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CRINER GJ, SUE R, WRIGHT S ET AL

A Multicenter RCT of Zephyr® Endobronchial Valve Treatment in Heterogeneous Emphysema (LIBERATE).

Am J Respir Crit Care Med. 2018 May 22

Placement of endobronchial valves (EBV) in patients with severe emphysema has been shown to achieve atelectasis and lung volume reduction if there is no collateral ventilation between the target lobe and an ipsilateral lobe. The LIBERATE study is the first multicentre RCT to evaluate safety and effectiveness of Zephyr EBV out to 12 months post placement.

190 emphysema patients were enrolled. Participants had an FEV1 15 – 45% predicted, TLC >100% predicted, RV >175% predicted and DLCO ≥20% predicted. Target lobe selection was based on a total destruction score >50%, absolute difference in total destruction score of >15% between target and ipsilateral lobes, and "collateral ventilation negative" based on Chartis assessment at bronchoscopy. Subjects were randomized to EBV placement (n=128) or standard of care (SoC) (n=62). EBV placement was performed immediately after Chartis assessment and patients hospitalised for 5 days post-procedure with daily chest xray and HRCT at 45 days to verify lobar occlusion, with revision procedure performed if necessary.

At 12-months post-procedure, 47.7% of EBV patients v. 16.8% of SoC patients achieved the primary endpoint of ≥15% increase in post-bronchodilator FEV1 (p<0.001, intention-to-treat analysis). Secondary endpoints of absolute change in FEV1, change in SGRQ and change in 6MWD were all significantly higher in the EBV group.

Respiratory serious adverse events were significantly higher in the EBV group (35.2%) compared to the SoC group (4.8%) up to 45 days post-procedure (p<0.001). Pneumothorax was the major adverse event, occurring in 46 subjects (34.4%) in the EBV group, with 3 resulting deaths. 35 (76%) pneumothoraces occurred within 3 days post-procedure. Subjects with pneumothorax experienced similar benefits to subjects without pneumothorax at 12-months. Within the EBV group, 35 patients under went 54 repeat procedures due to incomplete lobar occlusion (11), adverse event (28), clinical investigation (12) or perceived lack of benefit (3). At 12-month follow-up, 8 subjects (6%) had had all valves removed.

FINAL STATEMENT / Zephyr EBV placement provides clinically meaningful and statistically significant improvements in lung function, exercise tolerance and quality of life for carefully selected patients. However, high rate of pneumothorax and requirement for repeat procedure requires close follow-up post-procedure.

5

IS SEHGAL, DHOORIA S, AGGARWAL AN ET AL

Diagnostic Performance of Xpert MTB/RIF in Tuberculous Pleural Effusion: Systematic Review and Meta-analysis.

J Clin Microbiol 2016;54:1133-6

Sensitivities of pleural fluid microscopy and culture in the Diagnosis of tuberculous pleural effusion are in the range of 10% and 20%, respectively, with thoracoscopic pleural biopsy demonstrating higher yield but necessitating an invasive procedure. As a consequence, treatment of tuberculous pleural effusion is often empiric, based on high clinical suspicion without microbiological confirmation. Xpert MTB/RIF (GeneXpert) has performed reasonably in smear-negative pulmonary tuberculosis (sensitivity 67%, specificity 99%), hence in this systematic review and meta-analysis, authors evaluated the diagnostic performance of GeneXpert in the tuberculous pleural effusion.

From an initial search yielding 155 citations, 24 studies involving 2,486 participants were included in the analysis, with equal representation of developed and developing countries. Twenty-one studies used mycobacterial culture while ten studies used a composite reference standard to evaluate diagnostic accuracy of GeneXpert. Nine studies concentrated the pleural fluid by centrifugation prior to performing GeneXpert.

Pooled sensitivity and specificity of GeneXpert compared to mycobacterial culture were 51.4% (95% CI, 43.3-59.7) and 98.6% (95% CI, 97.1-99.6), respectively. Pooled sensitivity and specificity of GeneXpert compared to composite reference standard were 22.7% (95% CI, 12.8-36.9) and 99.8% (95% CI, 97.2-99.9), respectively. Concentration of pleural fluid prior to performing GeneXpert significantly increased sensitivity and specificity. On Bayesian analysis, GeneXpert had high positive predictive value in high TB prevalence areas while negative predictive value was not affected by TB prevalence.

FINAL STATEMENT / This study suggests that GeneXpert has poor sensitivity but high specificity for diagnosis of tuberculous pleural effusion, however conclusions are limited by the poor quality of reference standards used. Future work evaluating GeneXpert performance with reference to thoracoscopic pleural biopsy specimens would offer a more conclusive answer to the utility of this diagnostic tool. Nevertheless, given its high specificity and minimal invasiveness, there is a potential role for GeneXpert in diagnosis of tuberculous pleural effusion.

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Deadline Friday 25th January 2019

Irish Thoracic Society

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A. Menarini Pharmaceuticals

ATS Bursaries 2019

Call for Applications

Deadline Friday 25th January 2019

Call for Applications

Irish Thoracic Society/
A. Menarini Pharmaceuticals
ATS Bursaries 2019

The Irish Thoracic Society is pleased to offer two Bursaries to attend the American Thoracic Society (ATS) Meeting taking place in Dallas, Texas from the 17th -22nd May 2019, kindly supported by A. Menarini Pharmaceuticals.

The first bursary, to the value of €5,000, will be awarded based on an evaluation of abstracts submitted to the ATS. It is open to ITS Members who are SpRs on the Specialist Registrar Training Programmes in Respiratory Medicine or Paediatrics with an interest in Respiratory Medicine. Application details are available on www.irishthoracicsociety.com

The second bursary will be awarded to the ITS SpR Educational Officer 2019.

Deadline Friday 25th January 2019

ITS Journal Review

November 2018

We are pleased to bring you the following journal review by Dr Dan Ryan, ITS Educational Officer and Dr Laura Gleeson, Specialist Registrar, Respiratory Medicine..

Top Reads for 2018

1

LIPSON DA, BARNHART F, BREALEY N, BROOKS J, CRINER GJ, DAY NC, ET AL

Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD.

New England Journal of Medicine. 2018;378(18):1671-80

Triple inhaler therapy for COPD comprising ICS, LAMA and LABA is recommended in patients with clinically significant symptoms despite treatment with ICS/LABA or LAMA/LABA who are at risk of frequent exacerbations. Previously this required multiple inhalers but recently single inhalers containing ICS/LABA/LAMA have been developed. The Informing the pathway of COPD treatment (IMPACT) trial compared the relative benefits and risks of these three regimens.

The trial was a phase III randomized double-blind parallel group multicentre trial in an intention to treat population of 10,355 patients. The populations were divided into treatment arms of a triple inhaler device ICS/LAMA/LABA (Fluticasone/Umeclidinium/vilanterol) compared to LABA/ICS (Fluticasone/Vilanterol) or LABA/LAMA (Umcledinium/Vilanterol) in patients with CAT score>10, FEV1>50% and at least one exacerbation in the past year. Primary end point was rate of moderate to severe exacerbation with multiple secondary endpoints including change in FEV1 and quality of life scores.

The results showed significantly lower exacerbation rates in the triple device treatment arm (0.91 vs 1.07 vs 1.21 per annum p<0.001). Safety profile was similar to the dual therapy arms. Secondary end points such as improved FEV1 and QOL scores were also higher in the triple therapy device group.

FINAL STATEMENT / Once daily single inhaler triple therapy (ICS/LAMA/LABA) resulted in a significantly lower rate of moderate to severe exacerbations and better lung function and quality of life scores than treatment with equivalent device once daily ICS/LABA and LAMA/LABA with similar side effect profiles.

2

BYARS SG, STEARNS SC, BOOMSMA JJ

Association of Long-Term Risk of Respiratory, Allergic, and Infectious Diseases With Removal of Adenoids and Tonsils in Childhood.

JAMA otolaryngology-- head & neck surgery. 2018;144(7):594-603

Adenoids and tonsils are commonly removed in childhood. Understanding the long-term impact of the surgeries is critical because the Adenoids and Tonsils are parts of the immune system, have known roles in pathogen detection and defence and are usually removed at ages when development of the immune system is sensitive. Previous singles studies have shown subtle short-term changes in risk after surgery but no estimates for long term risks are available.

The trial, carried out in Denmark was a population-based cohort study of up to 1,189,061 children born between 1979 and 1999 and evaluated in linked patient registers up to 2009. Participants were classified as exposed if the Adenoids or Tonsils were removed within the 1st nine years of life.

17,460 patients had Adenoidectomy, 11,830 had Tonsillectomy and 31,377 had Adenotonsillectomy. There were 1,157,684 patients in the control group. Adenoidectomy and Tonsillectomy patients were associated with a 2-3-fold increase in diseases of the upper respiratory tract (Relative risk (RR); 1.99: 95% CI,1.51-2.63 and RR,2.72,95% CI,1.54-4.80 respectively). Similar increases in risk for infectious and allergic diseases were also found. Adenotonsillectomy was associated with a 17% increased risk of infectious disease (RR,1.17 95% CI,1.10-1.25) corresponding to an absolute risk increase of 2.14%.

In this study of 1.2 million children, surgeries for Adenoidectomy, Tonsillectomy and Adenotonsillectomy were associated with an increased long-term risk of respiratory, infectious and allergic diseases. The results suggest it is important to consider long term risks when making decisions to perform Tonsillectomy and Adenoidectomy.

FINAL STATEMENT / Surgery in childhood for Adenoids, Tonsils and Adenotonsillectomy is associated with an increased risk of respiratory, infectious and allergic diseases.

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HELLMANN MD, CIULEANU TE, PLUZANSKI A, LEE JS, OTTERSON GA, AUDIGIER-VALETTE C, ET AL

Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden.

The New England journal of medicine. 2018;378(22):2093-104

Standard of care therapy for previously untreated advanced Non-small cell lung cancer (NSCLC) without treatable driver mutations includes platinum-based chemotherapy and pembrolizumab for patients with a high level (> 50%) of PDL-1 expression. Nivolumab (PD1 antibody) and Ipilumab (CTLA4 antibody) are immune checkpoint inhibitors with complementary mechanism of action have shown superior efficacy in phase 1 trials compared to Novilumab monotherapy.

Tumour mutational burden is an emerging independent biomarker in immunotherapy driven cancer treatments including lung cancer. Previous studies have shown a tumour mutational burden of at least 10 mutations per megabase as an effective cut off for selecting patients most likely to have a response to immunotherapy, irrespective of PDL1 expression. This trial was an open label phase 3 trial where one of the co primary endpoints was to assess 1-year progression free survival with Nivolumab plus Ipilimumab versus chemotherapy in patients selected on the basis of tumour mutational burden. A high tumour mutational burden was defined as the presence of 10 or more mutations per megabase and low mutational burden was defined as < 10 mutations per megabase.

1649 patients had tumour samples available to assess tumour mutational burden. 444 patients had at least 10 mutations per megabase. I year progression free survival in the Nivolumab/ Ipilimumab group with high mutational burden was 42.6% versus 13.2% in the platinum chemotherapy group with median progression free survival of 7.2 months (45% CI 5.5 to 13.2) versus 5.5 months (95% CI, 4.4 to 5.8, p<0.001). This benefit was observed in patients regardless of levels od PDL1 expression.

FINAL STATEMENT / Progression free survival was significantly longer with Nivolumab/Ipilimumab than with chemotherapy in patients with advanced NSCLC and a high mutational burden. The results validate the role of Nivolumab plus ipilimumab as an effective 1st line therapy in NSCLC and tumour mutational burden as an important and independent biomarker in advances in NSCLC.