JOURNAL CLUB SUMMARIES

# What's hot that the other lot got

Janice Ward

## TB TREATMENT REGIMES IN PEOPLE LIVING WITH HIV

Intermittent dosing regimens to treat pulmonary tuberculosis (TB) are commonly implemented, particularly in the developing world, in an attempt to improve adherence, reduce costs and reduce side effects. Gopolan *et al* (*JAMA Intern Med* 2018;178:485-93) aim to test the efficacy of daily vs part daily (daily for the intensive phase followed by thrice weekly continuation phase) vs intermittent (thrice weekly) TB treatment in HIV positive individuals who were TB treatment naive. This question was pertinent in India as the Revised National TB Programme continued to recommend intermittent treatment. From September 2009 to January 2016 331 patients were allocated equally to the three arms. The trial was stopped early by the data monitoring and safety committee. In the modified intent-to-treat analysis, favourable responses at the end of TB treatment occurred in 89 of 98 patients (91%), 77 of 96 patients (80%), and 75 of 98 patients (77%) in the daily, part-daily, and intermittent regimens, respectively. Daily treatment was associated with an improved response (absolute increase in response rate 14%, 95% CI 4% to 25%, P=0.009) whereas part-daily was not (P=0.53). This trial shows that daily treatment for patients with pulmonary TB and HIV, as recommended by the WHO, is superior to intermittent regimens in an developing nation healthcare setting.

## MAKE MINE A DOUBLE… LUNG TRANSPLANT

Bronchiolitis obliterans syndrome (BOS) is pathological change seen post transplant that leads to significant morbidity and mortality. Fakhro *et al* (*J Cardiothorac Surg* 2017;12:100) used the Institute of Heart and Lung Transplant (ISHLT) definition of BOS to examine the effect of single or double lung transplantation on the diagnosis of BOS grade ≥2 and death as separate outcomes. All 278 lung transplants performed from 1990 to 2014 in one of two Swedish transplant centres were included. The incidence of BOS were numerically higher but not significantly different in double lung transplant (DLTx) recipients at 16%±3% at 5 years, 30%±4% at 10 years, 35%±5% at 15 years, and 37%±5% at 20 years compared with single lung transplant (SLTx) at 11%±3% at 5 years, 20%±4% at 10 years, 24%±5% at 15 years, and 24%±5% at 20 years. The relationship with mortality was reversed with non-significantly higher mortality in SLTx (34%±5% at 5 years, 71%±8% at 20 years) compared with DLTx (19%±3% at 5 years, 43%±7% at 20 years). The authors conclude that double lung transplantation should be favoured where possible. However, the results suggest that outcome is influenced significantly by other patient factors beyond BOS diagnosis. Transplant care has evolved considerably over the time frame of this study, and varies between centres making it hard to draw generalizable conclusions from this data.

## MAKE MINE A TRIPLE…INHALER

The optimum inhaled therapy for patients with severe COPD and frequent exacerbations remains unclear and was investigated in the IMPACT trial, a phase 3, double-blind, randomised clinical trial sponsored by GlaxoSmithKline (Lipson *et al*. *N Engl J Med* 2018;378:1671-80). Following a 2 week run-in period on usual therapy patients were randomised to either once-daily inhaled triple therapy with fluticasone furoate 100 µg, umeclidinium 62.5 µg and vilanterol 25 µg; dual therapy with fluticasone furoate-vilanterol or dual therapy with umeclidium-vilanterol. Primary outcome was the frequency of moderate or severe exacerbations of COPD in the 52 week treatment period. 10 355 patients were randomised between July 2014 and July 2017 from 37 countries (age 65±8 years, $FEV_1$ 46%±15%). 7991 remained in the per protocol population. Results from the intention to treat population showed a significantly reduced exacerbation frequency in the triple therapy group: 0.91 per year, compared with 1.07 per year among those treated fluticasone furoate–vilanterol (rate ratio with triple therapy, 0.85; 95% CI 0.80 to 0.90; P<0.001) and 1.21 per year in those treated with umeclidinium-vilanterol (rate ratio with triple therapy, 0.75; 95% CI, 0.70 to 0.81; P<0.001). There was no difference between the groups in numbers of serious adverse events, but in a time-to-first-event analysis there was a significantly increased risk of pneumonia in the fluticasone containing groups compared with the umeclidinium-vilanterol group (HR 1.53, 95% CI 1.22, P<0.001). The exacerbation results contrast with that of the FLAME trial, this is suggested to be due to the differing trial design with some patients have abrupt withdrawal of inhaled steroids on randomisation.

## RIOCIGUAT IN PORTOPULMONARY HYPERTENSION

The European Society of Cardiology recommend that treatment of portopulmonary hypertension (POPH) is the same as the other Group 1 causes of pulmonary hypertension (PH). However, evidence is lacking as most trials exclude patients with POPH. The PATENT −1 and 2 trials were large multicenter studies of riociguat treatment in PH and included 13 of 443 patients with POPH (11 in the treatment arm, two in the placebo arm); 12 continued on into PATENT-2 which was an open label 2 year follow-up study. Cartin-Ceba *et al* (*Pulm Circ* 2018;8:2045894018769305) performed a post-hoc analysis of the POPH subgroup of PATENT-1 and 2. The original PATENT-1 primary outcome was changes in 6 min walk test (6MWT) at week 12, the walk distance improved by a median of 48 (-2 to 104) m in the riociguat group and 3 (−6 to 11) m in the placebo group. Mean pulmonary artery pressure (mmHg) at week 12 changed by −7.5 (−14.7 -+4.0) in the riociguat group and −3 in the placebo group. Side effect profile appeared similar to that of the rest of the PATENT-1 cohort, the most common being headache and peripheral oedema. This study presents a small subset of patients, with very few controls, no information on their liver disease and most were pulmonary hypertension treatment naive; therefore, the authors were cautious to draw conclusions from the data. However, these data provide some evidence of safety and potential efficacy that should lead to inclusion of this patient group in future studies.

**Correspondence to** Janice Ward, University Hospital of North Durham, Durham DH1 5TW, UK; janice.higginson85@googlemail.com

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