement in the last 3 years. Smoking history was available for 35,027 (85%) of this cohort and 28,016 (68%) had both EOS + smoking history data available. 32% of patients with COPD had EOS > 300 cells/μL; 63% had EOS 100- 300 cells/μL and 5% had EOS < 100 cells/μL. 58% of COPD patients were self-reported former smokers, 24% were current smokers and 18% documented as never smokers.

Conclusion: The prevalence of elevated EOS in this large EHR-based COPD cohort is consistent with previously published results in the UK and USA (Vogelmeier et al. Respiratory Research 2019;20:178). Former smokers formed the majority of COPD patients (58%) in this cohort regardless of highest recent EOS level.

Funding: Sanofi and Regeneron.

S36

Effectiveness of a Reliever-based Digital System on Asthma Control

Flavia Hoyte, Giselle Mosnaim, Linda Rogers, Randall Brown, Michael Wechsler.

Introduction:The Reliever Digital System (RDS) comprises the Digihaler® integrated inhaler (albuterol 90μg) that transmits data wirelessly to a mobile application, which synchronizes with a Digital Health Platform to store and transfer data to a web-based dashboard. This allows patients and clinicians to track and review reliever inhaler usage and inhalation quality, to aid clinical decision making. This study aimed to evaluate asthma control as measured by the Asthma Control Test (ACT) in participants using RDS versus those in the standard of care (SoC) group using SoC albuterol reliever inhalers.

Methods: 333 eligible participants were randomized to RDS (N=167) or SoC (N=166) for 12-weeks. It was expected that the Dashboard would be checked at least once a week for each participant's inhalation data (usage, inhalation quality parameters). Primary outcome (N=313): proportion of participants achieving meaningful improvement, (ACT score ≥20 at week 12, or increase ≥3 units from baseline). Bayesian statistical analysis provided a posterior probability distribution for odds ratios with corresponding credible intervals (CrI).

Results: There was an 85.3% probability that participants using the RDS would have greater odds of achieving improvements in asthma control vs SoC after 3 months. The mean OR (95% CrI) for RDS/SoC was 1.33 (0.813, 2.050), demonstrating that, on average, participants in the RDS group had 33% higher odds of achieving meaningful improvement than those in the SoC group.

Conclusions: After 3 months, participants using the RDS had greater odds of clinically meaningful improvements in asthma control vs SoC. Further investigation of the potential of the RDS to help improve asthma management is warranted.

Funding: Teva Branded Pharmaceutical Products R&D Inc.

S37

Data from a Reliever-based Digital System Supports Patient-clinician Interactions in Asthma

Flavia Hoyte, Giselle Mosnaim, Linda Rogers, Randall Brown, Michael Wechsler

Introduction: The Digihaler® integrated inhaler (albuterol 90µg) records and wirelessly transmits reliever inhaler usage data to a patient-facing mobile application and a clinician Dashboard (altogether, the Reliever Digital System [RDS]). The CONNECT1 study evaluated the RDS in participants with asthma aged ≥13 years. This study aimed to explore differences in frequency and types of participant-clinician interactions undertaken for asthma management of participants using the RDS vs those in the standard of care (SoC) group using the SoC albuterol reliever inhalers.

Methods: Participants were randomized to RDS (N=167) or SoC (N=166) for 12 weeks. Clinicians obtained data on inhaler usage and inhalation quality via the Dashboard, recorded reasons for participant contact outside of scheduled visits, and answered Asthma Management questions at each visit. Adjusted between-group differences (RDS vs SoC) are reported with 95% credible intervals (CrI).

Results: Overall numbers of participant-clinician interactions were similar between RDS and SoC groups (239 vs 222; difference [95% CrI]: 0.40 [−0.106, 0.949]). Compared with SoC, the RDS was associated with increased technique-related participant-clinician interactions (52 vs 1; difference [95% CrI]: 2.00 [1.013, 3.416]) and fewer planned follow-up interactions (54 vs 104; difference [95% CrI]: −1.06 [−2.014, −0.513]). Inhaler technique/adherence discussions were more frequent in the RDS group (107 vs 44; difference [95% CrI]: 0.95 [0.476, 1.634]).

Conclusions: In this 12-week study, a link was observed between use of the RDS and interactions elicited by and leading to discussions on inhaler technique. Access to inhalation data may help clinicians target patients in need of intervention in a timelier fashion.

Funding: Teva Branded Pharmaceutical Products R&D Inc.

S38

Itepekimab significantly reduced hospitalizations or emergency department visits in former smokers with moderate-to-severe COPD

Klaus F. Rabe, MD, PhD, Bartolome R. Celli, MD, Amy Praestgaard, MS, Michel Djandji, MD, Xavier Soler, MD, PhD, Raolat M. Abdulai, MD, MMSc, David J. Lederer, MD, MS, Hélène Goulaouic, PhD, Michael C. Nivens, PhD, Shahid Siddiqui, MD, Juby A. Jacob-Nara, MD, MPH, DHSc, Yamo Deniz, MD, Paul J. Rowe, MD

Introduction: Hospitalizations and emergency department (ED) visits in patients with chronic obstructive pulmonary disease (COPD) have a significant healthcare burden. Itepekimab is a new human IgG4P monoclonal antibody against interleukin-33; a recent phase 2 study (NCT03546907) demonstrated that itepekimab 300 mg every 2 weeks vs placebo reduced exacerbation rates and improved lung function in the subgroup of former smokers with moderate-to-severe COPD during the 24–52-week treatment period. This post hoc analysis of the phase 2 study investigates the effect of itepekimab vs placebo on hospitalizations and ED visits in former smokers with COPD.

Methods: 187 (itepekimab 98; placebo 89) former smokers were assessed. The number of patients with 0, 1, or ≥ 2 hospitalizations or ED visits, adjusted annualized rates of hospitalizations or ED visits, and time to first hospitalization or ED visit are reported. Rate of hospitalizations or ED visits derived from negative binomial regression model. Probability of first hospitalization or ED visit derived using Kaplan-Meier estimates; HR derived using Cox regression model.

Results: Fewer former smokers with COPD treated with itepekimab experienced hospitalizations or ED visits than those treated with placebo (6% vs 17% overall; 5% vs 14% experienced 1, and 1% vs 3% had ≥2 hospitalizations or ED visits, respectively). Former smokers treated with itepekimab had a 70% reduced risk of hospitalization or ED visit (adjusted annualized rate [95% CI], 0.08 [0.03–0.18] for itepekimab vs 0.25 [0.14–0.46] for placebo; RR [95% CI], 0.30 [0.12–0.76]; $P = 0.01$) and had a longer time to first hospitalization or ED visit (probability at Week 24 [95% CI], 0.03 [0.01–0.08] for itepekimab vs 0.12 [0.07–0.20] for placebo; HR [95% CI], 0.31 [0.12–0.82], $P = 0.02$) vs placebo.

Conclusion: Itepekimab vs placebo significantly reduced hospitalizations or ED visits in former smokers with moderate-to-severe COPD.

Funding: Sanofi and Regeneron Pharmaceuticals, Inc.

S39

Lung function trajectories in patients with idiopathic pulmonary fibrosis (IPF): data from the IPF-PRO Registry

Megan L Neely, Shaun Bender, Anne S Hellkamp, Jamie L Todd, Timothy Liesching, Tracy R Luckhardt, Justin M Oldham, Eric S White, Scott M Palmer on behalf of the IPF-PRO Registry investigators

Introduction: IPF is a progressive fibrosing interstitial lung disease with a variable course. We used data from the IPF-PRO Registry to evaluate trajectories of lung function in patients with IPF.

Methods: Patients with IPF that was diagnosed or confirmed at the enrolling center in the previous 6 months were enrolled into the IPF-PRO Registry at 46 sites across the US between June 2014 and October 2018. Patients were followed prospectively with lung function data collected as part of routine clinical care. We assessed the trajectories of FVC % predicted and DLco % predicted during follow-up in the registry in subgroups based on time from enrollment to a terminal event (no event, ≤1 year, >1 to ≤2 years, >2 to ≤3 years, >3 years). A terminal event was defined as death, lung transplant, entry into hospice care, or withdrawal from the registry due to worsening of IPF. Trajectories were plotted using cubic functions fit through daily means. Analyses were descriptive and conducted in patients who had ≥1 usable measurement after or ≤30 days before enrollment.

Results: Of 1002 patients enrolled in the IPF-PRO Registry, 939 had ≥1 FVC measurement and 897 had ≥1 DLco measurement. In total, 675 patients had ≥2 FVC measurements within 12 months and 770 patients had ≥2 FVC measurements within 24 months of enrollment; 584 patients had ≥2 DLco measurements within 12 months and 686 patients had ≥2 DLco measurements within 24 months of enrollment. Patients who had shorter times to a terminal event had lower FVC and DLco % predicted values at enrolment and greater rates of decline in FVC and DLco % predicted.

Conclusions: Patients in the IPF-PRO Registry who had shorter times to a terminal event had lower starting values and steeper trajectories of decline in lung function.

Funding: Boehringer Ingelheim

S40

Indirect treatment comparison of tezepelumab versus other biologics for the treatment of severe asthma

Andrew Menzies-Gow, PhD, Jason Steenkamp, BSc, Sumeet Singh, MSc, Jennifer Rowell, MSc, Santiago Zuluaga Sanchez, MSc, Neil Martin, Jean-Pierre Llanos-Ackert MD, and Anna Quinton MSc

Objective: To compare the efficacy of tezepelumab with other approved biologics via indirect treatment comparisons (ITCs) in patients aged ≥ 12 years with severe, uncontrolled asthma.

Methods: Data from randomized controlled trials (RCTs) identified from a systematic literature review were synthesized using two ITC approaches: network meta-analysis (NMA) and simulated treatment comparison (STC). Outcomes of interest were changes from baseline in Asthma Control Questionnaire (ACQ) score, pre-bronchodilator forced expiratory volume in 1 s (FEV_1) and oral corticosteroid (OCS) dose. Potential heterogeneity between study populations was addressed using subgroup analyses for NMA (based on baseline biomarker levels), and adjustment by potential treatment effect modifiers for the STCs. Mean differences, odds ratios (with 95% confidence intervals) and ranking statistics (NMA only) are reported.

Results: Twenty-one RCTs were included to analyse ACQ and FEV_1; four were included for OCS. NMAs showed that all biologics (tezepelumab, dupilumab, benralizumab, mepolizumab, reslizumab and omalizumab) had similar efficacy. This similarity was largely consistent in subgroup and sensitivity analyses. The STCs of tezepelumab versus each biologic did not demonstrate any significant differences for ACQ or FEV_1, although tezepelumab was most likely to be ranked first across all outcomes in terms of change from baseline point estimates. For OCS, the STC estimations demonstrated a nominally statistically significant benefit favouring tezepelumab in one scenario. Heterogeneity in study populations, primarily in baseline blood eosinophil count, had an impact on NMAs for OCS dose, as evidenced by differing findings between primary and subgroup NMA and the STC, which is based on matched analysis.

Conclusion: Findings from both ITC approaches found tezepelumab to be as efficacious as other biologics in a broad patient population of severe uncontrolled asthma of any phenotype. For OCS outcomes, it is important to account for differences in study populations when comparing different biologics.

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S41

Application of Modified Delphi Expert Consensus Thresholds on SABA Reliever Use in Asthma to Data Obtained from a 12-week Study of a Digital Inhaler in Suboptimally Controlled Asthma Patients

John Oppenheimer, Maureen George, Jay Portnoy, Randall Brown

Introduction: US asthma experts developed clinical statements regarding excessive SABA reliever use via a rigorous consensus-building process, and agreed that clinical decision-making should optimally be based upon individualized insights into patients' reliever use profiles, with thresholds for clinical action informed by baseline and weekly usage data. These data obtained from the albuterol Digihaler (90µg/dose) can provide an objective platform for assessment of proposed clinical thresholds.

Methods: Previously, patients with ≥1 asthma exacerbation/prior year and suboptimal asthma control (ACQ ≥1.5) used albuterol Digihaler for 12 weeks in an open-label study (NCT02969408). In this analysis, clinical decision threshold rules derived from statements agreed upon during the modified Delphi process were applied to data downloaded from the devices.

Results: Of 359 patients who made ≥1 valid (peak inspiratory flow ≤120L/min with no use errors) inhalation and completed the study, 64 (18%) had a clinically confirmed in-study asthma exacerbation.104/359 (29%) exhibited a rate of SABA reliever use during the 12-week study, equivalent to ≥3 canisters/year, associated with increased risk of exacerbation and asthma-related death, including 33/64 (52%) of those who had exacerbation(s) during the study and 71/295 (24%) of those who did not. 319/359 (89%) of patients met a consensus decision threshold of usage ≥100% over their personal baseline during ≥1 study week(s); 260/359 (72%) met a very conservative threshold of usage ≥200% above their baseline. 62/359 (17%) made ≥25 valid inhalations in a week - a level of reliever usage associated with unanimous consensus of likely impending/ongoing exacerbation - including 40/295 (14%) patients without confirmed exacerbation(s).

Conclusions: These findings suggest that elevated SABA reliever use among suboptimally controlled asthma patients may be far more commonplace than previously understood. The advent of digital inhalers offers a new potential tool to address this challenge and meaningfully aid the development of informed individualized asthma preventive management.

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S42

US Expert Consensus on Short-acting Beta Agonist (SABA) Reliever Medication Use for Asthma Clinical Decision-making: A Mixed-method Delphi Adjudication Approach

Mario Castro, Greg Bensch, Rajan Merchant, Maeve O'Connor

Introduction: Increased use of SABA reliever medication has been recognized as a problem for >30 years and many guidelines lack specific overuse recommendations. Thus, updated expert-led review/consensus is needed to provide guidance on clinical action to take in response to reliever usage patterns.

Methods: In 2021, a rigorous iterative mixed-methods consensus-building process was undertaken: 1) online physician survey; 2) forum discussion with evidence review and SABA statement development; 3) Delphi adjudication videoconference/polling. Experts rated levels of agreement with statements on a 5-point Likert scale; median score and interquartile range were calculated. Consensus to accept was defined as lower quartile ≥4 ("agree").

Results: 100 primary/specialty physicians completed the survey. Subsequent expert panel consensus (median Likert score, IQR) directs, as reliever use of ≥3 SABA canisters/year is associated with increased risk of exacerbation/asthma-related death, refill rates should be monitored closely (5, 4.75-5) and SABA use history should be solicited at every patient encounter (5, 4.75-5). Individual SABA use data, rather than absolute thresholds, should typically guide clinical actions in response to SABA use (5, 4.5-5). SABA use episodes ≥50% and ≥100% above the patient's baseline (4, 4-4; 5, 4.75-5, respectively) are considered likely to indicate impending/ongoing exacerbation, as does reliever use exceeding ≥5 episodes/week (4.5, 4-5). Reliability of usage frequency information provided during patient assessment should be considered (4.5, 4-5); experts agreed that patient-sourced information is likely inaccurate (5, 5-5) and that pharmacy refill data may not correlate with actual use (4, 4-4.25); therefore, use of digital health tools to assess reliever medication use should be considered (4, 4-5).

Conclusions: Experts recommended consideration of thresholds/patterns for clinical action and basing action on individualized understanding of patients' asthma clinical profiles. Improving validity/reliability of reliever usage data offers potential to aid asthma management. Future asthma guidelines should include specific recommendations regarding this topic.

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S43

Continued nintedanib treatment in patients with progressive pulmonary fibrosis: interim analysis of INBUILD-ON

Wim A Wuyts, Francesco Bonella, Nazia Chaudhuri, Francesco Varone, Danielle Antin-Ozerkis, Heiko Mueller, Carl Coeck, Klaus B Rohr, Vincent Cottin

Introduction: In the INBUILD trial in patients with progressive fibrosing interstitial lung diseases (ILDs) other than idiopathic pulmonary fibrosis, nintedanib reduced the rate of decline in forced vital capacity (FVC) with a safety profile characterized mainly by gastrointestinal events. INBUILD-ON is an open-label extension study that is collecting data on adverse events and FVC decline in patients treated with nintedanib over the longer term.

Methods: Patients in the INBUILD trial had diffuse fibrosing ILD (reticular abnormality with traction bronchiectasis, with or without honeycombing) of >10% extent on HRCT, FVC ≥45% predicted, DLco ≥30%–<80% predicted, and met criteria for progression of ILD within the prior 24 months, despite management deemed appropriate in clinical practice. Patients who received nintedanib in INBUILD continued nintedanib in INBUILD-ON. Patients who received placebo in INBUILD initiated nintedanib in INBUILD-ON. A data snapshot was taken on 15 October 2021.

Results: A total of 434 patients were treated in INBUILD-ON (212 continued nintedanib, 222 initiated nintedanib). Median exposure to nintedanib was 22.0 months. The most frequent adverse event was diarrhea, reported in 48.6% of patients who continued nintedanib and 66.7% of patients who initiated nintedanib. Adverse events led to discontinuation of nintedanib in 17.9% and 29.3% of patients who continued nintedanib and initiated nintedanib , respectively. The observed change in FVC during INBUILD-ON over time was consistent with the rate of decline in INBUILD.

Conclusions: The adverse event profile of nintedanib in INBUILD-ON was consistent with that reported in INBUILD, supporting its manageable safety profile over continued use in patients with progressive pulmonary fibrosis.

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S44

Comparison of Exacerbation Risk and Health Outcomes among Patients with Chronic Obstructive Pulmonary Disease Initiating Maintenance Therapy with Tiotropium Bromide/Olodaterol or Fluticasone Furoate/Umeclidinium/Vilanterol

Sanjay Sethi, MD, Jennifer Quint, FRCP, Brendan Clark, PharmD, Asif Shaikh, MD, Gary T. Ferguson, MD

Introduction: Long-acting muscarinic antagonist (LAMA)/long-acting beta$_2$-agonist (LABA) dual bronchodilator therapy is recommended as an initial maintenance treatment in chronic obstructive pulmonary disease (COPD). Escalation to triple therapy (TT; LAMA/LABA/inhaled corticosteroid) is advocated for patients with continued exacerbations despite treatment with bronchodilators. Contrary to all recommendations, TT is commonly prescribed as first-line maintenance treatment.

Methods: Two retrospective, observational studies compared COPD exacerbations, pneumonia risk, and costs in maintenance treatment–naïve COPD patients (aged ≥40 years) initiating fixed-dose combinations of either LAMA/LABA (tiotropium/olodaterol [TIO+OLO]) or TT (fluticasone furoate/umeclidinium/vilanterol [FF+UMEC+VI]). Data were collected from administrative claim records of COPD patients included in the Optum Research database (study A: 06-01-2014 to 12-31-2019) and IQVIA database (study B: 09-15-2016 to 03-31-2020). Patients were continuously enrolled in health plans for at least 12 months before the index date and were matched 1:1 using propensity-score matching (PSM). Reference group for the risk analysis in both studies was TIO+OLO.

Results: After PSM, studies A and B had 3,025 and 2,951 pairs of maintenance treatment–naïve patients (mean age: 71 [population predominantly Medicare part D] and 61 years [population predominantly commercial insurance], respectively). No significant difference was observed in the risk of exacerbations between FF+UMEC+VI and TIO+OLO (adjusted hazard ratio [aHR]: 0.99; confidence interval [CI]: 0.88-1.10, Study A; HR [CI]: 1.13 [0.99-1.29], Study B). Pneumonia risk was not significantly different for FF+UMEC+VI versus TIO+OLO (aHR [CI]: 1.13 [0.95-1.36]), Study A; HR [CI]: 1.04 [0.85-1.27], Study B). Both studies indicated that TIO+OLO was associated with lower composite COPD+pneumonia-related costs compared with FF+UMEC+VI (22.8% and 10.0% in studies A and B, respectively).

Conclusions: In a maintenance treatment–naïve COPD population, TIO+OLO is as effective as FF+UMEC+VI but offers additional cost benefits. Initiating dual LAMA/LABA therapy as recommended by the GOLD strategy document has the potential to improve clinical and economic outcomes.

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