ADJUNCTIVE HOST-DIRECTED THERAPIES FOR PULMONARY TUBERCULOSIS: A PROSPECTIVE, OPEN-LABEL, PHASE 2, RANDOMISED CONTROLLED TRIAL

Despite effective antituberculous chemotherapy, there is significant morbidity following completed treatment regimens including lasting impact on lung function, which is linked with all-cause mortality. This has led to interest in the use of adjunctive host-directed therapies. In an open-label, phase 2, randomised control trial, Wallis *et al* (Lancet 2021;doi:10.1016/S2213-2600(20)30448-3) investigated the safety and preliminary efficacy of four adjunctive host-directed therapies for pulmonary tuberculosis. A total of 200 patients across three sites in South Africa with rifampicin-susceptible *Mycobacterium tuberculosis* were randomly assigned (1:1:1:1) to receive either CC-11050, everolimus, auranofin, ergocalciferol in addition to standard anti-tuberculosis therapy or standard therapy alone for 180 days. Three of 11 treatment-emergent serious adverse events were attributable to host-directed treatment: life-threatening thrombocytopenia in an auranofin recipient which resolved after auranofin discontinuation, intra-abdominal sepsis resulting in death in another auranofin recipient and tuberculosis spondylitis in an ergocalciferol recipient. The CC-11050 and everolimus groups did not contain any serious adverse events that could be attributed to treatment. Furthermore, relative to the control group, the CC-11050 and everolimus groups showed a greater improvement in mean forced expiratory volume in 1 s (FEV₁) at day 180 (6.30%, 95% CI 0.06% to 12.54%; $p=0.048$; and 6.56%, 95% CI 0.18% to 12.95%; $p=0.044$, respectively). No treatments showed a significant difference in forced vital capacity (FVC) or on measures of sputum culture status during the study. The authors conclude that encouraging safety and efficacy findings for CC-11050 and everolimus, including their effect on FEV₁ recovery, warrants further study.

MUC5B RS35705950 GENOTYPE IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS ON ANTIFIBROTIC TREATMENT: A POTENTIAL PROGNOSTIC MARKER?

The MUC5B rs35705950 genotype is the strongest genetic risk factor for sporadic and familial idiopathic pulmonary fibrosis (IPF), and although it has been identified as a predictor

of outcome, little is known about its influence on disease progression and survival for patients with IPF on antifibrotic treatment. In a longitudinal retrospective study, Biondini *et al* (Respiratory Research 2021;22:98) investigated disease progression in patients with sporadic IPF treated with either pirfenidone or nintedanib ($n=88$). Patients were divided into two groups based on their MUC5B genotyping: TT/TG genotype ($n=61$) and GG genotype ($n=27$), and followed up from 2014 until transplantation, death or end of follow-up in December 2019. There was no difference in progression-free survival, defined as absolute FVC predicted loss $\geq 5\%$ compared with the basal FVC % predicted, between patients with TT/TG and GG genotypes, with a median of 19 months and 20 months, respectively ($p=0.21$). Interestingly, GG genotype carriers demonstrated a significantly worse survival than TT/TG genotype carriers (42 vs 74 months, respectively; HR 2.59, 95% CI 1.24 to 5.40, $p=0.0082$). Multivariate analysis demonstrated that an earlier onset of respiratory failure at rest (HR 36.7, 95% CI 2.3 to 47.78; $p=0.006$) and a lower FVC at treatment initiation (HR 77.2, 95% CI 2.99 to 199.0 $p=0.009$) were independent predictors of mortality. The association between the MUC5B T allele and longer survival in patients with IPF on antifibrotic treatment highlights the importance of genetic data for clinical decision making.

HELMET NON-INVASIVE VENTILATION VERSUS HIGH-FLOW NASAL OXYGEN PATIENTS WITH COVID-19: THE CHOICE IS YOURS

The use of non-invasive respiratory support (high-flow nasal oxygen; HFNO and helmet non-invasive ventilation; HNIV) in the management of hypoxic respiratory failure secondary to COVID-19 has been widespread in the pandemic but high-quality data to suggest optimal delivery are limited. Grieco *et al* (JAMA 2021;325:1731) investigated the impact of HNIV on days free of respiratory support in patients with COVID-19 compared with HFNO. HENIVOT was an open-label, multicentre, clinical trial which randomised patients with COVID-19 infection and hypoxic respiratory failure to receive continuous HNIV ($n=54$) or HFNO ($n=55$) for at least 48 hours. From randomisation to 28 days, the median days free of respiratory support were: HNIV=20 (IQR 0–25) and HFNO=18 (0–22) ($p=0.26$). Interestingly, HNIV was associated with a lower rate of endotracheal intubation within 28 (30% vs 51%), with an absolute risk reduction of 21% ($p=0.03$). While HNIV did not significantly reduce the number of days of respiratory support compared with HFNO, these results do highlight the need for further

CONTINUOUS POSITIVE AIRWAY PRESSURE IN PATIENTS WITH HYPERTENSION AND OBSTRUCTIVE SLEEP APNOEA: IMPROVES BLOOD PRESSURE AND SERUM CARDIOVASCULAR BIOMARKERS

Current evidence for the impact of obstructive sleep apnoea (OSA) treatment on cardiovascular risk is conflicting. Lui *et al* (Eur Respir J 2021;doi:10.1183/13993003.03687-2020) report results of short-term continuous positive airway pressure (CPAP) therapy on ambulatory blood pressure (BP) and serum biomarkers of myocardial injury in subjects with OSA and treatment resistant hypertension. In a single-centre randomised (1:1) clinical trial, subjects between 18 and 65 years old with hypertension requiring at least three antihypertensive medications and moderate-severe OSA were allocated to receive either CPAP ($n=46$) or usual care without CPAP ($n=46$). Ambulatory BP and serum biomarkers were taken at baseline and reassessed at week eight. When compared with the control group, the CPAP group demonstrated a significant reduction in 24-hour systolic (-4.4 mm Hg, 95% CI -8.7 to -0.1 , $p=0.046$) and diastolic (-2.9 mm Hg, 95% CI -5.5 to -0.2 , $p=0.032$) BP. Counterintuitively the impact on BP manifested predominantly in day rather than night-time readings. Subgroup analyses revealed that CPAP resulted in a significant reduction in ambulatory BP only in non-dippers ($<10\%$ diurnal variation), but not in dippers. Furthermore, the CPAP group showed significantly reduced levels of both troponin I (-1.74 pg/mL, 95% CI -2.97 to -0.5 , $p=0.006$) and brain natriuretic peptide (-9.1 pg/mL, 95% CI -17.6 to -0.6 , $p=0.036$) compared with the control group. In addition to providing further control of ambulatory BP for difficult-to-treat hypertension, CPAP for OSA might help to reduce subclinical myocardial injury and strain the clinical importance of this level of reduction remains to be quantified.

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