JOURNAL CLUB SUMMARIES

What's hot that the other lot got

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WHICH COMBINATION INHALER SHOULD WE USE FOR COPD?

3362 patients with at least one exacerbation of COPD in the previous year were randomised to a long acting β agonist Indacaterol (LABA) and a Long acting muscarinic agonist (LAMA) Glycopyrronium or LABA Salmeterol and inhaled glucocorticoid fluticasone (doi: 10.1056/NEJMoa1516385). The outcome was annual rate of COPD exacerbation. In the LABA-LAMA group there was an 11% reduction in the exacerbation rate (3.59 vs 4.03; rate ratio, 0.89; 95% CI, 0.83 to 0.96; p=0.003) with comparison to the LABA-steroid group. There was also a longer time to first exacerbation (71 days (95% CI 60 to 82) vs 51 days (95% CI 46 to 57); HR, 0.84 (95% CI 0.78 to 0.91), representing a 16% lower risk; p<0.001). The annual rate of severe exacerbations was lower (0.98 vs 1.19; rate ratio, 0.83; 95% CI 0.75 to 0.91; p<0.001). The exacerbation rate was independent of the blood eosinophil count. The incidence of pneumonia was 3.2% in the LABA-LAMA group and 4.8% in the LABA steroid group (p=0.02).

DUPILUMAB FOR ASTHMA

Dupilumab is a fully human anti-interleukin-4 receptor α monoclonal antibody, which inhibits interleukin-4 and interleukin-13 signalling, these are drivers of type-2-mediated inflammation. This study was a double blind randomised placebo controlled, pivotal 2b clinical phase trial for Dupilomab (*Lancet* 2016;388:31–44). Adults receiving medium to high dose corticosteroids (equivalent to fluticasone proprionate ≥250 µg twice daily) and a long acting β agonist who were symptomatic with asthma Control questionnaire of score of 1.5 or higher with an FEV1 of 40–80% and reversibility were randomised to either dupilumab 200 or 300 mg every 2–4 weeks or placebo. Those included in the intention to treat analysis had eosinophils of at least 300/µL. The primary end point was a change in FEV1 at week 1. All the regimens except the duplulimab 200 mg every 4 weeks showed a significant increase in FEV1 (300 mg every 4 weeks, p=0.0212; 200 mg every 2 weeks, p=0.0008; 300 mg every 2 weeks, p=0.0063) the increase in FEV1 for all regimens from baseline at week 12 ranged from 0.35 to 0.43 L (0.05) and ranged from 0.17 L (95% CI 0.03 to 0.32) to 0.26 L (0.11 to 0.40) versus placebo these were sustained throughout the 24 week period and were significant (300 mg every 4 weeks, p=0.0401; 200 mg every 2 weeks, p=0.0264; 300 mg every 2 weeks, p=0.0345).

WHICH SMOKING CESSATION THERAPY IS SAFEST IN NEUROPSYCHIATRIC DISORDERS?

There are substantial concerns regarding variceline and buprenorphine in those with neuropsychiatric disorders. A randomised double blind placebo controlled trial with active controls was carried out in 16 countries (doi.org/10.1016/S0140-6736 (16)30272-0). A total of 8144 motivated to quit smokers were placed in 2 cohorts the first with no previous psychiatric diagnosis and the second with a psychiatric diagnosis of mood disorders including major depressive disorder or bipolar disorder; anxiety disorders including panic disorder, with or without agoraphobia, post-traumatic stress disorder, obsessive-compulsive disorder, social phobia, and generalised anxiety disorder; psychotic disorders including schizophrenia and schizoaffective disorders; or borderline personality disorder. They were randomised within their cohort to varenicline (1 mg twice a day) and bupropion (150 mg twice a day) or transdermal nicotine patch 21 mg/day with taper for 12 weeks with 12-week non-treatment follow-up. The overall incidence of the neuropsychiatric adverse events endpoint was similar across the four treatment groups: varenicline 4.0%, bupropion 4.5%, nicotine patch 3.9%, and placebo 3.7%. There was a higher incidence of events in the psychiatric cohort (5.8%) compared to the non-psychiatric cohort (2.1%). However the incidence of events remained the same between the treatment groups. As regards continuous abstinence this was similar for each treatment across both cohorts with varenicline showing superior efficacy (OR 3.61 (3.07 to 4.24) p<0.0001), bupropion (OR 2.07 (1.75 to 2.45) p<0.0001) and nicotine patch (OR 2.15 (1.82 to 2.54) p<0.0001) having similar efficacy.

WHAT IS THE RISK OF VENOUS THROMBOEMBOLISM IN LUNG CANCER?

A cohort of 10 598 patients with lung cancer diagnosed from 1997 to 2006 underwent cox regression analysis to see what factors independently affected the risk of venous thromboembolism (VTE) (doi: 10.1038/bjc.2016.143). The overall incidence of VTE was of 39.2 per 1000 person-years (95% CI 35.4 to 43.5). Factors which were associated with an increased VTE risk were metastatic disease (HR=1.9, CI 1.2 to 3.0); adenocarcinoma subtype (HR=2.0, CI 1.5 to 2.7) having chemotherapy (HR=2.1, CI 1.4 to 3.0); and diagnosis via emergency hospital admission (HR=1.7, CI 1.2 to 2.3), there was an increase in mortality in those with VTE of 50% compared to those without.

CAN THOSE WHO ARE AT RISK OF DEVELOPING TB BE IDENTIFIED?

A biomarker for predicting who develops a disease is the Holy Grail in medicine. This study aimed to see if RNA signatures in blood could predict those who would develop TB (*Lancet* 2016;387:2312–22). Teenagers from a study group in South Africa were enrolled if they had a positive QuantiFERON TB gold in-tube assay or tuberculin skin test therefore having latent TB. They were followed and those who developed intrathoracic TB were designated progressors, they were matched with healthy controls from their original group. An RNA TB signature was developed from this group. This was then adapted for multiplex quantitative real-time PCR (qRT-PCR) and used to predict the risk of developing TB in untouched samples from the original cohort and two separate independent cohorts of adults who were household contacts of people with active pulmonary disease. There were 46 progressors identified and from these a 16 gene signature was developed. This predicted TB progression with sensitivity of 66.1% (95% CI 63.2% to 68.9%) and a specificity of 80.6% (79.2% to 82.0%) in the 12 months preceding TB diagnosis. When validated in the untouched adolescent group (p=0.0095 for qRT-PCR) and in the independent cohorts (p values <0.0001 by qRT-PCR).

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