American Thoracic Society 2023

Washington D.C.
May 19 – 24 2023
ITS ATS A. Menarini Bursary 2023.
Dr. M. O'Callaghan & Dr. E. Lynn

Year in review

21st May 2023

Lung cancer update
Review of 2023 NEJM paper looking at chemotherapy with PDL1 inhibitor versus chemotherapy alone in patients with stage 1-3 resectable NSCLC. (TNM 7th edition) This was a phase 3 trial where patients were randomised to pembrolizumab (PDL1) or placebo with cisplatin-based chemotherapy prior to surgery and then adjuvant pembrolizumab or placebo. Two primary endpoints: eventfree survival (progression or recurrence or death) and overall survival. Better eventfree survival in pembro group and more likely to have complete pathological response to treatment but no significant between group difference in overall survival.

Covid 19 update
Review of treatments/ interventions in Covid 19
RCT looking at prone positioning in awake patients with covid-19 for a median duration of 5 hours. Included patients with mild-moderate disease. Primary outcome was need for endotracheal intubation (ETT) and there was no significant between group difference. Furthermore, there was no significant between group difference in mortality at 60 days or days spent ventilated in ICU. However a post-hoc analysis which looked at patients with mild hypoxia as defined by a sats: fi02 ratio of >150, demonstrated a statistically significant reduction in need for ETT in the prone positioning group.

Pegylated interferon lambda
RCT looking at single dose of pegylated interferon lambda versus placebo in early covid-19 disease (day 3) in those deemed to be at high risk of severe disease. Primary outcome was risk of hospitalisation and ED attendance. Pegylated interferon lambda cut down risk of attending the hospital by 50% versus placebo. There were no significant adverse effects and a clear benefit persisted even when adjusted for age, gender, BMI and vaccine status. The benefit was even more pronounced if Pegylated interferon lambda was started in patients who were more symptomatic at day 3.

PASC= post-acute sequelae of covid
Large study on PASC showed that patients admitted with covid19 are at higher risk of post covid symptoms or PASC at 6 months. Risk factors that conveyed a higher risk of PASC include female gender, receipt of supplementary 02 during admission, black race, older and more comborbidities. Furthermore this study showed that symptoms can settle at 1 month but recur before 6 months post admission. Paper suggests that there are 6 different phenotypes of patients who develop PASC and an AI model was proposed to identify who was at risk for what symptoms

PASC treatment
There is none. There is a reduced risk in vaccinated patients and an additional benefit with each consecutive vaccine.

New Treatment Approaches for Bronchiectasis

21st May 2023

Bronchiectasis is associated with significant morbidity and mortality. There is an unmet need in terms of treatment options for patients. While PA and haemophilus dominate there remains a lack of consistent microbiology in the bronchiectasis population. There is also concern regarding resistance due to antibiotic overuse. As a result, there is no common standard of care and a lack of approved drugs. Heterogeneity is a significant issue. Chalmers discussed the potential for inflammatory endotyping in bronchiectasis using proteomics. Severe disease is characterised by up-regulation of

neutrophil activity and as a consequence release of neutrophil elastase. This elastase drives mucus production and impairs innate immune system. The presenter referenced EMBARC (European Multicentre Bronchiectasis Audit and Research Collaboration and EMBARC-BRIDGE (Bronchiectasis Research Involving Databases, Genomics and Endotyping) collaborations looking at the molecular endotypes of bronchiectasis during stable disease and exacerbations. Chalmers also referred to the cohort of bronchiectasis patients with predominantly eosinophilic disease, who tend to exacerbate more frequently than those with neutrophilic inflammation. In these patients, the importance of out-ruling APBA was highlighted.

Leveraging Imaging and Biosamples to improve diagnosis and risk prediction in ILA and ILD (Poster discussion)

21st May 2023

Themed poster discussion with poster panel. General discussion around topics/ suggested areas for research:
Need to develop blood bio markers to predict disease progression in those with ILAs and early IPF. Currently 10% of ILAs are expected to progress to disease, opportunity to develop drugs to prevent that progression. Biomarkers can be used instead of reliance on radiology in these patients. How do we move them into clinical use? We still do not understand the early measurements of disease and are not yet there in terms of understanding the mechanisms of progression from early to advanced disease. By validating biomarkers and moving from lab to clinical use we can build confidence in these tools. This is relevant when deciding who to treat, need to know who will progress and take potential drug side effects into account when deciding when to initiate treatment.

Posters 805 – 807 Take home points:

- Discussion re potential to develop automated tools to recognise early UIP patterns
- Lower dose CT important for surveillance in patients who may require serial imaging to monitor progression
- The risk for progressive disease remains higher among older cohorts – should the focus be on these at-risk groups
- Should a screening tool be available to detect early IPF

Posters 808 – 815 Take home points:

- Again, use of software to diagnose ILD – would further negate need for biopsy
- Software would need to be user-friendly to facilitate use in non-ILD centres
- Aim to automate CTs in future
- Can algorithms be combined
- Make this software widely available
- What role does genetic testing play in excluding disease?

Posters 816 – 823 Take home points:

- Limited role for radiology and physiology over time as results can be variable so not always a reliable method for surveillance of patients
- Not always easy to assess disease progression over time
- Extent of reticulation is not a good predictor of progression, honeycombing is more useful
- Suggestion: Extent of fibrosis is a good biomarker, could that be used
- Role of phenotypes: does AI have a role here?
- Issue will be applying learning to individual patients in a consistent manner
- Would need to combine imaging models with exposure history and genomic data = precision medicine!

There is a need to determine disease activity in relation to how progressive that disease will then be. Once activity is defined, prediction to respiratory failure may be easier. There is a potential here for biomarkers to allow us to quantify activity and then to apply therapies in the treatment of these patients. The target for drug therapy may however be different that the target for prognostic biomarkers. Clinicians and researchers need to be very specific about the question they are asking!

Pulmonary physiology (poster discussion)

22nd May 2023

Oscillometry

Oscillometry measures the mechanical properties of the respiratory system during quiet tidal breathing by using oscillating pressure signals from the mouth. This is in contrast to traditional spirometry where forced respiratory effort is needed. Given the increased clinical application of oscillometry internationally, the ERS released guidelines on oscillometry standards in 2022. At this poster discussion session, a number of groups discussed their centres efforts at introducing oscillometry. One group looked at oscillometry v spirometry in adult patients with CF and found good correlation. Another group looked at impulse oscillometry in asthma and showed how it could be used to detect the presence airway hyperresponsiveness (AHR). They proposed this could circumvent the need for a metacholine challenge test in certain patients. Another group proposed an alternative method for standardising oscillometry and reducing variation during repeated readings suggesting that current methos ignore the reactance component of respiratory impedance. The novel algrorithm allowed for resistance and impedance variability over a range of frequencies and they demonstrated enhanced repeatability, feasibility and accuracy of oscillometry.

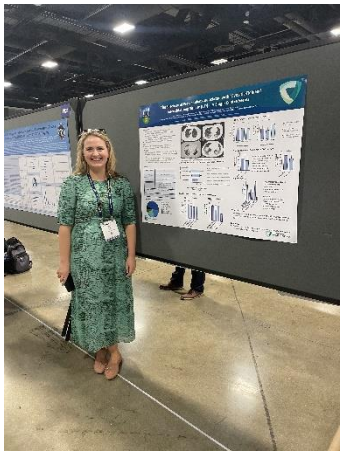
GLI

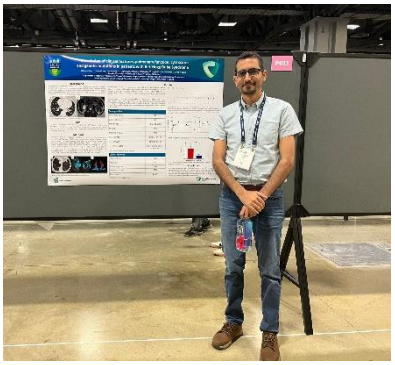
Traditional methods of spirometric measurements were based on coal-workers and Caucasian men. Estimates were then made for woman and non-caucasian races. Global lung function initiative (GLI) in contrast, correctly calculated normal expected spirometry for those previously not accounted for. One group looked at GLI in patients of different ancestral origins and another group looked at the accuracy of GLI in rare lung diseases. The first group found good concordance between traditional ECCS spirometric measurements and GLI for TLC in patients from different ancestral groups. The second group found discordance between ECCS and GLI in females with sarcoidosis and LAM with underestimation of FEV1 and overestimation of DLCO with GLU in both groups. A word of caution for those using GLI.

Imaging, biomarkers and machine learning in Lung cancer (poster discussion)

23rd May 2023

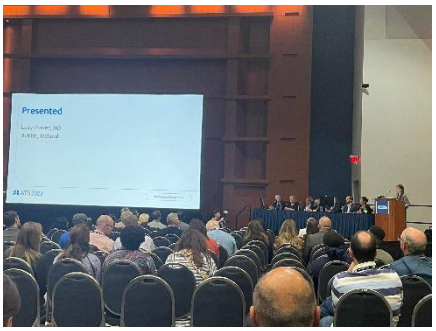
A number of posters jumped out at being interesting. Firstly, the potential role for neck US in staging of lung cancer and pulmonologist use of cervical lymph node sampling in diagnostics. This group performed either core needle biopsy or FNA of cervical lymph nodes in inpatients who were being worked up for lung cancer and found not only a diagnosis but also accurate staging in over 90% with a sample sufficient for ancillary studies in over 60% of samples. They suggest further studies are needed to determine if FNA is sufficient and how small a needle can be used. Secondly, a biomarker study looking at the potential role for exosomes in inducing EMT in LAM. This researcher found there are more extracellular vesicles (EVs) i in serum from LAM patients than healthy controls and that the number of EVs correlates negatively with FEV1 (widely accepted marker of disease severity in LAM). An A549 cell line was exposed to the EVs from LAM with an increase in vimentin expression, increased invasive capacity and increased TWIST1. These are all supportive of EMT suggesting these EVs in LAM might be playing a role in priming LAM cells for metastatic spread.



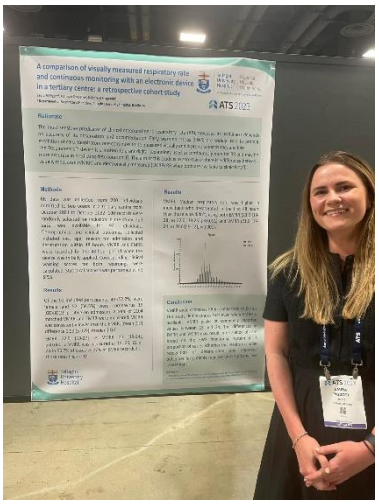


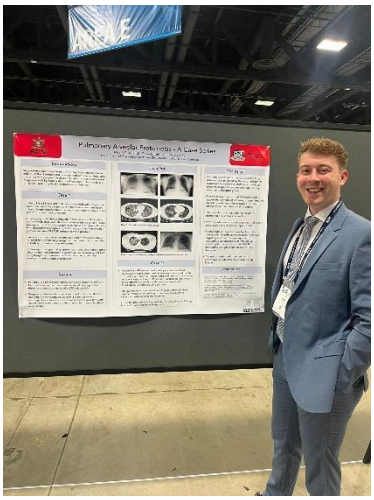
Dr. Jehangir Khan, St. Vincent's University Hospital

Dr. Cara Gill, St. Vincent's University Hospital



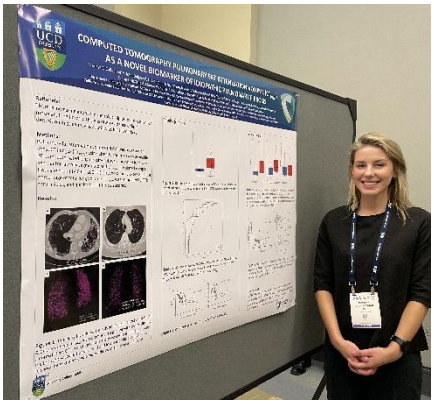
Dr. Lucy Power, Tallaght University Hospital



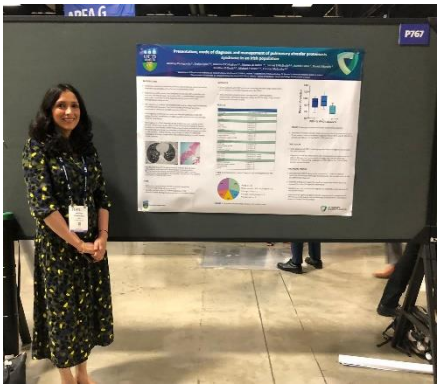


Dr. Jack Allen, Beaumont Hospital

Dr. Laura Piggott, Tallaght University Hospital

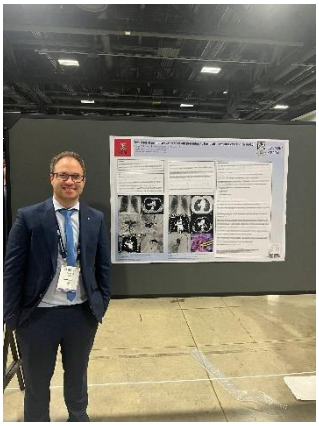


Dr. Marissa O'Callaghan, St. Vincent's University Hospital



Dr Maitreyi Penugonda, St. Vincent's University Hospital

Dr Evelyn Lynn, St. Vincent's University Hospital



Dr. Padraic Ridge, Beaumont Hospital